



Diamond-II | Advancing Science

Contents

1. Executive summary	2		
2. Background	4		
3. The Diamond-II synchrotron	6		
4. Beamlines and complementary technologies	9		
4.1. Benefit of Diamond-II for existing ID beamlines	9		
4.2. Optimising existing instruments using new mid section straights	10		
4.3. New instruments	12		
4.4. Development of complementary technologies	12		
5. The purpose of this document	14		
6. Diamond-II: Advancing life sciences	16		
6.1. Life science challenges	16		
6.2. Integrated structural biology	18		
6.2.1. Chromosome structure	19		
6.2.2. The prokaryotic cell surface	20		
6.2.3. Membrane proteins	20		
6.2.4. Dynamic studies	20		
6.3. Biotechnology and biological systems	24		
6.3.1. Engineering and applications of biomaterials	24		
6.3.2. Biological systems imaging	26		
6.4. Health and well-being	30		
6.4.1. Chemical imaging with X-rays	30		
6.4.2. Imaging of cells and biological materials	33		
6.5. Dark period mitigation	38		
6.6. New beamline opportunities	38		
7. Diamond-II: Advancing physical sciences	40		
7.1. Physical science challenges	40		
7.2. Energy	42		
7.2.1. Battery research	43		
7.2.2. Photovoltaics	47		
7.3. Chemistry	51		
7.3.1. Catalysis	51		
<i>In situ</i> experiments at the micro and nanoscales	52		
An increased sensitivity to ligands with spatial resolution	53		
New paradigms at the nanoscale	53		
Biocatalysis	54		
Catalyst characterisation: combination of techniques and using external triggers	54		
7.3.2. Advanced materials	55		
Porous materials	55		
Metal-Organic Frameworks	55		
Probing kinetic correlations in space and time	56		
7.3.3. Formulation	57		
Electronic structure of <i>in situ</i> nucleation of organic solutes	58		
7.4. Quantum materials	62		
7.4.1. Designing and controlling quantum materials	62		
7.4.2. Inhomogeneity and emergence in quantum materials	63		
7.4.3. Controlling emergence using phase separation	64		
7.4.4. A new dimension for magnetism	64		
7.4.5. Tuning coupled ferroic order	66		
7.4.6. The rise of 2D materials	67		
7.4.7. Topological matter	69		
7.5. Advanced Material Engineering and Processing	72		
7.5.1. Introduction	72		
7.5.2. New Materials and processes	72		
7.5.3. Materials <i>In-operando</i> and <i>Ex-situ</i> : Impact of Irradiation, Friction, Corrosion, Stress and Strain	74		
7.6. Earth, environment & planetary science	79		
7.6.1. Understanding global environmental issues: the organic carbon paradox	79		
7.6.2. Nuclear waste remediation	81		
7.6.3. Understanding global environmental issues: atmospheric pollution	82		
Appendix 1	87		
Appendix 2	89		
Acknowledgements	105		

1. Executive summary

Synchrotron radiation produced at storage rings has played a leading role in scientific discovery over recent decades, with five Nobel Prizes directly linked to research at synchrotrons. Synchrotrons make groundbreaking contributions to virtually all fields of science from physics, chemistry, biology to medicine, engineering and heritage science, and address a wide range of societal challenges from clean energy and the environment to well-being and an increasingly ageing population.

With funding from the UK Government and the Wellcome Trust, Diamond Light Source has established itself as a world-class synchrotron facility enabling research by leading academic and industrial groups in physical and life sciences. Diamond has pioneered a model of highly efficient and uncompromised infrastructure offered as a user-focussed service driven by technical and engineering innovation. We now propose Diamond-II, a co-ordinated programme of development that combines a major machine upgrade with complementary improvements to optics, detectors, sample delivery, detectors, and computing, as well as integrated and correlative methods, which will be transformative in speed and resolution, and will offer users streamlined access to enhanced instruments for life and physical sciences.

This document makes a science case for this next phase of Diamond, the Diamond-II programme.

The proposed new machine will be based on the multibend-achromat (MBA) technology that is transforming the performance of new and upgraded synchrotrons around the world, offering between one and two orders of magnitude reduction in the horizontal electron emittance which in turn can provide dramatic gains in photon brightness and coherence. Diamond has devised a novel implementation of MBA technology, offering not only dramatic gains in brightness and coherence but also additional source points (so-called mid-straight sections in each of the new cells) to install new photon sources based on insertion devices. This will enable the new machine to not only accommodate both high-performance beamlines that are currently based on bending magnets but will also offer additional sites for up to five new beamlines, offering greater capacity and flexibility to accommodate new science drivers and communities well into the future. A further design feature is an increase in electron beam energy from 3.0 GeV to 3.5 GeV, driven by the new scientific opportunities provided by the consequential boost in photon flux at higher energies.

The machine upgrade will go hand-in-hand with developments of beamlines and supporting infrastructure to adapt to and exploit fully the potential of the new beam characteristics: in addition to repositioning beamlines on bending magnets and insertion devices that will be displaced in the new lattice, new optical components must be developed and/or installed to handle finer, brighter beams, and many detectors will also have to be replaced to handle higher photon flux, much of which will be at higher

energies; brighter, finer beams will also demand sample delivery systems with higher throughput and more precise, stable positioning, higher flux at higher energy will require a wider range of *operando* sample environments, and there will also be a greater degree of integration with enhanced sample preparation facilities and complementary, often correlative measurements. All this must progress hand-in-hand with greatly enhanced capacity for data storage and transfer as photon flux and detector rates go through step changes, together with greatly enhanced computation speeds to enable raw data to be visualised and processed on timescales that allow user to make informed decisions about experiments in near-real time, adding substantial value to the experiment. The transformation required for the speed of data analysis will require both improvements to hardware and the development of more efficient data flows and algorithms, the latter increasingly exploiting AI methods to be developed in partnership with other facilities, institutes, university groups and industry.

Diamond-II will be a cauldron of life science research and development, integrating X-ray and electron scattering and imaging methods at all stages from sample preparation through to data analysis and interpretation. The new machine will provide a transformative improvement to the sensitivity and throughput of almost all life sciences beamlines allowing better delivery of existing methods as well as new methods and the possibility for additional beamlines to exploit the gains in brightness and coherence. These developments, alongside the continued developments in cryo electron microscopy, where Diamond intends to retain a leading position, will enable not only more and better traditional science but also will drive the transformation from reductive *in vitro* science to integrative *in situ*, and ultimately *in operando* science that will transform our view of biology. This is a scientific grand challenge, and its tractability rests on the assumption that nano-scale structures form into hierarchical assemblies which dictate emergent biological phenomena. In practical terms our aim is to be able to drill down from a field of view of many microns to the atomic level and, ultimately work under physiological conditions to address not only the structure but also the dynamics of life. We (somewhat arbitrarily) break this challenge down into three disciplines: 1) Integrated structural biology, where the 4th generation source will allow us to cover the important microsecond time domain – for instance enabling temporal as well as structural characterisation of ion channels and G protein-coupled receptors (GPCRs). 2)

Biotechnology and biological systems, where Diamond-II could enable true exploitation of SAXS tensor tomography up to map biomaterials at the sub-micron level, speeding experiments from days to an hour. 3) Health and well-being, where we expect imaging to be transformed by cryo X-ray ptychography at a resolution of nanometres over larger fields of view (mm) with data collection drastically reduced, perhaps to seconds. In each area we highlight a few examples of the transformative potential of Diamond-II. Enormous added value will come from bringing together beamline science with cryoEM (eBIC), and from adjacent activity in which Diamond is a partner, notably the Rosalind Franklin Institute (RFI) and the Research Complex at Harwell (RCAH), to form an internationally competitive centre for life sciences research. In this broader context Diamond-II will address major outstanding problems including sample preparation/environment, correlative imaging and beamline optimisation. We will work strategically, not only with academics but also with industry, to optimise the facility to maximise impact on applications including food security, bioenergy, bioremediation and the discovery of new therapeutics, from novel chemical entities, through biologics, to vaccines.

In the physical sciences, Diamond-II will deliver transformative gains in many areas of research in physics, chemistry, materials science and engineering. The gain in brightness and coherence will allow high throughput experiments able to map strain, morphology, chemical, structural, electronic and magnetic information at the sub-micron scale, even pushing the resolution of these techniques to a few nanometres using coherent diffraction techniques or to a time resolution of tens of nanoseconds (X-ray Photon Correlation Spectroscopy). Techniques that are currently highly specialised will be made much more widely available - for example, Resonant Inelastic X-ray Scattering (RIXS) will have a breakthrough capability in spectral resolution providing an unprecedented sensitivity for probing electronic properties in chemical processes (catalysis, battery cycling) and also fundamental excitations

in quantum materials. Greatly enhanced flux at higher energies will enable a much wider range of *operando* experiments to be performed and to do so far more quickly than currently possible, providing unique insights deep inside materials and processes in real time, for example innovative manufacturing processes, and transformations in operating batteries and catalytic systems. These developments will provide the most powerful tools to understand the next generation of systems and substances for which heterogeneity, nanoscale complexity, or non-equilibrium, emergent properties are key parameters. This in turn is essential to meet societal challenges in cleaner energy, transport, computation and communications, advanced manufacturing and the environment. Further details, with illustrative examples of ground-breaking applications are presented in sections on: 1) Energy, 2) Chemistry, 3) Quantum materials, 4) Engineering materials and processing, and 5) Earth, environment and planetary science. While these represent key areas of research at Diamond and reflect strengths and priority areas for UK research, they are by no means an exhaustive list and it is anticipated that new high impact applications will be found for Diamond-II, as is always the case when transformative technology becomes available for a vibrant research community.

The implementation of Diamond-II will require a significant shutdown. Other synchrotrons around Europe will be upgrading on a similar timescale to Diamond and although timings will often be dictated by National priorities, where feasible we will mitigate the effect on the user communities by coordinating shutdown timings, where possible, through the LEAPS (League of European Accelerator-based Photon Sources) consortium. In addition, we are investigating strategic collaborations with other facilities to provide alternative capacity during the dark period at Diamond and we expect that mitigation measures will be tailored to the characteristics of the different science communities.



2. Background

Diamond Light Source is enabling world-class science in universities and industry, both in the UK and internationally, to advance knowledge and underpin innovation in virtually all fields of research. Now in its 13th year of operations, Diamond offers access to 31 beamlines (Figure 1) and an impressive suite of complementary facilities – the Electron Bio-Imaging Centre (eBIC), the Electron Physical Science Imaging Centre (ePSIC), the MPL (Membrane Protein Lab), the XChem Fragment Screening service and the XFEL Hub, which develops technology for sample delivery and data analysis for Free Electron Lasers for life sciences; altogether making the offer to the user community unique in the world.

The information that Diamond provides is essential in understanding biological processes and the properties of materials, including biomaterials, for an immense range of science and technology, from drug design and catalysts, through electronic devices and high-performance engineering alloys to heritage science. The work that Diamond supports has a direct impact on some of the key challenges for our society, including healthcare and the environment, more efficient energy storage and transport.

During the past five financial years, Diamond has welcomed on average 7,500 external user visits per year (Figure 2) and has directly supported proprietary work for over 130 companies, while about 40% of all delivered beamtime in FY2017/18 had direct or indirect industrial access.

Its output includes steady stream of peer-reviewed articles, to date 8,000 (Figure 3), and a rate of deposition of structures in the Protein Data Bank that places Diamond as

one of the most productive synchrotrons in the world, and leading among medium energy synchrotrons. (Figure 4).

Such high throughput has been enabled by a remarkable level of automation, matched with efficient data analysis pipelines in close-to-real time; both now being rolled out across an increasing number of physical and life sciences beamlines to optimise workflows.

Since the beginning of operations, Diamond has welcomed over 12,000 direct users who have had an impact on a wider network of at least 24,500 researchers, positioning Diamond as one of the largest user bases amongst national facilities in Europe.

Diamond's output is not just characterised by volume. The institutional h-index currently stands at 128, and a recent analysis showed that 25% of publications are found in journals with an impact factor of nine and above. The

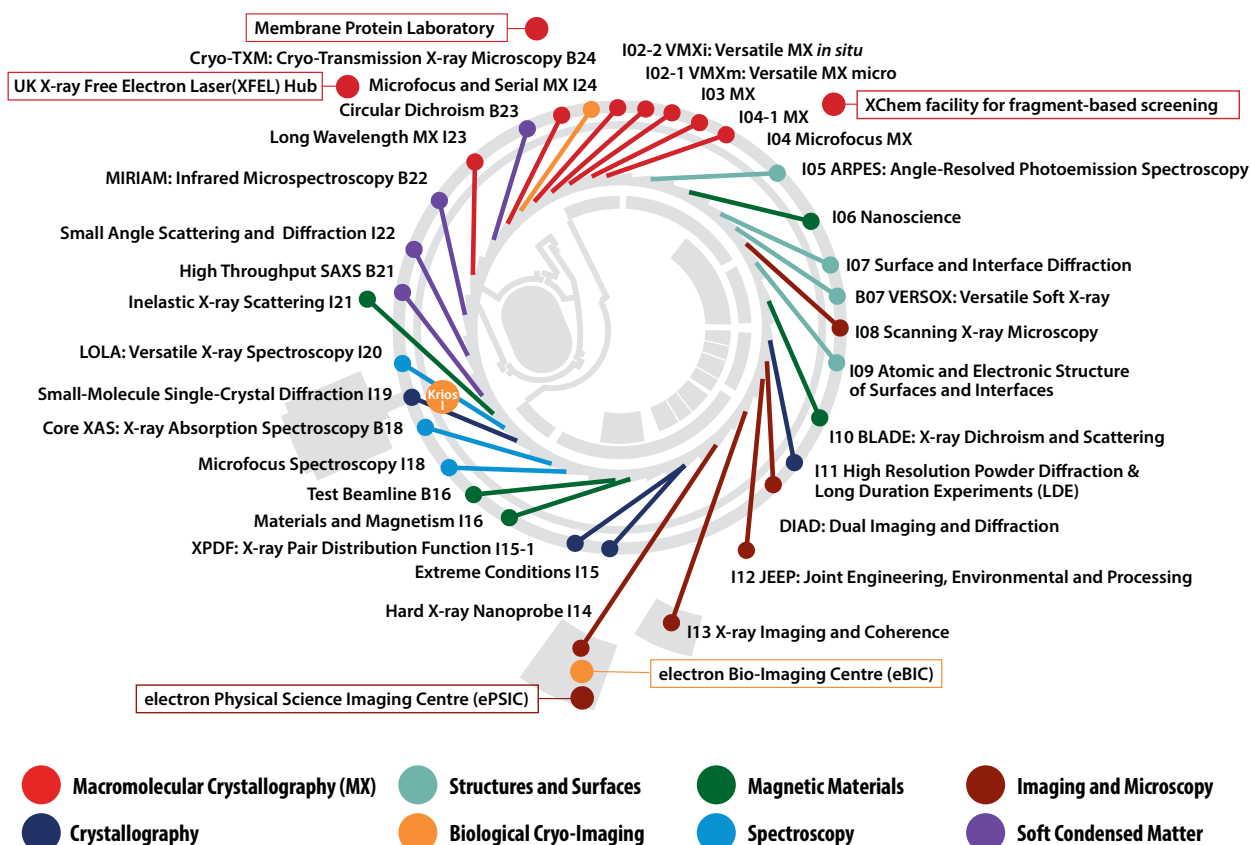


Figure 1: Instruments available within science groups and integrated facilities at Diamond. A detailed list of beamlines/instruments and their description is provided in Appendix 1.

completion of the Phase III instrument programme has added 10 beamlines, which ensures that the investment in Diamond fully maximises return on the initial capital investment. The impact of these new beamlines is already being felt, for example at I23 work around a plastic digesting enzyme is the epitome of the significant world leading instruments can make¹. The study of capture and storage of toxic iodine vapour from nuclear industry operation using metal organic frameworks (MOF)² at beam line I11 has led to more efficient and effective MOF designs by locating the position of captured iodine molecules within the MOF pore, which are less than 1 nm in size. As another example, the discovery of Weyl quasiparticles in condensed matter systems, using the beamline I05, has opened the door for future electronic systems that could potentially move electric charge at incredible speeds compared to current technology³.

The UK Government's Industrial Strategy⁴ highlights Grand Challenges to put the UK at the forefront of the industries of the future: to be a leader in artificial intelligence and big data revolution; to equip UK industry to be best prepared for clean growth; to be a world-wide leader in the mobility of people, goods and services; and to help meet the needs of an ageing society. We anticipate that Diamond-II will enable us to play a key role in all of these challenges, as well as enabling breakthroughs in research at the frontiers of knowledge.

* https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/664563/industrial-strategy-white-paper-web-ready-version.pdf

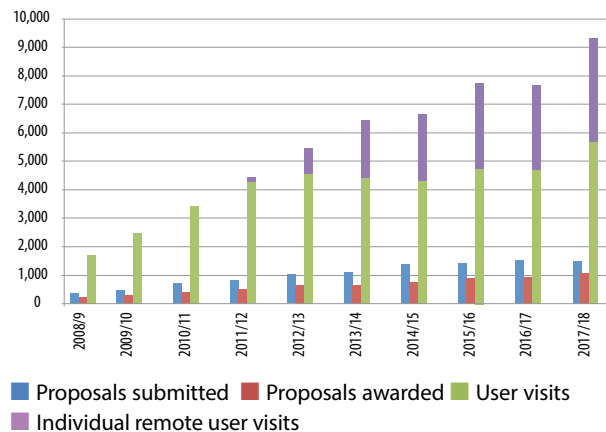


Figure 2: Total number of proposals for beamtime access and user visits per year.

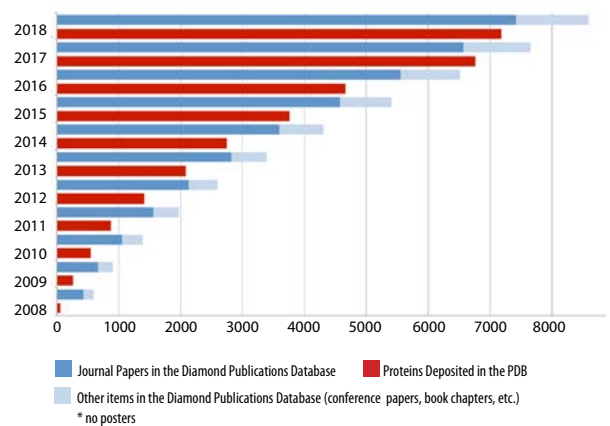


Figure 3: Cumulative number of publications by Diamond scientists and users, and cumulative number of structures deposited in the Protein Data Bank.

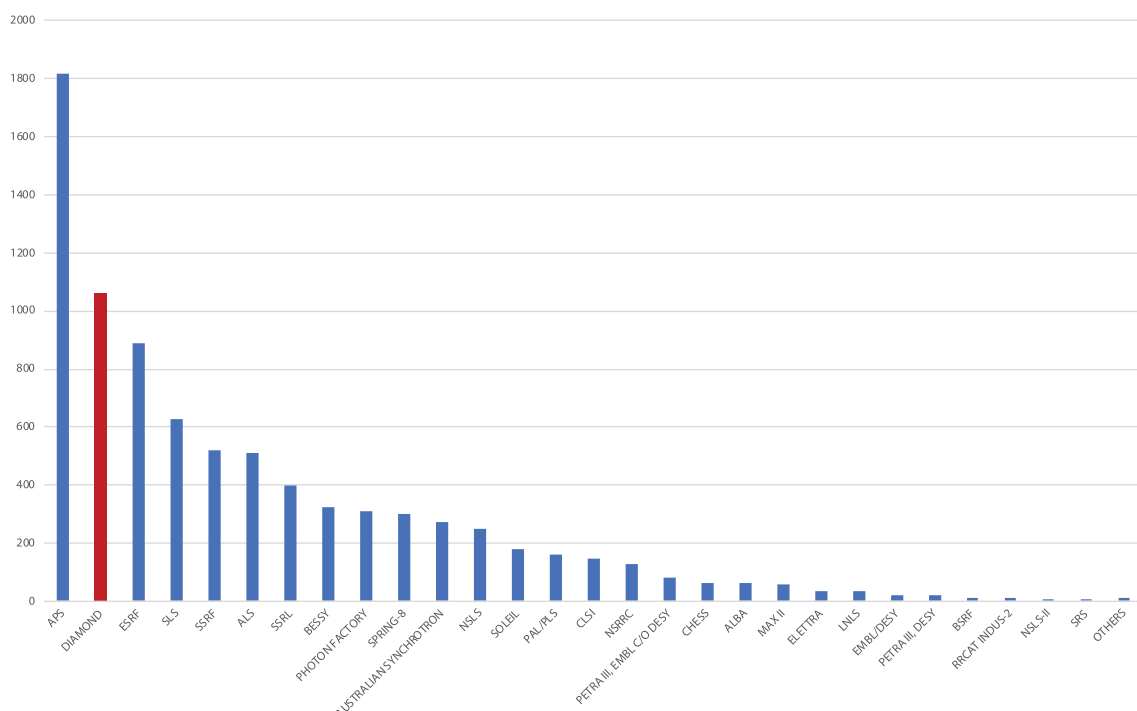


Figure 4: Average number of structures deposited in the Protein Data Bank per year for the period 2013 – 2018, for synchrotron facilities across the world. Please note that 2017 saw the beginning of significant PDB output from the XChem facility at Diamond where 100s of the same structure are deposited with or without bound small chemical fragments.

3. The Diamond-II synchrotron

We are entering a new era of opportunity with the advent of 4th generation sources, the so-called Diffraction Limited Storage Rings (DLSRs)⁴. This disruptive technology became a reality in 2016 with the operation of MAX IV, the world’s first multibend-achromat (MBA) light source. The progress in accelerator technology and the decrease of the electron horizontal emittance between one and two orders of magnitude, offers the scientific community the opportunity to exploit much brighter photon beams and an increased coherence over a large energy range. The gains are transformative in many areas of science, and consequently all major existing synchrotrons have proposed an upgrade to this new generation of magnetic lattice and are currently in various phases of their projects, from conceptual design to implementation for the EBS (Extremely Brilliant Source) upgrade at the European Synchrotron Radiation Facility (ESRF)⁵. It is vital for Diamond to realise such an upgrade in the years to come to remain competitive on the international scene and offer its academic and industrial users the very best opportunities in science enabled by synchrotrons.

Diamond has devised a novel implementation of MBA technology, offering not only dramatic gains in brightness and coherence but also additional spaces (so-called mid-straight sections in each of the new MBAs) to install new photon sources based on insertion devices. This will enable the new machine - Diamond-II - to accommodate both high-performance beamlines that are currently based on bending magnets and additional sites for new beamlines, offering greater capacity and flexibility to accommodate new scientific drivers and communities well into the future.

The full impact of the Diamond-II storage ring upgrade will

only be realised through complementary developments in sample preparation, sample environments, beamline optics and detectors, and the management and analysis of much larger and complex data sets. The new science opportunities afforded by Diamond-II will necessitate a wider review of beamline capabilities and will in some cases demand remodelling of existing beamlines or the development of completely new beamlines. For many beamlines, it is likely that Diamond-II will necessitate the renewal of beamline optics, sample environments and detectors, as well as substantial upgrades to our capacity and capability for data storage and computation. Many

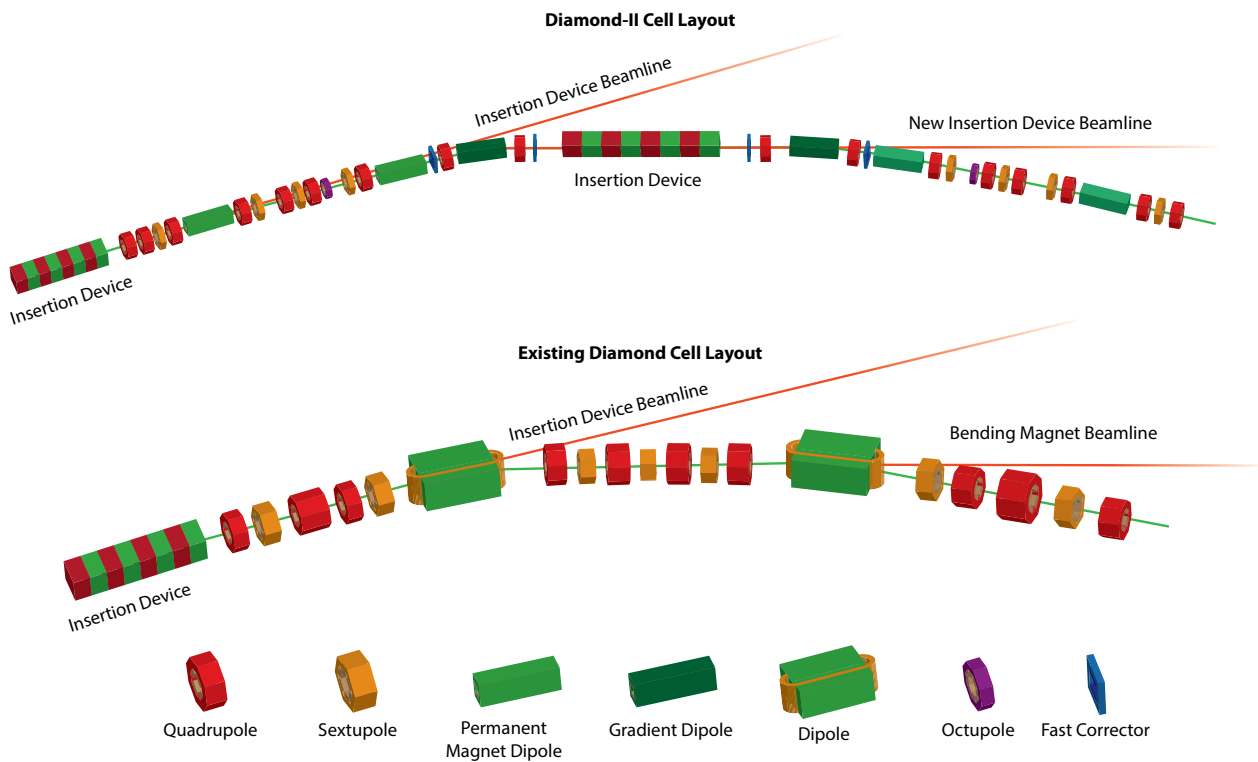


Figure 5: Schematic of the current Diamond DBA (Double Bend Achromat, bottom) and the proposed design for a DTBA (Double Triple Bend Achromat) for Diamond-II (top).

of these requirements are briefly outlined below, are described fully in the Conceptual Design Report (CDR) for the Diamond-II machine and will be elaborated at the Technical Design Report (TDR) stage of the Diamond-II project.

Given the strength and breadth of our user programme, our priority is to ensure that a maximum number of existing beamlines benefit from the upgrade to a low emittance machine. It is also critical that a maximum number of beamlines restart their user programmes as soon as possible after the end of the dark period. To minimise the down time, it is essential to preserve and reuse as much of the existing infrastructure as possible, including the existing optical layouts for insertion device beamlines. Finally we need to be able to take advantage of emerging methods that will be enabled by the characteristics of Diamond-II. With these factors in mind, we have been working on an outline design of the machine that offers a sweet spot for future science with respect to emittance, ring energy and capacity.

The new lattice

The brightness is the photon flux per unit area in 4D phase space and per spectral bandwidth and is maximised by either increasing the flux (higher electron current or using a higher ring energy, provided that such a choice is compatible with the photon energy range targeted), or by decreasing the transverse phase space volume. The current vertical emittance of 8 pm.rad at Diamond is state of the art, and most future gains in emittance are to be found in the horizontal direction.

We propose that the Diamond-II lattice will be based on Double Triple Bend Achromats (DTBAs). This “baseline” lattice, based on the 7BA lattice of the ESRF-EBS from which the central dipole has been removed, offers great advantages. It provides a reduction in horizontal emittance by at least an order of magnitude, with a resulting increase in photon brightness and coherent fraction that is described in greater detail in the next section. In addition, it introduces 24 new “mid-straight” sections that can be used for short (1.5 m) in vacuum insertion devices (Figure 5). We will not be able to exploit all of these mid-straight sections for insertion device (ID) sources, however up to five new beamlines are possible in addition to repositioning I04-1, B07-1 and I20-EDE and converting any other existing bending magnet beamlines to ID sources (either wigglers, 3-pole wigglers or undulators).

Choice of energy

The brightness and coherent fraction of the photon beams for Diamond-II will be dramatically increased due to the reduction in electron emittance, but some techniques are flux hungry and do not benefit directly from the brightness

increase. Increasing the energy of the machine (from 3 to 3.5 GeV) maximises photon flux at high photon energy but, as the emittance is proportional to the square of the energy, working with a higher ring energy increases the horizontal emittance (for a given lattice design). The decrease in the coherent fraction that this brings is offset by the marked increase in effective brightness at medium and high energies. The Diamond-II ring is based on a DTBA lattice with the highest practical ring energy of 3.5 GeV and a horizontal emittance of ~160 pm.rad. This choice of ring energy provides over one order of magnitude reduction in horizontal emittance and increases both the photon brightness and coherent fraction. These are plotted in Figures 6 and 7 for a set of IDs covering the entire energy range accessible at Diamond based on the examples of sources for the ARPES beamline I05 for the UV region, the RIXS beamline I21 for the soft X-ray regime, and the powder diffraction beamline I11 for harder X-rays. Whilst the coherent fraction decreases for the 3.5 GeV machine with respect to 3.0 GeV, it is marginal compared to the increase in brightness at higher energy (a factor of 4 at 25 keV for the Cryogenic Permanent Magnet Undulator (CPMU) to be installed on I11). Of course, increasing the electron current of the DTBA ring from 300 mA to 500 mA instead of ramping the energy was another option considered initially, but will not provide such a gain at the high energy end of the spectrum. The overall gain in brightness with respect to that of the current Diamond lattice over the entire spectral range is shown in Figure 8 alongside the operating energy ranges of existing beamlines. Clearly the selected lattice (3.5 GeV electron energy, 160 pm.rad emittance) maximizes impact for a large set of beamlines, without compromising the gain in brightness in the soft and tender X-ray regime, as shown by comparing the gain obtained for a 3 GeV ring, with 118 pm.rad emittance.

The Diamond-II science case provided in this document contains strong drivers to increase the flux and brightness in the hard X-ray regime, as highlighted by consultations with the user community in recent workshops. The advent of pixelated counters with high-Z materials (GaAs, CdTe) and excellent quantum efficiencies at high X-ray energy allows the very effective exploitation of high flux in this energy range, which finds many applications in imaging, diffraction and spectroscopy. We foresee that, combined with the continuous improvement of IDs - short CPMU^{6,7,8} periods, down to 14 mm, are achievable nowadays, providing very substantial gains at high energy - the appetite for flux-hungry or brightness limited hard X-ray applications will continue to grow and justify the choice of ring energy. Note that an upgrade to CPMU sources for several beamlines is already a major part of our current capital investment programme for the coming years (2019-2024). This ID upgrade programme will be extended and integrated as part of the Diamond-II project in order to fully exploit the benefit of the low-emittance upgrade and the increased energy of the ring.

The Diamond-II synchrotron

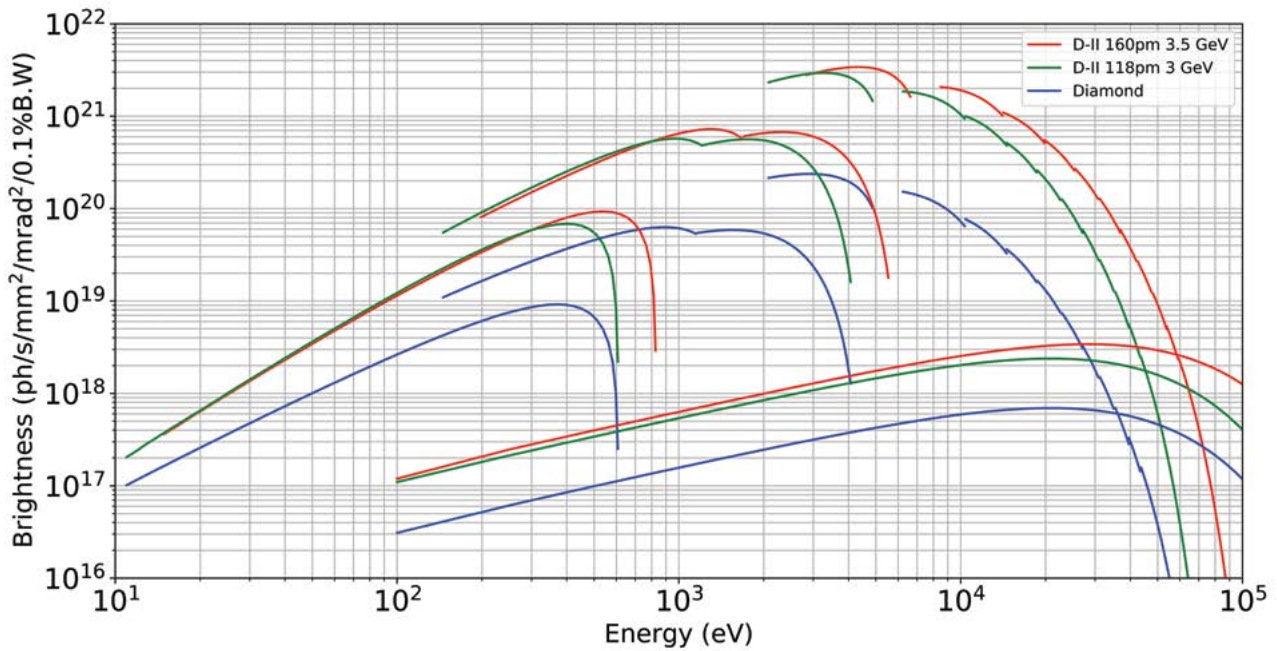


Figure 6: Brightness for a set of selected sources at Diamond (blue curves), Diamond-II at 3 GeV (green curves) and Diamond-II at 3.5 GeV (red curves). In the UV regime, soft X-ray regime and hard X-ray, the brightness curves are shown respectively for the I05, I21, the future CPMU 15.6 mm period (to be installed on I11 and VMXm), and for the superconducting wiggler on I12 (JEEP). All calculations have been made with Spectra⁹ using the Wigner function. A phase error of 3° for the undulators has been taken into account analytically¹⁰.

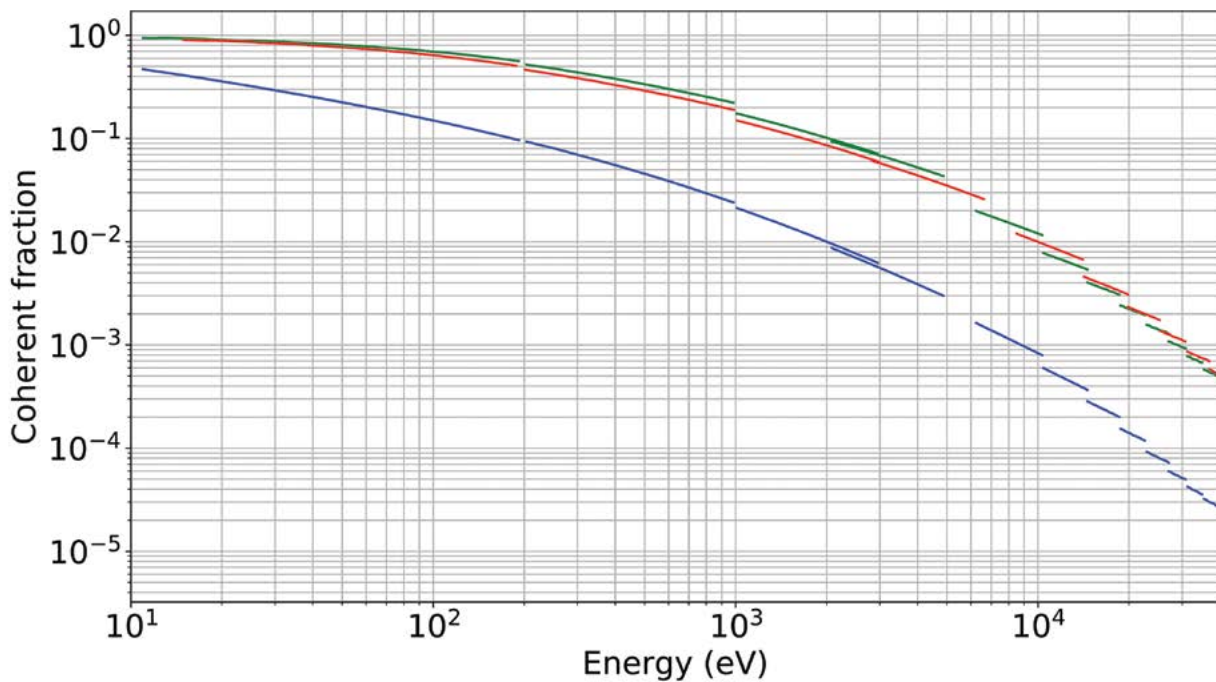


Figure 7: Coherent fraction in the horizontal direction as a function of Energy for Diamond (blue), Diamond-II at 3 GeV (green) and Diamond-II at 3.5 GeV (red). All curves have been produced with Spectra using the Wigner function and approximating the coherent fraction as the ratio between the Brightness and the Brightness calculated in the limit of zero emittance and zero energy spread.

4. Beamlines and complementary technologies

Achievements in super-resolution microscopy, gravitational waves (LIGO) and cryoEM underscore the idea that major leaps in science are often a consequence of technology-enabled improvements in sensitivity. For LIGO, a 3-fold improvement produced the required sensitivity, whereas in cryoEM a >10-fold improvement in detector frame rates opened the door to high-resolution reconstructions. Indeed, the present Diamond source generated several orders of magnitude increase over the previous facility; in Diamond-II, the 20-fold reduction in horizontal emittance will enhance the intrinsic signal-to-noise across all beamlines and the storage ring energy increase to 3.5 GeV will provide a substantial increase in flux at high photon energies (see Table I).

4.1. Benefit of Diamond-II for existing ID beamlines

Many X-ray beamlines will directly benefit from the lower emittance (and upgrade of IDs) and will be able to exploit the increased brightness, coherence and improved signal to noise for more accurate measurements at micron and sub-micron length scales. Table 2 lists current and planned beamlines at Diamond. Obviously, brightness limited instruments for 3D chemical tomography and imaging (I08, I18, I14, I13-1, I13-2) will directly benefit from the upgrade, but the gains for other instruments are also real step changes: powder diffraction (I11) for example will be able to work routinely at 30 keV, providing a much improved integration with *in situ* experimental setups and *operando* measurements of materials in their relevant operating environment. Small molecule crystallography (I19) will shift much of its user programme to using high-energy microfocussed beams, allowing single micron-sized grains to be analysed. A 40 keV instrument using an undulator source for micro-PDF will allow mapping of heterogeneity in disordered systems, nano-crystalline or amorphous components of the sample, currently inaccessible on the Wiggler source. Spectroscopy studies under geologically relevant high-pressures with nano-diamond anvil cells will be possible due to the much higher penetration.

Table 1 below summarises the gain in brightness at 1 keV, 25 keV and 40 keV with Diamond-II at both 3.0 and 3.5 GeV compared to the current machine, assuming a CPMU at 4 mm gap in a standard straight section in all cases, and a beam current of 300 mA. For the 25 and 40 keV cases a suitable undulator period is used which provides continuous tunability down to 6keV.

Photon energy (keV)	Gain in brightness Diamond-II at 3 GeV (118pm)	Gain in brightness Diamond-II at 3.5 GeV (160pm)
1	x 10	x 8
25	x 18	x 49
40	x 17	x 79

Table 1: Gain in brightness with Diamond-II at 3 or 3.5 GeV, calculated using the Wigner formulation.

In MX (Macromolecular Crystallography), XPCS (X-ray Photon Correlation Spectroscopy) or USAXS (Ultra-Small Angle X-ray Scattering), the improved horizontal emittance will map directly into gains in measurement signal-to-noise, especially for room temperature data or well-ordered crystals if complemented by small pixel detectors that match feature size. The reduction in measured X-ray background in such cases will extend data resolution and/or reduce the required dose for equivalent data quality. Due to the gains in brightness at higher energies, MX at 25 keV and above becomes a tractable method for substantially reducing radiation damage on micron sized crystals (as the mean path-length of the damaging photoelectrons exceeds the size of the crystal). Theoretical and experimental investigations^{11,12,13} indicate a gain of between 3 to 10-fold in crystal lifetime for micron sized beams at 20 - 25 keV.

But even for low energy beamlines the overall impact for Diamond-II will be substantial. For Diamond's IR beamline, B22, the Diamond-II lattice is expected to enhance the brightness by ~4-fold for the mid IR spectral range to ~10-fold for the THz range and allow improvements in noise and stability. Our Circular Dichroism (CD) beamline, B23, has invented a new imaging method with 50 micron spatial resolution. This has tremendous potential in microdevices, biosensors and polymers. The new lattice will enable an order of magnitude increase in spatial resolution. For I05, the ability to focus more efficiently micro-size beams (factor of 3) will open the door for experiments using a gate voltage or nanoscale strain as tuning parameters. Soft X-ray magnetic imaging with coherent beam will complement our current capabilities using photo emission electron microscopy (PEEM) and scanning transmission X-ray microscopy (STXM). Our soft X-ray RIXS beamline (I21) will be able to work efficiently in the tender X-ray regime and access 4D transition metals, and use multiplexed measurements by switching to a horizontal scattering geometry.

4.2. Optimising existing instruments using new mid-section straights

The new mid-section straights in the proposed machine with DTBAs mean that Diamond-II will enable us to retain and improve all existing high-performance beamlines while also offering increased capacity for new beamlines, and with it versatility of the beamline portfolio. More specifically, Diamond-II promises to do the following:

Ensure that current flagship bending magnet beamlines stay competitive

- Bending magnet beamlines B07, B16, B18, B21 could be converted to much brighter ID sources, whereas without a mid-straight, performance on the high energy bending magnet sources (particularly B16, B18 and B21) in Diamond-II would be reduced because of the lower dipole field. A higher field 2-pole or 3-pole wiggler would resolve this problem and lead to increased flux compared to the current situation and in particular for B18 a factor of 3 increase in flux at high energy. A CPMU located in the new mid-straight would provide vastly improved brightness for both B16 and B21. On B21, the CPMU will provide a flux gain from 10^{12} to 10^{14} photons per second with a much reduced background magnitude in the lowest resolutions (< 0.01 Angstroms⁻¹). The upgrade of B21 to a CPMU will allow the beamline to be completely windowless with all detectors in vacuum for optimal signal-to-noise.
- Beamlines B22, B23 and B24 could be converted to a dedicated ID source with a lower critical energy in order to increase the flux, and an *ad hoc* designed geometry in order to optimise the photon flux at the

sample position. It is worth underlining that at these wavelengths (IR, UV and soft X-ray, respectively) these beamlines are already diffraction limited. The natural synchrotron divergence of soft photons below the critical energy ($\epsilon_c \sim 8$ keV) decreases with the magnetic field of the source; the plan is to design a soft 3-pole wiggler that could provide a smaller opening angle of radiation and thus intrinsically increase the brightness at the source by several times.

Retain or improve several beamlines on insertion devices

- Without mid-straights J02 (VMXm) would be lost or would have to be moved and displace another beamline, since VMXm uses the mid-straight ID created by the recent DDBA upgrade.
- I04-1 (XChem) currently shares a canted straight section with I04 but is flux limited and its throughput would be transformed by an order of magnitude or more gain in flux which would be provided by a move of I04-1 to a dedicated straight section. This could only be achieved (without loss of existing beamlines) by the provision of new mid-straight capacity.
- DIAD (K11) could have a much better CPMU than the short mini-wiggler which has recently been installed. Otherwise, without a mid-straight DIAD would have to be accommodated on a 2-pole or 3-pole wiggler or potentially a superbend; this would exceed the brightness of the current mini-wiggler, but an undulator would clearly be brighter by an order of magnitude.
- I20-EDE could be relocated to an improved ID source at B19 and be disentangled from I20 XAS whilst allowing I20-XAS to improve its capability.

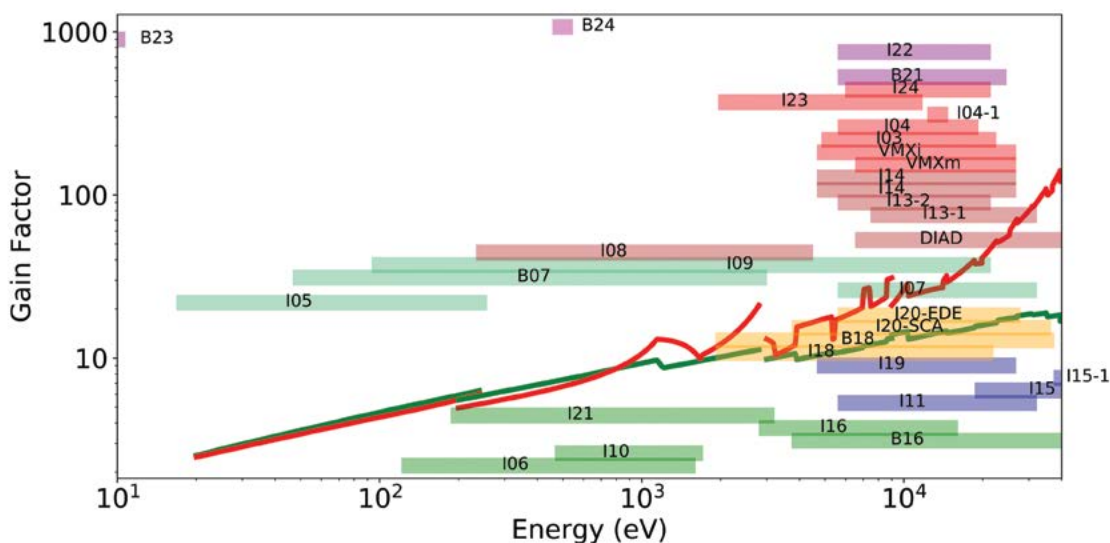


Figure 8: Gain in spectral brightness for a set of selected undulator sources for Diamond-II at 3 GeV, 118 pm.rad emittance (green curves) and Diamond-II at 3.5 GeV, 160 pm.rad emittance (red curves). In the UV regime, soft X-ray regime and hard X-ray, the brightness curves are shown respectively for the I05, I21, and the future CPMU 15.6 mm period (to be installed on I11 and VMXm). The photon energy ranges used for all current Diamond beamlines are represented by horizontal bars. Table 2 lists all current or planned beamlines at Diamond. Beamlines B22 (IR) and I12 (high-energy engineering) energies are outside of the range of this graph.

Diamond's beamlines: current operational status April 2019

Beamline Name and Number	Main Techniques	Energy / Wavelength Range
I02-1 - Versatile MX micro (VMXm)	Micro- and nano-focus in vacuum cryo-macromolecular crystallography (VMXm)	7 - 28 keV
I02-2 - Versatile MX <i>in situ</i> (VMXi)	<i>In situ</i> microfocus macromolecular crystallography, Serial Synchrotron Crystallography	10 - 25 keV
I03 - MX	Macromolecular crystallography (MX), Multiwavelength Anomalous Diffraction (MAD)	5 - 25 keV
I04 - Microfocus MX	MX, MAD	6 - 18 keV
I04-1 - Monochromatic MX	MX, XChem fragment screening	13.53 keV (fixed wavelength)
I05 - ARPES	Angle-Resolved PhotoEmission Spectroscopy (ARPES) and nano-ARPES	18 - 240 eV; 500 eV
I06 - Nanoscience	X-ray Absorption Spectroscopy (XAS), X-ray photoemission microscopy and X-ray magnetic circular and linear dichroism	80eV - 2200eV
I07 - Surface and Interface Diffraction	Surface X-ray diffraction, Grazing Incidence X-ray Diffraction (GIXD), Grazing Incidence Small Angle X-ray Scattering (GISAXS), X-ray Reflectivity (XRR)	6 - 30 keV
B07 - VERSOX: Versatile Soft X-ray	Ambient Pressure XPS and NEXAFS NEXAFS and High-Throughput XPS	250 - 2800 eV 50 - 2200 eV
I08 - Scanning X-ray Microscopy	Scanning X-ray microscopy, NEXAFS/ XANES, X-ray fluorescence	I08 branch: 250 eV - 4.4 keV J08 - Soft and Tender X-ray Ptychography branch: 250 - 2000 eV
I09 - Atomic and Electronic Structure of Surfaces and Interfaces	XPS (including HAXPES), X-ray Standing Waves (XSW), Near Edge X-ray Absorption Fine Structure (NEXAFS), energy-scanned photoelectron diffraction	Hard X-rays: 2.1 - 18+ keV Soft X-rays: 0.1 - 2.1 keV (currently 0.1 - 1.9 keV)
I10 - BLADE: Beamline for Advanced Dichroism Experiments	Soft X-ray resonant scattering, XAS and X-ray magnetic circular and linear dichroism	Circular: 400-1600eV; Linear Horizontal: 250-1600eV; Linear Vertical: 480-1600eV
I11 - High Resolution Powder Diffraction	X-ray powder diffraction	6 - 25(30) keV (0.5 - 2.1 Å)
DIAD: Dual Imaging and Diffraction	Simultaneous imaging and diffraction	8 - 38 keV
I12 - JEEP: Joint Engineering, Environmental and Processing	Time-resolved imaging and tomography (phase- and attenuation-contrast), time-resolved powder diffraction, single crystal diffraction, diffuse scattering, energy dispersive X-ray diffraction (EDXD), high-energy small angle X-ray scattering (under development)	53 keV - 150 keV monochromatic or continuous white beam
I13 - X-ray Imaging and Coherence	Phase contrast imaging, tomography, full-field microscopy (under commissioning), coherent diffraction and imaging (CXRD, CDI), ptychography and photocorrelation spectroscopy (XPCS) (under commissioning), innovative microscopy and imaging	Imaging branch: 8 - 30keV Coherence branch: 7 - 20keV
I14 - Hard X-ray Nanoprobe	Scanning X-ray fluorescence, X-ray spectroscopy, ptychography and transmission diffraction	5 - 23 keV
I15 - Extreme Conditions	Powder diffraction, single crystal diffraction	Monochromatic and focused 20 - 80 keV White beam
I15-1 - XPDF	X-ray Pair Distribution Function (XPDF)	40, 65, and 76 keV
I16 - Materials and Magnetism	Resonant and magnetic single crystal diffraction, fundamental X-ray physics	2.5 - 15 keV
B16 - Test beamline	Diffraction, imaging and tomography, topography, reflectometry	4 - 20 keV monochromatic focused 4 - 45 keV monochromatic unfocused White beam
I18 - Microfocus Spectroscopy	Micro XAS, micro Extended X-ray Absorption Fine Structure (EXAFS), micro fluorescence tomography, micro XRD	2.05 - 20.5 keV
B18 - Core XAS	X-ray Absorption Spectroscopy (XAS)	2.05 - 35 keV
I19 - Small-Molecule Single-Crystal Diffraction	Small-molecule single-crystal diffraction	5 to 25 keV / 0.5 to 2.5 Å
I20 - LOLA: Versatile X-ray Spectroscopy	X-ray Absorption Spectroscopy (XAS), X-ray Emission Spectroscopy (XES) and Energy Dispersive EXAFS (EDE)	Dispersive branch: 6 - 26 keV Scanning branch: 4 - 20 keV
I21 - Inelastic X-ray Scattering	Resonant Inelastic X-ray Scattering (RIXS), X-ray Absorption Spectroscopy (XAS)	Currently 250 - 1500 eV (to be upgraded to 250 - 3000 eV)
B21 - High Throughput SAXS	BioSAXS, solution state small angle X-ray scattering	8 - 15 keV (set to 13.1 keV by default)
I22 - Small Angle Scattering and Diffraction	Small angle X-ray scattering and diffraction: SAXS, WAXS, USAXS, GISAXS. Micro-focus.	7 - 20 keV
B22 - MIRIAM: Multimode InfraRed Imaging And Microspectroscopy	IR micro- & nano-spectroscopy, IR imaging, THz spectroscopy	nanoFTIR : 4000-900 cm ⁻¹ (2.5-11 μm) microFTIR: 10,000-100 cm ⁻¹ (1-100 μm) Spectroscopy (FTIR): 10,000-10 cm ⁻¹ (1-1000 μm) Imaging (FPA): 10,000-900 cm ⁻¹ (1-11 μm)
I23 - Long Wavelength MX	Long wavelength MX	3 - 8 keV (1.5 - 4.1 Å)
B23 - Circular Dichroism	Circular Dichroism (CD)	125-500 nm & 165-650 nm for CD Imaging at 50 μm resolution, 96-cell High-Throughput CD (HTCD) and High-Pressure CD up to 200 MPa
I24 - Microfocus and Serial MX	MX, MAD, Serial Crystallography	6.5 - 25.0 keV
B24 - Cryo Transmission X-ray Microscopy (TXM)	Full field X-ray imaging	200 eV - 2600 eV

4.3. New instruments

The significant initial capital investment in Diamond, followed by a series of upgrades to beamlines and enabling infrastructure, will be augmented by the proposed machine upgrade for Diamond-II. As will be seen from the case below this immediately suggests opportunities for transformational new beamlines which form a significant part of the justification for the machine upgrade. Being the only synchrotron photon source in the UK (unlike Germany with three sources), and serving a very diverse community, Diamond is heavily oversubscribed in many areas and must be able to provide maximum capacity as well as new capabilities. At the end of Phase III, Diamond will be operating 33 beamlines. The mid-straight option would allow an expansion to 38 beamlines, i.e. five new instruments in addition to promoting existing instruments to improved sources, as described in the previous section. Whether these new instruments provide only extra capacity for our most oversubscribed beamlines or deliver new capabilities remains to be established through a beamline prioritisation process in consultation with our user communities and the Diamond Science Advisory Committee (SAC) and Diamond Industrial Science Committee (DISCO) in the coming years. The machine upgrade presented here offers a great degree of flexibility in planning and will allow us to identify new beamline concepts as they emerge. With the improved coherence of the beam, new methods such as holography, ptychography and XPCS will grow rapidly. It is often not possible to foresee which methodological developments will have the strongest impact (for example the applications of 3D ptycho-tomography seem endless today but the method, being relatively slow, was not necessarily foreseen as transformative when the first dedicated beamlines were built). Leaving room to accommodate new beamlines, as scientists in the community become more familiar with the advantages of fourth generation sources, will be a strength. Cases provided later in this document already point to areas of science where new beamline designs could be transformative. As part of the full Diamond-II programme we propose to deliver two new beamlines within a year of operation of the new machine and a staged programme of delivery of further beamlines.

4.4. Development of complementary technologies

Sample Handling and Environments

The potential transformation in throughput and science output which the new machine offers can only be delivered if the necessary sample preparation and handling tools are provided in parallel. Engagement with Diamond's user community through the September 2018 workshops indicated overwhelming support for focussed effort in the areas of sample preparation, sample environments and

sample delivery. Integrated specialised facilities co-located at Diamond, and Harwell partners such as the Research Complex (RCaH), the Rosalind Franklin Institute (RFI), the Catalysis Hub or Faraday Institution (FI) will provide a supportive environment for implementing challenging sample preparation and new *operando* environments when coupled with world class expertise. Equally, in the same way that step-changes in MX throughput came about in the early 2000's from automation and standardisation efforts in collaboration with users (through SPINE¹⁴ and other EU initiatives), disruptive technological changes will be essential to truly unlock the high throughput capabilities of Diamond-II. Where practical, sample preparation capability should be distributed so that samples optimised for Diamond-II beamlines can be produced easily in appropriate quantities local to the users. It is therefore essential that where possible specialised apparatus for sample preparation is affordable.

We therefore propose, in support of life science activity at Diamond-II, in collaboration with our partners on campus and UK user groups, to initiate the development of new sample production, mounting and presentation methods for MX, SAXS and imaging that are matched to the throughput and technical requirements of Diamond-II with a particular focus on cross-instrument experiments (eg CD/SAXS and correlative light and electron or X-ray microscopy). To capitalise on the opportunities, we intend to establish a cross-beamline group for correlative bio-imaging.

Unprecedented gains in signal-to-noise have already been demonstrated from the in vacuum end station on I23¹⁵ and the in vacuum WAXS (Wide-Angle X-ray Scattering) detector on I22. In preparation for Diamond-II we will introduce a new approach to sample handling to provide direct laser-shaping of crystals to spheres and removal of extraneous, non-crystalline material. This will not only massively mitigate absorption differences that otherwise obscure anomalous scattering effects from lighter elements, the bread-and-butter activity of I23, but will also eliminate the largest contribution to noise for in vacuum X-ray crystallography (now extended to VMXm) and will potentially optimise all MX experiments.

The large reduction of horizontal emittance will also transform sample environments for physical sciences. By exploiting the improved horizontal divergence, some instruments (I16) will be switching to horizontal scattering geometry and will provide a much simpler vertical access for heavy sample environments such as cryostats and large cryomagnets (not available in magnetic scattering studies with hard X-rays at present) and also to in vacuum design for improved background. The larger penetration of the beam provided by the higher energy of the ring and new sources (CPMUs), will enable routine use of 30 keV energies for powder diffraction, for small molecule crystallography, and for surface XRD. It will open up new designs for

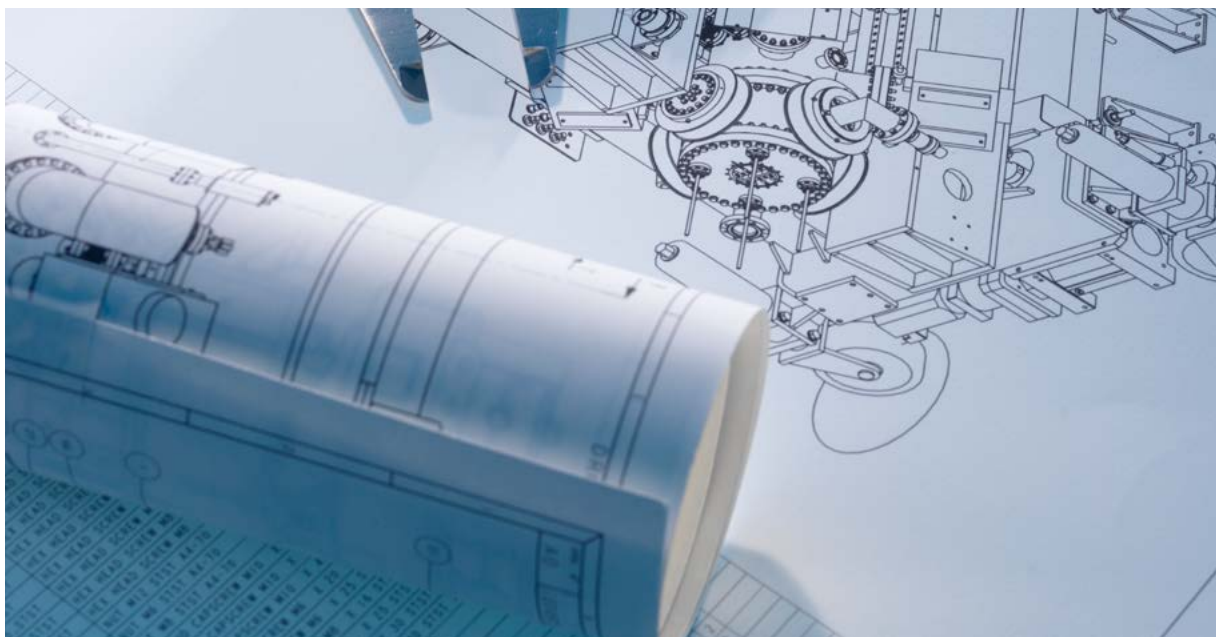
environments for *in situ* and *operando* science such as coin cells, flow cells and catalytic reactors, and allow rigs for new and developing processes such as additive manufacturing and new high temperature strain rigs to be developed. The improved micro-focussed flux will also open new avenues for multi-nodal mapping experiments in more realistic *operando* conditions on imaging instruments such as I08, I18, I14, I13.

Detector technology

The lower emittance and higher X-ray energies for many techniques coupled with orders of magnitude gains in incident photon counts rates is driving the requirement for new detectors. Current large area photon counting detector technology offers frame rates of a few hundred Hz with a choice of Si or CdTe sensors but for many MX, ptychography and XPCS applications the use of, for instance, multilayer monochromators combined with the Diamond-II source will cause incident count rates to exceed the thresholds for existing photon counting technology. A new generation of integrating detector technologies is emerging, driven principally by XFEL sources. Diamond-II and others will have a similar demand for multi-kHz framing, small pixels (< 10 micron), high-Z (to optimise detection efficiency at high energy), integrating technology in a modular format offering multiple geometries, capable of operating in vacuum. These requirements will also be needed for low energy beamlines in which CMOS technology is starting to be utilised, again initially driven by the XFEL sources. This will require both in-house/on-site development in collaboration with STFC and/or involvement in wider international partnerships to establish and mature this new technology in time for Diamond-II.

Data analysis, computing, big data

Data rates from Diamond are already approaching petabytes per month. The data rate from Diamond-II is expected to be at least an order of magnitude greater. This means that a major refresh of our network, data storage and analysis facilities is required. However, with increased data volumes come new challenges and exciting new opportunities for analysis. The vast quantities of data already available are enabling the use of deep learning and AI approaches that have particular applications in areas where, to date, human intervention has been essential for successful data analysis because analytical methods have not proven useful. Examples in the physical and life sciences include segmentation of tomography reconstructions¹⁶; the interpretation of poor quality or low resolution electron density maps; the interpretation of raw data to yield a qualitative impression of data quality; the interpretation of many-dataset experiments such as fragment screening¹⁷ and advancing data analysis for small angle scattering by allowing users to examine the size and shape of particles in a matrix using an AI driven algorithm. Other applications revolve around effective decision making in automated pipelines and workflows and have the potential to make more effective use of computing resource and generate real-time and useful feedback both to users conducting experiments at beamlines, and to expert systems controlling experiments. Current limitations for off-line analysis are the quality of metadata and annotation in existing databases, the challenge is to capture complete and meaningful metadata on-the-fly so that databases are AI ready. It is expected that by the time Diamond-II is online deep-learning classifiers will form an integral part of data collection and data analysis workflows. As part of the broader Diamond-II programme major investment in computation and data science will be required.



The purpose of this document

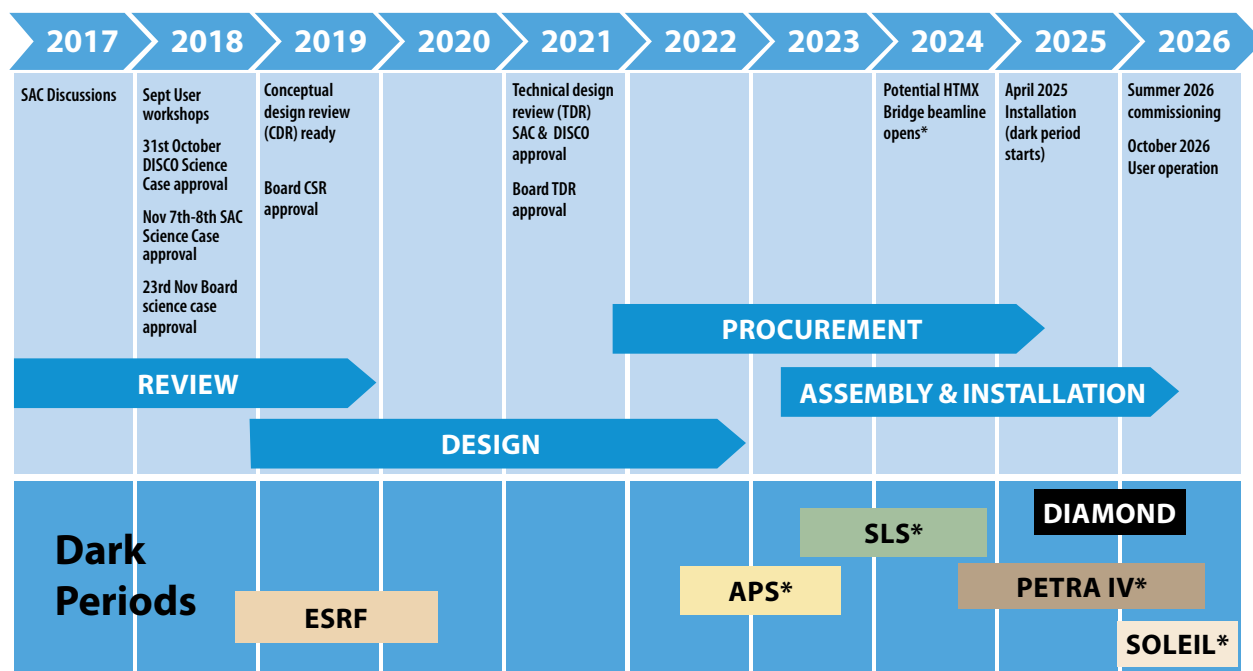
5. The purpose of this document

The principal aim of this document is to present the science case for Diamond-II and to do so for a particular implementation of the machine upgrade – i.e. with a lattice design that increases brightness and coherence by a factor of 79 (see table 1 on page 9), provides mid-section straights to retain and enhance all beamlines on bending magnets while offering additional sources for potential new beamlines, and which increases the electron beam energy from 3.0 to 3.5 GeV, providing greatly increased photon flux at higher energies. We provide examples that highlight the impact Diamond-II will have on key areas of research for which our user community in academia and industry is particularly strong, today and potentially in the future. The case has been developed by a wide range of Diamond scientists, with input from a series of workshops held with the UK user community and international experts in key areas of science and industry [See list of workshops and attendees in Appendix 2] and is organised into eight areas: Integrated structural biology; Biotechnology & biological systems; Health & well-being; Energy; Chemistry; Quantum materials; Engineering materials & processing; Earth, environment & planetary science. This document is complemented by a CDR document that was approved in April 2019 by an international expert panel, and a more detailed TDR will be developed over the following 24 months.

These plans are being developed in consultation with other European synchrotrons who are also planning significant machine upgrades, both bilaterally and collectively through the LEAPS (League of European Accelerator-based Photon Sources) consortium. LEAPS is drawing up a roadmap for such developments, and it is too early at this stage to have a coherent view across Europe of what is being proposed, beyond a very general understanding that certain facilities will have particular strengths and specialisations by virtue

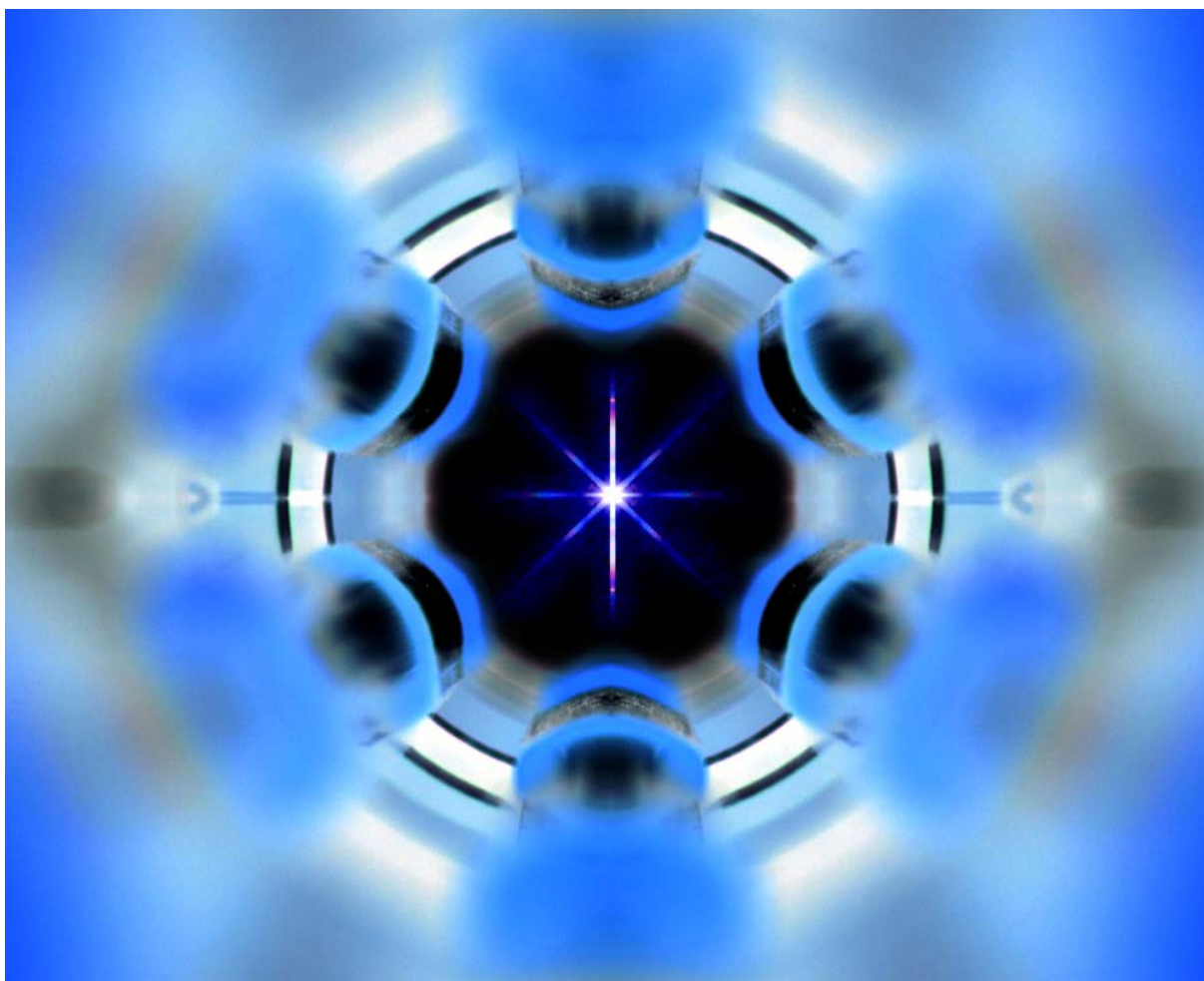
of key characteristics of their machines. For example, the ESRF will always be better suited than Diamond for beamlines operating with the very hardest X-rays. We are planning, as far as is practical, to avoid a situation in which our long shutdown coincides with shutdowns elsewhere (see Figure 9 for an indicative timeline for other dark periods), and will investigate strategic collaborations with other facilities to provide alternative capacity during the dark period at Diamond.

Diamond-II - Timeline



*to be confirmed. Discussions ongoing with European facilities

Figure 9: Timeline for planning, design, construction and commissioning for the Diamond-II machine upgrade. The dark period when Diamond is not operational will be of the order of 18 months, so steps will be taken to minimise the impact of this on the Diamond user community. This will include access to facilities outside the UK, co-ordinated to avoid dark periods. For this, it is important that plans for Diamond-II are coordinated within a road map of European facilities that is being drawn up through LEAPS. Current plans for dark periods at other facilities are shown.



References:

1. Austin, H. P. *et al.* Characterization and engineering of a plastic-degrading aromatic polyesterase. *Proc. Natl. Acad. Sci.* **115**, E4350 LP-E4357 (2018).
2. Zhang, X. *et al.* Confinement of Iodine Molecules into Triple-Helical Chains within Robust Metal–Organic Frameworks. *J. Am. Chem. Soc.* **139**, 16289–16296 (2017).
3. Xu, S.-Y. *et al.* Discovery of a Weyl fermion semimetal and topological Fermi arcs. *Science (80)*. **349**, 613 LP-617 (2015).
4. Eriksson, M., Van Der Veen, J. F. & Quitmann, C. Diffraction-limited storage rings-A window to the science of tomorrow. *J. Synchrotron Rad.* **21**, 837–842 (2014).
5. Culiuc, A. *et al.* ESRF Upgrade Phase II Status. (2015).
6. Hara, T. *et al.* Cryogenic permanent magnet undulators. *Phys. Rev. ST Accel. Beams* **7**, 50702 (2004).
7. Valléau, M. *et al.* Development of cryogenic undulators with PrFeB magnets at SOLEIL. *AIP Conf. Proc.* **1741**, 20024 (2016).
8. Patel, Z. *et al.* Insertion devices at Diamond Light Source: a retrospective plus future developments. in *8th Int. Particle Accelerator Conf.(IPAC'17), Copenhagen, Denmark, 14â 19 May, 2017* 1592–1595 (2017).
9. Tanaka, T. & RIKEN SPring-8 Center. SPECTRA - synchrotron radiation calculation code. (2015).
10. Walker, R. P. Phase errors and their effect on undulator radiation properties. *Phys. Rev. Spec. Top. Beams* **16**, 10704 (2013).
11. Cowan, J. A. & Nave, C. The optimum conditions to collect X-ray data from very small samples. *J. Synchrotron Rad.* **15**, 458–462 (2008).
12. Sanishvili, R. *et al.* Radiation damage in protein crystals is reduced with a micron-sized X-ray beam. *Proc. Natl. Acad. Sci.* **108**, 6127–6132 (2011).
13. Marman, H., Darmanin, C. & Abbey, B. The Influence of Photoelectron Escape in Radiation Damage Simulations of Protein Micro-Crystallography. *Crystals* **8**, (2018).
14. Cipriani, F. *et al.* Automation of sample mounting for macromolecular crystallography. *Acta Crystallogr. Sect. D* **62**, 1251–1259 (2006).
15. Wagner, A., Duman, R., Henderson, K. & Mykhaylyk, V. In-vacuum long-wavelength macromolecular crystallography. *Acta Crystallogr. Sect. D* **72**, 430–439 (2016).
16. Luengo, I. *et al.* SuRVoS: Super-Region Volume Segmentation workbench. *J. Struct. Biol.* **198**, 43–53 (2017).
17. Pearce, N. M. *et al.* A multi-crystal method for extracting obscured crystallographic states from conventionally uninterpretable electron density. *Nat. Commun.* **8**, 15123 (2017).

6. Diamond-II: Advancing life sciences

6.1. Life science challenges

Life science research is vibrant and continues to revolutionise the way we think about biology. The elucidation of the structure of DNA in 1953 kick-started this revolution and marked the start of modern structural biology. The recent genomics boom accelerated the growth and development of structural biology where the genetic interrelationships between organisms and viruses could be readily visualized by solving the structures of proteins encoded by their respective genes. Genomics is laying bare the relationships between organisms and, increasingly, the underpinnings of many diseases. Ultimately, this will lead to genuinely personalised medicine. The continued advancements in structural biology, through next generation synchrotrons, will enrich our understanding of biological structure across many scales and dimensions that include 1) spatial, where atomic level details describe life in terms of fundamental chemistry and 2) dynamic, where changes are measured at time-scales relevant to biology from one-billionth of a second to minutes. A series of grand challenges in basic science cascade from this and will be highlighted below.

The current strength of the UK academic sciences in these areas is demonstrated by the award of the Nobel prize for chemistry to a UK scientist in 2017 and 2018. The strength of UK industry is shown by the recent survey from the Office for Life Sciences*. The Biopharma and Medtech sectors employ over 240,000 people, generating approximately £70bn annual turnover. The largest segment in the industry (based on employees) is Biopharma, primarily involved in small molecule therapeutics, followed by contract manufacturers and research businesses. Diamond plays a key role in supporting these segments, with considerable industrial activity in MX, bioSAXS, and especially strong growth in demand in two life science areas, cryoEM (eBIC) and the XChem facility for fragment screening using MX. Eighty per cent of proprietary industrial use of Diamond is currently for life sciences and Diamond-II can contribute to strengthening the UK position across the life science sectors, both academic and industrial, through a cutting-edge, integrated user facility. The increased throughput and opportunities for new experiment modalities with Diamond-II are intended to match the requirements of a UK industrial sector that remains at the forefront of structure-based drug design (SBDD). It was stressed in our user consultation that Diamond's current approach of offering high-quality, high-throughput analysis must not be compromised in the search for new modalities; the current impact on biological discovery is enormous and will continue.

Diamond's activities have contributed to well over 3,000 life science peer-reviewed publications, addressing a vast range of science challenges in disease¹⁻⁴, ageing⁵, food security⁶⁻⁸, microbial drug resistance⁹⁻¹², vaccine development and delivery¹³⁻¹⁵, biotechnology^{16,17}, and healthcare product development¹⁸⁻²². These have been largely investigated through MX and Soft-Condensed Matter (SCM) beamlines. MX provides good examples of practical applications of life science, with impact exemplified by the development of new lead compounds for neurological glutamate

receptors²³, the protection of food crops from fungal *Phytophthora* infection⁷ and the development of the foot-and-mouth disease vaccine¹³. Indeed MX has been the "go-to" high-resolution structural technique, globally producing >136,000 structures of macromolecules from all kingdoms of life and from many disease causing pathogens and viruses. CryoEM is currently advancing rapidly and virus vaccine work, for instance, now largely uses this technology. We can expect much increased impact from cryoEM by the time Diamond-II becomes operational; however we should bear in mind that in 2018 the number of cryoEM structures determined was still less than 10% of the number determined by MX**.

Despite the wealth of atomic-level detail now available, the reductionist perspective of basic structural biology often struggles to explain the biological phenomenon under investigation. Why does a mutation in the BRCA gene lead to breast cancer or how does the polysaccharide structure within the dactyl club of the mantis shrimp withstand repeated impacts at 80 km per hour? These are emergent phenomena that will require structural biology investigations that are both multidisciplinary and integrative. Thus, the overarching challenge in the life sciences will be in relating our structural knowledge of a biological form (e.g. enzyme structure) to its function (e.g. catalysis) which is an emergent property resulting from hierarchical organisation.

This document is organised into three research areas - Integrated structural biology, Biotechnology and biological systems and Health and well-being - that map to high-level challenges in life science defined by the UK department for Business, Energy and Industrial Strategy (BEIS), UKRI and Wellcome: tackling antimicrobial resistance, healthy ageing, understanding health and disease, global food security and vaccine development. The Integrated structural biology theme covers the study of life at its most basic level, across many orders of length and timescales. It

* www.gov.uk/government/publications/bioscience-and-health-technology-database-annual-report-2017

** <http://www.rcsb.org/stats>

is here that questions of how the atomic and mechanistic details of a protein structure relates to an observed *in vivo* dynamic process will be addressed. The Biotechnology and biological systems theme describes the application of this understanding to biotechnology and the extension to more complex systems, the paradigm being to produce better materials, lifestyle products or breakthroughs in medicine by understanding nano-engineering and how nano-scaled structures assemble into hierarchical assemblies. Finally, the most pressing societal challenges in life sciences are addressed by the Health and well-being theme that encompasses improvements in human and animal health, and food security by i) establishing the underlying molecular basis of disease or vulnerability by high resolution structure determination of key proteins, ii) mapping key proteins to *in vivo* cellular chemistry and iii) imaging cells and tissue to aid in disease diagnosis for improved treatments and prevention.

In summary, Diamond-II will help our understanding of not only the component parts of biology but also how these structures assemble into hierarchical assemblies that form the basis of complete systems. Beyond this, lies the further challenge of understanding the dynamics of whole systems. This will be a major goal of the Rosalind Franklin Institute and much can be achieved for key timescales (microsecond and slower) at Diamond-II. Our judgements on how Diamond-II might address the science challenges described here take into account, as best we can, the likely developments in complementary fields. However, it is outside the scope of this document to describe these in any detail. Whilst we have tried to reconcile how technical advances in allied fields, for instance genomics, gene editing, organoid culture, cryoEM and XFEL might contribute to the landscape, the opportunities presented can be no more than exemplars; reality tends to be interestingly unpredictable.

References

- Oswald, C. *et al.* Intracellular allosteric antagonism of the CCR9 receptor. *Nature* **540**, 462-465, doi:10.1038/nature20606 (2016).
- Guillard, S. *et al.* Structural and functional characterization of a DARPin which inhibits Ras nucleotide exchange. *Nat Commun* **8**, 16111, doi:10.1038/ncomms16111 (2017).
- Hutchinson, J. P. *et al.* Structural and mechanistic basis of differentiated inhibitors of the acute pancreatitis target kynurenine-3-monooxygenase. *Nat Commun* **8**, 15827, doi:10.1038/ncomms15827 (2017).
- Abascal-Palacios, G., Ramsay, E. P., Beuron, F., Morris, E. & Vannini, A. Structural basis of RNA polymerase III transcription initiation. *Nature* **553**, 301-306, doi:10.1038/nature25441 (2018).
- Wauer, T., Simicek, M., Schubert, A. & Komander, D. Mechanism of phospho-ubiquitin-induced PARKIN activation. *Nature* **524**, 370-374, doi:10.1038/nature14879 (2015).
- Butler, H. J., Adams, S., McAinsh, M. R. & Martin, F. L. Detecting nutrient deficiency in plant systems using synchrotron Fourier-transform infrared microspectroscopy. *Vib Spectrosc* **90**, 46-55, doi:10.1016/j.vibspec.2017.03.004 (2017).
- Boutemy, L. S. *et al.* Structures of Phytophthora RXLR effector proteins: a conserved but adaptable fold underpins functional diversity. *J Biol Chem* **286**, 35834-35842, doi:10.1074/jbc.M111.262303 (2011).
- Sohn, K. H., Hughes, R. K., Piquerez, S. J., Jones, J. D. & Banfield, M. J. Distinct regions of the Pseudomonas syringae coiled-coil effector AvrRps4 are required for activation of immunity. *Proc Natl Acad Sci U S A* **109**, 16371-16376, doi:10.1073/pnas.1212332109 (2012).
- De Santis, E. *et al.* Antimicrobial peptide capsids of de novo design. *Nature Communications* **8**, doi:ARTN 2263 10.1038/s41467-017-02475-3 (2017).
- Stockbridge, R. B. *et al.* Crystal structures of a double-barrelled fluoride ion channel. *Nature* **525**, 548-551, doi:10.1038/nature14981 (2015).
- Hinchliffe, P. *et al.* Insights into the Mechanistic Basis of Plasmid-Mediated Colistin Resistance from Crystal Structures of the Catalytic Domain of MCR-1. *Sci Rep* **7**, 39392, doi:10.1038/srep39392 (2017).
- Yang, Y. *et al.* TRANSCRIPTION. Structures of the RNA polymerase-sigma54 reveal new and conserved regulatory strategies. *Science* **349**, 882-885, doi:10.1126/science.aab1478 (2015).
- Kotecha, A. *et al.* Structure-based energetics of protein interfaces guides foot-and-mouth disease virus vaccine design. *Nat Struct Mol Biol* **22**, 788-794, doi:10.1038/nsmb.3096 (2015).
- Porta, C. *et al.* Rational engineering of recombinant picornavirus capsids to produce safe, protective vaccine antigen. *PLoS Pathog* **9**, e1003255, doi:10.1371/journal.ppat.1003255 (2013).
- Renner, M. *et al.* Characterization of a potent and highly unusual minimally enhancing antibody directed against dengue virus. *Nat Immunol*, doi:https://doi.org/10.1038/s41590-018-0227-7 (2018).
- Butler, H. J. *et al.* Using Raman spectroscopy to characterize biological materials. *Nat Protoc* **11**, 664-687, doi:10.1038/nprot.2016.036 (2016).
- Armstrong, J. P. K. *et al.* Artificial membrane-binding proteins stimulate oxygenation of stem cells during engineering of large cartilage tissue. *Nature Communications* **6**, doi:ARTN 7405 10.1038/ncomms8405 (2015).
- Tang, T. Y. D. *et al.* Fatty acid membrane assembly on coacervate microdroplets as a step towards a hybrid protocell model. *Nat Chem* **6**, 527-533, doi:10.1038/Nchem.1921 (2014).
- Decandio, C. C. *et al.* Self-Assembly of a Designed Alternating Arginine/Phenylalanine Oligopeptide. *Langmuir* **31**, 4513-4523, doi:10.1021/acs.langmuir.5b00253 (2015).
- Edwards-Gayle, C. J. C. *et al.* Self-Assembly of Telechelic Tyrosine End-Capped PEO Star Polymers in Aqueous Solution. *Biomacromolecules* **19**, 167-177, doi:10.1021/acs.biomac.7b01420 (2018).
- Austin, H. P. *et al.* Characterization and engineering of a plastic-degrading aromatic polyesterase. *Proc Natl Acad Sci U S A* **115**, E4350-E4357, doi:10.1073/pnas.1718804115 (2018).
- White, M. D. *et al.* UbiX is a flavin prenyltransferase required for bacterial ubiquinone biosynthesis. *Nature* **522**, 502-506, doi:10.1038/nature14559 (2015).
- Dore, A. S., *et al.* (2014). Structure of class C GPCR metabotropic glutamate receptor 5 transmembrane domain. *Nature* **511** 557-562.(2014)

6.2. Integrated structural biology

The atomic level description of DNA accelerated molecular biology to the modern era. This simple, double helical structure illustrated how the complexities of genetics (e.g., DNA replication) could be readily understood in terms of an underlying structure. Biology remains immensely complicated and to understand the workings of cells through all forms of life requires in-depth, molecular level knowledge of many elaborate hierarchical structures. Deciphering the often weak and transient interactions between these structures, and the diverse roles they play in the makeup and biological functions of cells, is a unique strength of structural biology. The power of detailed atomic structures to explain biology will remain, and hence there will be strong requirements for MX and cryoEM analysis in Diamond-II, however alongside single technique analysis there will be increasing opportunities for deepening our understanding by correlative measurements. Beyond this, structural biology is now reaching towards the *in situ* cellular context, that is linking structure to cell biology (Figure 1). In this example, super resolution light microscopy pinpoints biology for correlation with X-ray tomography, which in turn links to electron tomography, electron microscopy and MX, ultimately allowing atomic level descriptions *in vivo* of states too fleeting and fragile to analyse *in vitro*. Such a molecular description of cellular organisation will transform fundamental science and our understanding of disease processes, allowing more effective definition of drug targets.

To achieve the goal of understanding the dynamics of complex systems, from subcellular organelles through to whole cells and tissues, we will work closely with

other infrastructures such as Instruct-ERIC (European Infrastructure for Integrated Structural Biology) and the RFI. Diamond is positioned as a major player that will attract innovators and users from the UK and beyond. The aim will be to reveal the inner workings of the cell, progressing towards a full dynamic picture of living organisms and, by linking with chemists and clinicians, to facilitate effective application in medicine and biotechnology. Of the many applications beyond the directly medical food security is a major concern for the future, prompting significant efforts in high resistance/high nutrition crop selection and transgenic modifications that leverage plant-microbe symbiotic interactions, and consequently depend less on anthropogenic (non-renewable) fertilisers. More generally, plant biology is an extremely important field of fundamental research, where there is a considerable role for integrated structural biology. For example, in the crucial aspect of mimicking photosynthesis where biophysical models can be tested and developed through ultrafast dynamic experiments.

Pooling atomic resolution information and *in vitro* reconstitution with *in vivo* imaging is one example of the way forward for cellular structural biology, especially when linked with the fourth dimension i.e. bringing dynamical systems to life. The integrated approach to structural biology (integrating imaging, scattering and spectroscopy, X-ray and electrons, *in situ* and *in vitro*) is exemplified in this section, however it weaves its way throughout the subsequent sections on Biotechnology and biological systems and Health and well-being.

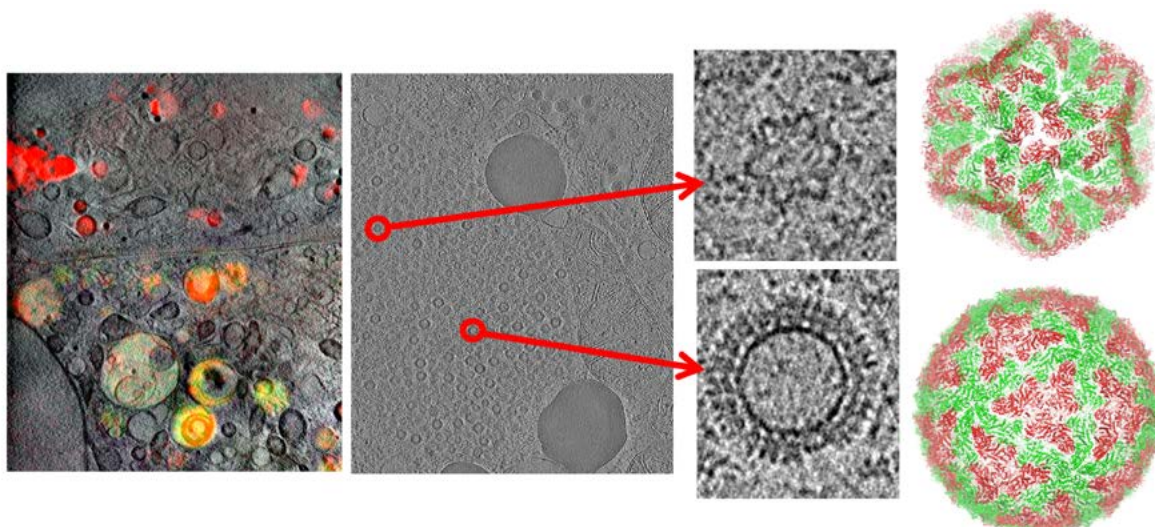


Figure 1: Integrated structural analysis allows atomic level description of transient structures in living cells. Here the left hand panel shows a virus infected mammalian cell imaged with both super-resolution cryo-light microscopy and cryo-X-ray tomography with the results correlated (colours show fluorescent labels). Central panels show cryo-electron tomography of a FIB milled slice of an infected cell (arrows point to two distinct assembly intermediates). Right: by averaging particles it was possible to fit atomic models (derived by crystallography from purified components) of these two intermediates (unpublished data from B24 and eBIC from the Grimes and Stuart groups, (U. Oxford & Diamond) and their collaborators).

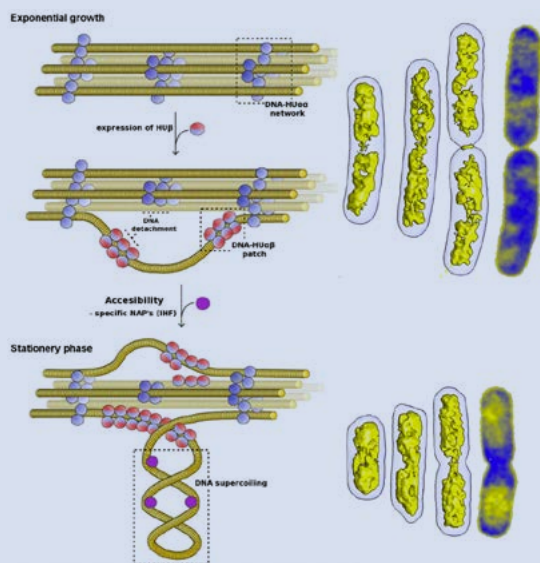
6.2.1. Chromosome structure

Despite the massive investments in genomics, we still have very little understanding of the organisation of genomic information in space in a non-dividing cell. This has proved a very difficult problem; the metazoan nucleus is so large and dense that electron microscopy has failed to penetrate it. We know there are well-defined structural domains, but the mechanism of organisation and structure underlying them is not known. It is hypothesized that genomic organization can be inherited and is a major contributor to the epigenetic phenomenon since selective compaction within a genome can readily influence gene expression patterns. Nevertheless, structural investigations of genomes will be difficult. Bacterial chromosomes are much smaller and easier systems to tackle. Despite compaction, the DNA must also be readily available for the variety of protein machines that include DNA replication, transcription and translation – recognizing that these are occurring at the same time. Nucleoid-associated proteins (NAPs) such as HU, Fis, IHF, StpA and H-NS facilitate chromosome organisation, and structural information on individual components has been available for many years, but the mechanism of action remains elusive due to a lack of tools for *in vivo* investigations, and these tools only probe a set of specific loci at a time. Super-resolution fluorescence microscopy showed that HU, Fis, IHF and StpA are largely distributed about the nucleoid, but H-NS forms two compact clusters per chromosome¹ with the genes regulated by H-NS sequestered into these clusters and transcription silenced in this condensed organisation.

Investigations into the widely distributed NAP HU in the nucleoid² (Exemplar 1) assembled data from the X-ray techniques of crystallography, small angle scattering (SAXS) and tomography. Together with mutational assays, the structural hierarchy spanned lengths from the nanoscale through mesoscale to the subcellular components of the chromosome and nucleoid structure. The crystallography was challenging due to the inherently non-specific nature of the HU protein interaction with DNA. In fact, structure determination would have been far more efficient if data were collected from sub-micron crystals. Whilst it was observed that the protein components supported the crystallographic lattice, the nucleotides within the bound DNA substrates were smeared. The higher flux, smaller beams enabled by Diamond-II will reduce the barriers to structure determination as we drive to collecting data from smaller crystals. Reducing radiation damage through high energy data collections, in vacuum sample environments and next generation detectors will expand our structural investigations to hierarchical phenomenon such as epigenetics.

The control of multimerisation of HU was shown to be an efficient mechanism to effect genetic response to external conditions, with effector molecules in pathogenic environments changing HU-mediated nucleoid condensation and consequently the bacterial transcription response. There continues to be a need to investigate the gamut of NAPs, their effects on nucleoid organisation and the role they play in multiple control mechanisms in reaction to stimuli. The dynamical response to effectors is ripe for investigation by multiple integrated methods of imaging,

Exemplar 1: Combining X-ray diffraction, scattering and imaging



invasive form.

The bacterial nucleoid forms the physical basis for cellular processes such as gene transcription and DNA replication. The nucleoid consists of the bacterial genome packed by nucleoid binding proteins (HU α and HU β) and is modulated at different growth phases and in response to environmental changes. HU α and HU β have distinct DNA binding modes which modulate bacterial chromosome packing and gene expression.

X-ray crystal structures and SAXS experiments were combined by Hammel *et al*² (LNBL, NCI, UCSF and University of Texas, USA) to determine the HU-DNA nucleoproteins in solution at near physiological conditions. The transition from HU α to HU α β complexes following expression of HU β results in condensation of the nucleoid and contraction at the cellular level as observed by soft X-ray tomography. The application of multiple X-ray techniques elucidated a detailed molecular mechanism that reprogrammes noninvasive *E. coli* into an

Hammel, M. *et al*. HU multimerization shift controls nucleoid compaction. *Sci Adv*, 2, e1600650, (2016).

Coordinated access to the beamlines I03, I04, B24, I23, I24, VMXi, VMXm, B21, Cryotomography/Ptychography in Diamond-II will enable such studies at new velocity and finer granularity following the large improvements in flux and coherence of Diamond-II coupled with improved instrumentation, data acquisition and analysis.

microscopy, scattering and diffraction. The improvements from the new machine, taken together with advances and developments in hardware and software, could see complete experiments from multiple samples performed much more quickly than the 12 hours in this example. Moreover, we expect the new tools available, including cryo-ptychography, to be able to extend such multi-modal analysis to the bigger challenge of the metazoan chromosome.

6.2.2. The prokaryotic cell surface

Another long-standing puzzle in the organisation of prokaryotic cells is the S (surface) layer, which forms part of the cell envelope and completely encloses nearly all archaeal and many bacterial cells (both gram positive and negative). S-layers form a crystalline-like lattice of (glyco) proteins and differ between organisms. Their structure and function has remained unclear, although it has been suggested that a major role is to protect against anti-microbial peptides. Clearly, with the anti-microbial resistance (AMR) problem overshadowing the fight against infectious diseases (see Health and well-being section) this is an area of great interest. The potential for the integrated use of high-end technologies to address a hierarchical problem is exemplified by the complete atomic S-layer structure of a gram-negative bacterium obtained. Here, a combination of *in vivo* cryo-electron tomographic imaging (at a 'molecular' resolution of 7.4 Å) was complemented by an atomic detailed crystal structure of a single S-layer protein³ (Exemplar 2). Using the soft X-ray MX capability of I23, divalent cations at dimeric, trimeric and hexameric interfaces implicated in a key role in stabilising the lattice were identified. The true potential of Diamond-II lies in integrating information from multiple, disparate techniques under a common scientific platform. Here, high resolution diffraction techniques with both X-ray and EM imaging pushed the boundaries to discover and map the location of metal ions *in vivo*, suggesting a new functional role for metal ions outside of the bacteria.

6.2.3. Membrane proteins

A key area where fundamental science is closely meshed with biomedical applications is in the understanding of membrane proteins. They make up nearly 30% of known eukaryotic proteins and yet constitute only 3.5% of structures in the protein data bank^{***}. Their therapeutic impact is immense. Diseases such as cancer, obesity, depression and heart disease are associated with mutations or misfolding of membrane proteins and approximately 60% of drugs currently target membrane proteins - mainly ion channels and G protein-coupled receptors (GPCRs). Extracellular signals (hormones, neurotransmitters, photons, ions and more) are relayed via membrane-bound GPCRs to trigger intracellular signalling through coupling with G proteins and arrestins.

*** <http://blanco.biomol.uci.edu/mpstruc/>

The need to study GPCRs and other membrane proteins led to Diamond establishing the Membrane Protein Laboratory, with Imperial College and Wellcome funding, which has helped drive developments at Microfocus MX beamlines. This has enabled GPCR structures⁴⁻¹⁴ from academic and industrial researchers, exemplified by a seminal series of advances reported by Heptares in seven Nature papers^{6,8-11,13,14} as shown in Exemplar 3. The capabilities of instruments and expertise and engagement of staff at Diamond with our industrial clients were key to these successes.

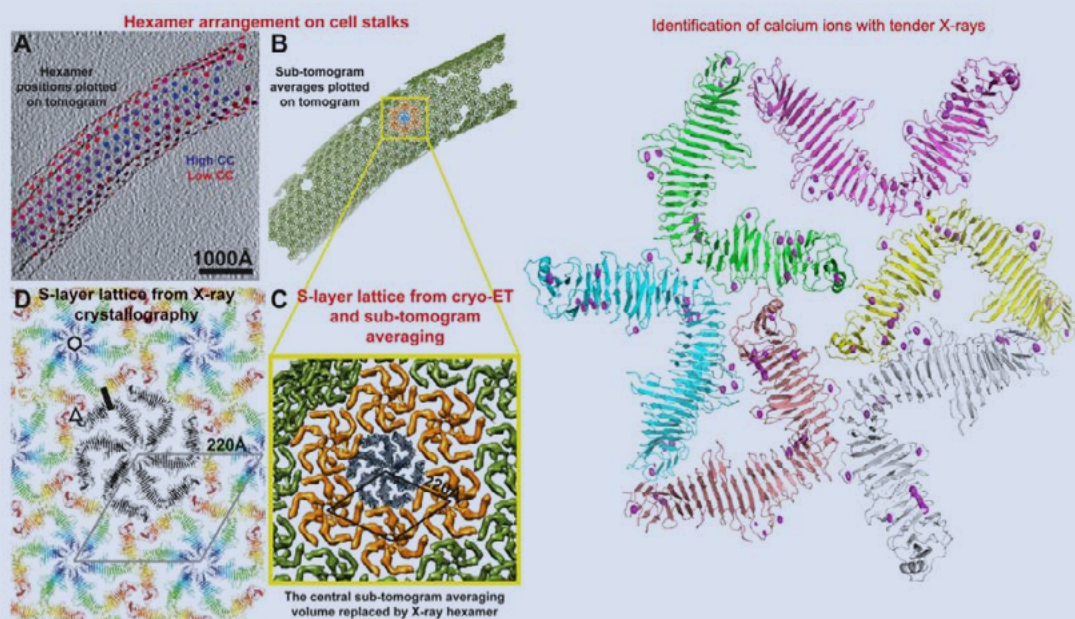
Nonetheless, GPCRs are highly dynamic molecules whereby ligands regulate receptor activity through conformational selection. A full understanding of their mechanisms requires investigating the conformational space and dynamics of receptor-ligand complexes. To date we have only scratched the surface of understanding. A target validation pipeline is envisaged that will exploit the imaging beamlines and eBIC, where gene editing and correlative microscopy techniques will map the ligand responses in the cell. GPCRs are at last showing signs that they will be susceptible to exploitation by Structure-Based Drug Discovery (SBDD)¹⁵ and Diamond-II, with its high-flux, microfocus MX and Small-Angle X-ray Scattering (SAXS) beamlines will address the next frontier of high-throughput screening. However Diamond-II not only represents a technical advance in the machine but also in how data is collected (sample environments) and processed. These advances will produce a step change in impact allowing the investigation of 1000s of such structures through accelerated versions of Serial Synchrotron Crystallography (SSX), sub-micron crystallography and room temperature fragment based drug discovery (as proposed in the Health and well-being section).

6.2.4. Dynamic studies

Life is a non-equilibrium thermodynamic process that changes through time, but we have little idea of how this operates at the microscale. If we understood the dynamics of macromolecules, and this could be combined with a mapping of the distribution of molecular species within the cell (including metabolites, ions, etc.), then it might be possible to quantitatively grasp this element of life. There is a resurgence of interest in observing the dynamics of molecules, largely driven by the advent of serial crystallography at XFELs. XFELs allow data collection at ambient temperature from femtosecond X-ray pulses, coupled (where appropriate) with complementary spectroscopic information. Ambient temperatures allow structural biology to link with functional dynamics, since suitably presented substrates can diffuse into micron-sized crystals on the microsecond time scale, much faster than the average 60 millisecond turnover time of enzymes (Figure 2)¹⁶. XFELs open up the femtosecond regime for studies, whilst time-resolved synchrotron serial crystallography at I24 and VMXi is already capable of investigating the millisecond regime. As seen in Figure 2 some of the most interesting biology occurs between these two regimes, a time domain that Diamond-II can address.

Exemplar 2: From atoms to cells - exploiting X-rays and electrons

S-layers are nearly crystalline, single-layered protein structures, consisting of repeating units of S-layer proteins, which protect many single-celled organisms from harmful extracellular molecules and provide mechanical stability. Bharat *et al*¹⁸ (MRC-LMB Cambridge, EMBL and Universities of Oxford and Indiana) elucidated the detailed, 2.7 Å atomic structure with *in vivo* imaging of the complete S-layer, exemplified here by the RsaA protein of the gram-negative bacterium *Caulobacter crescentus*. Tender X-rays on I23 unequivocally identified Ca²⁺ ions. Brought together, this combined information can help in understanding the protective mechanism that prevents access by phages, macromolecules and large filaments to the bacterial cell surface and may ultimately assist in the development of novel anti-bacterial drugs and therapies.



Reprinted by permission from Copyright Clearance Center: SpringerNature, *Nature Microbiology*, Structure of the hexagonal surface layer on *Caulobacter crescentus* cells, Bharat, T.A.M. *et al.*, Copyright (2017).

Coordinated access to the beamlines I03, I04, B24, I23, I24, VMXi, VMXm, B24 and Cryotomography/Ptychography in Diamond-II and eBIC will open up opportunities for *in vitro* to *in vivo* cellular biology.

The combination of upgrades outlined in section 3 make the microsecond domain accessible at Diamond-II, for dynamic studies this will fill in missing timescales down to the diffusion limit, in principle opening up the method to most enzymes. Historically drug design has focused on inhibitors with maximal binding affinity. However there is increasing interest in optimising target-drug kinetics, for example maximising the drug's residence time to ensure continuous effect between doses. The time domain enabled by Diamond-II matches closely the transient pathways of targets upon interaction with proteins, so that room temperature SSX will, in principle, provide a complete assessment of protein-drug kinetics and enable optimisation of drugs targeted to transition states.

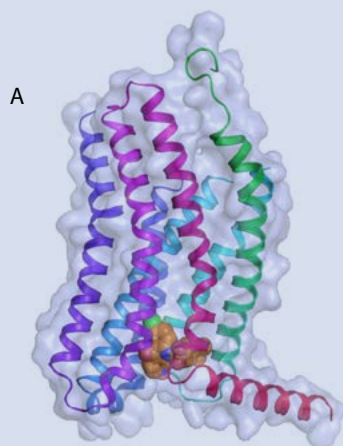
If we wish to rely on soaking substrates into crystals, then crystals will need to be submicron in size to approach single digit microseconds resolution¹⁷. This can be mitigated for non-light activated protein by pre-soaking crystals with a photocaged substrate and then using light to rapidly release substrate from the cage at the active site. Recent studies

with pink beam collections at the Advanced Photon Source demonstrated the accessibility of such time domains with synchrotron radiation¹⁸.

Currently, data from many hundreds of crystals is required to complete a room temperature SSX dataset. We envisage with Diamond-II that a useful dataset may be feasible from 50 or fewer crystals, due to increased signal-to-noise, reduced radiation damage, improved data analysis and a suitable choice of energy bandwidth. With improved sample preparation, delivery and collection methods, this could transform the throughput of SSX. Beyond fundamental science, the potential importance to drug discovery of studying the conformational landscape of proteins at room temperature and in large numbers has recently been shown^{19,20}, as is discussed in the Health and well-being section.

Such studies at Diamond-II complemented by XFEL-Hub supported access to femtosecond time resolution where required, combined with provision of fast-mixing

Exemplar 3: Cellular responses



Sosei Heptares exploit a structure-based drug design (SBDD) approach to deliver drug candidates against well characterised biomolecular pathways. To this end they have worked closely with Diamond's microfocus beamlines, in particular I24. A recent example of such work is the study of the CC chemokine receptor type 9 (CCR9) in complex with its antagonist vercirnon (a phase 3 clinical trial candidate in Crohn's disease of limited efficacy) [REF 13]. The GPCR Chemokine receptors aid immune defence by mediating the migration, activation and survival of immune cells and also play a role in tumour growth and metastasis and viral entry. Over 50 small-molecule drugs are in the pipeline however very few to date have reached the market. The elucidation of the structure of CCR9 in complex with vercirnon revealed it was bound to the intracellular side of the receptor – a long suspected theory details of which had not been revealed until this study. The necessity for compounds to reach the intracellular side of the receptor and knowledge of this newly identified site, which may be similar for other chemokines, is provoking a new way of looking at modulators for chemokines and CCR9 in particular and, opening up new treatment opportunities.

Copyright Diamond Light Source.

Coordinated access to MX using conventional and SSX methods, SAXS and imaging beamlines in Diamond-II and eBIC will transform the rate of information gathering and its depth, covering both spatial and temporal domains to truly understand this key superfamily of receptors important to human health.

technologies, will expand the searchable space for chemical probes for fundamental biology and for drug discovery. A concrete example of what is already starting to be possible is provided in Exemplar 4. The dissection of the sequential acylation and deacylation of the β -lactam ring by β -lactamases may enable the development of transition state inhibitors of this class of enzymes, of clear medical importance and relevance to the UK biopharma sector.

Finally, dynamics studies will be developed using other techniques, often sharing the same sample preparation problems. These include solution methods and cryo-imaging, where cryoEM methods are being developed at Diamond and elsewhere that will be transferable to cryo-X-ray imaging. An innovative solution based method that will be enabled by Diamond-II is X-ray footprinting mass spectrometry (XFMS), a recent addition to the synchrotron beamline portfolio, with the Advanced Light Source (Berkeley, CA) and NSLS-II (Brookhaven, NY) funding the first dedicated beam lines for time-resolved XFMS. The reconfiguration of B21 enabled by the new machine will uniquely enable routine time-resolved structural studies using both SAXS and XFMS. SAXS provides a structural snapshot of the particles at a resolution too low to directly correlate with sequence information whereas XFMS provides residue level information without regards to structure. The combination will inform on structural changes in complexes and isolated molecules within the microsecond regime.

In summary, Diamond-II will allow the observation of micro-second macromolecule dynamics through a combination of time-resolved synchrotron SAXS, MX and XFMS. This is a key time-window since most bio-molecular processes and catalysis occur more slowly than this (Figure 2).

References

- 1 Wang, W., Li, G. W., Chen, C., Xie, X. S. & Zhuang, X. Chromosome organization by a nucleoid-associated protein in live bacteria. *Science* **333**, 1445-1449, doi:10.1126/science.1204697 (2011).
- 2 Hammel, M. *et al.* HU multimerization shift controls nucleoid compaction. *Sci Adv* **2**, e1600650, doi:10.1126/sciadv.1600650 (2016).
- 3 Bharat, T. A. M. *et al.* Structure of the hexagonal surface layer on *Caulobacter crescentus* cells. *Nat Microbiol* **2**, 17059, doi:10.1038/nmicrobiol.2017.59 (2017).
- 4 Byrne, E. F. X. *et al.* Structural basis of Smoothed regulation by its extracellular domains. *Nature* **535**, 517-522, doi:10.1038/nature18934 (2016).
- 5 Carpenter, B., Nehme, R., Warne, T., Leslie, A. G. & Tate, C. G. Structure of the adenosine A(2A) receptor bound to an engineered G protein. *Nature* **536**, 104-107, doi:10.1038/nature18966 (2016).
- 6 Cheng, R. K. Y. *et al.* Structural insight into allosteric modulation of protease-activated receptor 2. *Nature* **545**, 112-115, doi:10.1038/nature22309 (2017).
- 7 Christopher, J. A. *et al.* Fragment and Structure-Based Drug Discovery for a Class C GPCR: Discovery of the mGlu5 Negative Allosteric Modulator HTL14242 (3-Chloro-5-[6-(5-fluoropyridin-2-yl)pyrimidin-4-yl]benzotrile). *J Med Chem* **58**, 6653-6664, doi:10.1021/acs.jmedchem.5b00892 (2015).
- 8 Dore, A. S. *et al.* Structure of class C GPCR metabotropic glutamate receptor 5 transmembrane domain. *Nature* **511**, 557-562, doi:10.1038/nature13396 (2014).
- 9 Hollenstein, K. *et al.* Structure of class B GPCR corticotropin-releasing factor receptor 1. *Nature* **499**, 438-443, doi:10.1038/nature12357 (2013).
- 10 Jazayeri, A. *et al.* Extra-helical binding site of a glucagon receptor antagonist. *Nature* **533**, 274-277, doi:10.1038/nature17414 (2016).
- 11 Jazayeri, A. *et al.* Crystal structure of the GLP-1 receptor bound to a peptide agonist. *Nature* **546**, 254-258, doi:10.1038/nature22800 (2017).

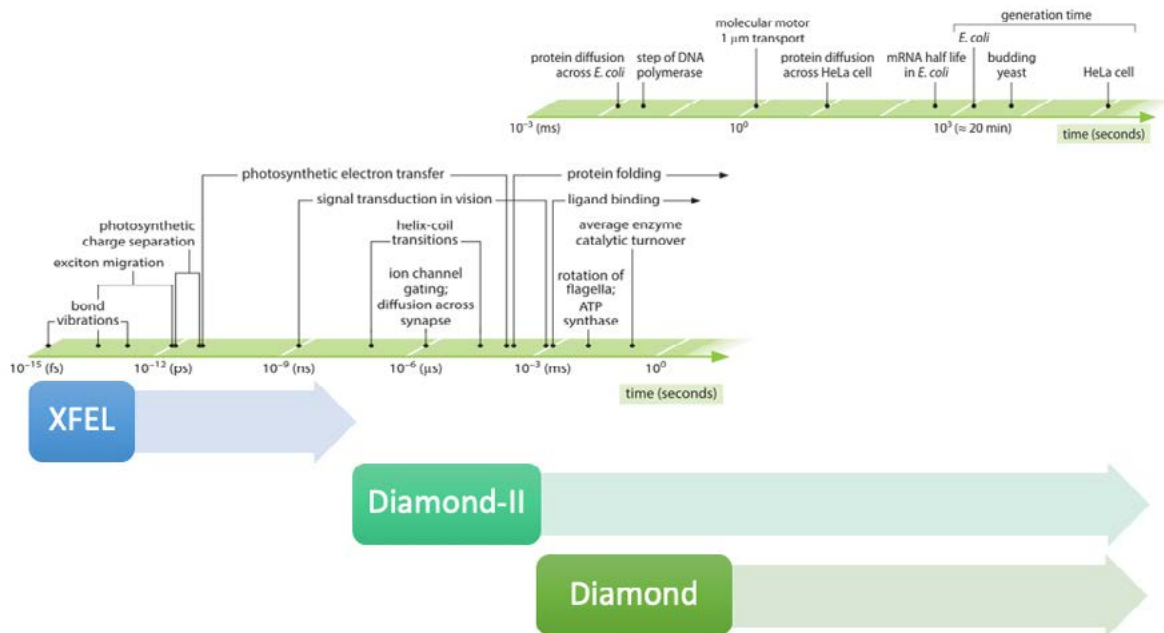
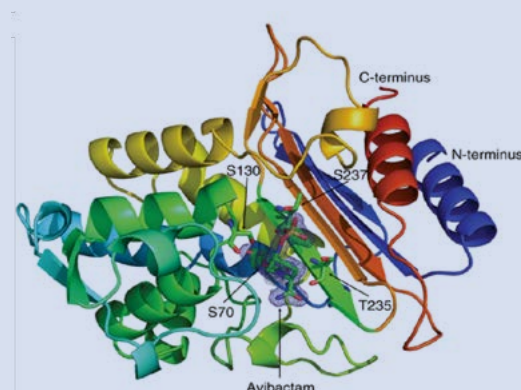


Figure 2: Timescales in biology where Diamond-II will play a role. Adapted from *Cell Biology by Numbers* by Ron Milo, Rob Phillips, Copyright 2015. Reproduced by permission of Taylor and Francis Group, LLC, a division of Informa plc.

<p>12 Lebon, G. <i>et al.</i> Agonist-bound adenosine A2A receptor structures reveal common features of GPCR activation. <i>Nature</i> 474, 521-525, doi:10.1038/nature10136 (2011).</p> <p>13 Oswald, C. <i>et al.</i> Intracellular allosteric antagonism of the CCR9 receptor. <i>Nature</i> 540, 462-465, doi:10.1038/nature20606 (2016).</p> <p>14 Robertson, N. <i>et al.</i> Structure of the complement C5a receptor bound to the extra-helical antagonist NDT9513727. <i>Nature</i> 553, 111-114, doi:10.1038/nature25025 (2018).</p> <p>15 Rucktooa, P. <i>et al.</i> Towards high throughput GPCR crystallography: In Meso soaking of Adenosine A2A Receptor crystals. <i>Sci Rep</i> 8, 41, doi:10.1038/s41598-017-18570-w (2018).</p> <p>16 Schmidt, M. Time-Resolved Macromolecular Crystallography at Modern X-Ray Sources. <i>Methods Mol Biol</i> 1607, 273-294, doi:10.1007/978-1-4939-7000-1_11 (2017).</p>	<p>17 Schmidt, M. Mix and Inject: Reaction Initiation by Diffusion for Time-Resolved Macromolecular Crystallography. <i>Advances in Condensed Matter Physics</i> 2013, 1-10, doi:10.1155/2013/167276 (2013).</p> <p>18 Meents, A. <i>et al.</i> Pink-beam serial crystallography. <i>Nat Commun</i> 8, 1281, doi:10.1038/s41467-017-01417-3 (2017).</p> <p>19 Keedy, D. A. <i>et al.</i> An expanded allosteric network in PTP1B by multitemperature crystallography, fragment screening, and covalent tethering. <i>Elife</i> 7, doi:10.7554/eLife.36307 (2018).</p> <p>20 Keedy, D. A. <i>et al.</i> Mapping the conformational landscape of a dynamic enzyme by multitemperature and XFEL crystallography. <i>Elife</i> 4, doi:10.7554/eLife.07574 (2015).</p> <p>21 Wiedorn, M. O. <i>et al.</i> Megahertz serial crystallography. <i>Nat Commun</i> 9, 4025, doi:10.1038/s41467-018-06156-7 (2018).</p>
-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Exemplar 4: Time is an illusion - dynamic structural biology

An area ripe for exploitation by time-resolved methods is understanding the structural and kinetic changes that occur during the interaction of β -lactams with their target penicillin binding proteins and with β -lactamase enzymes. β -lactamases provide multi-resistance to β -lactam antibiotics such as penicillins, cephalosporins, cephamycins and carbapenems – a significant risk to human health. Traditional X-ray crystal structures reveal only partial insights into



function and mechanism, through snapshots of ground states. Time resolved data collection methods at synchrotrons and FELs of systems undergoing catalysis will reveal transition states previously unobservable by diffraction methods at high resolution. First experiments at the European XFEL beamline SPB/SFX with a large international consortium elucidated a structure of CTX-M-14 β -lactamase from *Klebsiella pneumoniae* soaked with the inhibitor avibactam (shown as sticks with electron density in grey)²¹.

Megahertz serial crystallography. *Nature Communications*, 9, 4025, (2018) <https://creativecommons.org/licenses/by/4.0/>.

Coordinated access to the beamlines B21, I24 and VMXi in Diamond-II alongside the XFMS, XFEL-Hub and XChem can open up transition state targeted drug discovery.

6.3. Biotechnology and biological systems

Biotechnology benefits the agricultural, medical, energy, and environmental sectors. The “penicillin miracle” established biotechnology as a tool in the medical industry and the process of fermentation, used for thousands of years for the production of beer and wine, is increasingly applied to biodiesel production and synthetic biology. Whilst today, biotechnology is largely identified with the array of enzymes for industrial and medical applications it also includes the burgeoning field of biomaterials and the engineering of biological systems. Since the field of medical technology has a turnover of £16 billion, advances in biomaterials will be transformative for both our economy and our health¹.

The development of biomaterials into widespread commercial and medical applications would mark a new era of renewable and bio-compatible products. This will be facilitated by an understanding of the nanoscale structure of materials and how bulk properties emerge from the hierarchical assembly. This level of physical characterisation and precision measurement demands: 1) brighter/harder X-ray sources to improve depth of penetration, 2) improved spatial resolution to image sub-micron features, 3) new technologies in chemical mapping including circular dichroism (CD) spectroscopy, infrared (IR) spectroscopy and X-ray fluorescence imaging and 4) beam characteristics (coherence, emittance and divergence) that are not available as part of Diamond’s current offer. The proposed machine upgrade addresses each of these technical demands and we anticipate that this will lead to a substantial increase in demand from both industrial and academic users.

6.3.1. Engineering and applications of biomaterials

Biomaterials encompass the range of bio-inspired, bio-mimetic or bio-derived materials, with synthetic rubber representative of a commonly encountered bio-mimetic. Many of these (*e.g.* laundry detergents, pharmaceutical formulations and lubricants) form nano-scaled structures during processing that contribute to stability or bulk material properties. Preserving these structures over long-time scales and conditions is critical to function.

Polymers permeate every aspect of our day and the polymers industry is the second largest employer in the UK, with £23.5 billion in annual sales. Environmental awareness is driving a need for bio-inspired materials that provide environmentally-friendly polymers derived from natural sources. Such biopolymers are expected to become a significant feedstock source. While there has been much interest in converting biomass into a liquid energy source

such as ethanol or biodiesel, there is significant untapped potential to develop biomass into suitable feedstock for the polymer industry. Thus in 2016, the United States produced 702 million tons of dry biomass from agricultural and forestry waste, more than twice its total production of plastic (335 million metric tons)^{****}.

Biomaterials

Unlike petrochemical-based polymers, biopolymers are derived from renewable sources² and current applications include additives, biocomposites, drug delivery systems, scaffolds for tissue engineering and hydrogels. Biopolymer additives can improve injection moulded manufacturing by modifying viscosity and friction of the feedstock polymer during injection³. As biocomposites, biopolymers are widely used in the rubber industry and recent applications include processing of cellulosic feedstocks to create robust nanostructured membranes for water filtration⁴. In drug delivery, nano- to micron-sized colloidal biopolymer particles can be loaded with drugs for timed or site-specific release⁵. Nevertheless the very limited adoption by industry (~2% of total production) underscores two significant science-based challenges^{6,7}: 1) how can renewable biomass feedstocks be efficiently transformed into appropriate monomers for production and 2) how can biopolymers be modified or used to improve material properties with the requisite thermal resistance and mechanical strength?

Engineering new biomaterials

Bio-inspired systems are leading to new forms of paint, hydrophobic and anti-bacterial structures. As an example, cicada wings (Exemplar 1) are superhydrophobic and anti-bacterial and these properties are due to the nanoscale-structure of the wing¹². The height, diameter and spacing of nano-pillars (50-100 nm in diameter) present on the wing cause sufficient localised stretching and strain of a bacteria’s membrane to induce cell rupture, which has been replicated using templating techniques. Gecko’s feet are arrays of 200-500 nm hydrophilic hairs, where the diameter and length of hairs provides very high adhesive force through a combination of capillary and van der Waals forces. The colour of many creatures in nature isn’t from a dye but rather from complex nanostructures that selectively scatter light¹³ and this is being used to develop new paints that remove the need for carbon-intensive production of titanium oxide or zinc oxides. Coherent imaging techniques can play a critical role in understanding these structures, but the technique is flux-limited. Diamond-II’s upgraded machine will offer increased coherent flux, faster detectors and improved data acquisition and analysis strategies, opening up opportunities to drive the engineering of future bio-inspired materials.

**** <https://www.energy.gov/eere/bioenergy/2016-billion-ton-report>

Natural products

Cellulosic biomass is a massive source of biomaterial that can be readily converted into a cellulose nanocrystalline¹⁵ biomaterial through acid hydrolysis. The nanocrystalline material (helical segments of cellulose) can be structured into pores and functionalised to endow it with different chemical properties. To understand the effects and efficiency of this processing requires biophysical characterisation. Questions difficult to answer using X-ray methods, such as homogeneity of the crystalline state or functionalisation could be answered by CD-imaging¹⁶ (Exemplar 2). Current CD-imaging capabilities can show heterogeneous surfaces that would otherwise go unnoticed, in this case revealing orientation of helical cellulosic nanocrystals. Such information will underpin improved processing and material reliability. The lower emittance of the new Diamond-II machine, will improve the resolution of CD-imaging by at least an order of magnitude (currently: 50 microns).

Medical engineering

Improvements in source emittance and brightness will lead to a 20-fold improvement in divergence and 30-fold increase in brilliance at our SAXS/WAXS (Small Angle/Wide Angle X-ray Scattering) beamline, I22, leading to a corresponding improvement in our ability to probe materials simultaneously at the nano- to meso-scales. These scales provide an observation window for the analysis of biomaterials under mechanical deformation, where nanoscale flaws introduced during manufacturing ultimately defeat the desired mesoscale property such as durability.

Consider an artificial heart valve, the material must withstand ~100,000 open-close cycles per day where each cycle is approximately one second, but the valve movement occurs in only 1/20th of a second. Over the course of 10 years, the biomaterial durability must be sufficient for ~500 million cycles while being biocompatible with the patient. Self-assembling, cylinder forming block copolymers have been engineered as a durable material for prosthetic heart valves¹⁷⁻¹⁹ (Exemplar 3). The triblock copolymers have a “rubbery” middle that self assembles with outer “glassy” ends forming hexagonal arrays. Current Diamond capabilities have achieved 1 millisecond time resolution at a spatial resolution of 10 microns. Since the valves are only 300 microns thick, the current spatial resolution is insufficient for understanding how defects occur during manufacturing or use. The block copolymers form layered structures during injection moulding where the shear forces during flow dictate how the hexagonal arrays orient and pack and intrinsic strains (defects) are introduced where shear forces cause subtle structural variations in the final annealed material. Understanding and controlling how these defects arise during processing is critical to making a valve with the desired mechanical properties.

More importantly, detecting these defects in valves prior to use is not possible with existing instrumentation. The enhanced beam profile of Diamond-II, in both the Infrared and X-ray regimes, offers the possibility of correlating SAXS tomography (Exemplar 4) to identify defects at sub-micron spatial resolution with the analysis of chemical environments by nano-IR spectroscopy and visualisation by soft-X-ray imaging.

Protein design

Bioengineering of proteins and enzymes has considerable untapped potential and in recent work solution-state SAXS, computational protein folding prediction and high-throughput recombinant technologies have been combined to successfully engineer proteins with specified topologies^{21,22}. Whilst designer proteins or enzymes remain a largely unrealised goal the potential impact was recently hinted at by the engineering of a plastic-degrading enzyme capable of breaking down the common plastic PET²³. This combined the power of natural evolution (starting from a bacterial enzyme which had evolved to allow bacteria to colonise waste sites), with rational design. A high-resolution structure of the natural enzyme was used to guide mutations in the enzyme that optimised interactions with PET. The throughput increases envisaged for Diamond-II will allow an integrated approach to such engineering, looping between computation and high-throughput characterisation. The increase in the photon flux and reduction in beam size will impact both X-ray scattering and CD beamlines. CD immediately reveals the particle's structural state (i.e. folded vs unfolded) and can provide high-throughput validation of a recombinant topological library. In addition, ultra-high-throughput SAXS will be within reach with Diamond-II where total data collection times of < 1-second per 300 nanolitre sample will be achievable, implying that a 96-well plate will require < 3 minutes total measurement time. This will be transformative as thousands of compounds, conditions, and mutants would be readily tested within a single 8-hour shift. High-throughput experimental feedback will be critical to the development of the requisite computational algorithms for protein engineering. This cannot be overstated. In the era of big data and machine learning, multi-parameter optimisation problems such as protein engineering will become tractable as long as experiments at synchrotrons can efficiently deliver large and robust datasets.

6.3.2. Biological systems imaging

Human biology derives from four fundamental tissue types: epithelial, connective, muscle and nervous. A layered combination of epithelial and connective tissue can form the transparent material of the cornea whereas a different layered combination will form the opaque tissue of skin. The desired function emerges from the types of structures

present, how they are arranged and the additional small molecules and metal ions that are selectively sequestered. Defects often lead to undesirable properties in bone, myelin sheaths, or cornea, resulting in disease. The challenge of imaging such systems is multi-scale and also requires chemical imaging of compartmentalised environments.

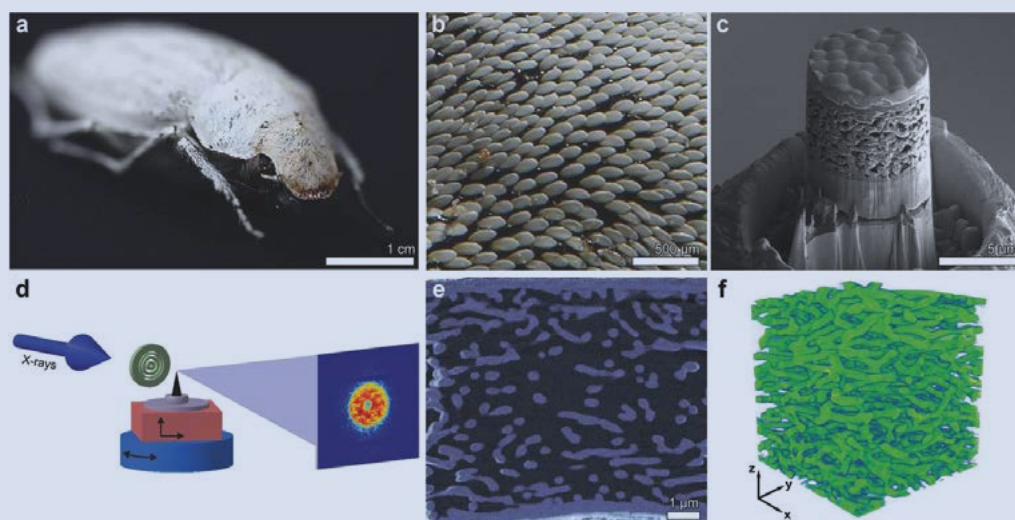
Hierarchical decomposition

Coronary artery plaques result from fatty-fibrous deposits on arterial surfaces. These plaques can be stable or unstable and the transformation to an unstable plaque, called a rupture, is associated with high mortality rate heart attacks²⁴. Plaque formation can occur over decades and undergo compositional changes such as calcification and accumulation of cholesterol and protein. However, the factors that contribute to destabilise a plaque to rupture are unknown. Can imaging techniques such as SAXS tensor tomography²⁵ reveal structured elements within the deposits? Are these deposits correlated with specific metal ions during mineralisation and destabilisation? How do the lipid, protein, nucleic acid and water compositions vary throughout the plaque? Are there sub-micron structures unique to destabilisation? These are challenging questions

that require *in situ* measurements at high spatial resolutions and brightness. With the new machine and beamline upgrades Diamond-II will transform the capabilities of beamlines I14, I22, B22, B23 and B24, providing a comprehensive approach to addressing this multi-scale problem. Understanding the multi-scale internal structure of stable and unstable plaques may reveal the key factors that lead to plaque rupture and aid in treatment.

The relationship between structure, organisation and mechanical properties can be readily appreciated through our current knowledge of bone, however, this underscores our lack of understanding of effective treatments for bone diseases and recovery from traumatic injuries. Over 3 million patients are treated annually by the NHS for the aging related bone disease osteoporosis and hip-fractures from falling are associated with a 3- to 5-fold increase in mortality in individuals older than 65 years. Therefore, a detailed understanding of the mechanisms behind changes in bone stiffness and strength will lead to new developments in biomaterials for bone repair and replacement. In human bone, toughness is determined by crack deflection and twist at cement lines at the micron scale, whereas strength results from collagen fibre bridging

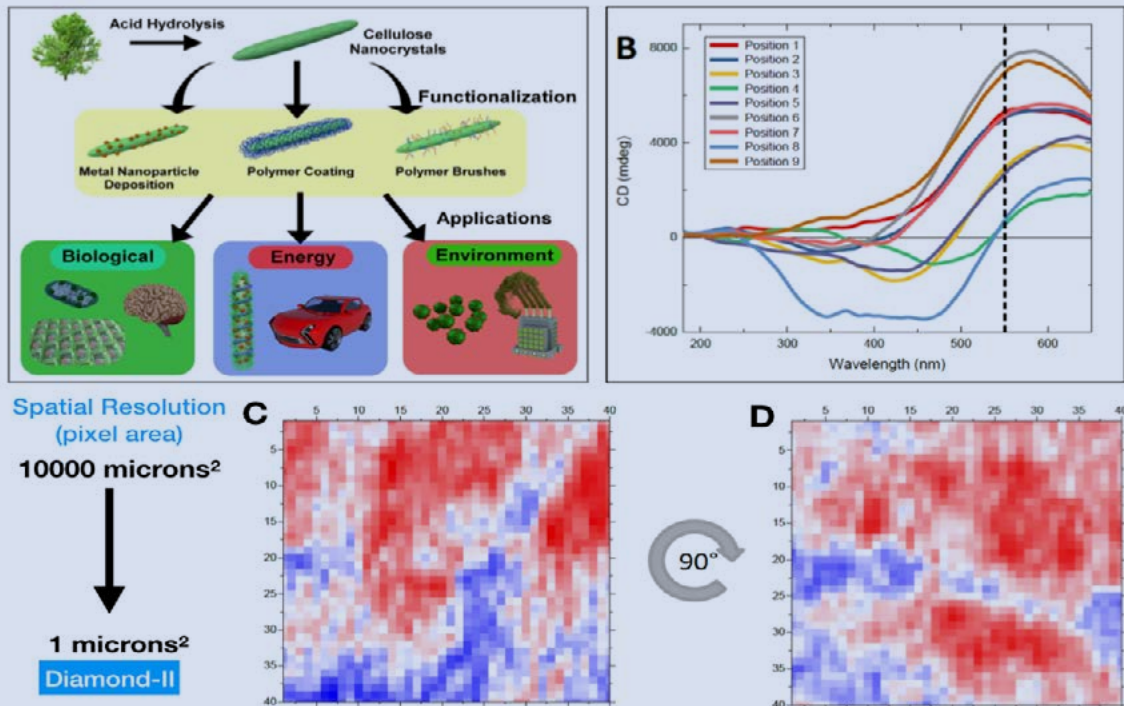
Exemplar 1: An X-ray ptychography-tomography study of the ultra white scales of the beetle *Cyphochilus*¹⁴



(a) An optical image of a *Cyphochilus* specimen, (b) a light microscopy image of the scale decoration on the surface of the beetle's elytra. (c) A focussed ion beam prepared region from the centre of an individual *Cyphochilus* scale, imaged using SEM, (d) shows a schematic representation of the X-ray nanotomography setup used to image the internal nanostructure of the region in (c). Briefly the sample is scanned and rotated through the beam (indicated by arrows) while recording the diffraction pattern. (e) An individual high-resolution tomographic slice used to reconstruct the full 3D volume and (f) a 3D volume reconstruction of the inner structure of a beetle wing scale of sides 7 μm acquired using cryo-tomography. The increase in coherence flux with Diamond-II will improve resolution, scan speed (dramatically) and potentially provide a tool for probing dynamics.

Wilts, B. D. et al. Evolutionary-Optimized Photonic Network Structure in White Beetle Wing Scales. *Adv Mater* 30, e1702057, (2018).

Exemplar 2: Biophysical characterisation of biomaterials by Circular Dichroism



A) Applications of nanocrystalline cellulose (Tang *et al.*, 2017)¹⁶. **B)** UV-Vis CD spectra of NCC as a 3x3 grid area measured at 1mm interval **C)** CD 2D image generated from the scanning of 1600 points at fixed wavelength of a 40x40 grid area of NCC film at 23 °C. **D)** CD 2D image generated from the scanning at fixed wavelength of a 40x40 grid at 100 micron interval (approximately 16mm²) of the same NCC film at 23 °C as panel C) but rotated clockwise around the incident axis direction by 90°. The fact that the orientation of the domains following the sample rotation of 90° retained the same colour hue, CD sign and intensity magnitude is an indication that there were no artefacts in the measured CD data. That means that the changes in terms of sign for the 2D images or the spectral shape are due to conformational changes that affect the helical structure of the cellulose.

Copyright Diamond Light Source.

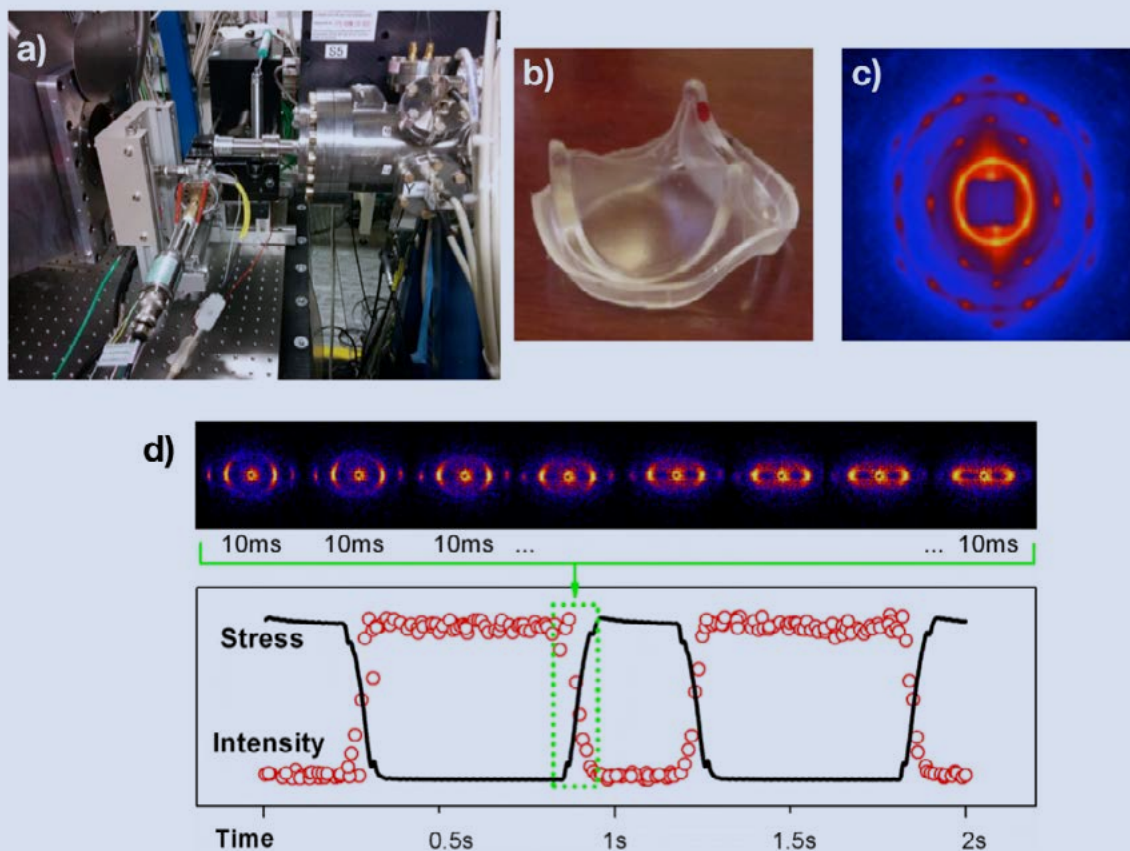
and intrinsic plasticity at the nano- to micron-scales. A combination of biomimetic studies (synthetic analogues) and investigations of the collagen-mineral interface in bone and mineralised bone cells over a range of length scales are needed, but this approach is currently limited in resolution, number of samples and the timescale of measurements. We still need to answer fundamental questions regarding how disease affects bone structure from nano- to macro- length scales, and therefore its mechanical response, as well as how treatments for conditions such as osteoporosis affect bone's performance. How can we design a new generation of implants that are safer and longer lasting? Why, despite encouraging results in small animal models, has bone or cartilage regeneration using tissue engineering scaffolds failed to achieve clinical success in humans? Diamond-II will provide greatly enhanced chemical and structural nano-imaging capabilities. For example, on DIAD flux gains of 70-fold and spot size reduction to 1µm will allow for

highly dynamic loading studies of crack propagation and local strain and structure from bones or biomimetics.

References

- 1 *Biomedical Materials*, <<http://www.royce.ac.uk/research-areas/biomedical-materials/>>
- 2 Zhu, Y., Romain, C. & Williams, C. K. Sustainable polymers from renewable resources. *Nature* **540**, 354-362, doi:10.1038/nature21001 (2016).
- 3 Scaffaro, R., Dintcheva, N. T., Marino, R. & La Mantia, F. P. Processing and Properties of Biopolymer/Polyhydroxyalkanoates Blends. *Journal of Polymers and the Environment* **20**, 267-272, doi:10.1007/s10924-011-0385-2 (2011).
- 4 Carpenter, A. W., de Lannoy, C. F. & Wiesner, M. R. Cellulose nanomaterials in water treatment technologies. *Environ Sci Technol* **49**, 5277-5287, doi:10.1021/es506351r (2015).
- 5 J. Joye, I. & Julian McClements, D. Biopolymer-Based Delivery

Exemplar 3: Understanding nano-scale architecture to improve material performance and durability



a) *In situ* measurements during injection moulding of heart valves can help reveal how defects form during manufacturing. b) Block copolymer heart valve produced by injection moulding. c) SAXS pattern showing the presence of a hexagonal lattice. d) Functional measurements of the heart valve at 10 millisecond (ms) resolution.

Images 7a) and 7b) courtesy of G. D. Moggridge. Image 7c) Stasiak, J et al. A bio-inspired microstructure induced by slow injection moulding of cylindrical block copolymers. *Soft Matter*, 10, 6077-6086, (2014). Published by The Royal Society of Chemistry. Image 7d) Reproduced from Stasiak, J et al. A real time SAXS study of oriented block copolymers during fast cyclical deformation, with potential application for prosthetic heart valves. *Soft Matter*, 7, 11475-11482, (2011) with permission from The Royal Society of Chemistry.

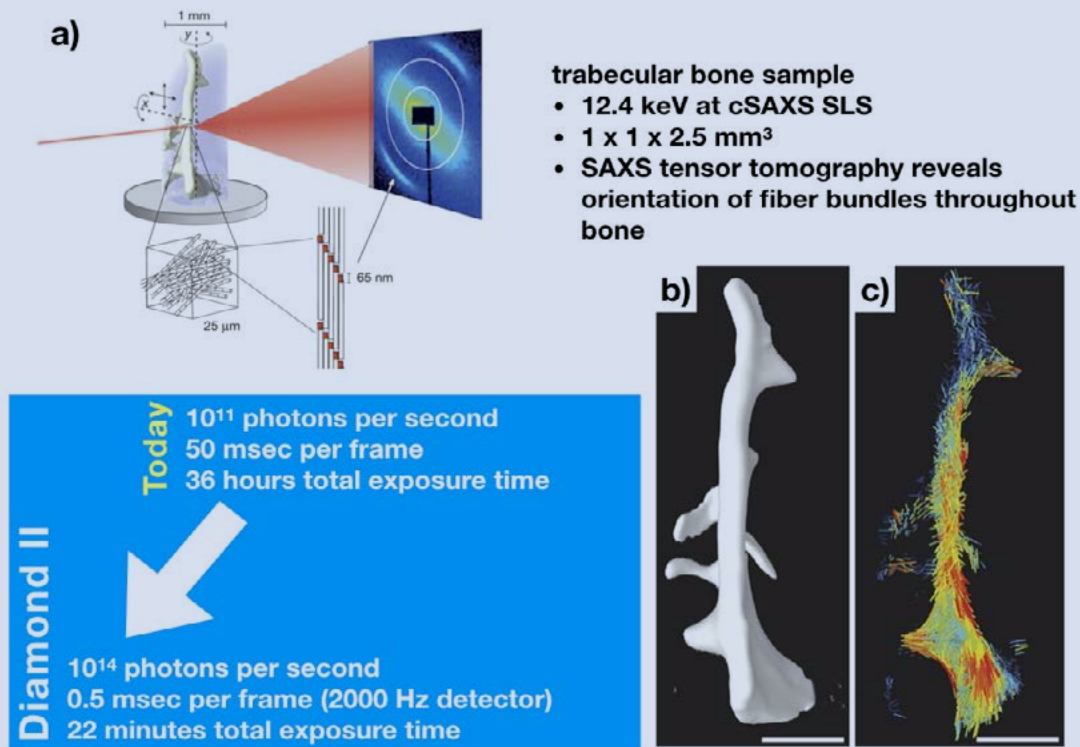
Systems: Challenges and Opportunities. *Current Topics in Medicinal Chemistry* **16**, 1026-1039, doi:10.2174/1568026615666150825143130 (2015).

- 6 Sam, S. T., Nuradibah, M. A., Chin, K. M. & Hani, N. Current Application and Challenges on Packaging Industry Based on Natural Polymer Blending. *Olatunji O. (eds) Natural Polymers. Springer, Cham* (2016).
- 7 Storz, H. & Vorlop, K.-D. Bio-based plastics: status, challenges and trends. *Appl Agric Forestry Res* **4**, 321-332 (2013).
- 8 Tan, J. C., Bennett, T. D. & Cheetham, A. K. Chemical structure, network topology, and porosity effects on the mechanical properties of Zeolitic Imidazolate Frameworks. *Proc Natl Acad Sci U S A* **107**, 9938-9943, doi:10.1073/pnas.1003205107 (2010).
- 9 Falcaro, P. et al. MOF positioning technology and device fabrication. *Chem Soc Rev* **43**, 5513-5560, doi:10.1039/c4cs00089g (2014).
- 10 Ryder, M. R. et al. Identifying the role of terahertz vibrations in metal-organic frameworks: from gate-opening phenomenon

to shear-driven structural destabilization. *Phys Rev Lett* **113**, 215502, doi:10.1103/PhysRevLett.113.215502 (2014).

- 11 Greenaway, A. et al. *In situ* synchrotron IR microspectroscopy of CO₂ adsorption on single crystals of the functionalized MOF Sc₂(BDC-NH₂)₃. *Angew Chem Int Ed Engl* **53**, 13483-13487, doi:10.1002/anie.201408369 (2014).
- 12 Pogodin, S. et al. Biophysical model of bacterial cell interactions with nanopatterned cicada wing surfaces. *Biophys J* **104**, 835-840, doi:10.1016/j.bpj.2012.12.046 (2013).
- 13 Burg, S. L. & Parnell, A. J. Self-assembling structural colour in nature. *J Phys Condens Matter* **30**, 413001, doi:10.1088/1361-648X/aadc95 (2018).
- 14 Wilts, B. D. et al. Evolutionary-Optimized Photonic Network Structure in White Beetle Wing Scales. *Adv Mater* **30**, e1702057, doi:10.1002/adma.201702057 (2018).
- 15 Lam, E., Male, K. B., Chong, J. H., Leung, A. C. & Luong, J. H. Applications of functionalized and nanoparticle-modified nanocrystalline cellulose. *Trends Biotechnol* **30**, 283-290, doi:10.1016/j.tibtech.2012.02.001 (2012).

Exemplar 4: SAXS tensor tomography is an exciting new technique that allows 3-D reconstruction of an object based on unique scattering features.



A mounted sample is measured along two rotation axes and scanned to produce a collection of SAXS/WAXS patterns. Since each SAXS pattern is a projection of the material through the beam path, several measurements at different angles help resolve the SAXS patterns into voxels describing the smallest measured unit. In this case, trabecular bone is analysed to determine the orientation of the collagen fibres throughout the larger structured material. Current methods require nearly two days of beam time. However, Diamond-II could reduce acquisition times to < 1 hour. Image adapted from Liebi *et al*²⁰.

Reprinted by permission from Copyright Clearance Center: Springer Nature, *Nature*, Nanostructure surveys of macroscopic specimens by small-angle scattering tensor tomography, Liebi, M. *et al.*, Copyright (2015).

- Tang, J., Sisler, J., Grishkewich, N. & Tam, K. C. Functionalization of cellulose nanocrystals for advanced applications. *J Colloid Interface Sci* **494**, 397-409, doi:10.1016/j.jcis.2017.01.077 (2017).
- Ghanbari, H. *et al.* Polymeric heart valves: new materials, emerging hopes. *Trends Biotechnol* **27**, 359-367, doi:10.1016/j.tibtech.2009.03.002 (2009).
- Stasiak, J. *et al.* A bio-inspired microstructure induced by slow injection moulding of cylindrical block copolymers. *Soft Matter* **10**, 6077-6086, doi:10.1039/c4sm00884g (2014).
- Stasiak, J. *et al.* Structural changes of block copolymers with bi-modal orientation under fast cyclical stretching as observed by synchrotron SAXS. *Soft Matter* **11**, 3271-3278, doi:10.1039/c5sm00360a (2015).
- Liebi, M. *et al.* Nanostructure surveys of macroscopic specimens by small-angle scattering tensor tomography. *Nature* **527**, 349-352, doi:10.1038/nature16056 (2015).
- Boyken, S. E. *et al.* De novo design of protein homo-oligomers with modular hydrogen-bond network-mediated specificity. *Science* **352**, 680-687, doi:10.1126/science.aad8865 (2016).
- Fallas, J. A. *et al.* Computational design of self-assembling cyclic protein homo-oligomers. *Nat Chem* **9**, 353-360, doi:10.1038/nchem.2673 (2017).
- Austin, H. P. *et al.* Characterization and engineering of a plastic-degrading aromatic polyesterase. *Proc Natl Acad Sci U S A* **115**, E4350-E4357, doi:10.1073/pnas.1718804115 (2018).
- Chen, Y. C., Huang, A. L., Kyaw, T. S., Bobik, A. & Peter, K. Atherosclerotic Plaque Rupture: Identifying the Straw That Breaks the Camel's Back. *Arterioscler Thromb Vasc Biol* **36**, e63-72, doi:10.1161/ATVBAHA.116.307993 (2016).
- Schaff, F. *et al.* Six-dimensional real and reciprocal space small-angle X-ray scattering tomography. *Nature* **527**, 353-356, doi:10.1038/nature16060 (2015).
- Reznikov, N., Bilton, M., Lari, L., Stevens, M. M. & Kroger, R. Fractal-like hierarchical organization of bone begins at the nanoscale. *Science* **360**, doi:10.1126/science.aao2189 (2018).
- Fratzl, P. & Weinkamer, R. Nature's hierarchical materials. *Progress in Materials Science* **52**, 1263-1334, doi:10.1016/j.pmatsci.2007.06.001 (2007).

6.4. Health and well-being

Improving public health is a critical driver for advancing chemistry and biology. Life expectancy has increased dramatically in Europe, from the low 60's in the 1950s to more than 80 years of age (projected) by 2050****. This contributes to the world's growing population, which is likely to increase to 9.7 billion by 2050, creating many new challenges in public health, food security and environmental sciences.

Combatting non-communicative (NCD) and infectious diseases builds upon multi-disciplinary basic sciences, due to their inherent hierarchical complexity. NCDs, which include cardiovascular disease, cancers, chronic respiratory diseases and diabetes, are responsible for 63% of all deaths and impact all age groups (a quarter of these deaths are of people aged 60 or less)¹. These are extremely tough problems, cancer remains a leading cause of morbidity and mortality despite decades of research. And likewise, extending life expectancy has revealed an insidious link to incidences in neurodegenerative disorders. Of the total human disease burden, ~35% is attributed to brain disorders, with an economic cost estimated at twice that of cancer, due to their chronic and incurable nature² (dementia costs the UK £17 billion a year alone³). The impact of NCDs on the world economy is considerable, with an estimated 15% increase in NCD deaths by 2020 and a projected cost of nearly £36 trillion over the next two decades¹.

Research in health and well-being aims to improve quality of life and prognosis, and Diamond-II will enable further innovation. Recent developments in synchrotron X-ray imaging tools can now directly reveal the intricate structural changes during tumorigenesis in a single cancer cell whereas advancements in nano-imaging and nano-spectroscopy can identify and map the distribution of metal ions throughout brain tissue. This high level of detail is uncovering relationships which suggest new leads towards the next generation of medicines and treatments.

Infectious diseases represent another significant public health challenge⁴. Latrogenic infections, which are hospital-acquired like Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* (C.diff), are a global problem occurring in every hospital, and in the UK alone, result in >300,000 patient infections and >9,000 deaths per year. Major progress in fighting infections such as HIV, tuberculosis and malaria has come from large-scale research investments, but the rise of resistance to antibiotics is now one of the major public health problems of the 21st century. It is estimated that 10 million people a year will die by 2050 and the United Nations General Assembly (UNGA) acknowledged the threat of antimicrobial resistance to global health security. The UNGA emphasized the need for a coordinated global effort to combat infection diseases that

**** <http://www.un.org/en/development/desa/publications/world-population-prospects-2015-revision.html>

includes continued investments in basic research. Coupled with the advanced imaging and X-ray capabilities of Diamond-II, research will reveal the origin of antimicrobial resistance mechanisms and aid in the development of new antimicrobials, vaccines and diagnostic tools.

Synchrotron techniques provide unique capabilities for addressing these public health challenges. In particular, Diamond has allowed us to understand the underlying chemistry of a variety of public health related proteins, enzymes, macromolecular complexes and viruses from the atomic level through to the whole cell. It has also established itself as a critical resource for various start-ups in the growing biotech industry, both as a center for training scientists in cutting-edge methods, and as a leader in innovation. The new capabilities of Diamond-II will not only improve and accelerate existing activities such as MX and SAXS but also will greatly enhance the possibilities for hard and tender X-ray imaging, opening new analytic possibilities to academia and industry.

6.4.1. Chemical imaging with X-rays

Metal ions are essential to many physiological processes including electron transport, redox reactions, the immune response, cell adhesion, DNA repair, enzymatic catalysis (~30% of enzymes use metals). Metal ion concentrations are tightly regulated, with both deficiencies and overloads leading to disease. Hypertension, a leading cause of cardiovascular disease, results from an imbalance in metals ions in the blood. Metal ions are also critical to the nervous system and deficiencies are associated with a variety of neurological diseases⁵. Excessive metal ion levels in the brain may alter neurotransmission and lead to neurodegeneration; with metal-induced neurotoxicity associated with Alzheimer's, Huntington's and Parkinson's disease.

Neurodegenerative disease

Although the altered regulation of metal ion metabolism is ubiquitous in neurodegenerative disorders, it remains comparatively poorly understood despite extensive research and presents a tremendous analytical challenge. Thus, there are conflicting observations and limited mechanistic insight into the role of metal ions in neurodegenerative disorders⁶⁻⁸. For example, the biometals: calcium, manganese, iron, copper, zinc, and selenium⁹⁻¹³ are implicated in disease, along with the more canonical metals associated with disease pathology such as lead, mercury, and aluminium¹⁴.

Synchrotron spectroscopy and spectromicroscopy offer the greatest diversity of instrumentation, and unique sensitivity and specificity to investigate spatial and temporal aspects of metal ions in biological systems^{14,15}. In addition to investigating toxicity mechanisms in

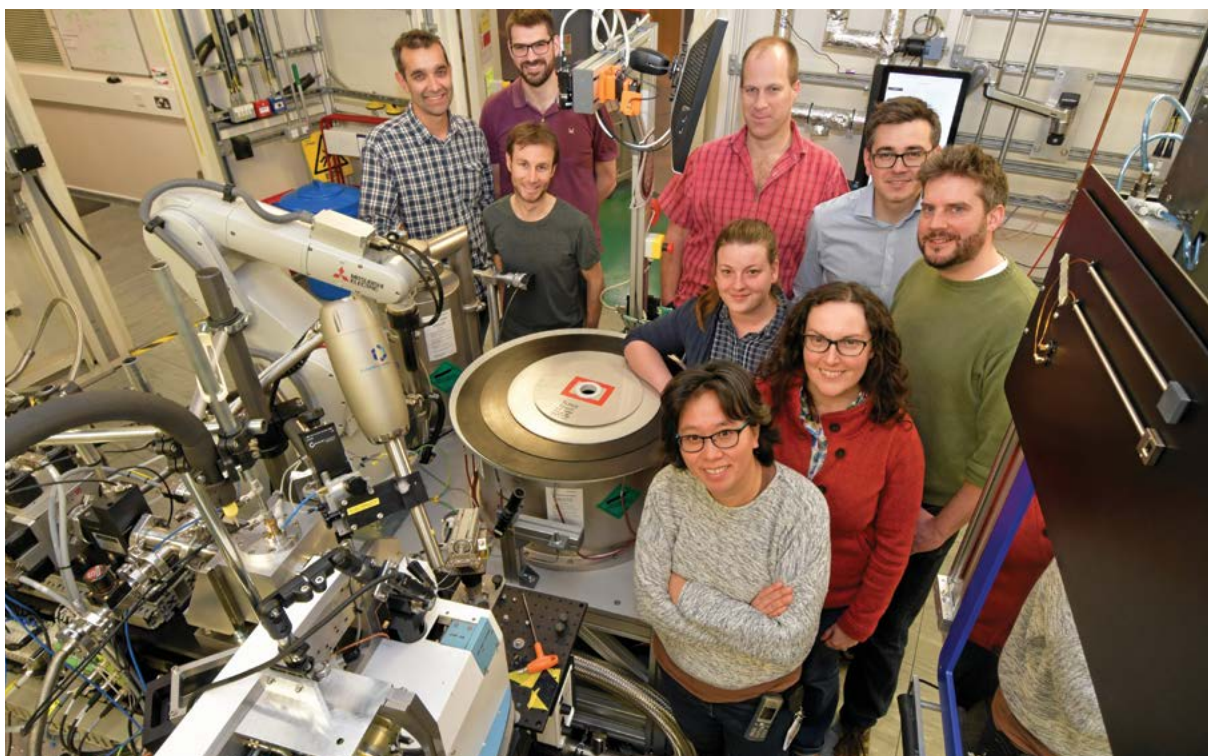
relevant cells, metal-modifying drugs such as chelators offer under-explored potential for earlier intervention to delay progression¹⁶. Diamond-II will enable *in situ* analysis of both the inorganic and organic components in the sample¹⁰, with scope for full quantification of constituent elements¹⁷. Diamond-II will provide a nano-sized, low divergence beam for quantitative metal spectroscopy that can be coupled to simultaneous mass spectroscopy for site-specific proteomics within tissues. This would provide unparalleled insights into the speciation of metals in their local environments on length scales relevant to understanding disease.

The wider use of spectroscopy and spectromicroscopy to study human tissues, and study the processes hypothesised to drive cell degeneration *in-vivo*, is currently limited by factors which Diamond-II will resolve. Current limitations include acquisition times on dilute systems (typically < parts-per-million), issues with sample preservation, limited access to temperature control (for sample presentation), atmospheric control (e.g. to avoid auto-oxidation of samples), and limited flexibility to move between spatial resolutions, required for surveying tissue and its constituent cells¹⁴.

These limitations fundamentally restrict the number of samples that can be reasonably investigated and produce poor statistical support for the observations. Therefore, sample throughput is critical to providing statistically sound data. For example, the trafficking of metal particulates from air pollution in the brain implicated in dementia¹⁸, and PM₁₀ particulates implicated in Parkinson's disease¹⁹, will only be understood if greater numbers of

cell and tissue sample replicates can be included in an experiment. There may be multiple pathways involved in the uptake, digestion or excretion of particulates by the central nervous system. Observing these processes will be critical to testing and refining hypotheses to describe factors contributing to the mechanisms of neurodegeneration, and, importantly, to bring new insight to the opportunities offered by chelation therapy²⁰. New opportunities for 3D analysis, including ptychography and chemical topography¹⁷, are a high priority in this context. For example, to distinguish environmentally-acquired industrially-produced particulates from those of biogenic origin¹⁰. However, these techniques currently suffer from limited sample throughput. Factors that contribute to sample throughput such as reduced data acquisition times, sample environments, detector technology and improved signal-to-noise will all be improved in Diamond-II. In totality these gains will provide a step-change.

Advancing the science of metallomics (the role of metals in biology) is a high priority. The majority of synchrotron studies of metals in neurodegenerative disorders sample a single time-point in the process¹⁴. Increased flux and better spatial resolution, coupled with greater control over sample environments, will enable new insights into the way that cells, proteins and polymers take up and release biometals and disease-relevant metal ions and minerals. High dose X-ray measurements can improve signal-to-noise but require techniques such as cryoprotection and atmospheric controls to preserve the fragile samples. The increased brilliance of Diamond-II will enable sampling over larger areas (an order of magnitude greater diameter



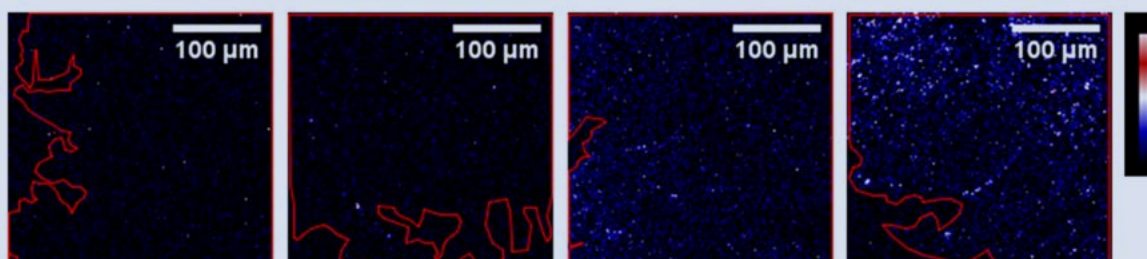
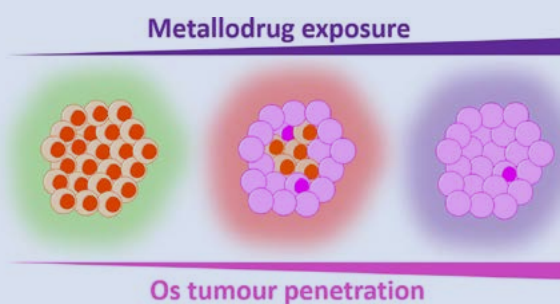
samples than can be achieved with the nanoprobe I14 and I08 beamlines), but will bring the in-plane resolution into the subcellular regime, supporting single cell analysis at a level that has not previously been possible (see Exemplar 1). This bridges a critical gap in provision for life sciences experiments, overcoming current constraints at nanoprobe beamlines worldwide. It will be a powerful opportunity for mammalian and plant science, where greater sample areas will be accommodated on an electron microscopy grid, and where spatial resolutions enabling wide area surveying (e.g. several cm²) and spectroscopic evaluation of individual sites at cellular or subcellular resolution are required.

6.4.2. Imaging of cells and biological materials

Imaging of cells and biological materials has been dominated by light and electron microscopy. These techniques will continue to flourish as super-resolution microscopy and CryoEM^{22,23} readily provide 0.1 to 10 nm resolution imaging within cells and their correlation provides a platform to study cellular dynamics – a biological process of interest is followed by fluorescent markers and structurally resolved using electron microscopy. An example of such correlated analysis is given in Figure 1 in

Exemplar 1: Metal drugs to combat cancer

Metal-based chemotherapy drugs hold much promise for development of selective activity to specific cancer cell types, although the precise cellular targets for many of these compounds remains unclear. Organometallic complexes of ruthenium, iridium and osmium promise this selective activity with low levels of toxicity. μ X-ray techniques (X-ray Fluorescence Imaging and X-ray Absorption Spectroscopy) can offer useful insights into the action of these complexes by spatially probing the chemistry and interactions between the



introduced agents and their biological targets. It is essential to probe these interactions using therapeutically relevant concentrations of the drug, which is challenging at present as the signal from the metal compounds is extremely weak and restricts the extent of usefulness of X-ray spectroscopy. Notwithstanding this, the potential is evident in a recent study by Sanchez-Cano *et al*²¹ that assessed penetration of an organo-osmium drug candidate into the interior of tumour models, leading to cellular changes that suggest nuclear damage and initiation of cell death events.

Distributions of Os particles in spheroids exposed to the drug for different incubation times were obtained (see mapping inset), demonstrating that the drug candidate penetrates into the core of the tumour in a time-dependent manner. Conversely, acquisition of XAS spectra (providing information on the chemical properties of the drug once inside the spheroid) was achieved on a few hot spots with high concentration of the metal, but the low quality and signal-to-noise ratio of the spectra obtained did not allow extensive analysis. Higher flux would allow high-quality XAS data to be collected in a time frame that would help to moderate radiation damage. Diamond-II's increased flux and more focused beam will facilitate more such studies where the metal levels are dismally low and within pharmacologically-relevant ranges, and where high spatial resolution in 3D is imperative.

Sanchez-Cano, C *et al*. Microfocus X-ray fluorescence mapping of tumour penetration by an organoosmium anticancer complex. *Journal of Inorganic Biochemistry*, 185, pp.26-29 (2018), <https://creativecommons.org/licenses/by/4.0/>.

Coordinated access to I14, I18, B24 and eBIC provides a platform for chemical and molecular imaging of cells and tissue.

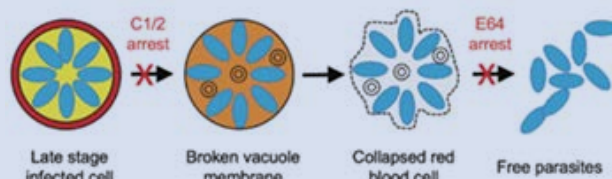
section 6.2. The main limitation of cryoEM arises from the poor penetration depth of electrons so that only thin slices (~100-200 nanometres) of a biological specimen can be imaged. Sectioning the sample and imaging by CryoEM is a complex and time consuming process. In contrast, X-rays have a high penetration depth and avoid the need for labelling as electron density is directly probed. Each type of atom in the periodic chart can uniquely resonate at a specific X-ray energy and for the atoms commonly found in life sciences (i.e., carbon, nitrogen and oxygen), these atoms will resonate in the so-called “soft” X-ray region (< 1000 eV). By selectively resonating during imaging, X-ray microscopy can delineate or segment the different regions in the image readily identifying water, lipids, proteins and nucleic acids. Although the resolution achievable from X-ray imaging is much lower than CryoEM, X-rays nonetheless provide complementary information

that bridges light and electron imaging, both in terms of resolution and sample size (both thickness and area).

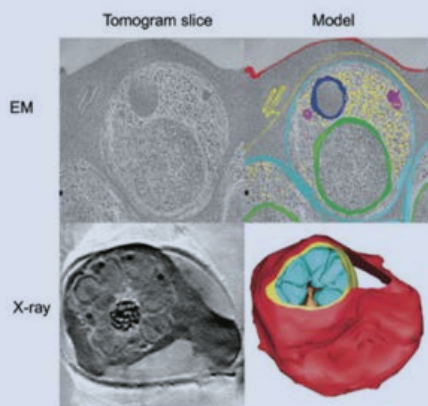
Full-field soft X-ray cryo transmission microscopy (cryo-TXM), our newest capability at Diamond allows imaging of whole cells (up to 10 microns in thickness), exploiting the excellent absorption contrast in the so-called water window (~500 eV X-rays). High-pressure freezing, together with higher energy or sectioning, can be used to investigate tissues or organoids. This is of great interest with the growing importance of organoids, which approximate mini-organs in tissue culture, showing some functional attributes of actual organs. Organoids are formed by culturing stem or progenitor cells in a 3D medium, followed by treatment with the appropriate growth factors. These are far more useful models for academic and industry research than the classical lines used for cell culture, which are notoriously unrepresentative.

Exemplar 2: Combining X-ray and electron tomography to visualise key steps in the malaria infection process

Malaria parasites develop within red blood cells inside a membrane-enclosed parasitophorous vacuole. An essential step in their life cycle is the exit of mature parasites from the blood cell, a multistage process termed egress. To do this, the parasites orchestrate a highly-regulated sequence of membrane permeabilisation and breakage steps, culminating in the explosive release of parasites for a new round of infection.



Schematic of the main steps in egress with points of arrest by compound 1/2 and E64 indicated



Electron and X-ray tomograms of cells arrested early in egress by Compound 1 or 2. Red cell membrane, red; vacuole membrane, yellow; parasite cell membranes, cyan. Other colours, parasite organelles and ribosomes.

Using a combination of cryo X-ray and electron tomography, Hale et al²⁷ discovered a previously unidentified permeabilisation of the vacuolar membrane at the start of egress that preceded membrane rupture. To collect these data, parasites inside red blood cells were synchronised so that they were at a similar stage of the infection cycle. Two pharmacological blockers (Compounds C1/2 and the cysteine protease inhibitor E64, see schematic) were used that could stall egress at different stages. The strategy enabled visualisation of the final minutes of egress, revealing that the blood cell membrane abruptly loses its structural rigidity and collapses around the parasites. The image is rich in detail and provides significant context, however, it is just one of a small, limited dataset. The increase in flux and sample throughout in Diamond-II would provide suitable datasets for machine learning. Already, we are seeing that machine learning algorithms can improve protein folding predictions, cancer screening and guide self-driving cars. Diamond-II will enable larger numbers of

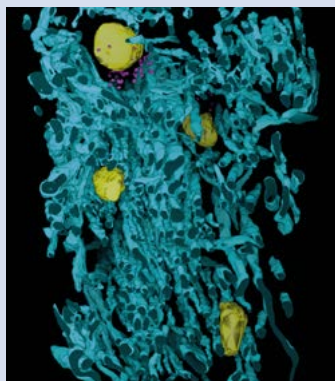
samples to be measured that will not only increase their statistical relevance but also provide deeper insights through the application of artificial intelligence.

Coordinated access to B24, Super resolution fluorescence microscopy and eBIC provides a platform for *in situ* cellular imaging of biological materials

Copyright Diamond Light Source.

Exemplar 3: 3D Imaging of biological tissue

High-throughput 3D cryogenic imaging of biological specimens is now possible through a variety of light, X-ray and electron-based techniques, which bring with them their own advantages and disadvantages. CryoElectron tomography can provide high resolution images of biological specimens but is limited to thin sections (a couple of 100s of nanometres). Fluorescence microscopy is limited by resolution, as is X-ray tomography although to a lesser extent and it can image cells with thicknesses up to 10 microns. When used in integrative correlative studies these three techniques can dissect the ultrastructure of cells and tissues to high resolution. That being said, cryogenic imaging of thick biological samples remains a challenge.



Semi-automated colour-segmentation of a reconstructed mouse brain tomogram, based on the contrast differences within the sample. Yellow = nuclei, Pink = lysosomal LF and putative PAVs, Aqua = Myelinated axons.

volumes up to $48,000 \mu\text{m}^3$. The increased coherence provided by Diamond-II, improved source and optics will bring X-ray bioimaging of tissue and organoids to the fore by allowing imaging of biological tissues on a larger scale and at higher resolutions, which can be applied to the understanding of disease states. The example here illustrates how X-ray imaging can potentially transform our understanding of neurological disorders through the use of a dedicated cryo-ptychography beamline at Diamond-II.

Shahmoradian, S. H. et al. Three-dimensional imaging of biological tissue by cryo X-ray ptychography. *Scientific Reports*, 7, (2017). <https://creativecommons.org/licenses/by/4.0/>.

Coordinated access to a new cryo-biological imaging beamline, B24 and eBIC will provide a platform for imaging of cells and tissue in their near-native state across a range of length and resolution scales.

Proof-of-principal application of hard X-ray cryo-ptychography to mouse brain tissue has been recently demonstrated. Shahmoradian et al³² succeeded in imaging of mouse brain, allowing the visualisation of myelinated axons as well as sub-cellular features at a spatial resolution of ~ 100 nanometres and thicknesses approaching 100 microns with

The resolution of cryo-TXM is limited by the focusing device (zone plate objective). Currently, zone plates provide tens of nanometres resolution, but the technique can be easily combined with super resolution light microscopy (we have developed cryo-SIM to provide a correlative light-X-ray workflow). The technique has been applied to many key cellular processes, such as chromatin rearrangement²⁴, virus-host interactions²⁵, cell motility²⁶, parasite life cycle²⁷, and lymphocyte activation and function²⁸. Although Diamond-II will provide modest gains, together with concerted development in sample preparation methods, data analysis pipelines and correlative workflows we expect markedly increased impact of the method. The power of the technique in combination with CryoElectron tomography is exemplified by the recent work of Hale et al²⁷ (Exemplar 2) who applied these techniques to elucidating key steps in the malaria parasite egress from red blood cells.

Coherent diffraction Imaging (CDI), currently a niche technique, will potentially be transformed by Diamond-II. The reduced emittance in the new machine will see significant gains in coherent flux of nearly 4-orders of magnitude. Pioneering work, initially with plane wave CDI show the potential for imaging of bacteria²⁹ and more recently hydrated whole yeast cells at 25 nm resolution in 2D³⁰. Developments in the use of cryo-ptychography have ignited the field, as the limitations placed on the imaged object are in essence determined only by the experimental setup and the technique delivers a unique combination of quantitative electron density contrast and high-resolution 3D imaging. The technique has been applied to a few proof-of-principle examples in biology, but with the expected reduction in scan times and the potential to utilise higher energy X-rays to reduce the impact of radiation damage to biological materials, imaging at 10s of nanometre resolutions for large tissue samples becomes tractable with Diamond-II.

A flavour of the potential impact of cryo X-ray ptychography is illustrated by imaging of neuronal tissues, which is the current state-of-the-art for the technique and is summarised in Exemplar 3. The total data acquisition time required was 23 hours; we estimate that the increased coherent flux of Diamond-II could reduce this to an equivalent number of seconds, whilst allowing an increased field of view and improved resolution. Coherent imaging will be a sought-after and important capability of next-generation synchrotrons.

The high-resolution structural imaging techniques are performed on cryo-preserved cells and tissues. To complement such studies *in vivo*, live-cell IR microspectroscopy developed at our IR beamline provides the capability of following the living mammalian cell responses to treatment. Our IR imaging informs on the metabolism at sub-cellular resolution, showing changes inside the cell's biochemical machinery via the IR molecular fingerprint at the level of organelles. Diamond-II seeks

to increase the IR photon flux and flux density 3- to 4-fold for IR-imaging and microspectroscopy, for widening the field of view to multiple cells and improving the molecular sensitivity. Determining the factors that influence cellular uptake of drugs and their metabolism is key to developing effective treatments for cancer. Full IR-spectral imaging will be a critical complementary technique to correlative studies that bridges the knowledge gap between high-resolution imaged cells and the flow of small molecules that comprise the cell's metabolic signature.

Structure-based therapeutic discovery

Diamond supports a large volume of commercial investigations in the area of structure-based therapeutic discovery and we expect the demand for synchrotron radiation to continue through to Diamond-II. The dark period represents a severe risk to this area and we will investigate possible risk mitigation strategies (see section 6.5). There is recognition that features of Diamond-II will be helpful in both New Biological Entity (NBE) and New Chemical Entity (NCE) drug discovery benefiting both basic sciences and industry.

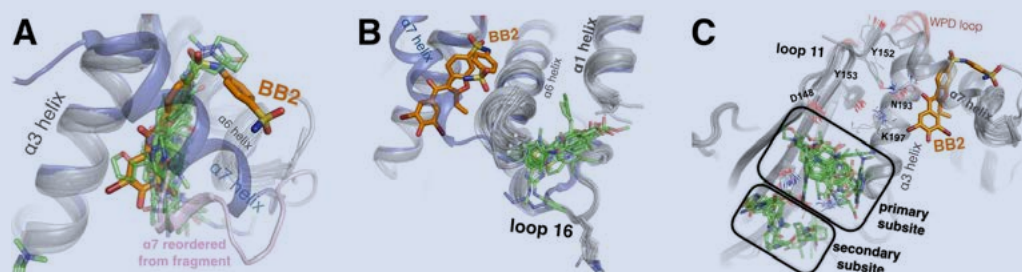
In NCE discovery more difficult crystallographic systems

such as GPCRs still remain challenging samples but have become relatively routine due to the improved beam capabilities of microfocus beamlines and will be further enhanced by the Diamond-II upgrade. Excitingly, major improvements in signal-to-noise, sample throughput and detector technology will create a potentially transformative opportunity for NCE design, by facilitating kinetic studies with target proteins that would link the potency of compounds to conformational sampling and catalysis. Indeed the recent proof of principle demonstration outlined below is creating excitement in the industry.

Over the last few years, industry has become increasingly heavily committed to the design/discovery of NBEs, perhaps most notably antibodies, with the global market for monoclonal antibodies hitting nearly £77 billion in 2017. Recent trends in antibody discovery are towards the rational design and engineering of multiple variable regions (the regions involved in target recognition), which are usually generated inefficiently in low-throughput. Here, proposed work of the Rosalind Franklin Institute (RFI) and the Research Complex at Harwell (RCaH) with industry, aimed at the parallelisation and miniaturisation of target production through the use of microfluidics, might allow a step change in throughput when matched with the

Exemplar 4: X-ray-based discovery chemistry – probing conformational space for novel therapeutic strategies

Proteins are dynamic molecules and carry out many of their essential biological functions by using concerted molecular motions in processes such as enzyme catalysis and protein:protein and protein:ligand interactions. Understanding protein dynamics at the atomic level opens the way to identify novel molecular mechanisms for targeting specific disease genes. This was recently illustrated by Keedy *et al*⁹⁹, who used XChem screening and room-temperature crystallography (now available on VMXi) to probe the dynamics of a long-pursued but consistently refractory target of diabetes, the phosphatase PTP1B, which reduces how well cells can respond to insulin. Thus, inactivating this enzyme could help to treat diabetes. Collectively, the structures, captured both at room temperature and from the high-throughput XChem FBDD platform, allowed for the first time the identification of allosteric sites, one of which was determined to be far more amenable to small molecules targeting than the positively-charged active site pocket of the enzyme (see figure below: Keedy, D.A. *et al*. *An expanded allosteric network in PTP1B by multitemperature crystallography, fragment screening, and covalent tethering*. *eLife*, (2018).) – a major milestone in the fields of both phosphatases and diabetes.



Fragments cluster at three binding hotspots distal from the active site of PTP1B

This work demonstrates the route to studying allostery in general and opens the path to a host of new targets and targeting modalities in drug discovery. To offer this as a routine experiment will require the extremely high-throughput infrastructures that Diamond-II will offer with XChem and VMXi.

increased sensitivity and throughput offered by Diamond-II for solution, single particle and crystal analysis.

Finally, an area where we believe there is still enormous unexplored potential is structural vaccinology, where structural knowledge is used to improve the properties of vaccine antigen. Diamond has already contributed to work on synthetic foot-and-mouth-disease virus and poliovirus vaccines^{33,34}. For full capsid vaccines we expect cryoEM to be the dominant methodology in the future. However, for the many products based on individual protein antigens X-ray analysis at Diamond-II is the most attractive route for the facilitation of structure-guided design^{35,36}.

Fragment based drug discovery (FBDD)

This approach to drug design was first proposed in the late 1980s following the impact of molecular biology advances and the acceleration of structure determination by X-ray crystallography. FBDD has succeeded in developing over 30 clinical drug candidates with 3 FDA-approved drugs in oncology³⁷. The XChem facility at Diamond has set a new paradigm for FBDD and, even though based at the significantly flux-limited beamline I04-1, has achieved an order-of-magnitude increase in the efficiency of early-stage drug discovery. This has transformed the take-up of fragment screening by X-ray crystallography and has led to the democratisation of FBDD in academia and small companies, as a result of the small size and cost of fragment libraries and the accessibility and ease of use of XChem. Further ways of probing potential drug targets have also been made possible recently by high-throughput methods (see Exemplar 4). Nevertheless, the full potential of FBDD, to quickly (in weeks), cheaply (<£10k) and routinely generate potent and bioactive compounds against any target of interest is still unrealised. Such a capability would unlock a flood of drug discoveries and new chemical probes³⁸. Such probes are powerful tools for exploring fundamental biological mechanisms and validating the druggability of targets, yet they remain rare due to the prohibitive cost of generating them. Bespoke probes, essentially on-demand, would transform biological research in a similar way to gene editing. Thus, for instance, mechanisms of antimicrobial resistance (AMR) could be quickly dissected in chemical detail and then by-passed through nimble compound design, allowing rapid restocking of the antibiotic arsenal to side-step the looming AMR crisis. Diamond-II by combining an upgraded machine and a new purpose-built beamline for high-throughput drug discovery is projected to increase baseline throughput 20-fold, providing a platform for UK industry and academia to take FBDD to the next level, offering both cryo and room temperature screening.

References

- 1 Bloom, D. E. *et al.* The Global Economic Burden of Noncommunicable Diseases. *Geneva: World Economic Forum.* (2011).
- 2 McGovern Institute, M. *Brain Disorders: By the Numbers*, <<https://mcgovern.mit.edu/brain-disorders/by-the-numbers>> (2014).
- 3 MRC. *Neurodegenerative diseases and dementia*, <<https://mrc.ukri.org/funding/science-areas/neurosciences-mental-health/our-science-and-contacts-nmhb/neurodegenerative-diseases-and-dementia/>> (2018).
- 4 Dye, C. After 2015: infectious diseases in a new era of health and development. *Philos Trans R Soc Lond B Biol Sci* **369**, 20130426, doi:10.1098/rstb.2013.0426 (2014).
- 5 Chen, P., Miah, M. R. & Aschner, M. Metals and Neurodegeneration. *F1000Res* **5**, doi:10.12688/f1000research.7431.1 (2016).
- 6 Friedman, A., Galazka-Friedman, J. & Kozirowski, D. Iron as a cause of Parkinson disease - a myth or a well established hypothesis? *Parkinsonism Relat Disord* **15 Suppl 3**, S212-214, doi:10.1016/S1353-8020(09)70817-X (2009).
- 7 Oakley, A. E. *et al.* Individual dopaminergic neurons show raised iron levels in Parkinson disease. *Neurology* **68**, 1820-1825 (2007).
- 8 Schrag, M., Mueller, C., Oyoyo, U., Smith, M. A. & Kirsch, W. M. Iron, zinc and copper in the Alzheimer's disease brain: a quantitative meta-analysis. Some insight on the influence of citation bias on scientific opinion. *Prog Neurobiol* **94**, 296-306, doi:10.1016/j.pneurobio.2011.05.001 (2011).
- 9 Dusek, P. *et al.* The neurotoxicity of iron, copper and manganese in Parkinson's and Wilson's diseases. *J Trace Elem Med Biol* **31**, 193-203, doi:10.1016/j.jtemb.2014.05.007 (2015).
- 10 Everett, J. *et al.* Nanoscale synchrotron X-ray speciation of iron and calcium compounds in amyloid plaque cores from Alzheimer's disease subjects. *Nanoscale* **10**, 11782-11796, doi:10.1039/c7nr06794a (2018).
- 11 Koeppen, A. H. *et al.* Friedreich's ataxia causes redistribution of iron, copper, and zinc in the dentate nucleus. *Cerebellum* **11**, 845-860, doi:10.1007/s12311-012-0383-5 (2012).
- 12 Kruger, P. C. *et al.* Abundance and Significance of Iron, Zinc, Copper, and Calcium in the Hearts of Patients With Friedreich Ataxia. *Am J Cardiol* **118**, 127-131, doi:10.1016/j.amjcard.2016.04.024 (2016).
- 13 Solovyev, N. *et al.* Selenium, selenoprotein P, and Alzheimer's disease: is there a link? *Free Radic Biol Med* **127**, 124-133, doi:10.1016/j.freeradbiomed.2018.02.030 (2018).
- 14 Collingwood, J. F. & Adams, F. Chemical imaging analysis of the brain with X-ray methods. *Spectrochimica Acta Part B: Atomic Spectroscopy* **130**, 101-118, doi:10.1016/j.sab.2017.02.013 (2017).
- 15 Porcaro, F., Roudeau, S., Carmona, A. & Ortega, R. Advances in element speciation analysis of biomedical samples using synchrotron-based techniques. *TrAC Trends in Analytical Chemistry* **104**, 22-41, doi:10.1016/j.trac.2017.09.016 (2018).
- 16 Martin-Bastida, A. *et al.* Brain iron chelation by deferiprone in a phase 2 randomised double-blinded placebo controlled clinical trial in Parkinson's disease. *Scientific Reports* **7**, 1398, doi:10.1038/s41598-017-01402-2 (2017).
- 17 Yang, Y. *et al.* Quantitative Nano-imaging of Cells with a High Energy X-ray Cryo Nano-probe. *Microscopy and Microanalysis* **24**, 402-403, doi:10.1017/s1431927618014290 (2018).

- 18 Maher, B. A. *et al.* Magnetite pollution nanoparticles in the human brain. *Proc Natl Acad Sci U S A* **113**, 10797-10801, doi:10.1073/pnas.1605941113 (2016).
- 19 Chen, C.-Y. *et al.* Long-term exposure to air pollution and the incidence of Parkinson's disease: A nested case-control study. *PLoS ONE* **12**, e0182834, doi:10.1371/journal.pone.0182834 (2017).
- 20 Dusek, P., Schneider, S. A. & Aaseth, J. Iron chelation in the treatment of neurodegenerative diseases. *J Trace Elem Med Biol* **38**, 81-92, doi:10.1016/j.jtemb.2016.03.010 (2016).
- 21 Sanchez-Cano, C., Romero-Canelon, I., Geraki, K. & Sadler, P. J. Microfocus X-ray fluorescence mapping of tumour penetration by an organoosmium anticancer complex. *J Inorg Biochem* **185**, 26-29, doi:10.1016/j.jinorgbio.2018.04.014 (2018).
- 22 Balzarotti, F. *et al.* Nanometer resolution imaging and tracking of fluorescent molecules with minimal photon fluxes. *Science* **355**, 606-612, doi:10.1126/science.aak9913 (2017).
- 23 Bartesaghi, A. *et al.* Atomic Resolution Cryo-EM Structure of beta-Galactosidase. *Structure* **26**, 848-856 e843, doi:10.1016/j.str.2018.04.004 (2018).
- 24 Le Gros, M. A. *et al.* Soft X-Ray Tomography Reveals Gradual Chromatin Compaction and Reorganization during Neurogenesis In Vivo. *Cell Rep* **17**, 2125-2136, doi:10.1016/j.celrep.2016.10.060 (2016).
- 25 Hagen, C. *et al.* Structural Basis of Vesicle Formation at the Inner Nuclear Membrane. *Cell* **163**, 1692-1701, doi:10.1016/j.cell.2015.11.029 (2015).
- 26 Ramirez-Santiago, G. *et al.* Clathrin regulates lymphocyte migration by driving actin accumulation at the cellular leading edge. *Eur J Immunol* **46**, 2376-2387, doi:10.1002/eji.201646291 (2016).
- 27 Hale, V. L. *et al.* Parasitophorous vacuole poration precedes its rupture and rapid host erythrocyte cytoskeleton collapse in *Plasmodium falciparum* egress. *Proc Natl Acad Sci U S A* **114**, 3439-3444, doi:10.1073/pnas.1619441114 (2017).
- 28 Cruz-Adalia, A. *et al.* T cells kill bacteria captured by transinfection from dendritic cells and confer protection in mice. *Cell Host Microbe* **15**, 611-622, doi:10.1016/j.chom.2014.04.006 (2014).
- 29 Miao, J. *et al.* Imaging whole *Escherichia coli* bacteria by using single-particle X-ray diffraction. *Proc Natl Acad Sci U S A* **100**, 110-112, doi:10.1073/pnas.232691299 (2003).
- 30 Nam, D. *et al.* Imaging fully hydrated whole cells by coherent X-ray diffraction microscopy. *Phys Rev Lett* **110**, 098103, doi:10.1103/PhysRevLett.110.098103 (2013).
- 31 Suzuki, A., Shimomura, K., Hirose, M., Burdet, N. & Takahashi, Y. Dark-field X-ray ptychography: Towards high-resolution imaging of thick and unstained biological specimens. *Sci Rep* **6**, 35060, doi:10.1038/srep35060 (2016).
- 32 Shahmoradian, S. H. *et al.* Three-Dimensional Imaging of Biological Tissue by Cryo X-Ray Ptychography. *Sci Rep* **7**, 6291, doi:10.1038/s41598-017-05587-4 (2017).
- 33 Kotecha, A. *et al.* Structure-based energetics of protein interfaces guides foot-and-mouth disease virus vaccine design. *Nat Struct Mol Biol* **22**, 788-794, doi:10.1038/nsmb.3096 (2015).
- 34 Marsian, J. *et al.* Plant-made polio type 3 stabilized VLPs-a candidate synthetic polio vaccine. *Nat Commun* **8**, 245, doi:10.1038/s41467-017-00090-w (2017).
- 35 Wright, K. E. *et al.* Structure of malaria invasion protein RH5 with erythrocyte basigin and blocking antibodies. *Nature* **515**, 427-430, doi:10.1038/nature13715 (2014).
- 36 Lennartz, F. *et al.* Structural basis for recognition of the malaria vaccine candidate Pfs48/45 by a transmission blocking antibody. *Nat Commun* **9**, 3822, doi:10.1038/s41467-018-06340-9 (2018).
- 37 Blundell, T. L. Protein crystallography and drug discovery: recollections of knowledge exchange between academia and industry. *IUCrJ* **4**, 308-321, doi:10.1107/S2052252517009241 (2017).
- 38 Arrowsmith, C. H. *et al.* The promise and peril of chemical probes. *Nat Chem Biol* **11**, 536-541, doi:10.1038/nchembio.1867 (2015).
- 39 Keedy, D. A. *et al.* An expanded allosteric network in PTP1B by multitemperature crystallography, fragment screening, and covalent tethering. *Elife* **7**, doi:10.7554/eLife.36307 (2018).



6.5. Dark period mitigation

The Diamond-II upgrades will be disruptive to the UK academic and industrial community. An 18-month dark period will especially affect the competitiveness of communities who rely on regular access. The most obvious example is perhaps MX, our users produce over 370 publications and 1180 PDB depositions per year (based on recent 4 year average) this success is a result of having access to our exceptional beamline staff, automation and data processing tools. Furthermore, the proposed Diamond-II dark period will create ~24,000 hours of MX demand amongst our European synchrotron community. It will not be possible to absorb this demand even if the likely overlap of dark periods with for instance PETRA and SOLEIL could be avoided. Engagement with Diamond's users at the Diamond-II workshops (Sep 2018) indicated overwhelming support for the proposal that Diamond seeks to help mitigate the dark period by seeking alternatives/substitutes.

Diamond will therefore urgently explore a range of strategies to mitigate the dark period. Here we simply lay out some options that will be analysed. We note that resources are likely to be limiting, even if options are affordable putting them in place before the shutdown will place additional strain on a workforce already fully occupied with Diamond operations and Diamond-II preparations.

The most radical would be to construct a new ring, for instance a smaller ring built to support a limited number of relatively simple but highly automated beamlines aimed at certain core high throughput communities (for example crystallography, spectroscopy, certain imaging applications). Such a machine might free-up Diamond-II to focus on the less routine aspects. The major difficulty with this approach is likely to be the lack of resources to execute a new build alongside the Diamond-II programme.

A less ambitious approach would be to analyse the needs of the different communities and to seek bespoke mitigations proportionate to the scale of the impact of the dark period.

Thus, a possible strategy for the large MX community might be: 1) a replacement beamline that will be built on a new mid-straight section (existing B04) before decommissioning I04-1 and at the start of the dark period. This will provide users access to a new, Diamond-II beamline as soon as possible, whilst making the most efficient use of engineering resources. 2) In order to retain capacity during the dark period for academic and industrial users we might establish a new, satellite beamline, HTMXBridge, at another European synchrotron. HTMXBridge would be a fully-automated ultra-high-throughput beamline with access managed for both academic and industrial users through Diamond and the host institute and could also serve as a test-bed for new technologies for Diamond-II beamline

upgrades. HTMXBridge would help maintain relationships with our existing users, keep our beamline scientist's knowledge and expertise up-to-date, and promote and strengthen relationships between the UK and Europe.

Small angle X-ray scattering (SAXS) capabilities could be maintained through a distributed strategy where less challenging SAXS experiments could be managed through our offline SAXS instrument and via a network of home sources found throughout the UK. This might be complemented by a strategic sample-environment collaboration with a SAXS beamline at another European synchrotron, SXBridge, comparable to the SAXS imaging capabilities at our multi-purpose beamline I22. Mail-in bioSAXS experiments would be managed through securing time at various bioSAXS beamlines in Europe and the United States.

For the IR and UV beamlines, B22 and B23 it might only be possible to maintain baseline capacity through the offline IR/THz source and CD instrumentation.

As a general principle learnt in the run-up to Diamond through the UK-ESRF BM14 collaboration, working on new instruments at other facilities offers the opportunity to learn, build strong links and strengthen both user communities, whilst minimising disruption to UK user groups.

6.6. New beamline opportunities

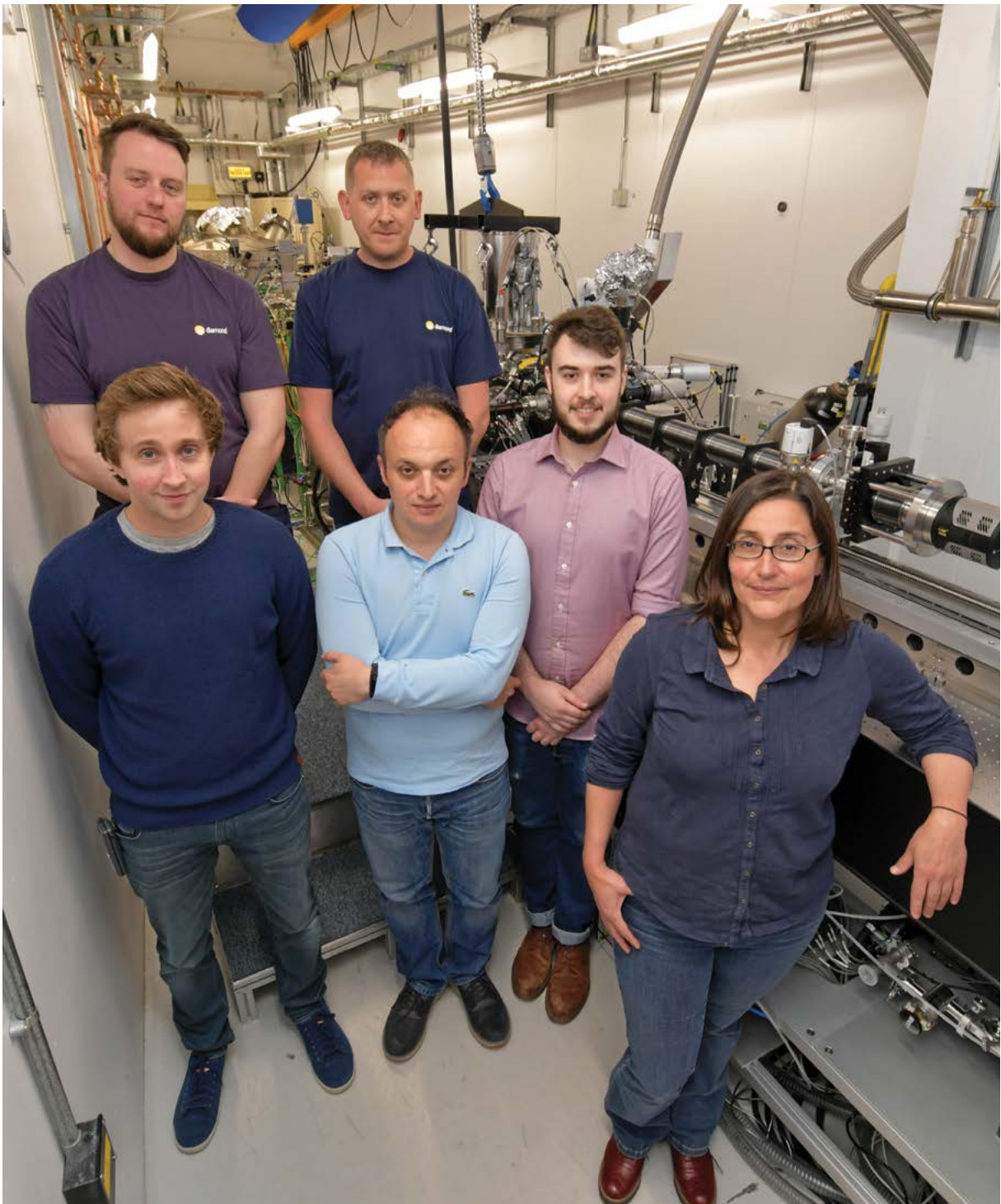
We would expect to strongly develop imaging and note that holography benefits from a low emittance source and can provide images with less phase retrieval errors than CDI or ptychography³¹. An instrument capable of ptychography (near and far field), holography and scanning spectroscopy would cover a broad range of imaging requirements for biology and benefit significantly from Diamond-II. It is likely that this would require a purpose-built life science beamline that could exploit cryo-ptychography, holography and fluorescence microscopy, to complement the full-field imaging capability of our cryo-soft X-ray imaging beamline, B24. The target of such a beamline would be to offer 3D cryo imaging with a field of view of approaching a mm laterally and perhaps a third of a mm in depth and a resolution for optimum samples of ~12 nm. A capability that we believe is currently unique at Diamond is the ability to work on biological samples requiring containment level 3 (at beamline I03) and we see the future for such experiments increasingly moving towards including *in situ* imaging of the interactions of pathogens with cells. The beam properties of I03 would be well suited to such applications, so we will also explore imaging options on I03.

In addition we note that the X-ray scattering instruments at Diamond are insufficient for measuring the entire

range of length scales from 0.1 nanometres to 10 microns. Diamond-II offers the opportunity to build a unique X-ray scattering instrument that can simultaneously measure the USAXS (ultra-small angle), SAXS and WAXS ranges. The high flux, low divergence beam would enable new studies in structured-products, i.e. materials such as lubricants or colloids that self-assemble into mesoscale structures critical to function. These materials are designed to work in extreme, turbulent or non-equilibrium conditions and have been poorly studied in their *in operando* environments.

Diamond has allowed the study of structured materials in their equilibrium states. The next frontier will be studying these materials in their non-equilibrium, point-of-use conditions.

ⁱ Further bibliometric analysis (Mean Normalised Citation Score) shows that citations of published work performed at Diamond is significantly higher than both the European and UK average across all of the key areas of science it serves.



7. Diamond-II: Advancing physical sciences

7.1. Physical science challenges

Physical science research transforms our understanding of the world at the atomic and planetary level. For instance, unlocking the secrets of superconductivity allowed MRI scanning to revolutionise healthcare, whilst understanding the quantum world led to the development of the transistor, computers and lasers and is nowadays unearthing ever more subtle sides of nature promising dissipationless electronics and quantum computing. Basic research in physical sciences is then a key driver of productivity and economic growth providing solutions to the health, environmental and technological challenges facing our society today. The latest investments made in the Henry Royce Institute for Advanced Materials (£235 million), Maxwell Centre (£45 million), Bragg Centre for Materials Research and the Faraday Institution (£246 million) demonstrate the strong commitment made by government and industry to promote step changes in the discovery of novel materials and processes ranging from nanoscale research to large-scale manufacturing. These investments pay huge dividends for the UK. In little over a decade, the remarkable properties of graphene were uncovered, revolutionary developments in electron microscopy were made, and scientists realised the importance of topology in quantum physics. These breakthroughs can be directly linked to UK research and have been recognised by six recent Nobel prizes in Physics and Chemistry.

Diamond plays a pivotal role in physical science research, nurturing UK innovation by creating the best environment for research excellence via access to world-leading facilities, cutting edge technologies and leading expertise. The strength of physical science research at Diamond is brought into sharp relief by the prolific number of peer-reviewed journal articles achieved to date (>5000), with over 26% of those articles published in journals with an impact factor greater than seven. Physical science research spans diverse areas, which will directly benefit from the Diamond-II upgrade by exploiting the increase in brightness and coherence, the higher photon flux and the extra capacity. In the electronics sector, worth £16 billion every year to the UK economy, employing 300,000 people in over 12,000 companies*, the enabling capacity of Diamond-II will be essential to understand phenomena at the heart of future technologies. For instance, advanced X-ray imaging achieves 14 nm resolution¹ currently and exactly matches Intel's state-of-the-art process technology. The well documented challenges of achieving a 10 nm process technology then serve only to highlight the importance of improved cutting edge X-ray tools to drive forward technological innovation. X-ray microscopy, has also helped to develop addressable antiferromagnetic semiconductors, critical as the underpinning technology behind extremely secure storage devices². The improvements to coherent diffraction imaging methods³ will allow such materials to be probed with much higher definition and hence drive forward device performance. The ability to probe the electronic states of nanoscale 2D materials and

heterostructures controlled by engineered strain or voltage gates in greater detail also holds enormous potential for new concepts in electronics.

Generating electricity from renewable sources is vital for the decarbonisation of the UK energy system, but weather-driven energy sources are intermittent by nature so that cost-effective energy storage is required to better match electricity demand with supply. Diamond-II and the neighbouring Faraday Institution will be at the forefront of efforts to improve the efficiency of rechargeable batteries and to develop new technologies based on solid electrolytes and low cost electrodes⁴. In addition, research conducted into fuel cells will directly feed into the Road to Zero Strategy** with a direct impact on the battery supply chain. This is a highly attractive opportunity for UK industry with the electric vehicle battery industry estimated to be worth £2.7 billion per year by 2030***.

Corrosion is estimated to cost the UK economy around £80 billion a year and cuts across sectors including marine and automotive transport, aerospace and oil and gas exploration. Meeting the challenges of corrosion requires an understanding of fatigue and fissures at the nanoscale as well as the development of robust coatings whilst mapping the alloying in metals after exposure in a reactor is crucial to control corrosion kinetics. Chemical state mapping using nanotomography using Diamond-II will give disruptive insights allowing preventative strategies for the impact of corrosion, building on recent pioneering imaging studies⁵ of encapsulated waste products for long-term nuclear waste storage.

In chemistry, innovation will be key to meet carbon budgets and reach the UK goal to develop sustainable low carbon, energy secure pathways towards 2030. X-ray research in catalysis will also continue to play a vital role in unveiling the microscopic mechanisms during chemical reactions. With

* <https://www.gov.uk/government/publications/electronics-and-it-hardware-in-the-uk-investment-opportunities/electronics-and-it-hardware-in-the-uk-investment-opportunities>

**<https://www.gov.uk/government/news/government-launches-road-to-zero-strategy-to-lead-the-world-in-zero-emission-vehicle-technology>

***https://www.apcuk.co.uk/app/uploads/2018/06/E4tech_Report_UK-chemical-supply-chain-for-EV-batteries_25June2018-1.pdf

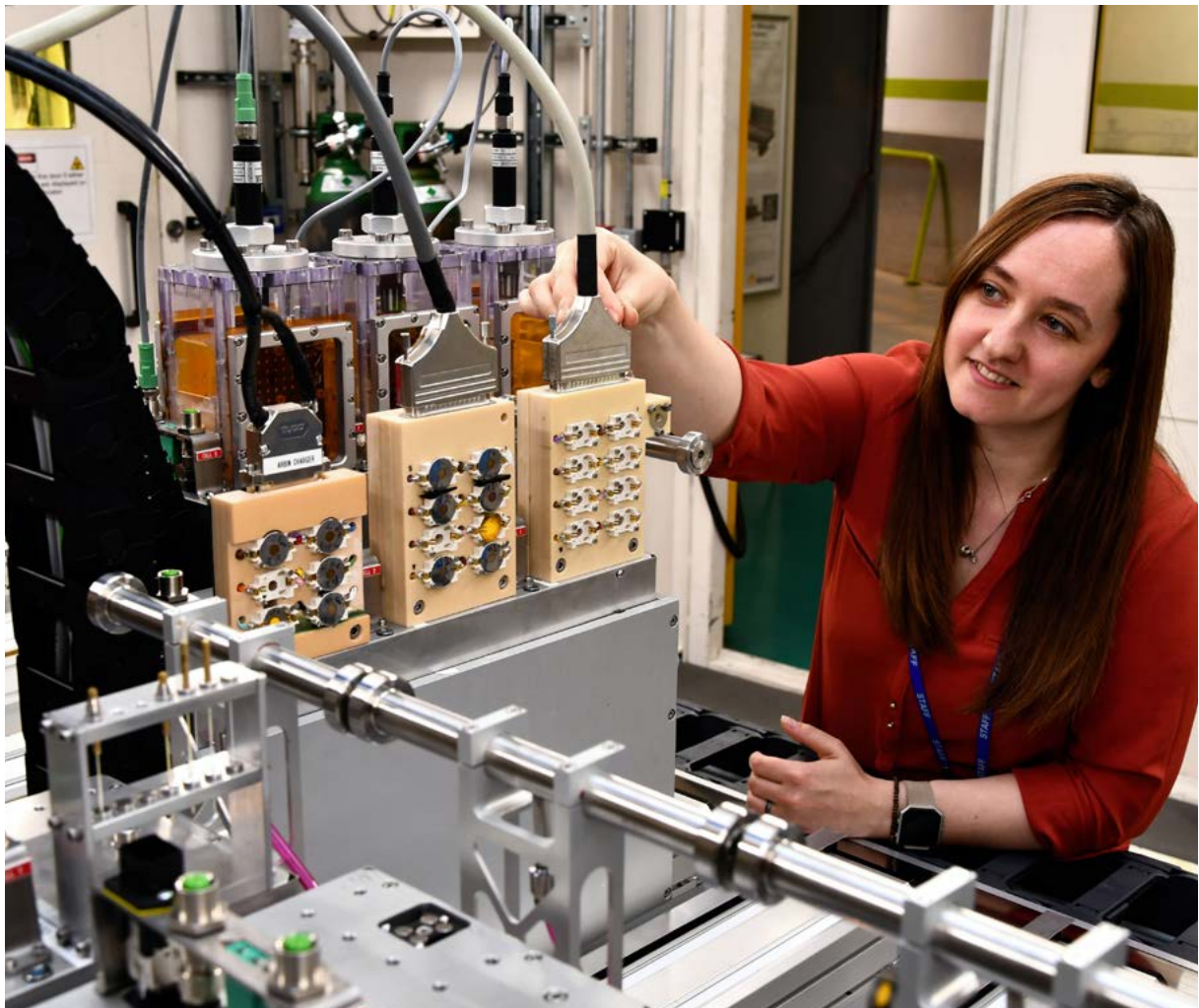
Diamond-II, 3D chemical tomography at the submicron level can be realised, allowing the role of nanoscale strain and interfaces in catalytic activity, as well as biocatalysts, to be probed with unprecedented sensitivity.

Diamond-II will deliver transformative gains in many areas of X-ray research in physical sciences through ground breaking technical innovation. For example, the improved energy resolution of spectrometers will allow unprecedented sensitivity to the speed of electronic changes during chemical processes, catalysis, battery charging and the elementary excitations in quantum materials. The dramatic gains in coherence and brightness will allow simultaneous 3D morphological, electronic and magnetic mapping for the first time at a spatial resolution of a few nanometres using coherent diffraction techniques. These gains will also allow unprecedented insights into the fast dynamics of materials as they condense from one phase into another promoting the development of new functional materials. Diamond-II will push our understanding of emerging nanoscale complexity and heterogeneity and therefore feed directly into the Industrial Strategy which sets out

Grand Challenges focussing on artificial intelligence and data, the ageing society, clean growth and the future of mobility. The different challenges and areas of most impact in physical science research for the Diamond-II upgrade have been broken down into five major areas: Energy, Chemistry, Quantum materials, Engineering materials & processing and Earth, environment & planetary science.

References

1. Holler, M. *et al.* High-resolution non-destructive three-dimensional imaging of integrated circuits. *Nature* **543**, 402–406 (2017).
2. Wadley, P. *et al.* Spintronics: Electrical switching of an antiferromagnet. *Science* (80-.). **351**, 587–590 (2016).
3. Donnelly, C. *et al.* Three-dimensional magnetization structures revealed with X-ray vector nanotomography. *Nature* **547**, 328–331 (2017).
4. 10 years left for redesign of Li battery. *Nat.* **559**, 467–471 (2018).
5. Stitt, C. A. *et al.* In-situ, time resolved monitoring of uranium in BFS:OPC grout. Part 2: Corrosion in water. *Sci. Rep.* **8**, 1–12 (2018).



7.2. Energy

Energy demands are increasing throughout the world, for both static (e.g. electricity grid) and mobile (e.g. vehicle) applications. The provision is currently met by a mix of technologies including fossil fuels, nuclear power, hydroelectricity and increasingly through sustainable energy power sources. Inevitably the future balance will evolve rapidly, with predictions (see Figure 1) indicating a surge in the uptake of technologies such as solar and wind power. Energy efficiency will also become a focus, including development of low power electronics and ultra-efficient engine technology with, for example, associated improvements in lubricants.

Many challenges need to be overcome to realise this global energy revolution through improving aspects of energy conversion, storage, transmission and low-power device efficiency in order to limit the detrimental effects on the planet, as highlighted in the UKRI strategy document¹. Solutions must be found that allow expanding energy use whilst reducing the environmental impact, in order to meet the UK obligations under the Paris Agreement on Climate Change² and the ambition of a net zero emissions energy policy by 2050. Energy conversion technologies will focus on the transition from polluting fossil fuels to low-carbon sources such as wind, tidal and solar power, complemented at least in the immediate future by nuclear energy. These technologies inherently produce an intermittent supply of energy and therefore must integrate with highly efficient grid and off-grid storage solutions such as batteries or chemical storage.

Synchrotron investigations are crucial in understanding details of the structure, chemical nature and electronic states of energy materials, not only in their pristine state, but as they evolved during the reaction or process. Indeed, many materials developed through discovery-based studies, such as the development of perovskite based photovoltaic materials, are starting to appear in commercial products. This combination of discovery led development of new materials together with challenge-based improvements in material and device performance is key to exploiting the potential of energy materials.

In this section, we focus on two major areas of research, metal-ion batteries and photovoltaics, as examples of where Diamond-II will be truly transformative. We outline how some of the techniques will be developed to understand the materials and devices in greater detail than ever before. Beyond these topics, however, there is a much broader range of relevant research areas that will also benefit from Diamond-II, including solid oxide fuel cells, supercapacitors, bioenergy, solar-to-fuel, solid-state batteries, hydrogen storage and flow cells amongst many others. This research is of direct relevance to two of the UK government Grand Challenges³, clean growth and future mobility, by helping to develop low carbon and mobile battery technologies. It also contributes directly to the areas that are the focus of the Faraday Challenge that includes specific goals for the automotive sector, such as increasing the power density of batteries by a factor of four (from 3kW/kg to 12kW/kg), increasing the battery lifetime from 8 to 15 years and improving the recyclability from 10-50% to 95%, all by 2035. Similarly, the Henry Royce Institute has a focus on materials innovation to drive economic growth,

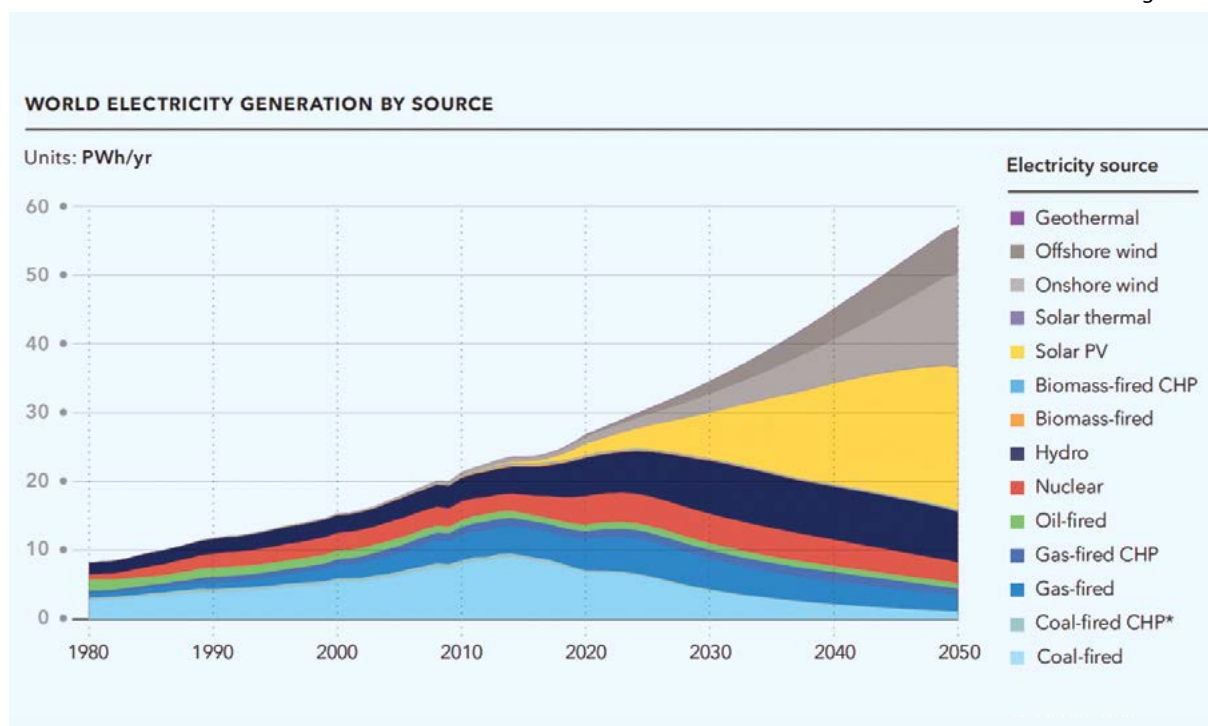


Figure 1: Projected world electricity generation by source. Figure taken from DNV-GL Energy Transition Outlook Report 2017, <https://eto.dnvgl.com/2017/main-report>.

including research into energy storage materials with the aim to solve the challenges involved in an all-solid-state battery and materials for energy efficient ICT such as in low power processing and memory materials.

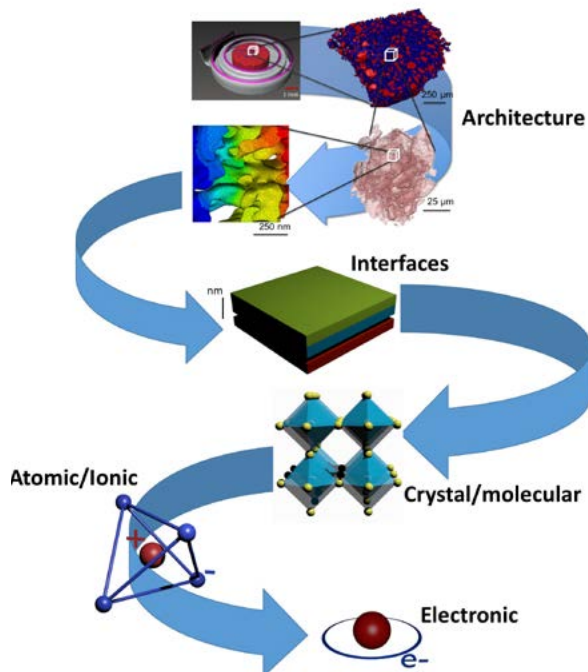


Figure 2: Schematic representation of the multiscale challenge in energy research with reference to a battery cell. Processes are governed at many length scales, ranging from the macrostructure down to the level of electronic states. Copyright Diamond Light Source. Courtesy of P. Shearing for the top part of the figure.

Synchrotron science has a significant role to play in helping to develop these new technologies, in particular through: supporting the discovery of new materials that are both more efficient and robust against degradation; improving new device architectures that are likely to be more complex multi-component structures; and through a thorough understanding of the electronic, chemical and structural state of the devices at a range of length scales and under *operando* conditions. This relies on a coordinated approach, involving a wide range of spectroscopy, imaging and scattering techniques from across Diamond and the wider synchrotron community. Figure 2 shows this hierarchical approach as applied to battery materials, where many of the important processes occur on these different length scales. For example, conduction pathways may be governed by the granular microstructure, whilst degradation could be due to atomic scale phase changes, interface effects or nanoscale coarsening.

Device architectures are increasingly being customised so that different materials are brought together to form more complex device stacks that improve the device functionality. It is widely recognised that interface effects

between the materials play a crucial role in device performance and future challenges include having to identify the interface effects with ever greater spatial and time resolution, chemical sensitivity and under realistic operating conditions. This can be addressed using synchrotron light but requires *operando* spectroscopic and scattering studies that exploit extremely focussed beams, high beam energies and coherence; all factors that are greatly improved by the proposed Diamond-II upgrade. One example is research into developing solid oxide electrochemical cells (fuel cells, electrolyzers) where a key consideration is the processes that are occurring at the gas to solid and solid to solid interfaces. These dictate the overall cell performance as they limit the charge transfer and mass transport. In operating cells, the interfaces of critical importance are those that are electrochemically active, i.e. in regions close to the ceramic electrolyte. As the electrodes are typically of the order of 30 μm thick, and the active region is only the 2-3 μm close to the electrolyte, the challenge for cell developers is to probe the *buried* interface. Whilst it is feasible to probe model systems currently, the opportunity to probe these interfaces in operational devices is extremely challenging given that the fuel/electrolyte/air electrode interfaces are of equal interest. This means that ideally a single measurement would provide correlative information on structure, electrochemistry, redox processes and microstructure, requiring high spatial resolution and depth penetration, as well as innovative sample environment design.

7.2.1. Battery research

Since the proposal by Goodenough to use lithium-cobalt oxide as the cathode for a battery in 1980³, and its commercialisation by Sony Corporation, the Li-ion battery market has grown exponentially with predictions that it will reach \$93 billion globally by 2025⁴. The ever-increasing need for portable electronics and electric vehicles places heavy demands on battery capacity, calling for further improvements of energy density and a continuous reduction of cost. Likewise, the energy needs for information and communication technology is growing rapidly⁵ with data centres of the big five global information traders already using 1% of global electricity, whilst forecasts of the electricity use by the information industry predict an increase of up to 8% of the projected global demand by 2030⁴. Although the energy supply from renewable technology is rising rapidly (Google is currently the largest corporate purchaser of renewable energy⁵), the need for affordable large-scale grid storage solutions is urgent. This will rely on a range of solutions including chemical or hydrogen storage whilst battery technology can also play a major role, where sustainable long-term viability will require a step-change improvement of materials cyclability and low production costs, likely requiring solutions beyond Li-ion technology and minimising the use of strategic metals. The UK aims to become a world leader in battery

Diamond-II: Advancing physical sciences

technology for the automotive sector by investing in the Faraday Challenge⁶, a mission-driven research, innovation and scale up programme announced in 2017, as part of the Industrial Strategy Challenge Fund. In addition to novel large-scale manufacturing solutions, the challenge resides in developing new materials, and gaining a fundamental understanding of electronic, chemical and structural properties (from atomic scale to architectures at the mesoscale). This aspect aligns very well with the Atoms to Devices theme of the Henry Royce Institute and will likely lead to breakthroughs in storage capacity, longevity and safe operation of batteries.

Synchrotron X-ray experiments have been at the heart of this materials challenge since the end of the 1980s, with the first experiment to probe the atomic structure using spectroscopy⁷, and contributing to several key discoveries ever since. For example, one of the very first *in situ* synchrotron X-ray diffraction (XRD) experiments on a plastic commercial Li-ion battery in 1999⁸ revealed a tiny reduction of the O-O interplanar distance at high potential, and suggested that the oxygen ions are active contributors to the redox reaction in this regime. After 20 years of active research, and further experimental evidences by a range of characterisation methods including X-ray spectroscopy, the anion (O,S) redox mechanism is considered nowadays as a serious contender⁹ to engineer high capacity cathode materials in the so-called Li-rich phases but also for N-ion batteries¹⁰. Whilst the cathode capacity in these Li-rich materials is at least 25% higher than current technology, the batteries suffer from the voltage-fade problem, i.e. a gradual reduction of the voltage upon cycling. This is a true

multidimensional problem (electronic, chemical, structural) and also a complex multiscale problem¹¹ with a lot of open fundamental questions that need tackling by experiments and theory. Whilst the Faraday Institution has recognised this through its “*Multiscale modelling*” fast track project, provision of a “*Multiscale X-ray measurements*” programme is also essential to push the frontiers of knowledge that will feed advances in technology.

At the electronic level, the recent progress in energy resolution and efficiency of soft-Resonant X-ray Inelastic Scattering (RIXS) has enabled exquisitely detailed studies of the electronic properties of oxygen and sulphur ions in Li-rich and Na cathodes, as the potential is varied^{12–15}. Strong evidence of an electronic reconstruction due to oxygen redox at a specific potential have emerged, encoded in weak inelastic excitations. This is clearly visible in the two dimensional (2D) scattering intensity maps as a function of the excitation and emission energy (Figure 3), but difficult to interpret in a conventional X-ray absorption spectroscopy (XAS) experiment due to the signal integration in one dimension. These types of experiments are extremely time consuming at present, as they require recording of the emission energy spectra for each value of the scanned excitation energy. A multiplexed version of the RIXS spectrometer (Figure 3)¹⁶, only possible at a low emittance source (or a FEL) will allow data collection rates to be increased by a factor 100 at Diamond-II and would have great applicability for battery research. The improved brightness in the tender X-ray range (1-5 keV) offered by the Diamond-II 3.5 GeV upgrade (factor of 20 at 2.5 keV) will also open the possibility for fast studies of redox processes

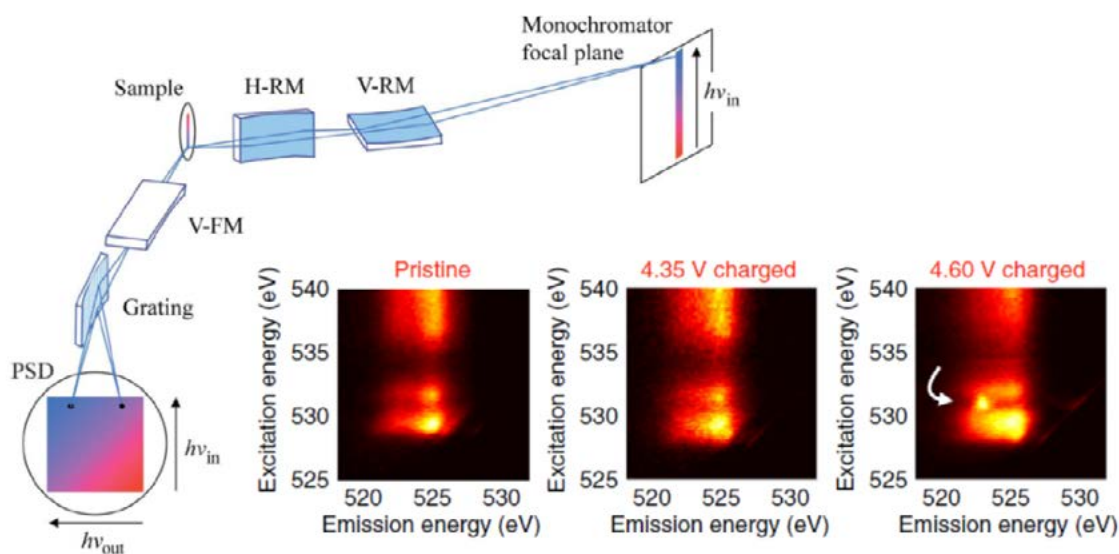


Figure 3: Concept of the multiplexed RIXS instrument proposed by Strocov¹⁶ and oxygen K-edge RIXS collected at different voltage for $\text{Li}_{1.17-x}\text{Ni}_{0.21}\text{Co}_{0.08}\text{Mn}_{0.54}\text{O}_2$ ¹⁴. Left: Strocov, V. N. Concept of a spectrometer for resonant inelastic X-ray scattering with parallel detection in incoming and outgoing photon energies. *J. Synchrotron Rad.* 17, 103–106 (2010). Right: Gent, W. E. et al. Coupling between oxygen redox and cation migration explains unusual electrochemistry in lithium-rich layered oxides. *Nat. Commun.* 8, 2091 (2017) <https://creativecommons.org/licenses/by/4.0/>.

in Li-sulphur batteries¹⁷, a highly promising material class for which the capacity fading problem needs to be understood. Moreover, the low emittance of Diamond-II will naturally allow expansion of the technique to nano-RIXS¹⁸ enabling spatial mapping of excitations to probe electronic structures when inhomogeneity is a relevant parameter, as certainly is the case in battery electrodes.

Many of the processes that occur in an operational battery rely on the movement or changing chemical state of light ions or atoms. Monitoring these processes has been challenging due to either lack of probe penetration or poor resolution. Diamond-II could address this through development of novel techniques such as a state of the art X-ray Raman Scattering (XRS)¹⁹ instrument to perform spectroscopy studies of light elements using hard X-rays, enabling *in situ* and *operando* studies with bulk sensitivity, that would complement the soft X-ray surface studies available at beamlines such as B07. Spectrometers with a much increased efficiency (due to the large arrays of analyser crystals used²⁰) have recently been employed to perform studies on Li electrode materials^{21,22}, but also to study electrolyte solutions (C and O K-edge) in a flow cell²³. Such an instrument would complement our current spectroscopic capabilities, in particular since the increased brightness of Diamond-II will push the energy-resolution of XRS further²⁰.

At the structural level, XRD measured on *ex situ* electrodes provides insights into, for example, the intercalation reactions in LiFePO_4 at the atomic scale²⁴. Such steady-state investigations, however, reveal only a snapshot of quasi-equilibrium conditions. Only *in situ* and *operando* experiments can provide information about non-equilibrium phase transitions, metastable phases or phase separation under realistic high-rate cycling conditions²⁵. Furthermore, small angle X-ray scattering (SAXS) combined with the pair-distribution function (PDF) technique is a powerful combination to probe the particle size and shape²⁶. Although such experiments provide valuable information, based on an ensemble average, they are not able to distinguish intra-particle or inter-particle multi-phase reactions.

In the field of battery research, μXRD provides the spatial resolution required to understand the processes that limit battery performance, such as capacity, power, and lifetime, from the atomic scale upwards. The degradation mechanisms associated with, for example, the solid-electrolyte interphase (SEI) that forms at interfaces within the battery are on a length scale of tens of nanometres to several micrometres. Monitoring the formation and changes that occur in real time and during operation with chemical sensitivity (for example tuning to X-ray absorption edges) will give unparalleled structural information including the role that the granular structure plays. Time-resolved *operando* experiments would provide key information of dynamic and kinetic processes

during charging and discharging of real devices, and the effects of rapid charging could be studied. There would be significant potential to develop optimised interface geometries that could extend battery lifetimes, improve charging rates and limit failure modes. Diamond-II, together with recent developments of μXRD ²⁷ (including high spatial and temporal resolution²⁸) would improve studies of subtle structural effects, which can influence both conductivities and rates of ion diffusion in batteries. This will go beyond current XRD experiments that revealed, for example, volume changes associated with the (de)lithiation of an intermetallic “Sn-based, Li-alloying anode” during (dis)charging cycles²⁹. Higher spatial resolution data are needed to correlate these structural effects with the diffusion and chemical reaction kinetics, a multi-technique approach that could lead to an increased cycle life of this type of anode. The potential of μXRD is highlighted by an experiment carried out at the ESRF using X-rays at 40 keV and a beam size of $1.7 \mu\text{m}$ ³⁰, where it was possible to reveal cycling rate-dependent phase transformation mechanisms within individual grains of a LiFePO_4 electrode. The results show that at high (dis)charge rates, dynamically induced diffuse interfaces avoid the build-up of local coherent lattice strain at sharp phase boundaries and hence prevent the formation of cracks. These challenging experiments will become possible at Diamond-II (due to the increased energy and better focussing of the photon beam) and could be combined with Bragg CDI³¹ (see Figure 4) to match the atomic scale parameters to the grain size, shape and nanoscale strain.

Several battery characteristics rely on the interaction between different materials and phases, including both crystalline and amorphous structures. A multi-technique approach of PDF in combination with SAXS could establish links between the structure and chemistry across multiple length scales²⁶. High-flux and high-energy X-rays with a micrometre sized beam size would be required to distinguish intra- or inter-particle multi-phase reactions. Furthermore, the combination of the PDF technique and Computed Tomography (CT) makes it possible to produce a detailed spatial map with quantitative structural parameters, including the crystalline and nano-crystalline or amorphous components of the sample³². This technique was used to study specific components of a Na-ion battery and to extract spatially resolved information on crystalline and amorphous phases present during cycling³³. At Diamond-II, it will be possible to use high-energy X-rays with micrometre beam size and high flux for combined diffraction and PDF-CT studies.

At the micro and mesoscale, soft and hard X-ray imaging techniques are already regularly employed for battery research, in particular radiography and tomography³⁴ to understand the failure mechanisms and developing certification processes. This is critical given both the surge in Li battery-powered devices and some of the high profile

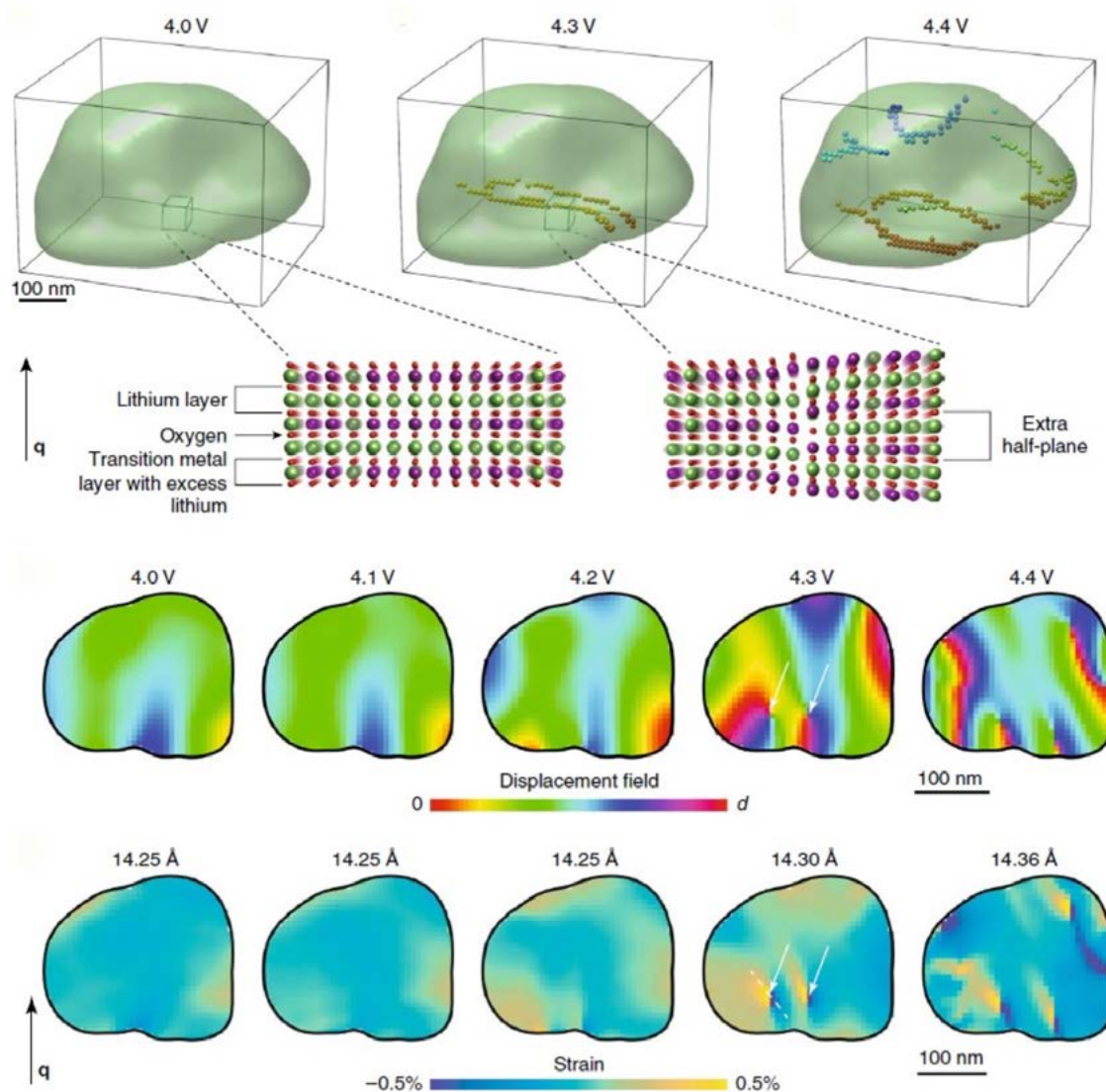


Figure 4: (Top) Nanoscale dislocations in a Li-rich particle measured during charging, by Bragg Coherent Diffraction Imaging. (Second row) Schematic of an edge dislocation. (Third row) The changes in the displacement field along q in a plane through the nanoparticle during charge. The voltage vs. Li^+ is indicated. Two edge dislocations are identified as singularities of the displacement field and are indicated at 4.3 V vs. Li^+ (white arrows). Additional dislocations emerge at 4.4 V vs. Li^+ . (Bottom) The strain along the (001) direction (perpendicular to the layers) inside of the nanoparticle calculated from the 3D displacement fields. The strain is shown around the average lattice constant indicated at the top of each strain field. Figures taken from Ref³¹. Reprinted by permission from Copyright Clearance Center: SpringerNature, Nature Energy, Nucleation of dislocations and their dynamics in layered oxide cathode materials during battery charging, Singer, A. et al., Copyright (2018).

safety issues seen with products such as the Boeing 787 Dreamliner³⁵ and Samsung Note 7. Imaging morphological changes that occur during the lifetime of rechargeable batteries is necessary to understand how these devices fail. For example, structural buckling of electrodes is known to occur in abused batteries and was the failure mode of the Samsung Note 7³⁶, while more subtle distortions found in normal use are poorly understood. Local inhomogeneity in the electrode materials can lead to current focussing and formation of “hot spots” that can seriously compromise safety, and certainly impair battery performance. However, most battery materials are air sensitive making sample preparation for analysis by electron microscopy and traditional optical microscopy difficult, requiring imaging of the full battery assembly or within a specialist cell.

Diamond-II will enable *operando* studies of large devices, such as imaging the growth and evolution of Li dendrites, chemical evolution in the battery or transport in the solid-electrolyte interphase. The increased brilliance and phase contrast (x20) available at Diamond-II will have a significant impact by allowing studies with greater spatial and time resolution, improving the sensitivity to fine scale changes and dynamics. Combined *in situ* imaging and diffraction mapping of normal and abnormal phase changes during battery cycling with improved spatial resolution (currently $\sim 8\mu\text{m}$) would provide a better match to the important grain sizes that are typically a few micrometres or smaller in battery devices. The Diamond-II upgrade would enable a $1\mu\text{m}$ focal spot and increased intensity (gain factor of 70 at 10 keV, and 10 at 35 keV) for microscale studies of operational devices.

Emergent phenomena can develop in battery materials and influence the device characteristics. For example, the chemical composition and microstructure of the SEI, or leeching of material from the electrodes has a direct impact on charging rates and capacity. Understanding the 3D elemental and structural information over a large field of view but with high resolution is key to understanding these processes at the nanoscale. One key technique, still in its infancy for battery research is soft X-ray ptychography-tomographic reconstruction. Initial experiments have focused on individual nanoparticles of LiFePO_4 , revealing the phase boundaries in 3D with 11 nm resolution³⁷ and highlighting the importance of size effects on the electrochemical activity. Another recent study using Bragg CDI³¹ has revealed a high rate of dislocations in nanoparticles of Li-oxide rich phases compared to other oxides, directly linking this phenomena to the voltage fade problem, but also reporting that thermal annealing recovers the initial properties. The increase in brightness available at Diamond-II, combined with broad bandwidth radiation will make these techniques routine at the 10 nm scale and will allow access to sub 5 nm resolution. It is also important to note that many of these materials do not suffer from radiation damage, so that the increased brightness gained by some technique such as soft X-ray ptychography can be efficiently exploited.

7.2.2. Photovoltaics

The ability to convert solar radiation, which delivers a vast amount of power to the Earth's surface, is limited by a number of factors such as efficiency, ability to withstand long-term exposure to solar radiation, materials degradation, toxicity of the materials used and cost. The global photovoltaic market is forecast to grow to an output level of 200 GW by 2022, with emerging technologies predicted to account for 25% of this³⁸. Solar cell technology is rapidly developing due to the wide range of materials systems that are being developed in parallel. Whilst silicon remains dominant as the market leader in both its

crystalline and amorphous forms due to its high power conversion efficiency of greater than 26% (close to the theoretical limit of 29%) and mature processing methods, it has drawbacks including its rigid panel requirements and indirect band gap. Several technologies³⁹ are based around low cost solution processing or vacuum deposition that are scalable and could potentially provide global power on the terawatt scale. The low temperature processing also means that these layered structures can be grown on flexible substrates opening up new markets. Independent of the specific material systems studied, there are a number of factors that affect the efficiency of the solar cell including the absorption rate of the incident photons, their ability to create an electron hole pair, reducing detrimental recombination routes and improving the conduction pathways to the electrodes. Addressing these challenges involves understanding the device structure, composition and dynamic processes over a wide range of length scales and timescales.

Improving the active layer in photovoltaic materials is a significant research effort including development of ternary and quaternary semiconductors such as CIGS ($\text{CuIn}_x\text{Ga}_{1-x}\text{Se}_2$) or kesterite structures like CZTS ($\text{Cu}_2\text{ZnSnS}_4$), halide perovskite structured semiconductors such as methylammonium lead iodide ($\text{CH}_3\text{NH}_3\text{PbI}_3$) and organic photovoltaic (OPV) structures based on a bulk heterojunction morphology. Equally important is the device architecture with a move towards thin film multi-junction geometries, where the layers are tailored to a specific role to improve processes such spectral absorption, charge transfer or to limit recombination. Controlling these parameters can be achieved in a number of ways including through band engineering by doping/defect incorporation through production of vacancies, concentrator geometries to increase the incident flux levels or modifying the microstructure. Whilst understanding pristine devices is a key requirement, identifying and limiting the degradation processes that occur over time is equally critical. Diamond-II will offer improved insight into photovoltaic structures in a number of important ways; smaller spot sizes will enable

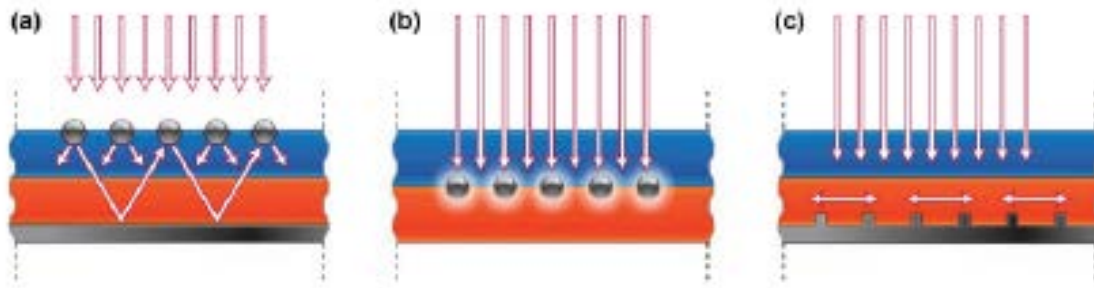


Figure 5: Plasmonic light trapping processes in thin film solar cells. (a) Scattering from the metal nanoparticles increases the effective light path leading to increased absorption, (b) localised surface plasmons on the particles are excited, creating an electric field enhancement around the particles, leading to increased absorption and (c) surface plasmon polaritons are excited at the metal dielectric interface leading to improved coupling. Ahn, S., Rourke, D. & Park, W. Plasmonic nanostructures for organic photovoltaic devices. *J. Opt.* 18, 033001 (2016). © IOP Publishing. Reproduced with permission. All rights reserved.

greater structural, chemical and electronic understanding of microstructured samples, an increase in flux at higher energies will allow deeper penetration through more complex device stacks and under *operando* conditions and the higher coherent flux can be used to study the effects of the strain profile in nanoparticle additives.

At the electronic and chemical level, valence band states and electronic core levels can be probed using synchrotron techniques including XAS, RIXS and hard X-ray photoelectron spectroscopy (HAXPES). This is elegantly shown in studies of the ternary bismuth halide $\text{Cs}_3\text{Bi}_2\text{I}_9$, where the combined techniques gave insight into atomic level electronic structure⁴⁰. This is a material of potential interest for photovoltaic application due to its replacement of toxic lead by bismuth and potential benefits such as improved stability. By studying the material and its related precursors the authors were able to establish that during the processing, the iodine states shifted to different positions within the valence and conduction bands associated with a changing degree of hybridisation with the bismuth states. Links were made as to how the crystal structure created a small perturbation to the electronic state. This material also has a relatively large band gap (2.2 eV) meaning that it has potential application in tandem solar cell devices (where two light absorbing layers with different band gaps are deposited onto the substrate to enhance the wavelength response of the device). Diamond-II will provide increased penetration for such studies, the energy tunability of the incoming X-rays allows depth profiling of the chemical and electronic states; information that will be critical in developing these more complex multi-junction devices.

These techniques are also able to give insight into degradation processes, such as those that occur through oxygen interaction with dopants in silicon photovoltaic structures⁴¹. Light induced degradation has been observed in boron doped silicon, attributed to the formation of B-O defect pairs introducing a deep state in the band gap that acts as an efficient non-radiative recombination centre⁴². There is, as yet, no consensus as to the underlying atomistic processes, details of which could be investigated using Diamond-II and the techniques described above. The dilute nature of the dopants and the requirement to understand the distribution of the defect centres would benefit from the small spot sizes and higher energies that will be available.

At the structural level, microstructure or nanoscale additives can affect the recombination and conduction pathways. The ability to control the distribution of point defects in films has been discussed by Park *et al*⁴², who identify the role that interstitial atoms, vacancies and grain boundary structure can have on the device efficiency. Dopants can introduce defect levels within the band gap leading to improvement in the photon absorption whilst strain in the structures can also shift the electronic energy

levels. Diamond-II with its smaller spot sizes and increased coherent flux will enable detailed measurement of the strain (see Figure 4) or mapping of dopant distribution within the materials.

In organic photovoltaic systems, intermixed blends of organic semiconductors are created to produce and carry the electric charge. The generation of an exciton has to occur within ~10 nm of an interface so that it can diffuse to it and be split into free charge carriers that are then transported to their respective electrodes on efficient conduction pathways; critical is the right balance between separating every photo-generated exciton (more mixed materials) and efficient transport pathways (coarser structures). These nanoscale and microscale features can be investigated by a number of powerful techniques including grazing incidence small angle and wide angle X-ray scattering (GISAXS, GIWAXS)^{43,44}. The scattering features reveal information on the size, shape, separation and orientation of the nanostructures. The smaller beam sizes provided by Diamond-II together with new fast detectors and increased flux at higher energies will enable studies under 'real world' conditions, opening up the prospect of revealing dynamics of materials during processing or operation.

Another promising direction for developing the next generation of photovoltaic materials is based on intrinsic or induced chiral organic polymers packed in supramolecular helical structures. The efficiency of the OPV films depends on the formation of stable helical structures. The B23 beamline for synchrotron radiation circular dichroism (SRCD) is the only tool worldwide that can directly identify and quantify these crucial helical structures in solid state thin films and image large areas at an unprecedented spatial resolution of 50 micrometres. It is more difficult to determine unambiguously the presence and handedness of helical structures in thin films using other synchrotron techniques. The upgrade of B23, envisaged as part of Diamond-II, will enable the CD imaging of OPV structures and also of circularly polarised organic emitting diodes (CP-OLED), the next generation of display materials, at 1 micrometre spatial resolution.

The perovskite family of materials offers huge potential with record efficiencies rising from 4% to 22% in less than a decade. The performance of the perovskite is linked to defects associated with the nano and microstructural properties of the films and current research is focussed both on understanding this link, optimising processing steps (e.g. annealing) and on moving away from toxic lead based compositions⁴⁵. A combination of imaging and diffraction techniques with smaller spot sizes, together with grazing incidence XRD and X-ray reflectivity would enable detailed analysis of the structure including the distribution of defects during operations such as solution-based processing and drying.

At the device level, there is significant effort to reduce the

losses that occur at the interfaces of all of the component layers. Every operating device must have at least two interfaces between the active layer and the electrodes, whilst multicomponent thin film morphologies will have many more. There will be a significant role for studies of model systems, to gain real details of the interfaces. Crystal truncation rod (CTR) analysis is able to accurately identify the interface structure in single crystal model systems, including any strain or the registry between the layers – important factors that affect characteristics such as the Schottky barrier height that can lead to energy losses. Some studies of complex perovskite thin films have been reported, based around novel Bayesian analysis methods⁴⁶ that are likely to become essential to interpret data from more complex multi-layered structures. The higher energies and small beams available at Diamond-II will enable faster measurement of these structures under real operating conditions, giving insight into the energy loss mechanisms.

The incorporation of plasmonic structures into different regions of the organic photovoltaic stack is already making an impact on device performance⁴⁷. The structures include embedded metal nanoparticles, patterned electrodes and plasmonic metamaterials. They can operate in different ways within the structure (Figure 5); for example, metal nanoparticless can improve OPV performance due to enhanced scattering and local field enhancement resulting from the excitation of localised surface plasmon resonances at the interface between the metal and dielectric. This causes a concentration of the electric field at the interface leading to an increase in optical absorption. Patterned electrodes provide a localised field enhancement and increased optical path length by coupling into the surface plasmon polaritons.

It is essential to control and optimise the distribution of metal particles within the device as the plasmon resonances depend critically on parameters such as particle size, composition, strain in the structure and the surrounding environment. Diamond-II will enable chemical mapping with small beams together with studies of the strained particles by microdiffraction or coherent imaging under *operando* conditions (including under illumination) that will enable optimisation of the processing conditions.

Studies of energy materials and processes will remain important for years to come, addressing the requirements of increasing demand for energy while reducing the impact on the environment. The two areas that have been highlighted as examples show how synchrotron science will be crucial in these developments. The techniques discussed will be applicable across the whole research area and have already had major impact in fields such as hydrogen storage technology, solid oxide fuel cells or bioenergy. Diamond-II will be transformative for energy research and will require input from all of the science

groups, real space imaging combined with diffraction to determine structural information, spectroscopic studies of the chemical and electronic states, studies of interface phenomena and detailed studies of low power quantum devices will all add to the drive to produce a global sustainable energy economy.

References

1. UKRI Strategy Document. (2018). Available at: <https://www.ukri.org/files/about/ukri-strategy-document-pdf/?pdf=Strategic-Prospectus>.
2. Agreement, T. P., Contributions, N. D. & Agreement, T. P. The Paris Agreement on Climate Change. *Mini-Symposium Paris Agreem. Clim. Chang.* **1**, 1–4 (2015).
3. Mizushima, K., Jones, P. C., Wiseman, P. J. & Goodenough, J. B. $\text{Li}_x\text{CoO}_2(0 < x \leq 1)$: A new cathode material for batteries of high energy density. *Solid State Ionics* **3–4**, 171–174 (1981).
4. Grand View Research. *Lithium-Ion Battery Market Analysis By Product (Lithium Cobalt Oxide, Lithium Iron Phosphate, NCA, LMO, LTO, Lithium Nickel Manganese Cobalt (NMC)), By Application, And Segment Forecasts, 2018 - 2025.* (2017).
5. Jones, N. How to stop data centres from gobbling up the world's electricity. *Nat.* **2018** 5617722 **561**, 163–166 (2018).
6. GOV.UK. Faraday battery challenge: Industrial Strategy Challenge Fund - GOV.UK. GOV.UK (2018). Available at: <https://www.gov.uk/government/collections/faraday-battery-challenge-industrial-strategy-challenge-fund>. (Accessed: 16th October 2018)
7. McBreen, J., O'Grady, W. E. & Pandya, K. I. EXAFS: A new tool for the study of battery and fuel cell materials. *J. Power Sources* **22**, 323–340 (1988).
8. Tarascon, J. M. *et al.* *In Situ* Structural and Electrochemical Study of $\text{Ni}_{1-x}\text{Co}_x\text{O}_2$ Metastable Oxides Prepared by Soft Chemistry. *J. Solid State Chem.* **147**, 410–420 (1999).
9. Assat, G. & Tarascon, J. M. Fundamental understanding and practical challenges of anionic redox activity in Li-ion batteries. *Nat. Energy* **3**, 373–386 (2018).
10. Zhao, C. *et al.* Review on anionic redox for high-capacity lithium- and sodium-ion batteries. *Journal of Physics D: Applied Physics* **50**, (2017).
11. Yang, W. Oxygen release and oxygen redox. *Nature Energy* (2018). doi:10.1038/s41560-018-0222-0
12. Maitra, U. *et al.* Oxygen redox chemistry without excess alkali-metal ions in $\text{Na}_2/3[\text{Mg} 0.28 \text{Mn} 0.72]\text{O}_2$. *Nat. Chem.* **10**, 288–295 (2018).
13. Gent, W. E. *et al.* Coupling between oxygen redox and cation migration explains unusual electrochemistry in lithium-rich layered oxides. *Nat. Commun.* **8**, (2017).
14. Yang, W. & Devereaux, T. P. Anionic and cationic redox and interfaces in batteries: Advances in soft X-ray absorption spectroscopy to resonant inelastic scattering. *Journal of Power Sources* **389**, 188–197 (2018).
15. Kavčič, M. *et al.* *Operando* Resonant Inelastic X-ray Scattering: An Appropriate Tool to Characterize Sulfur in Li-S Batteries. *J. Phys. Chem. C* **120**, 24568–24576 (2016).
16. Strocov, V. N. Concept of a spectrometer for resonant inelastic X-ray scattering with parallel detection in incoming and outgoing photon energies. *J. Synchrotron Rad.* **17**, 103–106 (2010).

17. Kang, W. *et al.* A review of recent developments in rechargeable lithium-sulfur batteries. *Nanoscale* **8**, 16541–16588 (2016).
18. Schmitt, T., De Groot, F. M. F. & Rubensson, J. E. Prospects of high-resolution resonant x-ray inelastic scattering studies on solid materials, liquids and gases at diffraction-limited storage rings. *J. Synchrotron Rad.* **21**, 1065–1076 (2014).
19. Miedema, P. S. Raman Spectroscopy with X-Rays. *Raman Spectrosc. Appl.* (2017). doi:10.5772/65427
20. Sala, M. M. *et al.* A high-energy-resolution resonant inelastic X-ray scattering spectrometer at ID20 of the European Synchrotron Radiation Facility. *J. Synchrotron Rad.* **25**, 580–591 (2018).
21. Pascal, T. A. *et al.* Finite temperature effects on the X-ray absorption spectra of lithium compounds: First-principles interpretation of X-ray Raman measurements. *J. Chem. Phys.* **140**, 34107 (2014).
22. Braun, A. *et al.* Hard X-rays in-soft X-rays out: An *operando* piggyback view deep into a charging lithium ion battery with X-ray Raman spectroscopy. *J. Electron Spectros. Relat. Phenomena* **200**, 257–263 (2015).
23. Ketenoglu, D. *et al.* X-ray Raman spectroscopy of lithium-ion battery electrolyte solutions in a flow cell. *J. Synchrotron Rad.* **25**, 537–542 (2018).
24. Delmas, C., Maccario, M., Croguennec, L., Le Cras, F. & Weill, F. Lithium deintercalation in LiFePO₄ nanoparticles via a domino-cascade model. *Nat. Mater.* **7**, 665–671 (2008).
25. Liu, H. *et al.* Capturing metastable structures during high rate cycling of LiFePO₄ nanoparticle electrodes. *Science (80-.)*. **344**, 1–23 (2014).
26. Wiaderek, K. M. *et al.* Mesoscale effects in electrochemical conversion: Coupling of chemistry to atomic- and nanoscale structure in iron-based electrodes. *J. Am. Chem. Soc.* **136**, 6211–6214 (2014).
27. Ice, G. E., Budai, J. D. & Pang, J. W. L. The Race to X-ray Microbeam. **334**, 1234–1240 (2011).
28. Huang, Z. *et al.* Grain rotation and lattice deformation during photoinduced chemical reactions revealed by *in situ* X-ray nanodiffraction. *Nat. Mater.* **14**, 691–695 (2015).
29. Glazer, M. P. B. *et al.* In *operando* X-ray diffraction strain measurement in Ni₃Sn₂-Coated inverse opal nanoscaffold anodes for Li-ion batteries. *J. Power Sources* **367**, 80–89 (2017).
30. Zhang, X. *et al.* Direct view on the phase evolution in individual LiFePO₄ nanoparticles during Li-ion battery cycling. *Nat. Commun.* **6**, 1–7 (2015).
31. Singer, A. *et al.* Nucleation of dislocations and their dynamics in layered oxide cathode materials during battery charging. *Nature Energy* 1–7 (2018). doi:10.1038/s41560-018-0184-2
32. Jacques, S. D. M. *et al.* Pair distribution function computed tomography. *Nat. Commun.* **4**, 1–7 (2013).
33. Sottmann, J. *et al.* Chemical Structures of Specific Sodium Ion Battery Components Determined by *Operando* Pair Distribution Function and X-ray Diffraction Computed Tomography. *Angew. Chemie - Int. Ed.* **56**, 11385–11389 (2017).
34. Finegan, D. P. *et al.* Characterising thermal runaway within lithium-ion cells by inducing and monitoring internal short circuits. *Energy Environ. Sci.* **10**, 1377–1388 (2017).
35. Williard, N., He, W., Hendricks, C. & Pecht, M. Lessons learned from the 787 dreamliner issue on Lithium-Ion Battery reliability. *Energies* **6**, 4682–4695 (2013).
36. Moynihan, T. Samsung Finally Reveals Why the Note 7 Kept Exploding. 1–9 (2017). Available at: <https://www.wired.com/2017/01/why-the-samsung-galaxy-note-7-kept-exploding/>. (Accessed: 16th October 2018)
37. Yu, Y. S. *et al.* Three-dimensional localization of nanoscale battery reactions using soft X-ray tomography. *Nat. Commun.* **9**, (2018).
38. Global Photovoltaic Market Report 2018-2022. Available at: <http://www.pvmarketalliance.com/downloads/flagship-report-number-one-2016/>.
39. Pearson, A. J. Structure formation and evolution in semiconductor films for perovskite and organic photovoltaics. *J. Mater. Res.* **32**, 1798–1824 (2017).
40. Phuyal, D. *et al.* The electronic structure and band interface of cesium bismuth iodide on a titania heterostructure using hard X-ray spectroscopy. *J. Mater. Chem. A* **6**, 9498–9505 (2018).
41. Lindroos, J. & Savin, H. Review of light-induced degradation in crystalline silicon solar cells. *Sol. Energy Mater. Sol. Cells* **147**, 115–126 (2016).
42. Park, J. S., Kim, S., Xie, Z. & Walsh, A. Point defect engineering in thin-film solar cells. *Nature Reviews Materials* **3**, 194–210 (2018).
43. Agostinelli, T. *et al.* Real-Time Investigation of Crystallization and Phase-Segregation Dynamics in P3HT:PCBM Solar Cells During Thermal Annealing. *Adv. Funct. Mater.* **21**, 1701–1708 (2011).
44. Dippel, A.-C. *et al.* Local atomic structure of thin and ultrathin films via rapid high-energy X-ray total scattering at grazing incidence. *IUCr* **6**, 290–298 (2019).
45. Ban, M. *et al.* Solution-processed perovskite light emitting diodes with efficiency exceeding 15% through additive-controlled nanostructure tailoring. *Nat. Commun.* **9**, 3892 (2018).
46. Anada, M., Nakanishi-Ohno, Y., Okada, M., Kimura, T. & Wakabayashi, Y. Bayesian inference of metal oxide ultrathin film structure based on crystal truncation rod measurements. *J. Appl. Crystallogr.* **50**, 1611–1616 (2017).
47. Ahn, S., Rourke, D. & Park, W. Plasmonic nanostructures for organic photovoltaic devices. *J. Opt.* **18**, 033001 (2016).

7.3. Chemistry

Chemistry is a fundamental science to modern life that has been directly responsible for improvements in health (pharmaceuticals), agriculture (fertilisers and pest control) and energy (petrochemicals). From a national perspective, chemistry will be an essential tool for realising the technologies required to deliver on the Clean Growth Grand Challenge identified by the UK Government, detailed in the 2018 policy document¹. In 2016, the UK chemicals sector accounted for £12.1 billion of the UK economy's Gross Value Added² and directly provides approximately 100,000 jobs³. The Chemical Industry Association estimates that chemical and pharmaceutical businesses in the UK contribute £60m of added value every single working day to the UK's Gross Domestic Product (GDP).

Examples of chemical impact in modern society include the realization of new routes for water splitting and methods for the efficient production of biofuels as solutions for future energy needs. Major efforts are also directed to the search for new catalysts that can be used as alternatives to the currently dominant "strategic" metals (mostly elements of the platinum group), as these rare elements have limited long-term availability and their access are subject to geopolitical risks. Chemistry's role in the discovery and development of new functional materials, and the innovative uses of existing materials, is vitally important to maintain steady technological progress. Here the main challenge is threefold: discover new generations of materials, reduce time to market from a new material discovery; a process that currently can take from 5 to 10 years⁴, and finally push the frontiers of knowledge by acquiring a fundamental understanding of how materials work.

For many decades now, synchrotron radiation facilities have made major contributions to the development of chemical knowledge. The use of spectroscopy and scattering techniques, and more recently imaging, is providing a detailed understanding of the geometrical and electronic structures of the different species involved in chemical processes and relates this knowledge to function. The development of high-brilliance third-generation sources has freed us from studying model systems primarily under vacuum, enabling us to follow fast processes near-*operando* and under realistic reaction conditions of concentration, temperature, and other external parameters, all of this at very different length scales, from probing the atomic structure, the long-range order structure or obtaining information at the meso-scale.

The advent of fourth generation synchrotron sources, such as Diamond-II, with a strongly reduced horizontal emittance, will provide new tools to understand processes and develop advanced materials. The increased brightness of Diamond-II, together with the improvement of detector technology and nanofocussing optics, will enable the study of chemical processes under real conditions of operation

with unprecedented spatial resolution down to nanometers. New techniques exploiting the increased coherence of the photon beam, for example Bragg Coherent Diffraction imaging (Bragg-CDI), will provide routine access to parameters such as strain in nanoparticles during catalytic reactions.

7.3.1. Catalysis

Catalysis research is fundamental to the sustainability of our modern way of life. Catalysts are involved in the process of more than 80% of manufactured products; most of them used by modern societies for fuels, chemicals, polymers, and pharmaceuticals, as well as for abatement of air and water pollution. Estimates suggest that 90% of all chemical processes make use of a catalyst⁵, and according to the North American Catalysis Society, this translates, through their role in the fossil fuel cycle, to 35% of global GDP being reliant on catalytic processes. Research in this area using Diamond is strengthened by the collaboration with the UK Catalysis hub. The hub, created in 2013 with Engineering and Physical Sciences Research Council (EPSRC) funding for five years and recently renewed until 2023, aims to establish a world-leading and cooperative programme of catalytic science that will enable the UK to regain and retain its world-leading position in this area of science, with a scientific mission to develop the knowledge required to be able to custom-design catalysts for a variety of chemical processes. To achieve this goal, it is essential to develop a detailed mechanistic understanding of how catalysts work, informing new strategies for materials design and synthesis⁶. Constant improvement in the techniques probing the electronic, chemical and structural degrees of freedom is at the heart of this challenge. Diamond-II offers step changes in capabilities in some of these areas

The 21st century CO₂ challenge aiming to cap the upward trend in global CO₂ emissions and atmospheric CO₂ levels is a key societal target requiring new strategies and the development of new catalysts. The UK government has targeted an 80% reduction in CO₂ emissions (from 1990 levels) by 2050, with an interim target of 34% reduction by 2020⁷. Direct CO₂ activation and utilisation⁸⁻¹⁰ is critical to achieve the CO₂ reduction target required by governments. An in-depth understanding of the activation processes, in particular for emerging directions of research such as the plasmon-enhanced catalytic process at the nanoscale¹¹, is essential to design new catalysts and develop new systems under a range of activation methods e.g. thermal, electrochemical, plasma and solar. Many of these processes require hydrogen production and storage, and yet our chemically engineered materials capabilities are currently limited in the liquid and gas phases due to the low capacity of storage materials and by the undesired deactivation of many systems. A more detailed understanding of catalytic process for water splitting is also required so that CO₂ can be transformed into other useful chemicals.

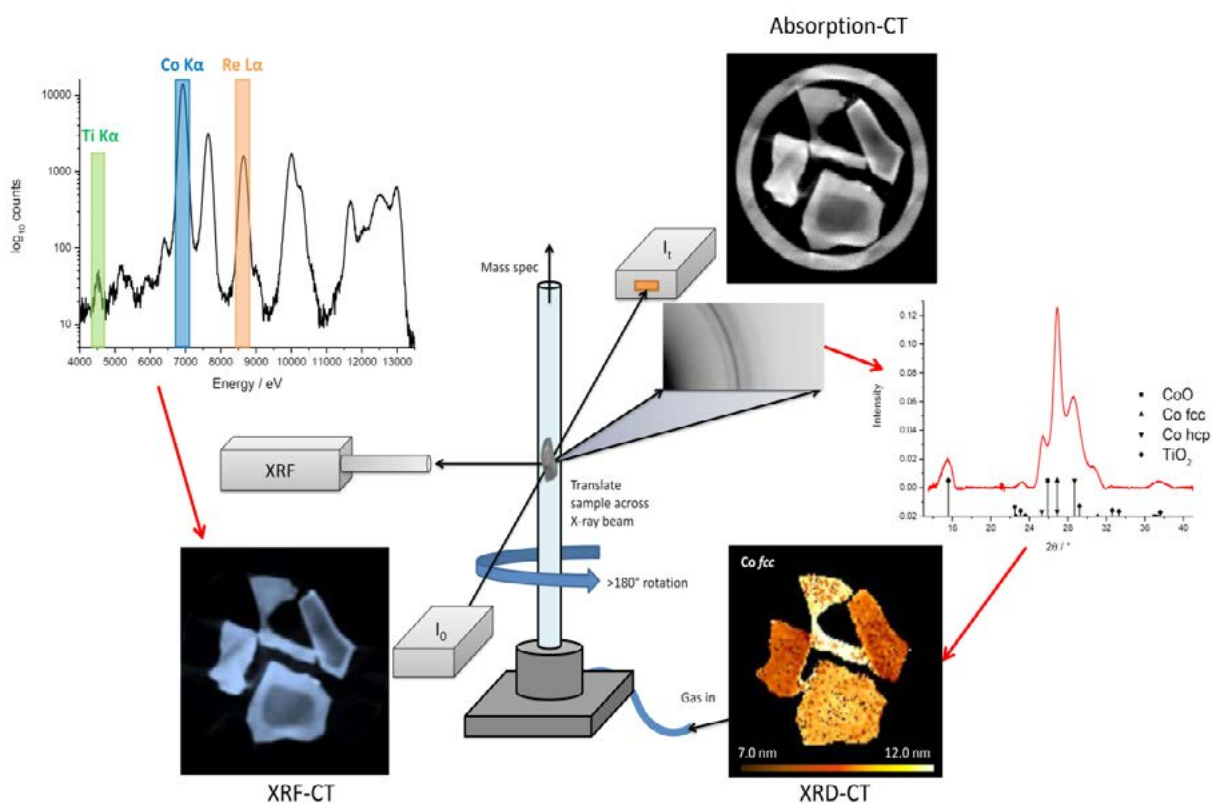


Figure 1: Schematic of an *in situ* multimodal micro-tomography catalytic study¹³. Price, S. W. T. et al. Chemical imaging of Fischer-Tropsch catalysts under operating conditions. *Sci. Adv.* 3, e1602838 (2017). See text for details.

***In situ* experiments at the micro and nanoscales**

There is still much to be understood fundamentally about how catalytic performance is influenced by formulation. The mixture of catalyst, support structure, microstructure and nanostructure and the resulting correlations with selectivity, function and performance, remains a challenging multidimensional problem. One approach to addressing this challenge is the continued development of *in situ* multimodal micro computed-tomography studies (μ -CT) that have been pioneered at the Diamond microfocus spectroscopy beamline, I18^{12–15}. For example, this multimodal approach has been recently used under *operando* conditions to study the Fischer-Tropsch synthesis of synthetic natural gas into functional hydrocarbons, catalysed by cobalt. Through combination of μ -XRD-CT, μ -XRF-CT, and μ -absorption-CT (Figure 1), the effect of the chemical distribution and composition on the activity and the selectivity of the catalyst has been determined accurately. This study has provided unique insight into the behaviour of the cobalt active phase, the titanium modified silica support, the rhenium promoter, and the importance of the (co)location by following all these species through the reaction's lifetime, from the preparation of a pre-active state to the evolution of the catalyst into the active state. This work demonstrated the power of multimodal approaches for catalytic studies, but the flux available currently limits the speed (approximately 100 min per data

per slice) and spatial resolution (down to 5 μ m) at which the catalytic process can be monitored. As a result of the long collection times, experiments are limited to imaging slices through a single particle rather than a full particle imaging. Also, the size of the X-ray beam cannot be tuned below 2 micrometres, and there is a need to match the beam to the particle size at smaller scales. The increased brightness of Diamond-II by a factor 20 at 10 keV (see Figure 8 in Chapter 4.2), will make high-throughput multi-dimensional (multimodal) catalytic studies a reality. It will become feasible to create a Z-stack of 2D time-resolved measurements within controlled sample environments, a term recently described as 5D imaging^{16,17}. Such an approach is important for multivariate problems and scale-up of laboratory-based processes to plant-scale manufacture- critically the point at which many new production technologies struggle.

At the nanoscale, Diamond-II will equally offer attractive gains for catalytic science as CDI techniques, in particular ptychography, is rapidly evolving towards a routine technique, with Diamond strategically investing in this area (I14, I13 and J08). In the hard X-ray regime, the 20 fold gain in brightness will be combined with broad bandwidth radiation, for example the entire wavelength range produce by an undulator harmonic (typically $\Delta E/E \sim 1\%$), or even pink beam, to produce an overall gain in excess of 2000 compared to monochromatic radiation. Such an improvement in beamline performance will reduce the time required for *in situ* studies of full particle imaging from

one day to less than 1 minute. This step change will not only allow imaging of full particle, but additionally, important parameters such as intra- and inter-particle variations or pore structure will become accessible (in the range of 10's of nm), with very precise electron density maps extracted by phase contrast. Equally, at the nanoscale, XRD-CT relies on single crystal diffraction spots rather than overlapping powder rings, so that spatially-resolved crystalline identification can be carried out using broad bandwidth radiation with $\Delta E/E \sim 1\%$. As for ptychography, a gain of three orders of magnitude for nano-XRD will be a step change for catalytic research.

An increased sensitivity to ligands with spatial resolution

The increased brightness of Diamond-II will facilitate the further development of photon-in/photon out techniques such as High Energy Resolution Fluorescence Detected X-ray Absorption Spectroscopy (HERFD-XAS)¹⁸ and Valence to Core X-ray Emission Spectroscopy (VtC-XES)¹⁹. These photon-hungry techniques are increasingly used to determine catalytic mechanisms²⁰. In particular, VtC-XES has all the benefits of standard XAS for the study of chemical processes but overcomes its main limitation - the inability to distinguish ligands that are neighbours in the periodic table, such as carbon, nitrogen and oxygen. Overcoming the XAS limitation is a serious advantage for the study of chemical reactions, particularly in the field of heterogeneous catalysis, where most systems are composed of oxide materials or are catalysts on an oxide support used for the conversion of small molecules consisting mainly of C, N and H. Additionally, the ability of VtC-XES to determine absorbed species during a reaction, makes it a powerful tool for the study of catalysts. Although there are some very interesting examples in the literature demonstrating the usefulness of VtC-XES for the study of catalysts²¹⁻²³, only a handful of investigations have so far been performed *in situ* or under operational conditions, due to the very weak signals of the emission lines. The first *in situ* VtC-XES experiment studied the propane ammoxidation reaction by vanadium supported catalysts²⁴. A number of subsequent investigations have been performed under *operando* conditions in steady-state, focussing on the reduction reaction of NOx by NH₃ over Fe²⁵ and Cu^{26,27} based catalysts. A more recent investigation used²⁸ Mo VtC-XES to study the methane dehydro-aromatization over Mo containing zeolites, but the XES study was limited to quenched samples due to the long acquisition times of the order of 4 hours per sample. With Diamond-II, the availability of new straight sections will open the door for the construction of a new instrument that optimally exploit broad bandwidth or pink-beam radiation²⁹, not easily accommodated on existing high resolution spectroscopy instruments, producing a flux 300 times higher than what is available at present for VtC-XES, reducing the time for performing these experiments

to minutes. Such an instrument would open the door to performing VtC-XES studies in a time-resolved manner, or probing elements in much lower concentrations. In addition, the availability of smaller beams will open the possibility of recording VtC-XES in a spatially resolved manner, in a similar fashion to what is done routinely using conventional XAS³⁰.

New paradigms at the nanoscale

In recent years, the engineering of complex multi-functional structures at the nanoscale, such as the so-called "Antenna-reactor nanostructures"³¹⁻³³ (Figure 2), has been attracting a significant amount of attention in the field of catalysis. In these materials, excitations induced by visible light inside a plasmonic metal assist the transfer of hot or excited electrons to an active catalyst grafted onto the nanostructures or embedded in a core-shell structure, increasing the efficiency and selectivity of the process³⁴. This developing area of research is potentially delivering transformative changes. For example, CO₂ reduction through the dry-reforming of methane reaction assisted by light recently produced a reaction rate 2.4 times higher than that of the thermocatalytic reaction¹¹. Research shows that the nanoscale strain, the morphology of the particle or particle assemblies, and the defects in the nanoparticles are factors that influence the catalytic process. Strain engineering itself has been employed to control the catalytic activity by using nanorods³⁵, or by tuning the morphology of the nanoparticles³⁶. It is consequently important to be able to measure the strain in the nanoparticle and to correlate this with the catalytic activity. The recent development of Bragg-CDI has made the nanoscale study of the strain field in 3D a reality, as shown in a recent experiment probing the strain induced by a catalytic reaction in gold nanoparticles³⁷. To date however, the use of this technique has been largely part of proof of concept experiments on existing diffraction beamlines, but new dedicated and optimized facilities are needed to fully exploit the brightness of the source.

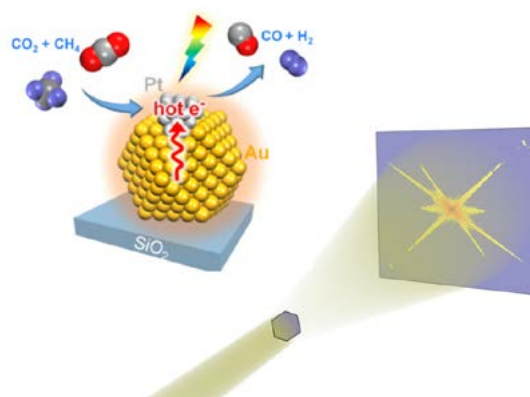


Figure 2: The principle of antenna-reactor catalysis where surface plasmons assist a metallic catalyst, adapted from¹¹. Bragg-CDI can be used to determine the influence of nanoscale strain and dislocations on the catalytic properties.

Bragg-CDI requires the coherence length of the incident X-ray wave to be larger than the sample size which results in a diffraction spot intensity that is strongly modulated by interference scattered from all parts of the sample or nanoparticle. The diffraction spot intensity scales directly with coherent flux on the sample so the gain in coherent flux from Diamond-II (x30-x1000 depending on upgrades and energy bandwidth) along with the additional capacity for a dedicated Bragg-CDI facility has the potential to completely transform our tools to investigate plasmon-assisted and strain-assisted catalysis.

Biocatalysis

Biocatalysis, the use of modified protein-based catalysts beyond their evolved functions, is characterised by a higher efficiency and selectivity when compared with chemical catalysis. However, it is highly substrate-specific, and usually can only occur under tightly-controlled conditions of temperature, pressure and pH^{38,39}. Some newly-designed enzymes are able to perform reactions that are of major industrial and environmental interest under less favourable conditions^{40,41}. Among these are the metalloenzymes capable of converting abundant biomass into commodity fuels, in particular the conversion of methane to methanol⁴² and of cellulose to soluble sugars which can then be fermented to bioethanol^{43,44}. Both of these catalytic bioconversions are of critical importance in the search for sustainable sources of fuel. The role of the metal ion in recruiting oxygen (from the air) to then oxidise the substrate is not fully understood, and there is a real need to determine the electronic and geometric structure of the reactive intermediates occurring during the catalytic cycle of the enzyme. The structural study of these intermediates relies on the use of advanced spectroscopic techniques, of which XAS and XES are major contributors.

XAS, together with X-ray Diffraction (XRD), is frequently

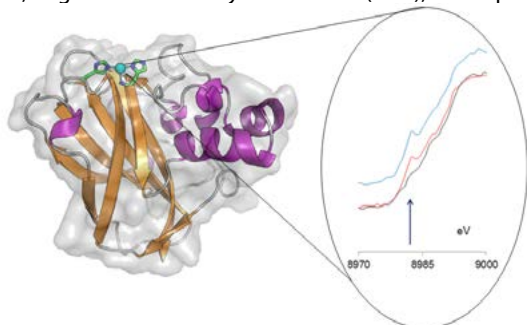


Figure 3: Copper-containing lytic polysaccharide monoxygenase enzyme which is used in bioconversion of cellulose to bioethanol, alongside inset of Cu K-edge XAS spectrum showing change in copper oxidation state and coordination geometry. Adapted from Ref. ⁴³. Reprinted with permission from Hemsworth, G. R. et al. *The copper active site of CBM33 polysaccharide oxygenases*. *J. Am. Chem. Soc.* 135, 6069–6077. Copyright (2013) American Chemical Society.

used to elucidate the structure of metalloenzymes such as hydrogenase⁴⁵, methane monoxygenase⁴² and lytic polysaccharide monoxygenases^{43,46} (Figure 3). However, the limited sensitivity of the spectroscopy techniques, and in particular of XES, has prevented these studies from being extended to more dilute systems. The increased flux provided by Diamond-II will enable the study of metalloenzymes at concentration values closer to operational conditions, widening the range of enzymes that can be studied. Alternatively, for those enzymes that are stable at high concentrations, real time studies under operating conditions will be feasible, allowing the structural determination of reactive intermediates that cannot be isolated, but hold the key to the operation of these enzymes, and ultimately their catalytic power for bioconversion.

Catalyst characterisation: combination of techniques and using external triggers

In most cases it is insufficient to investigate chemical processes with a single structural and/or spectroscopic technique, and the evolving paradigm prescribes the application of multidisciplinary methods to obtain the comprehensive insight required for knowledge-guided process optimisation. To date, the successful use of combined techniques in a single experiment such as XAS/DRIFTS/MS/UV-Vis, XAS/XRD/UV-visible/Raman, or SAXS/WAXS/Raman/UV-visible has proved to be very powerful for elucidation of reaction mechanisms and improving catalytic systems^{47–49}. The increased flux density provided by Diamond-II will provide an opportunity to extend the combination of X-rays with spectroscopy from infrared (IR), Raman and UV-vis measurements to include NMR and EPR, which have not yet been developed, due to the requirement for the beam to penetrate more challenging environments.

For a number of catalytic process, we will also be able to exploit Diamond-II's brightness to perform measurements under modulation excitation, for a range of spectroscopy and scattering techniques. Typically, an applied periodic perturbation coupled with phase sensitive detection, allows to study the structure of minority active species which signal would otherwise be masked by the contribution from the chemically inert bulk background. The Diamond-II upgrade will enhance the sensitivity of these methods further, helping to determine reaction mechanisms of dilute systems.

7.3.2. Advanced materials

The synthesis of new materials designed with specific properties for technological applications is one of the main research areas in chemistry and materials engineering. The

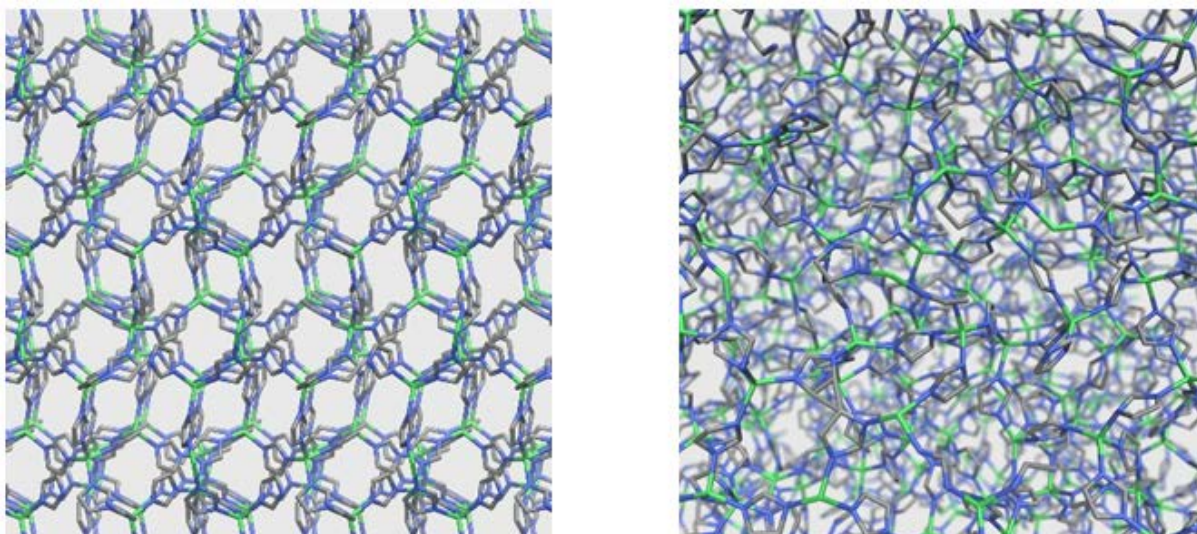


Figure 4: (left) Crystalline structure of the ZIF-4 material at room temperature; (right) Disordered structure of ZIF-4 at high temperature. Image courtesy of FX. Coudert & T. Bennett⁷¹

combination of leading-edge synthetic methods and the availability of more accurate modelling tools and advanced characterisation techniques is behind the development of a wide range of functional materials used in diverse areas such as health, technology and clean energy.

Porous materials

A large number of porous materials such as zeolites, metal organic frameworks (MOFs), covalent organic frameworks (COFs) and nanoporous polymers are currently being used for various different applications such as catalysis, ion exchange, gas storage, sequestration or separation.

One of the applications of porous materials is their use as filters to reduce the presence of pollutants in the air, and the development of new materials with better storage capacity and selectivity is needed. High concentrations of atmospheric smog poses a significant health risk and environmental problems worldwide⁵⁰, and the World Health Organisation (WHO) suggests that poor air quality is directly responsible for one eighth of total global deaths⁵¹. The health risk posed by smog containing NO_x and SO_x is most pronounced in cities and countries with high population densities⁵². Controlling emissions of these two harmful pollutants is a highly complex issue, not least because these gases are highly reactive, oxidising and corrosive in nature⁵³.

A wide spectrum of materials has been tested for adsorptive removal of these pollutants, but most of these materials are not sufficiently stable for use over multiple cycles. Understanding the mechanism by which these materials bind guests at a molecular level, by unravelling the precise role of the active sites, is of critical importance in designing and optimising successive generations of materials. On one hand, a comprehensive knowledge about competitive adsorption among different gases will

provide valuable information needed to design materials for use in industrial gas streams, typically made of complex mixtures of components. On the other hand, information about the durability of these materials under different environmental conditions is key for materials qualification and process validations for future real-life integration.

The use of *in situ* sample cells and gas-delivery systems integrated with powerful synchrotron scattering and absorption techniques, has already transformed our understanding of porous materials for gas adsorption and separation. The increased brightness of Diamond-II will enable faster (sub microsecond) and more sensitive measurements under real conditions of operation or enable higher throughput in-situ experiments allowing researchers to probe a large portion of the materials and environment (T, P, flow, ...) phase-space.

Metal-Organic Frameworks

Since their discovery in 1989⁵⁴, MOFs have become the subject of extensive research, due mainly to their exceptionally high porosity and chemical versatility. These properties have made them attractive for applications in gas storage and separation⁵⁵, having been recently used as storage for hazardous gases in the electronics industry⁵⁶ and for removing pollutants from the air⁵⁷⁻⁵⁹. MOFs are also being studied as vectors for drug delivery⁶⁰, in water harvesting⁶¹, ion conduction⁶² and for heterogeneous catalysis^{63,64}, including asymmetric catalysis when using chiral MOFs⁶⁵. The state of the art within this field has moved considerably in just a few years, with MOFs no longer being recognised as just rigid, defect free, static structures⁶⁶. It has been shown that the introduction of correlated defects improve catalytic efficiency, where simple lattice and interstitial vacancies control diffusion and ionic conductivity, and point defects affect the guest-host interactions⁶⁷⁻⁶⁹. Non-crystalline MOFs^{70,71}, the extreme case of disorder,

have also received a considerable amount of interest in recent years as membrane materials for gas separation⁷². Synchrotron experiments have been used extensively to characterise the structure of these materials, both in crystalline and non-crystalline forms. Early studies were performed using single crystal and powder XRD. More recently, techniques such as XPDF, XAS and synchrotron μ -IR spectroscopy have become essential to comprehensively characterise and elucidate the atomic and molecular bonding in increasingly chemically-complex structures, as well as their host-guest sorption behaviour^{73,74}. More recently, non-crystalline structures (Figure 4) have been characterised by techniques such as XPDF which allow to probe their local bonding environment and degree of disorder with respect to their crystalline counterparts. Numerous synchrotron studies have been performed *in situ* to elucidate the electronic and geometric structure of MOFs upon gas adsorption or whilst undergoing a chemical reaction. The *in situ* formation of MOFs is also of considerable interest, as a detailed understanding of formation processes is required if we are to develop methods that allow us to exercise a greater degree of control over their structures and properties⁷⁵.

At present, the majority of synchrotron time-resolved studies are performed under steady-state conditions. The proposed Diamond upgrade will allow the collection of fast kinetic data, providing information about the mechanisms that govern the structural transformations. For example, in the case of the High-Resolution Powder Diffraction beamline, I11, the higher critical energy of the ring combined with the upgrade of the insertion device (either a CPMU or SCU with a period of 15.6mm and maximal field of 1.24T) will provide a 36-fold increase in flux at the sample at 25keV. This will reduce the data collection time down to milliseconds, enabling the study of fast processes under real conditions of operation. For instance, acquiring knowledge of the 'real-time' deformation of MOFs upon pelletisation or extrusion has important implications for the use of polydisperse microcrystalline MOF powders. These materials are limited in their applicability in industrial settings due to poor handling, dust formation, mass transfer limitations and strong pressure drops in packed beds⁶⁶. As a consequence, methods for their preparation as mesoscopically-structured objects with hierarchical pore architectures are highly sought after, but this is currently a difficult problem to address due to the loss of crystallinity and nanoporosity upon pelletisation via mechanical compression or extrusion⁷⁶. For single crystal diffraction, which does not suffer from the peak overlap problem of powder diffraction, it is possible to relax the energy resolution from typically 10^{-4} to 1%. With the non-structured undulator spectrum generated by a low-emittance source, it becomes possible to extract efficiently the radiation from a single harmonic, for example by separating the harmonics by a simple prism, generating a flux density 2000 brighter than currently available on I19. The advent of detector technology using

event-driven data collection and sub microsecond time resolution, as currently developed in the Tristan project (Diamond detector group, first module releaser in February 2019), will completely transform fast kinetic experiments. This certainly applies to phase transformations in MOFs, as rapid and high-quality measurements are needed to properly investigate sharp transitions.

Whilst not accessing timescales relevant for electronic phenomena as available at XFELs and attosecond lasers, moving into the microsecond regime opens already a very large playground to study emergent structures or functions, i.e. probing reactions where the resulting products do not necessarily depend on the individual constituents alone but vary greatly with the environmental conditions. By enabling high throughput measurements and accessing sub microsecond dynamic, Diamond-II will open the door for studying emergent phenomena.

The increased brightness of Diamond-II will also enhance the sensitivity of the measurements, and this will enable the study of host-guest interactions in cases where the host is present only in low concentrations (a few %), as in the case of MOFs used as filters of toxic gases, or as drug delivery vectors.

The delivery of smaller beams at Diamond-II will allow spatially resolved studies with sub-micron resolution for tomographic imaging of MOF materials, for probing the variance of local structure and composition in cases where multiple metal or organic components are used. Accessing the nanoscale spatial dimension will also be critical for systems used in pollution mitigation, medical and industrial applications.

Synchrotron μ -IR has also been used extensively for the study of MOFs upon gas adsorption in individual crystallites. These studies have been used to determine the diffusion rate of gases into the channels and pores of the material, but are often limited to one crystal due to the limited flux available at the sample^{77,78}. The increased brightness of Diamond-II and new source for the IR beamline will translate into measurements an order of magnitude faster, enabling the study of more than one crystal during the gas adsorption. This will provide valuable information about the effect of the morphology of the crystals on the diffusion rate of gases.

Probing kinetic correlations in space and time

A relatively new technique that is bringing fresh insight into these nanoporous materials is X-ray Photon Correlation Spectroscopy (XPCS)⁷⁹, which makes use of the coherence properties of the X-ray beam to measure dynamical processes through the variation of the speckle pattern in the measured diffraction image⁸⁰. XPCS measures the dynamical structure factor in the time regime rather than

in the frequency regime, but has been limited to processes slower than, typically, tens of milliseconds^{80,81}. Because XPCS is a two-photon process, the time regime accessible varies with the square of the brightness, so that an increase in brightness of Diamond-II, combined with the progress in detector technology, can provide access to dynamical processes occurring down to the tens of nanoseconds⁸². This would bridge the gap with other time-domain spectroscopy techniques such as neutron spin-echo, providing diffusion coefficient and jump parameters⁸³ (and references therein) to be compared with the results of molecular dynamic simulations. XPCS would also uniquely provide the additional benefit of elemental sensitivity by using resonant edges, performing element-specific dynamics studies. The length and time scales accessible by XPCS are well matched to investigating migration of gases and liquids through the porous networks of nanoporous materials, giving additional insight into the dynamical aspects of gas adsorption and separation and mechanisms of catalytic performance of these materials.

7.3.3. Formulation

Product formulation is used to optimize how material mixtures behave and interact to provide enhanced properties, improved processing and stability, or delivery of an active ingredient in a convenient and useable form. Consequently, product formulation is an important aspect for many consumer goods such as cosmetics, detergent agents, foods, drugs, etc.

In the case of pharmaceuticals, the chemistry and particle engineering of drugs and their excipients must be understood and optimised in order to produce products with the required physical properties to maximise biological efficacy in dosage forms. For licensing and regulation, the quality and consistency of dosage forms is key, including in many cases the consistency of dose concentration through the complex formulated product. The imperative for Diamond-II is to provide a range of capabilities that map to this key driver. In terms of techniques, the summary here focuses on diffraction, imaging and spectroscopy, but other techniques are also crucial, notably surface diffraction.

This area has moved on dramatically from a focus solely on the primary particle (crystal) structure. A larger vision embraces both this core underpinning requirement and the need to develop enhanced tools to examine more complex, multi-component and often heterogeneous systems, which may lack long range order to an extent, and looks at the evolution of these throughout the process for producing a final pharmaceutical product. This ideally matches the aspiration for Diamond-II to allow real-time studies of critical physical, chemical (and in this case manufacturing) processes. These experimental requirements are essential complements to the parallel digital design priorities in this area. The aim is to produce

end-to-end processes matching experimentally-driven process design with a predictive digital twin capability, where the modelling (fully informed by prior experiment), with high level multiscale computational methods spanning from the molecule to the product, is augmented by contemporary approaches such as machine learning/AI to enhance predictive capability.

The significance of this vision is reflected in a number of national and international consolidated efforts in this area including CMAC⁸⁴, ADDoPT⁸⁵, National Formulation Centre⁸⁶, MMIP (Medicines, Manufacturing Industrial Partnership)⁸⁷, representing high profile efforts that underpin the UK's aspiration to remain a world leader in a hugely important area for the UK economy and a powerful example of combining basic research & industrial R&D to translate fundamentals into applications.

Examples of the type of materials processes and characteristics that are important include: i. The effect of additives and impurities, in the bulk, at the surface and at the molecular scale, including control and exploitation of defects and disorder. A full characterisation of these (quantitative, and often at low levels, <1%) is essential; the extra brightness of Diamond-II is crucial here, ii. The structure (in its broadest sense) at the molecular, crystalline (and non-crystalline) domain, particle and bulk macroscopic level. Determining the structure at the micro-domain level in developed products that are deliberately heterogeneous in order to enhance critical physical properties such as dissolution rate. Understanding of the 2D and the 3D interfaces and how to engineer these will benefit from smaller beams. Consistency of bulk structure and contents is critical to control of dosage, iii. Assembly from molecule to product, including *in situ* studies of upstream crystallisation, particle formation and processing to final formulated (complex) product, which may contain crystalline and non-crystalline domains, and iv. *Operando* conditions and timescales must be replicated, and materials probed, during processes such as solution-mediated crystallisation and phase transitions, dispersion, spray drying, compression, 3D printing and hot melt extrusion to final product dosage form. Both of these will benefit from better sample environment integration and faster data collection

A recent example from work on coupling flow synthesis and crystallisation illustrates some of the dynamic polymorphic effects that cannot be probed at present⁸⁸. The effluent of this flow reactor was directly linked to a tri-segmented tubular crystalliser (KRAIC), providing a seamless transition from flow synthesis to crystallisation, with control over solid form and particle characteristics (Figure 5). In a case like this the aim is to study evolving particle information in its fullest sense, to tune process parameters, to control particle size and shape and polymorphic form, i.e. to use diffraction information across a range of length scales to examine the dynamic processing of active pharmaceutical materials

Diamond-II: Advancing physical sciences

and formulations and to interact in real time with these processes. The control of polymorph is not simply a matter of allowing the thermodynamically stable product to emerge and then finding out what it is, but monitoring, controlling and interacting with the kinetics of the process to direct the crystal form *in situ* and to deliver the desired form into downstream processing.

Enhanced spatial resolution, resulting from a smaller and more tuned beam size at the sample, will allow us to scan rapidly the microstructure of complex, often heterogeneous, product particles. Intensity enhancements (and related *in situ* environment capabilities) will allow real-time *operando* experiments to be carried out for various stages of the pharma manufacturing process, across the whole of the key driver space noted above, using Diamond-II. Such dynamic polymorph control of form is achieved with API products in solution-mediated environments, rather than via solid-state phase transitions. In addition, a separate sample environment development, integrating crystalline-non-crystalline characterisation capabilities (software and modelling, XPDF, etc.) is essential to understand the molecular level interactions in complex, potentially heterogeneous materials. Removing this boundary recognises that in real materials this is a continuum, and optimal properties can sit anywhere along that continuum.

There is an increasing demand for developing amorphous drugs. At least two-thirds of drugs in the pipeline are poorly soluble but well-permeable drugs (BCS Class II), and the amorphous form can improve the 'apparent' solubility. As the preferred means of delivery of these types of drugs is still oral, it is essential to develop polymeric excipients that i. maintain drugs in a dispersed, amorphous state in tablets form during storage, ii. deliver drugs by dissolving in the gastrointestinal tract, and iii. somehow suppress drug crystallisation before it can pass through the intestinal lining and into the blood stream⁸⁹. Regarding i., it is very difficult to assess whether a given drug is molecularly dispersed, and to detect the first onset of crystallization. The high flux and unprecedented spatial resolution obtainable

with Diamond-II will make it possible for the first time to screen solid dispersions for uniform drug dispersion and confirm the absence of crystals. In terms of iii., the current hypothesis is that successful excipients sequester drugs in amorphous nanoparticles, that acts a reservoir during passage through the body. There is recently good evidence for this hypothesis in a couple of cases, using a powerful combination of SAXS and cryo-TEM⁹⁰. In the future it will be important to screen the appearance and disappearance of such nanoparticles in real time, which is quite demanding as the concentration is typically low, the particles are very small, and the contrast can be weak.

The direct relevance to industry of all developments outlined in formulation is endorsed in the roadmap for MMIP⁸⁷.

Electronic structure of *in situ* nucleation of organic solutes

An additional benefit from Diamond-II that will improve our knowledge in formulation will be the addition of a new X-ray Raman Scattering (XRS) instrument to our suite of beamlines that will allow the study of the electronic structure of low Z materials such as C and N, using hard X-rays, which is highly complementary to experiments that are currently undertaken using B07. This instrument will, for example, enable the *in situ* study of nucleation of organic solutes during the first stages of crystallisation, a process that is important to understand in detail if we are to develop methods to control the physical and chemical properties of crystalline products. To date, these studies have been primarily performed using soft X-ray Near-Edge X-ray Absorption Fine Structure (NEXAFS) spectroscopy^{91,92}, but a recent proof of concept study has shown how XRS can be used to study relevant systems *in situ*, characterising the solute speciation during the crystallisation process of imidazole⁹³. This study shows how the penetration of the hard X-rays allows us to circumvent some of the limitations of soft X-ray spectroscopy for the study of nucleation of organic molecules. The provision of extra straight sections

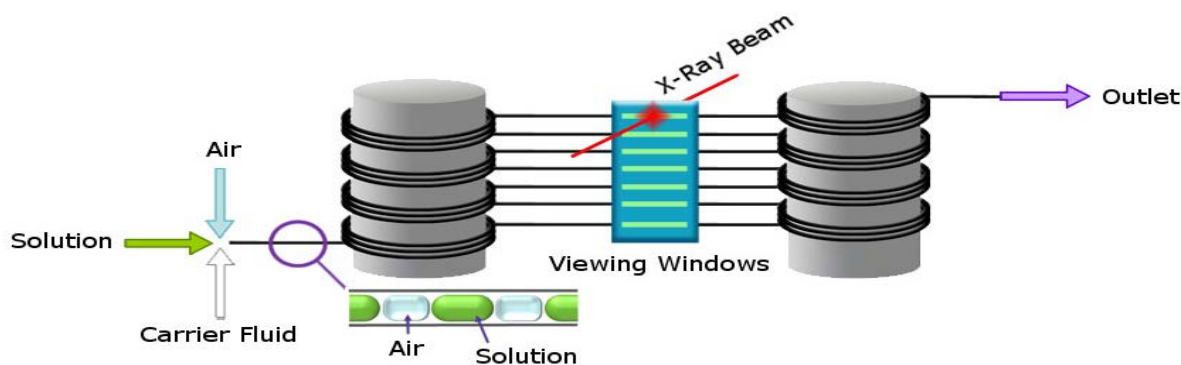


Figure 5: KRAIC-D cartoon of set-up being developed at Diamond to monitor crystallisation as a single end-to-end process. Copyright Diamond Light Source.

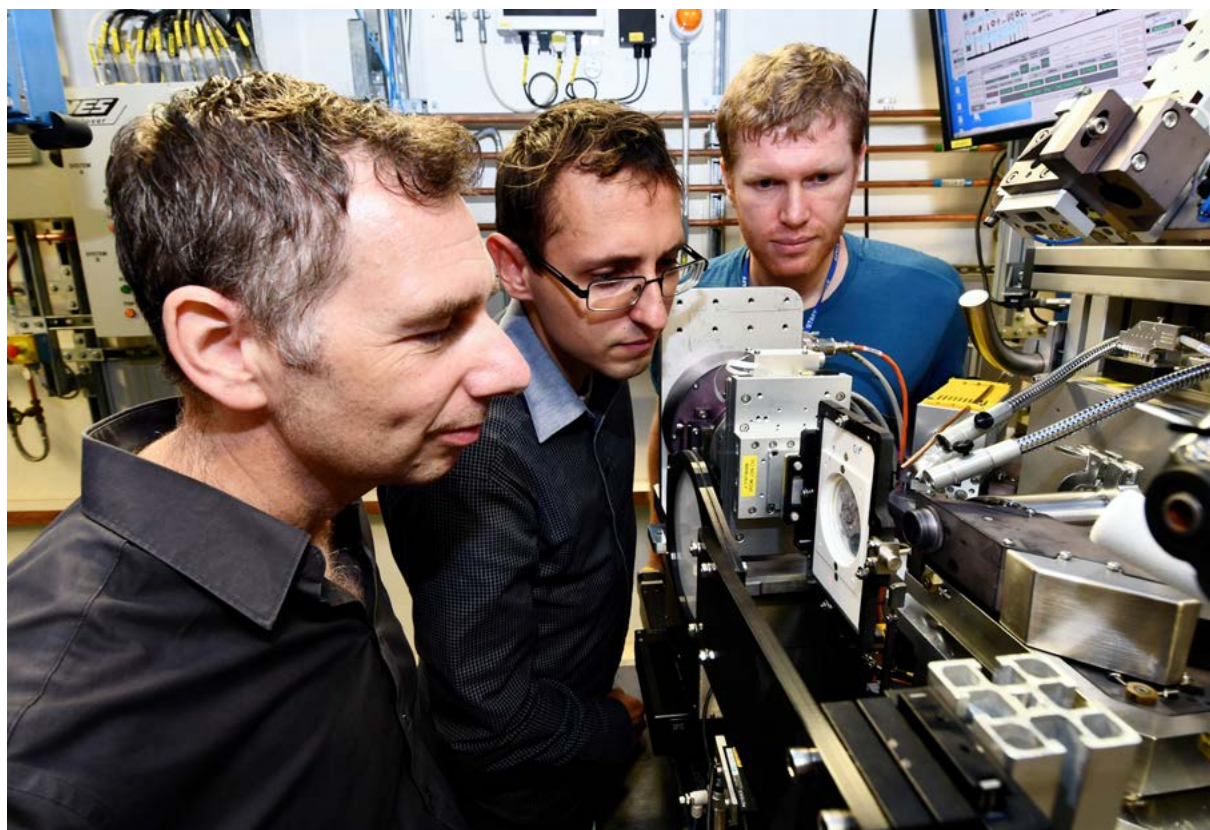
in Diamond-II will allow this complementary technique to be added without compromising the current capabilities in XAS, while the increased brilliance of Diamond-II will enhance the spatial resolution achievable, particularly in the horizontal plane, from hundreds to tenths of microns.

References

- The Grand Challenges. Available at: <https://www.gov.uk/government/publications/industrial-strategy-the-grand-challenges/industrial-strategy-the-grand-challenges#clean-growth>.
- GDP(O) Low Level Aggregates National Accounts, ONS, 2017. Available at: <https://www.ons.gov.uk/economy/grossdomesticproductgdp/datasets/ukgdpolowlevelaggregates/current>.
- 'Employee Jobs by Industry', ONS, September 2017. Available at: <https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/employmentandemployeetypes/datasets/employeejobsbyindustryjobs03/current>.
- Maine, E. & Seegopaul, P. Accelerating advanced-materials commercialization. *Nat. Mater.* **15**, 487–491 (2016).
- Ertl, G., Knözinger, H., Schüth, F., Weitkamp, J. & Ed. *Handbook of Heterogeneous Catalysis*. (Wiley-VCH, Weinheim, 2008).
- Hutchings, G. *et al. Modern Developments in Catalysis*. (WORLD SCIENTIFIC (EUROPE), 2017). doi:10.1142/q0035
- Government funding to reduce the carbon emissions from UK industry. Available at: <https://www.gov.uk/guidance/funding-for-low-carbon-industry>.
- Porosoff, M. D., Yan, B. & Chen, J. G. Catalytic reduction of CO₂ by H₂ for synthesis of CO, methanol and hydrocarbons: Challenges and opportunities. *Energy Environ. Sci.* **9**, 62–73 (2016).
- Ahn, S. *et al.* Poly-Amide Modified Copper Foam Electrodes for Enhanced Electrochemical Reduction of Carbon Dioxide. *ACS Catal.* **8**, 4132–4142 (2018).
- Zhao, G., Huang, X., Wang, X. & Wang, X. Progress in catalyst exploration for heterogeneous CO₂ reduction and utilization: A critical review. *J. Mater. Chem. A* **5**, 21625–21649 (2017).
- Song, H. *et al.* Light-Enhanced Carbon Dioxide Activation and Conversion by Effective Plasmonic Coupling Effect of Pt and Au Nanoparticles. *ACS Appl. Mater. Interfaces* **10**, 408–416 (2018).
- Price, S. W. T. *et al.* Chemical imaging of single catalyst particles with scanning u-XANES-CT and u-XRF-CT. *Phys. Chem. Chem. Phys.* **17**, 521–529 (2015).
- Price, S. W. T. *et al.* Chemical imaging of Fischer-Tropsch catalysts under operating conditions. *Sci. Adv.* **3**, e1602838 (2017).
- Sheppard, T. L. *et al.* In Situ Multimodal 3D Chemical Imaging of a Hierarchically Structured Core@Shell Catalyst. *J. Am. Chem. Soc.* **139**, 7855–7863 (2017).
- Price, S. W. T. *et al.* In Situ Microfocus Chemical Computed Tomography of the Composition of a Single Catalyst Particle during Hydrogenation of Nitrobenzene in the Liquid Phase. *Angew. Chemie - Int. Ed.* **54**, 9886–9889 (2015).
- Beale, A. M., Jacques, S. D. M., Gibson, E. K. & Di Michiel, M. Progress towards five dimensional diffraction imaging of functional materials under process conditions. *Coord. Chem. Rev.* **277**, 208–223 (2014).
- Vamvakeros, A. *et al.* 5D tomographic *operando* diffraction imaging of a catalyst bed. *Nat. Commun.* **9**, 4751 (2018).
- Safonova, O. V. *et al.* Identification of CO Adsorption Sites in Supported Pt Catalysts Using High-Energy-Resolution Fluorescence Detection X-ray Spectroscopy. *J. Phys. Chem. B* **110**, 16162–16164 (2006).
- Gallo, E. & Glatzel, P. Valence to core X-ray emission spectroscopy. *Adv. Mater.* **26**, 7730–7746 (2014).
- Bauer, M. HERFD-XAS and valence-to-core-XES: New tools to push the limits in research with hard X-rays? *Phys. Chem. Chem. Phys.* **16**, 13827–13837 (2014).
- Delgado-Jaime, M. U. *et al.* Identification of a single light atom within a multinuclear metal cluster using valence-to-core X-ray emission spectroscopy. *Inorg. Chem.* **50**, 10709–10717 (2011).
- Swarbrick, J. C. *et al.* Ligand Identification in Titanium Complexes using X-ray Valence-to-Core Emission Spectroscopy. *Inorg. Chem.* **49**, 8323–8332 (2010).
- Lee, N., Petrenko, T., Bergmann, U., Neese, F. & Debeer, S. Supporting Information: Probing valence orbital composition with iron K-beta x-ray emission spectroscopy. *J. Am. Chem. Soc.* **132**, 9715–9727 (2010).
- Safonova, O. V., Florea, M., Bilde, J., Delichere, P. & Millet, J. M. M. Local environment of vanadium in V/Al/O-mixed oxide catalyst for propane ammoxidation: Characterization by *in situ* valence-to-core X-ray emission spectroscopy and X-ray absorption spectroscopy. *J. Catal.* **268**, 156–164 (2009).
- Boubnov, A. *et al.* Selective Catalytic Reduction of NO over Fe-ZSM-5: Mechanistic Insights by *Operando* HERFD-XANES and Valence-to-Core X-ray Emission Spectroscopy. *J. Am. Chem. Soc.* **136**, 13006–13015 (2014).
- Günter, T. *et al.* Structural snapshots of the SCR reaction mechanism on Cu-SSZ-13. *Chem. Commun.* **51**, 9227–9230 (2015).
- Giordanino, F. *et al.* Interaction of NH₃ with Cu-SSZ-13 catalyst: A complementary FTIR, XANES, and XES study. *J. Phys. Chem. Lett.* **5**, 1552–1559 (2014).
- Lezcano-Gonzalez, I. *et al.* Molybdenum Speciation and its Impact on Catalytic Activity during Methane Dehydroaromatization in Zeolite ZSM-5 as Revealed by *Operando* X-Ray Methods. *Angew. Chemie - Int. Ed.* **55**, 5215–5219 (2016).
- Kvashnina, K. O., Rossberg, A., Exner, J. & Scheinost, A. C. Hard X-ray emission spectroscopy with pink beam. *Annual Report 2016, Institute of Resource Ecology, HZDR - Helmholtz-Zentrum Dresden-Rossendorf*, **30** (2016).
- Doronkin, D. E. *et al.* *Operando* Spatially- and Time-Resolved XAS Study on Zeolite Catalysts for Selective Catalytic Reduction of NO_x by NH₃. *J. Phys. Chem. C* **118**, 10204–10212 (2014).
- Robatjazi, H. *et al.* Plasmon-induced selective carbon dioxide conversion on earth-abundant aluminum-cuprous oxide antenna-reactor nanoparticles. *Nat. Commun.* **8**, 27 (2017).
- Zhang, C. *et al.* Al-Pd Nanodisk Heterodimers as Antenna-Reactor Photocatalysts. *Nano Lett.* **16**, 6677–6682 (2016).
- Swearer, D. F. *et al.* Transition-Metal Decorated Aluminum Nanocrystals. *ACS Nano* **11**, 10281–10288 (2017).
- Aslam, U., Chavez, S. & Linic, S. Controlling energy flow in multimetallic nanostructures for plasmonic catalysis. *Nat. Nanotechnol.* **12**, 1000–1005 (2017).
- Ling, T. *et al.* Activating cobalt(II) oxide nanorods for efficient

- electrocatalysis by strain engineering. *Nat. Commun.* **8**, 1509 (2017).
36. Kuo, C. H. *et al.* The effect of lattice strain on the catalytic properties of Pd nanocrystals. *ChemSusChem* **6**, 1993–2000 (2013).
 37. Ulvestad, A. *et al.* *In Situ* 3D Imaging of Catalysis Induced Strain in Gold Nanoparticles. *J. Phys. Chem. Lett.* **7**, 3008–3013 (2016).
 38. Schramm, V. L. Introduction: Principles of enzymatic catalysis. *Chem. Rev.* **106**, 3029–3030 (2006).
 39. Bornscheuer, U. T. *et al.* Engineering the third wave of biocatalysis. *Nature* **485**, 185–194 (2012).
 40. Chapman, J., Ismail, A. & Dinu, C. Industrial Applications of Enzymes: Recent Advances, Techniques, and Outlooks. *Catalysts* **8**, 238 (2018).
 41. Truppo, M. D. Biocatalysis in the Pharmaceutical Industry: The Need for Speed. *ACS Med. Chem. Lett.* **8**, 476–480 (2017).
 42. Ro, S. Y. *et al.* From micelles to bicelles: Effect of the membrane on particulate methane monooxygenase activity. *J. Biol. Chem.* **293**, 10457–10465 (2018).
 43. Hemsworth, G. R. *et al.* The copper active site of CBM33 polysaccharide oxygenases. *J. Am. Chem. Soc.* **135**, 6069–6077 (2013).
 44. Hemsworth, G. R., Johnston, E. M., Davies, G. J. & Walton, P. H. Lytic Polysaccharide Monooxygenases in Biomass Conversion. *Trends Biotechnol.* **33**, 747–761 (2015).
 45. Kampa, M., Pandelia, M. E., Lubitz, W., Van Gestel, M. & Neese, F. A metal-metal bond in the light-induced state of [nife] hydrogenases with relevance to hydrogen evolution. *J. Am. Chem. Soc.* **135**, 3915–3925 (2013).
 46. Kjaergaard, C. H. *et al.* Spectroscopic and computational insight into the activation of O₂ by the mononuclear Cu center in polysaccharide monooxygenases. *Proc. Natl. Acad. Sci.* **111**, 8797–8802 (2014).
 47. Newton, M. A. & Van Beek, W. Combining synchrotron-based X-ray techniques with vibrational spectroscopies for the *in situ* study of heterogeneous catalysts: A view from a bridge. *Chem. Soc. Rev.* **39**, 4845–4863 (2010).
 48. Bentrup, U. Combining *in situ* characterization methods in one set-up: Looking with more eyes into the intricate chemistry of the synthesis and working of heterogeneous catalysts. *Chem. Soc. Rev.* **39**, 4718–4730 (2010).
 49. Gibson, E. K. *et al.* Restructuring of AuPd nanoparticles studied by a combined XAFS/DRIFTS approach. *Chem. Mater.* **27**, 3714–3720 (2015).
 50. Edwards, P. M. *et al.* High winter ozone pollution from carbonyl photolysis in an oil and gas basin. *Nature* **514**, 351–354 (2014).
 51. WHO (World Health Organisation). 7 million premature deaths annually linked to air pollution. (2016). Available at: <http://www.who.int/mediacentre/news/releases/2014/air-pollution/en/>.
 52. Chen, Z., Wang, J.-N., Ma, G.-X. & Zhang, Y.-S. China tackles the health effects of air pollution. *Lancet* **382**, 1959–1960 (2013).
 53. Rezaei, F., Rowanghi, A. A., Monjezi, S., Lively, R. P. & Jones, C. W. SO_x/NO_x Removal from Flue Gas Streams by Solid Adsorbents: A Review of Current Challenges and Future Directions. *Energy & Fuels* **29**, 5467–5486 (2015).
 54. Hoskins, B. F. & Robson, R. Infinite Polymeric Frameworks Consisting of Three Dimensionally Linked Rod-like Segments. *J. Am. Chem. Soc.* **111**, 5962–5964 (1989).
 55. Mason, J. A., Veenstra, M. & Long, J. R. Evaluating metal-organic frameworks for natural gas storage. *Chem. Sci.* **5**, 32–51 (2014).
 56. Frameworks for commercial success. *Nat. Chem.* **8**, 987 (2016).
 57. Han, X. *et al.* Reversible adsorption of nitrogen dioxide within a robust porous metal-organic framework. *Nat. Mater.* **17**, 691–696 (2018).
 58. Yang, S. *et al.* Irreversible network transformation in a dynamic porous host catalyzed by sulfur dioxide. *J. Am. Chem. Soc.* **135**, 4954–4957 (2013).
 59. Decoste, J. B. & Peterson, G. W. Metal-organic frameworks for air purification of toxic chemicals. *Chem. Rev.* **114**, 5695–5727 (2014).
 60. Horcajada, P. *et al.* Metal-organic frameworks in biomedicine. *Chem. Rev.* **112**, 1232–1268 (2012).
 61. Kim, H. *et al.* Water harvesting from air with metal-organic frameworks powered by natural sunlight. *Science (80-.)*. **356**, 430–434 (2017).
 62. Campbell, M. G., Liu, S. F., Swager, T. M. & Dinc, M. Chemiresistive Sensor Arrays from Conductive 2D Metal-Organic Frameworks. *J. Am. Chem. Soc.* **137**, 13780–13783 (2015).
 63. Stubbs, A. W. *et al.* Selective Catalytic Olefin Epoxidation with MnII-Exchanged MOF-5. *ACS Catal.* **8**, 596–601 (2018).
 64. Yan, Z.-H. *et al.* Photo-generated dinuclear {Eu(II)}₂ active sites for selective CO₂ reduction in a photosensitizing metal-organic framework. *Nat. Commun.* 1–9 (2018). doi:10.1038/s41467-018-05659-7
 65. Bhattacharjee, S., Khan, M., Li, X., Zhu, Q.-L. & Wu, X.-T. Recent Progress in Asymmetric Catalysis and Chromatographic Separation by Chiral Metal-Organic Frameworks. *Catalysts* **8**, 120 (2018).
 66. Dissegna, S., Epp, K., Heinz, W. R., Kieslich, G. & Fischer, R. A. Defective Metal-Organic Frameworks. *Adv. Mater.* (2018). doi:10.1002/adma.201704501, 1704501
 67. Cheetham, A. K., Bennett, T. D., Coudert, F. X. & Goodwin, A. L. Defects and disorder in metal organic frameworks. *Dalt. Trans.* **45**, 4113–4126 (2016).
 68. Dissegna, S. *et al.* Tuning the Mechanical Response of Metal-Organic Frameworks by Defect Engineering. *J. Am. Chem. Soc. jacs.8b07098* (2018). doi:10.1021/jacs.8b07098
 69. Cliffe, M. J. *et al.* Correlated defect nanoregions in a metal-organic framework. *Nat. Commun.* **5**, 1–8 (2014).
 70. Bennett, T. D. & Horike, S. Liquid, glass and amorphous solid states of coordination polymers and metal-organic frameworks. *Nat. Rev. Mater.* doi:10.1038/s41578-018-0054-3
 71. Gaillac, R. *et al.* Liquid metal-organic frameworks. *Nat. Mater.* **16**, 1149–1155 (2017).
 72. Denny Jr., M. S., Moreton, J. C., Benz, L. & Cohen, S. M. Metal-organic frameworks for membrane-based separations. *Nat. Rev. Mater.* **1**, 16078 (2016).
 73. Gallo, E. *et al.* Effect of Molecular Guest Binding on the d-d Transitions of Ni²⁺ of CPO-27-Ni: A Combined UV-Vis, Resonant-Valence-to-Core X-ray Emission Spectroscopy, and Theoretical Study. *Inorg. Chem.* **56**, 14408–14425 (2017).
 74. Chapman, K. W., Sava, D. F., Halder, G. J., Chupas, P. J.

- & Nenoff, T. M. Trapping guests within a nanoporous metal-organic framework through pressure-induced amorphization. *J. Am. Chem. Soc.* **133**, 18583–18585 (2011).
75. Surblé, S., Millange, F., Serre, C., Férey, G. & Walton, R. I. An EXAFS study of the formation of a nanoporous metal-organic framework: Evidence for the retention of secondary building units during synthesis. *Chem. Commun.* 1518–1520 (2006). doi:10.1039/b600709k
 76. Su, Z., Miao, Y. R., Zhang, G., Miller, J. T. & Suslick, K. S. Bond breakage under pressure in a metal organic framework. *Chem. Sci.* **8**, 8004–8011 (2017).
 77. Greenaway, A. *et al.* In situ synchrotron IR microspectroscopy of CO₂ adsorption on single crystals of the functionalized MOF Sc₂(BDC-NH₂)₃. *Angew. Chemie - Int. Ed.* **53**, 13483–13487 (2014).
 78. Savage, M. *et al.* Selective Adsorption of Sulfur Dioxide in a Robust Metal–Organic Framework Material. *Adv. Mater.* **28**, 8705–8711 (2016).
 79. Grübel, G. & Zontone, F. Correlation spectroscopy with coherent X-rays. *J. Alloys Compd.* **362**, 3–11 (2004).
 80. Grübel, G., Madsen, A. & Robert, A. X-Ray Photon Correlation Spectroscopy (XPCS). in *Soft Matter Characterization* 953–995 (2008). doi:10.1007/978-1-4020-4465-6_18
 81. Shpyrko, O. G. X-ray photon correlation spectroscopy. *J. Synchrotron Rad.* **21**, 1057–1064 (2014).
 82. Sandy, A. R., Zhang, Q. & Lurio, L. B. Hard X-Ray Photon Correlation Spectroscopy Methods for Materials Studies. *Annu. Rev. Mater. Res.* **48**, 167 (2018).
 83. O'Malley, A. J., Parker, S. F. & Catlow, C. R. A. Neutron spectroscopy as a tool in catalytic science. *Chem. Commun.* **53**, 12164–12176 (2017).
 84. CMAC: Future Manufacturing Reserach Hub. Available at: <https://www.cmac.ac.uk/>. (Accessed: 24th October 2018)
 85. ADDoPT – advanced digital design transforming pharmaceutical development and manufacture. Available at: <https://www.addopt.org/>. (Accessed: 24th October 2018)
 86. National Formulation Centre - CPI. Available at: <https://www.uk-cpi.com/contact/locations/national-formulation-centre>. (Accessed: 24th October 2018)
 87. Medicines Manufacturing Industry Partnership (MMIP) | ABPI. Available at: <https://www.abpi.org.uk/what-we-do/collaboration-and-partnership/manufacturing-and-supply/medicines-manufacturing-industry-partnership-mmip/>. (Accessed: 24th October 2018)
 88. Scott, C. D. *et al.* Integrated plug flow synthesis and crystallisation of pyrazinamide. *React. Chem. Eng.* (2018). doi:10.1039/C8RE00087E
 89. Liu, H., Taylor, L. S. & Edgar, K. J. The role of polymers in oral bioavailability enhancement; a review. *Polymer (Guildf)*. **77**, 399–415 (2015).
 90. Ricarte, R. G. *et al.* Direct Observation of Nanostructures during Aqueous Dissolution of Polymer/Drug Particles. (2017). doi:10.1021/acs.macromol.7b00372
 91. Thomason, M. J. *et al.* Self-association of organic solutes in solution: A NEXAFS study of aqueous imidazole. *Faraday Discuss.* **179**, 269–289 (2015).
 92. Meyer, F. *et al.* Site-specific electronic structure of imidazole and imidazolium in aqueous solutions. *Phys. Chem. Chem. Phys.* **20**, 8302–8310 (2018).
 93. Al-Madhagi, L. H. *et al.* X-ray Raman scattering: a new *in situ* probe of molecular structure during nucleation and crystallization from liquid solutions. *CrystEngComm* (2018). doi:10.1039/C8CE00929E



7.4. Quantum materials

7.4.1. Designing and controlling quantum materials

In the 21st century, limitations imposed by thermodynamics and quantum mechanics imply that historical projections governed by Moore's Law and Koomey's Law start to breakdown. Basic research in quantum materials is then key to advancing knowledge and identifying applications for industry. For instance, with the global photonics and telecommunications market reaching £396 billion in 2015 and the semiconductor industry £260 billion, the impact of condensed-matter physics research into quantum materials, along with the associated improvements in technology, will be transformative. Furthermore, by 2024 the global market for graphene materials is predicted to reach £300 million. These atomically thin materials, capable of being combined in various ways, then require state-of-the-art analytical tools to visualise and characterise their properties in order to harness their potential.

Condensed-matter physics is concerned with the study of systems where the assembly of many identical particles leads to complex collective phenomena (e.g. magnetic ordering, superconductivity or superfluidity) that are not encoded in the properties of the individual constituent particles. The *emergent* properties can be used to engineer new materials to underpin the development of information and storage technologies. Historically, technological developments have arisen through an understanding of material properties in terms of symmetry breaking and order parameters. Symmetry breaking remains at the heart of many research streams; for example, certain complex antiferromagnetic materials violate parity and time-reversal symmetry to enable magnetoelectric control. Today condensed matter physics has entered a new era following the discovery that the physics of quantum materials is not necessarily governed by a local order parameter, but by global properties encoded in topology. The emergence of new physics and phenomena arising from symmetry breaking, as well as symmetry-protected topological phases of matter, has generated enormous interest from both a basic research and application perspective in recent years.

In systems with strong interactions, a topological charge can emerge from a non-trivial magnetisation distribution at the nanoscale (in real space) in, for example, the now well-studied skyrmions¹. Non-trivial topology can also be an intrinsic property of the internal structure of the wavefunction (in momentum space), as, for instance, in topological insulators. The topological charge of skyrmions can be used for information storage^{1,2}. Equally, the potential applications of topological insulators are extremely diverse, from low-power-consumption electronics using

magnetic topological insulators³, to fault-tolerant quantum computation using Majorana bound states engineered in topological superconductors⁴⁻⁶. Moreover, the interest in these new systems has already transferred to other disciplines. For example, in chemistry it is anticipated that the ultra-high carrier mobility of Weyl semimetals can accelerate catalytic processes⁷.

Quantum materials present immense challenges to our existing understanding of material properties, so that realising their full potential requires the development of new and advanced analytical tools. In this respect, experimental probes based on polarised synchrotron Vacuum Ultraviolet (VUV), soft and hard X-ray scattering, absorption and spectroscopy have given unrivalled insights into quantum materials, unveiling a host of complex phenomena at the electronic and magnetic level and from the atomic to mesoscale. However, the fundamental length and time scales relevant for emergent phenomena remain largely inaccessible with X-rays, impeding our understanding of quantum materials and limiting their deployment in functioning devices. For instance, the competition between charge-ordering and superconductivity in cuprates has been a topic of intense activity in recent years, with Angle-Resolved Photoemission Spectroscopy (ARPES) and hard and soft X-ray scattering making significant contributions⁸⁻¹², but the fundamental driving forces of phase separation and percolation remain elusive. The dynamics of artificial spin ice can be tailored to match current experimental capabilities¹³, but the interactions at the fundamental timescales of, for instance, ferromagnetic and antiferromagnetic fluctuations close to phase transitions in bulk materials remain largely unexplored.^{14,15} The explosive growth of 2D material production (e.g. graphene) also means that there is also an urgent need to probe electronic properties of engineered nanoscale heterostructures *in operando* when a gate voltage is applied to 2D materials or when strain is applied to tune the quasiparticle energy close to the Fermi energy.

The transformative research directions outlined below describe how the new capabilities offered by Diamond-II can help unravel some of the fundamental interactions governing the properties of quantum materials and therefore help develop processes to design, create and control such materials for future applications. The development of advanced X-ray methodologies at Diamond-II will therefore accelerate our ability to probe, predict, and exploit the properties of quantum materials. The increased flux, brilliance, stability and coherent fraction of Diamond-II will equip the UK with a unique suite of polarised VUV, soft and hard X-ray facilities, building on the success of beamlines such as I05, I06, I09, I10, I16 and I21. The upgrade of these facilities, as well as the construction of new facilities, will allow the investigation of quantum materials with unprecedented spatial and temporal resolution.

7.4.2. Inhomogeneity and emergence in quantum materials

Quantum materials often exhibit rich phase diagrams arising from the subtle interplay among the charge, spin, orbital and lattice degrees of freedom. For example, an anomalous conducting phase can emerge in correlated insulators or Mott insulators through a temperature change or chemical doping. In such a correlated metal, the mobile charges experience strong competing interactions leading to exotic phases, including the pseudogap state in cuprates and manganites, high-temperature superconductivity, charge density waves in cuprates, and even phase separation in some manganites and cuprates. Scanning synchrotron-radiation X-ray microdiffraction discovered that the ordering of oxygen interstitials, in the $\text{La}_2\text{O}_{2+y}$ spacer layers of $\text{La}_2\text{CuO}_{4+y}$ is characterised by a fractal distribution up to a maximum limiting size of 400 nm. Intriguingly, this fractal distribution of dopants seems to enhance superconductivity.¹⁶ In the cuprate superconductor $\text{HgBa}_2\text{CuO}_{4+y}$ charge density wave (CDW) puddles have been found to have a highly inhomogeneous distribution arising from oxygen interstitials (O_i) in spacer layers anticorrelated with the CDW domains in the CuO_2 planes (Figure 1), leading to a complex emergent spatial landscape for superconductivity.¹⁷

In the colossal magnetoresistance (CMR) manganites disorder can sometimes lead to new and unexpected effects. $\text{Re}_{0.5}\text{Ba}_{0.5}\text{MnO}_3$ (where Re is a rare earth element) can be prepared both in ordered and disordered forms, depending on the Re-Ba distribution¹⁸. Remarkably, only the disordered phase was found to exhibit CMR, suggesting that when phases compete the effect of small amounts of quenched disorder can result in dramatic properties that are very different from those of a slightly impure material. Disorder in the regime of phase competition is then not a mere perturbation, but alters qualitatively the properties of the material.

The emergent inhomogeneity of competing phases also exists in the metal-insulator transition (MIT) of correlated materials. In vanadium dioxide, scanning infrared microscopy has directly imaged metallic submicron size puddles at the on-set of the MIT. Such metallic puddles, manifested as an inhomogeneous mixture of insulating and metallic domains, behave as an incipient strongly correlated metal with a divergent quasi-particle mass.¹⁹

In systems where multiple phases coexist on the nanometer scale, the dynamical properties of these individual electronic phases remain largely unexplored because methods to study charge, spin or lattice dynamics lack the required spatial resolution. Over the last decade, Resonant Inelastic X-ray Scattering (RIXS) has emerged as a powerful tool to characterise spin excitations in cuprates, nickelates and iron pnictides^{20–23}. With the unprecedented energy resolution achieved recently (on ID32 at the ESRF and I21 at Diamond), RIXS has been shown to be capable of probing the electron-phonon coupling and dynamical CDWs in highly correlated quantum materials.²⁴ With an upgrade to Diamond-II, the reduction of the horizontal beam size and divergence will allow spatially-resolved RIXS on the nanoscale (nano-RIXS) with the possibility of mapping the dynamic structure factor of quantum materials in real space to trace the origin of emergent phenomena opening up the possibility of engineering new materials with technologically relevant properties.

The I21 design initially proposed a novel RIXS concept in its planning phase, where the energy dispersive plane of the RIXS spectrometer is orthogonal relative to the incoming beam (the so called μ2 RIXS concept).²⁵ Such a transformative design has two key advantages: (1) the X-ray photon throughput can be enhanced by an order of magnitude without compromising the total energy resolution; (2) it has a strong potential to implement nano-RIXS for the study of disorder or phase separation. However, to realise such a concept, one needs to achieve

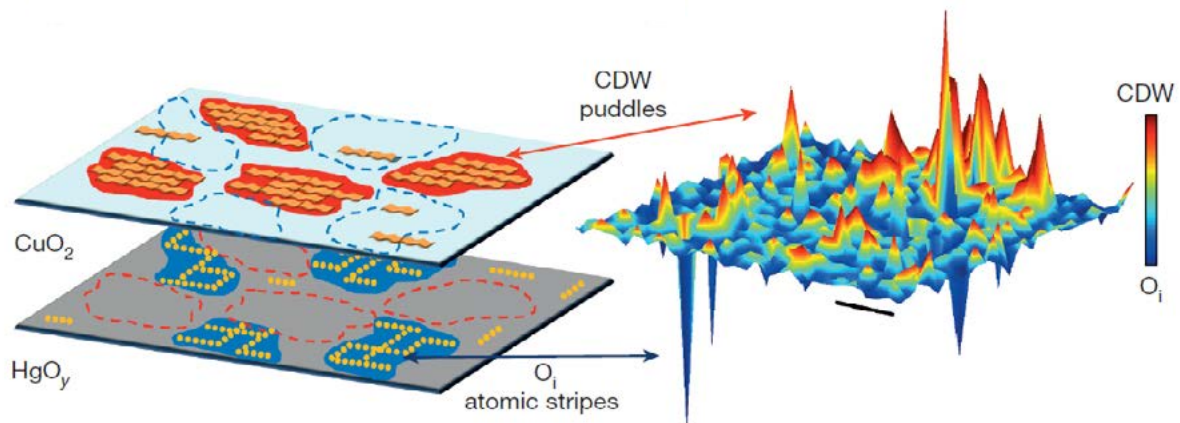


Figure 1: (left) Schematic view of the anticorrelation between the CDW puddles and the O_i interstitial stripes in $\text{HgBa}_2\text{CuO}_{4+y}$, (right) Difference map of CDW and O_i regions generated using X-ray microdiffraction. Adapted from Ref¹⁷. Reprinted by permission from Copyright Clearance Center: SpringerNature, *Nature*, Inhomogeneity of charge-density-wave order and quenched disorder in a high-Tc superconductor, G. Campi et al., Copyright (2015).

a submicron horizontal beam size at the sample position using KB focussing mirrors or zone plates as refocussing optics. The requirement was deemed too challenging due to the large horizontal size and divergence of the source at the time. With the Diamond-II upgrade, the reduction of the horizontal emittance will make such an implementation possible. It is noteworthy that the hv2 concept will make the realisation of <10 meV energy resolution more realistic because of the significant enhancement of the photon flux. The unique combination of high spatial resolution and an energy range covering many 3d and 4d transition metals will then enable electronic phase separation as well as spin, charge, lattice and orbital dynamics in quantum matter to be probed with unprecedented energy resolution in both real space and reciprocal space. In the long term, the development of nano-RIXS can be applied to the study of nanoscale structures and quantum devices.

7.4.3. Controlling emergence using phase separation

To understand and manipulate the microscopic mechanisms leading to emergent phenomena such as superconductivity, magnetoelectric coupling and magnetism it is imperative to develop a broad spectrum of X-ray techniques capable of decoding phase fluctuations with nanometer spatial and nanosecond temporal resolution. Here, X-ray Photon Correlation Spectroscopy (XPCS) to play a key role since it probes the dynamical structure factor in the time domain. The spatial correlations are then given by the scattering wavevector. Currently, up to millisecond dynamics, on length scales of hundreds of nanometres to several Ångströms, are routinely probed using third-generation sources using XPCS^{26,27}. Since the time-resolution improves as the square of the coherent flux an upgrade to Diamond-II allows the possibility of nanosecond dynamics with the increase in flux allowing spatial correlations to be probed on smaller length scales. For instance, spin ice has been the subject of intense experimental and theoretical activity for many years since the discovery of magnetic monopole by leading UK groups²⁸ and Kagomé ice states²⁹ being fascinating realisations low-temperature and field-dependent magnetic behaviour. Magnetic skyrmions are considered to be stabilised by spin fluctuations arising from the competition between the symmetric and antisymmetric exchange interactions giving rise to disordered phases with skyrmion-like short range order close to the ordering temperature in MnSi.³⁰ Element-resolved XPCS would give transformative insights into the dynamics of skyrmion formation and the relevant order parameters. XPCS would also make a huge impact on the development of nanoscale phase separation, which has the potential to create materials with new properties as opposed to conventional phase separation, which leads to a trivial superposition of the contributing phases. Since electronic fluctuations of individual domains become faster as the domains become smaller, the increased coherence of

Diamond-II is essential to develop and control materials on the nanoscale. The ability of XPCS to cover timescales from ~1Hz to ~1GHz in an element- and site-selective manner (not available with neutron spin-echo) would allow access to a range of dynamics currently inaccessible in a single technique ushering in a new era of understanding and exploiting electronic and magnetic phase transitions.

To realise nanoscale spatial resolution and higher frequency magnetisation dynamics in soft X-ray XPCS requires the highest possible coherent flux up to ~1keV, whereas in the hard X-ray range the highest possible coherent flux gives access to higher-*q* fluctuations representing atomic scale structural dynamics. A particular ordering, or correlation, can then be picked out by characteristic Bragg peaks, while the intensity distribution in and around the peaks is determined by the domain morphology. In the hard X-ray range, where magnetic sensitivity is rather weak, XPCS would then be predominantly a structural probe offering the potential to understand phonon modes during phase separation processes if sufficient time resolution could be realised. In this respect, the development of full-field fast readout detectors capable of time stamping events from single bunches in the soft and hard X-ray range will allow a time resolution of a few ns. Sub-ns readout times are some way off into the future, but it is possible to conceive of improvements to, for instance, streak-cameras to achieve the highest time resolution.

7.4.4. A new dimension for magnetism

Magnetic materials have been developed into innovative technologies for thousands of years, from the discovery of magnetite for navigation to electricity generation to the use of exchange bias in modern data storage centres. Hand-in-hand with this progress has been the dramatic rise of predictive theories, along with advances in sample fabrication and characterisation tools that have underpinned many of the developments made in the last century. Today, magnetic materials are ubiquitous in the production and transformation of energy³¹, sensing, data storage and biomedicine.³² In the future they will continue to enable key technologies that will make our economy more efficient, greener and highly automated.^{31,32} The properties of applied magnetic materials - whether in the form of bulk permanent magnets, inductor and transformer cores, or in the form of thin films memories and sensors - are determined by the interaction of a highly inhomogeneous magnetisation (a 3D vector field) with the material microstructure. Material performance is optimised (e.g. in permanent magnets³¹) and new functionalities are unlocked (e.g. giant magnetoresistance in the spin valve sensor³³) when we achieve good control of this complex 3D interaction. Currently available experimental techniques are unable to capture this complexity.

Macroscopic measurement probes give an average of all material properties and thus give, at best, only indirect information about the key role of magnetic and microstructural inhomogeneities. Magnetic microscopy currently provides 2D maps of the magnetisation vector field, which has revolutionised the performance of thin films used in devices. However, more than a century after the beginning of modern research in magnetism,^{34,35} and more than eighty years after the first magnetic imaging experiments³⁶, the inner 3D workings of a permanent magnet have never been observed, and thus the processes that govern magnetic reversal remain elusive. However, recent X-ray results³⁷ have shown the way forward (Figure 2). Magnetic X-ray Tomography (MXT) can provide element-selective 3D mapping of the magnetisation of thick samples with nanometer scale spatial resolution. As shown by the impact of MRI tomography on life sciences, 3D imaging has the potential to unlock transformative science, and MXT can be expected to do so in several areas of magnetism.

In particular, imaging magnetisation reversal in 3D has the potential to solve a classic micromagnetic problem known as the Brown paradox^{38,39}, i.e. the fact that the highest coercive field attainable never exceeds a very small fraction of the theoretically predicted value. Apart from the fundamental interest, this problem is extremely relevant in practice because the coercive field is a measure of the energy density that can be stored in a magnet³¹. MXT imaging will allow the mechanisms responsible for coercivity to be linked to nucleation and pinning of magnetic domain walls in the presence of defect morphology and compositional inhomogeneity. Controlled design of permanent magnets with optimum coercivity (and therefore energy density) will become possible by adding suitable dopants to modify the microstructure following insights gained through MXT. This will be transformative, since the permanent magnet generator concept based on NdFeB magnets is currently setting a new standard for wind turbines.⁴⁰ Furthermore,

permanent magnet motors alone are estimated to consume £34.5 billion of electrical energy in the US annually,³¹ so that improvements in material performance (e.g. by an increase in energy density that can lead to the use of smaller magnets) could give huge economical gains as well as environmental benefits.

In ferromagnetic thin films, geometrical confinement and topological properties stabilise isolated chiral objects (domain walls, skyrmions and vortices) with complex 3D spin structures, unique physical properties and great potential for information storage.^{1,2,41,42} This is at the cutting-edge of magnetism research, and it can be expected that it will become more mainstream in the coming years. Here, MXT could transform the field because it will permit direct 3D imaging of how the position, velocity and chirality of these isolated magnetic objects can be controlled by spin polarised currents, magnetic and electric fields.

Recently, the near surface switching of antiferromagnetic order in CuMnAs and Mn₂Au thin films has generated considerable interest in the community.^{43,44} The work represents the combined strength of predictive theoretical modelling, advanced sample synthesis methods and state-of-the-art X-ray imaging tools. Understanding the effects of inhomogeneity, defect pinning, magnetostriction and switching using full tomographic imaging will be key to developing antiferromagnetic materials to the level of device performance. One of the most exciting new prospects for future technology is the prediction that antiferromagnetic systems, including CuMnAs, host Dirac quasiparticles.^{45,46} These are topologically-protected electronic features that provide excellent functionality such as ultrahigh electron mobilities and quantised Hall effects. Uniquely to antiferromagnets, their very existence in these systems is linked to the magnetic order, leading to the tantalising prediction of a topological metal insulator transition (TMIT). By rotating the magnetic order, for example using electrical currents,⁴³ one should

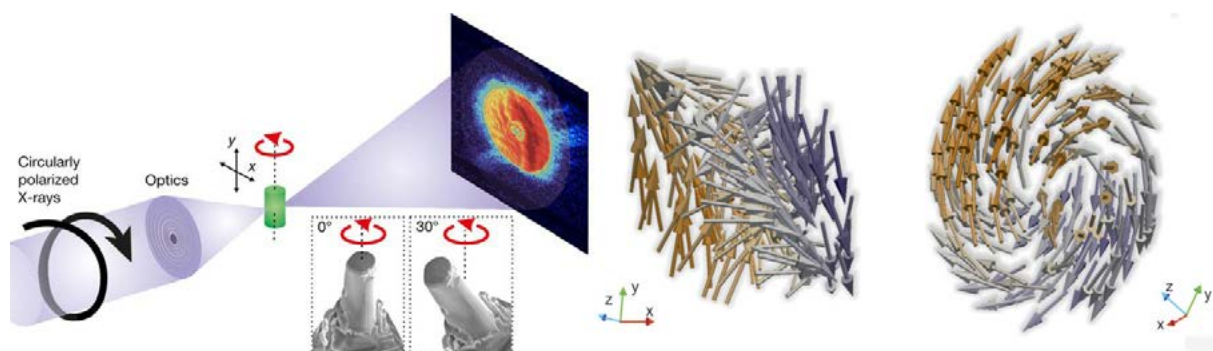


Figure 2: Experimental geometry (left) to determine the three-dimensional magnetisation structures in a microcylinder of GdCo₂, revealing the internal details of domain wall and vortex structures (right). Adapted from Ref³⁷. Reprinted by permission from Copyright Clearance Center: SpringerNature, Nature, Three-dimensional magnetization structures revealed with X-ray vector nanotomography, C. Donnelly et al., Copyright (2017).

be able to switch between semiconducting and metallic conduction. The dependence of the TMIT on the direction of the antiferromagnetic spin axis, with respect to the crystal axes, means that accurate 3D magnetic mapping together with high-resolution nano-ARPES (both only practical using Diamond-II) will be essential for device development. In this respect, polarised X-rays are a unique probe of antiferromagnetic order, which is hard to study by conventional means due to the absence of stray magnetic fields. Combining tomographic methods with X-ray magnetic linear dichroism offers the possibility of obtaining 3D images of frustrated spin structures in antiferromagnetic materials, and to investigate their behaviour in response to external stimuli such as pulsed currents. While challenging, such approaches have the potential to provide a step change in our understanding of electrically-driven antiferromagnetic domain switching, and so offer a route to exploiting their ultrafast properties for new information and communication technologies.

MXT also has the potential to drive the development of an entirely new field, namely 3D nanomagnetism, where thin films with thicknesses in the 50 nm range extending over tens of micrometres, are shaped into 3D configurations using advanced two-photon lithography techniques. This new field has the potential to permit the development of transformative 3D storage technologies based on the controlled movement of novel domain wall structures.⁴⁷ The exploration of emergent spin textures³² using MXT³⁷ can then lead to the discovery of new forms of magnetic ordering arising from the interaction between spatially confined spins in 3D curved geometries.

Lensless imaging, such as Coherent Diffraction Imaging (CDI) and Ptychography, have developed considerably in recent years achieving a spatial resolution of ~15 nm in 3D under favourable circumstances.⁴⁸ A low-emittance machine would increase the coherent fraction by at least an order of magnitude from 500 eV to 10 keV, and together with improvements to the insertion devices and beamline optics, could lead to an increase in the coherent flux at the sample by several orders of magnitude. This then enables 3D nanotomography to become a routine tool with which to explore the magnetic landscape of functional devices *in operando*. The aim would be to acquire 3D magnetic nanotomographs on timescales comparable to those currently achieved on beamline I12 (~10 tomographs per second). CDI, which can be performed in a magnetic field, would also complement insights provided by the PhotoEmission Electron Microscope (PEEM) on beamline I06 which cannot image in strong magnetic fields, but does provide spectroscopic information not as easily obtained using coherent imaging.

The increased coherence and brilliance of the source would also require the development of MHz frame rate detectors (preferably operating at 500eV and above), alongside stringent requirements for sample stages with

fast scanning velocities to fully exploit the new source. The RASOR diffractometer on I10, with suitable upgrades, would be an obvious instrument to explore 2D and 3D spin textures on the nanoscale and would complement the improved capabilities of an upgrade to I16 providing similar probes in the hard X-ray range.

7.4.5. Tuning coupled ferroic order

The coupling between magnetic and electric order parameters has led to several potentially ground-breaking applications of multiferroics such as magnetic read heads, magnetoelectric memory and logic devices.⁴⁹ In recent years, hard X-ray diffraction has revealed the most subtle changes in crystal structure due to magnetoelastic interactions^{50,51} so that multiferroics are currently intensely studied to improve the coupling of magnetic and ferroelectric properties at room temperature. By far the most studied material is BiFeO₃ since it is magnetic above room temperature and therefore potentially suitable for applications. The cycloidal domains in BiFeO₃ have been imaged directly on the surface of a single-domain polar BiFeO₃ crystal using non-resonant magnetic X-ray diffraction on beamline I16.⁵² However, for thin films of BiFeO₃ the domains were beyond the spatial resolution available on I16 and required the PEEM combined with X-ray Magnetic Linear Dichroism (XMLD) on I06 to uncover the nanoscale domain structure arising from monoclinic distortions in the thin film⁵³. Nanocrystalline materials are also of immense interest, with electronic properties shaped by their large surfaces, crystal morphology, strain and defects. Direct measurement of magnetic and electronic ordering is, however, extraordinarily challenging due to the weak scattering cross-section and low scattering volume. Nevertheless, several glimpses of future opportunities using Diamond-II are found in CDI studies of strain in multiferroic nanocrystals. Optically induced-strain in BiFeO₃ can not only be determined using CDI, but also reveals that the strain is localised to surface layers.⁵⁴ Photostriction is known to undergo significant modification from magneto-electric effects, emphasising the familiar story of competing ordering phenomena in strongly-correlated systems. The development of electronic, spin and strain domain mapping using the much higher hard X-ray coherent flux of Diamond-II will bring new insight to nanocrystalline material development. Here, the low emittance offered by Diamond-II would increase the spatial resolution of diffraction imaging using, for instance, compound refractive lenses or coherent diffraction, which would allow the details of magnetic ordering and femtoscale structural distortions to be determined with nanoscale spatial resolution.

This incredible sensitivity to structural distortions^{55,56} now requires improvements to sample environment in order to relate the atomic displacements to the effects of magnetic and electric fields at low temperatures,

which can only be realistically achieved using horizontal scattering geometries made possible by the low emittance of Diamond-II. Hard X-ray diffraction would then provide a transformative opportunity to discover and understand spontaneous ordering of atomic-scale electronic and magnetic properties in crystals, thin films and micron sized single-grain samples. The gains in emittance, with low horizontal beam divergence and focus, will allow measurements to be performed using a fully optimised horizontal scattering geometry with microfocused beams extending down to the lower energy $4d$ L -edges, instead of the currently employed vertical geometry. A high-stability, fully-optimised horizontal geometry will then facilitate a much wider range of research, allowing complex electronic and magnetic structures (magnetic frustration, spiral/cycloidal, Kitaev systems) to be probed under variable low temperatures and high magnetic fields, allowing links to be made to fundamental atomic-scale interactions. The development of a new diffractometer with a smaller sphere of confusion would then allow a scattering response from single-domain or micron sized samples or volumes, giving key insights into magnetic and electronic ordering that has remained elusive. For instance, distinguishing between multi- q structures (e.g. a skyrmion lattice) and single- q multidomain structures (e.g. helical skyrmion precursor phases) is currently a significant challenge. There are also long-standing mysteries surrounding the nature of the hidden order in materials such as URu_2Si_2 , where improved X-ray domain mapping would give more conclusive insights.

Soft X-ray Resonant Diffraction (SXR) has led to some remarkable insights into multiferroic ordering. In ground-breaking experiments, SXR revealed the correlated, long range polarisation of the O sites in $TbMn_2O_7$, as well as revealing a competition between non-collinear ordering during the ferroelectric phase transition in $TbMnO_3$.^{57,58} $TbMnO_3$ is a prototypical type-II multiferroic and has generated considerable interest since the domain walls have unexpected structures and are predicted to behave as novel nanoreactors⁵⁹. Here, spatially resolved SXR using, for instance, efficient zone plate focussing could reveal the 2D details of magnetic and electronic ordering at the domain walls, opening up new avenues of research into novel phases of matter only present at domain walls. The interplay between hard and soft X-ray science at synchrotron facilities often leads to new fields of activity. For instance, hard X-ray scattering, originally used to understand orbital ordering in manganites, led directly to the development of soft X-ray diffraction,⁶⁰ which has revolutionised our understanding of multiferroic ordering, superconductivity and ultrafast spin dynamics. In the spirit of these developments, it is possible that new facilities dedicated to exploiting the coherent properties of Diamond-II could be proposed to develop 2D and 3D imaging in the soft and hard X-ray range with complementary strengths and sample environments.

7.4.6. The rise of 2D materials

The incredible success of graphene has inspired the explosive growth of research into atomically thin 2D materials, such as Transition Metal Dichalcogenides (TMDCs), with appealing properties including transparency, flexibility and very large carrier mobility.⁶¹ In particular, flexible nanoelectronics stand to benefit greatly from the development of 2D materials because of their unrivalled device physics and mechanics on polymer substrates. However, these materials also provide an incredible opportunity to design and manipulate novel electronic structures and magnetic phenomena arising from a confined geometry. For instance, conventional electronic devices based on nanostructured components typically exploit the electron spin and charge degrees of freedom. On the other hand, electrons in 2D materials with a honeycomb lattice structure (e.g. graphene, MoS_2) possess another degree of freedom (pseudospin) due to valley points in the band structure. For graphene, it has been suggested⁶² that a valley degree of freedom could be used to carry information in electronic devices if a controllable way is found to produce valley polarisation. In contrast to graphene, monolayer MoS_2 is a direct band gap semiconductor possessing an inversion asymmetric honeycomb lattice structure that readily facilitates optical and electrical control. The direct energy gaps in monolayer MoS_2 are located at inequivalent K and K' valleys of the Brillouin zone so that electrons moving in the two valleys experience opposite, but equal, effective magnetic fields due to the inversion asymmetry and large spin-orbit coupling. The electrons in the K and K' valleys therefore experience opposite Lorentz-like forces and so move in opposite directions perpendicular to the drift current. This effect, known as the valley Hall effect, arises from the coupling of the valley degree of freedom to the orbital motion of the electrons. Circularly polarised light can then be used to create a population imbalance between the two valleys, which gives rise to a measurable valley Hall effect and a means to detect and control a quantity known as the pseudospin⁶³ which can arise from the sublattice, the band structure valley points, the layer for bilayers or the actual spin. The electrical generation of a valley magnetisation (a magnetoelectric effect) has also recently been reported in a strained MoS_2 monolayer⁶⁴ opening up the possibility of tuning the interaction between the different pseudospins with the aim of developing new semiconducting optoelectronics.

Theoretically, magnetic ordering in a 2D isotropic Heisenberg model (at finite temperatures) is prohibited by the Mermin–Wagner theorem. However, magnetic anisotropy removes this restriction by creating a spin wave gap and so, in principle, enables the possibility of 2D Ising ferromagnetism. To date, most van der Waals bulk crystals are magnetically soft with a small easy-axis anisotropy in the direction normal to the 2D plane.

Diamond-II: Advancing physical sciences

Harnessing long-range ferromagnetic order in 2D van der Waals crystals therefore relies on retaining a sufficient magnetic anisotropy in the 2D regime, which represents a significant challenge. Nevertheless, pristine $\text{Cr}_2\text{Ge}_2\text{Te}_6$ and CrI_3 atomic layers have been shown to possess long range ferromagnetic order^{65,66} with unprecedented control of the ferromagnetic transition temperature using small magnetic fields of $\sim 0.3\text{T}$.

Bright and stable single photon emitters can be realised using monolayer WSe_2 with localised light sources found at random positions on the edges of the material. However, attempts to position the emitters on the microscale by scratching the WSe_2 monolayer with a metal tip or by introducing microscale holes were limited in success. Recently, single-photon emitters in WSe_2 have been developed by draping a monolayer across a nanoscale gap between two single-crystalline gold nanorods.⁶⁷ The novel method to introduce a variable strain landscape in the monolayer led to the formation of a potential well, so that single-photon emitters were realised and localised to around 100 nm. Remarkably, the polarisation of the emitted light was also oriented with respect to the nanoscale gap.

In general, layered van der Waals materials, such as MoS_2 , $\text{Cr}_2\text{Ge}_2\text{Te}_6$ and CrI_3 , discussed above, allow mechanical exfoliation from bulk single crystals, leading to a huge number of possible 2D materials of which only a handful have been realised and developed. The challenges are significant with monolayers being plagued by vacancies, impurities and lattice distortions as well as the unavoidable influence of the substrate material and gating contacts. The availability of so many 2D materials with various electronic structures allows the construction of artificial heterostructures by stacking individual atomic layers. As a

pioneering example, 2D photodetectors have been realised by sandwiching semiconducting TMDCs, such as WS_2 and MoS_2 , between transparent graphene electrodes.⁶⁸

ARPES has made significant contributions to the rise of 2D materials, but the lack of high spatial and spin resolution has limited progress. For instance, spin-polarised studies are hampered by a low polarisation arising predominantly from twin domains requiring the development of single domain layers which are only now being realised.⁶⁹

Here, the higher spatial resolution of spin-resolved nano-ARPES will be essential to understand and develop the unique electronic landscape of 2D materials and will only become feasible with the increased flux available using Diamond-II. Higher spatial coherence is also required to increase the photon flux transmitted by the diffractive optics, and to achieve better nano-focussing (10-100 nm) at the sample on the nano-ARPES system. This increase in flux, combined with a new generation of spin detector, would give access to a spin-resolved nano-ARPES capability that would transform the characterisation of the local electronic structure in new 2D materials. In particular, it is of enormous interest to be able to perform such measurements while manipulating the material properties *in situ*. This would be transformative both for understanding the operation of prototypical devices, and more generally for tuning between exotic quantum many-body states and phases in complex solid materials to address fundamental questions on the nature of their collective states. Exciting possibilities include implementing field-effect doping schemes, which are the mainstay of semiconductor microelectronics, to tune between correlated phases of 2D materials. Additional opportunities include mechanically-straining transition-metal oxides to drive topological

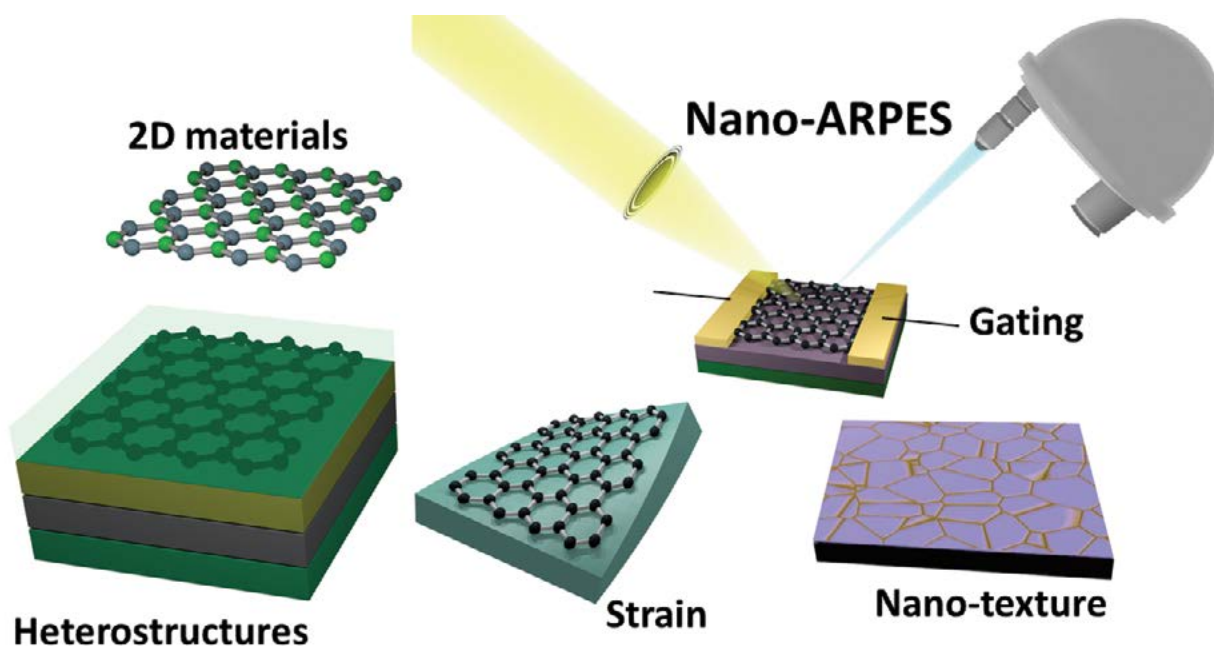


Figure 3: Schematic showing classes of 2D materials and *in situ* control processes that would open up novel science areas through the exploitation of small beams and nano-ARPES techniques at Diamond-II. Copyright Diamond Light Source.

transitions of their Fermi surface and probing the effect of changing an applied potential for tuning metal-insulator transitions for possible applications in “Mottronics”. Figure 3 represents some of the possibilities for future studies of 2D materials, the effects of strain on the system and the ability to monitor the structures whilst under electronic control and biasing.

7.4.7. Topological matter

In the 1980s, the discovery of the quantum Hall effect in a 2D electron gas, under the influence of a magnetic field, introduced the importance of topological order in condensed matter physics. However, it was unclear if these states could exist in materials that were not subjected to very low temperatures and high fields, until 2005, when key theoretical advances predicted that non-magnetic insulators could possess stable edge-states in the absence of a magnetic field⁷⁰. The idea that the role of magnetic field could be assumed by spin-orbit coupling within the material led to many experimental studies, targeting two key features that would act as markers of the topological state: dissipationless transport and separation of the different spin states moving in opposite directions around the edge of 2D samples. The spin-orbit coupling was found to be ideal in heavy atom, small bandgap semiconductors, with initial experimental confirmation of the topological insulator (TI) state found in (Hg,Cd)Te quantum well structures.⁷¹ These structures were still 2D in nature through the heterostructure geometry, which stimulated the search for 3D TI structures that would be insulating in the bulk, but have protected metallic states at the surface. The first confirmation of this behaviour was observed in $\text{Bi}_x\text{Sb}_{1-x}$ ⁷² using ARPES as a direct probe of the band structure. The dispersion of the states in the band structure clearly showed the bulk band gap (insulator) with single surface states crossing the gap and meeting at a single Dirac point at the Brillouin zone centre. In the last decade, there has been intense activity to discover other materials that can host the TI state, including Bi_2Se_3 and Bi_2Te_3 . Studies are evolving to understand how TI materials may be utilised in future applications, for example, through studies of the Aharonov-Bohm effect in Bi_2Se_3 nanoribbons subjected to a magnetic field along the ribbon.⁷³ Reducing the dimensionality further, 1D systems such as Sb_2Te_3 nano-wires exhibit quantum transport that is governed by the presence of nontrivial topological surface states. It has been shown using nano-ARPES that the metallic-like surface state around the wire cross section is characterised by a Dirac cone dispersion⁷⁴. This research field has also stimulated a great deal of interest in trying to stabilise novel emergent states, including the creation of Majorana Fermions, theoretically predicted to occur at the interface between a TI and a superconductor⁷⁵. These states have even been suggested as a future technology for use in a topological quantum computer.⁷⁶

Topological insulators form one group of material systems that gain their properties through topological protection, whilst other novel phases of matter are also being investigated with respect to the role that topology plays. Weyl and Dirac semimetals belong to a newly discovered class of 3D topological materials, where two or more bands at the Fermi energy are exactly degenerate at specific points in \mathbf{k} -space, forming nodes that are topologically protected and dictate unusual transport properties. Weyl phases exist in materials that are close to the transition between a trivial insulator and a topological insulator, but where inversion symmetry is broken. In these systems, the topological protection is achieved not through the bulk band gap but through the separation (in momentum space) of the gapless Dirac nodes. These states have been experimentally observed in materials including TaAs, NbAs and TaP^{77,78} using high resolution VUV ARPES and soft X-ray ARPES (SX-ARPES). However, the electronic structure in many systems is simply inaccessible due to grain averaging so that illumination by the smaller photon beam available at Diamond-II will allow new insights into a much broader range of materials with a view to developing high-mobility carriers for electronics applications as well as underpinning progress in quantum field theory.

In lower dimensional systems, a single atomic layer 2D-TI is expected to exhibit a Quantum Spin Hall Effect (QSHE) effect localised at the edge of the layer, where robust helical edge states dominate the transport.⁷⁹ The experimental evidence for such states has been inferred from conductivity measurements,⁸⁰ suggesting that edge state phenomena would greatly benefit from the increased sensitivity of nano-ARPES. This would then allow a much more detailed understanding of the changing nature of the electronic structure across small grains and is essential in developing our knowledge of the mechanism of topological protection. Adding in the possibility of spin-detection to the probe would transform the field, as the spin state of each feature could be quickly and easily identified. It has also been predicted theoretically that a QSHE state could be induced by an electric field in monolayer transition metal dichalcogenides (TMDCs) via a topological phase transition.⁸¹ The ability to measure the electronic structure under gating control would be transformative, since changes to the electronic structure could be directly related to the topological phase determined using nano-ARPES.

A number of opportunities exist with the Diamond-II upgrade. For example, in the Weyl semimetals, SX-ARPES is required to observe the Weyl nodes or Dirac points in the 3DI systems, because the so-called k_z broadening effect becomes less severe at higher photon energies. To compensate the intensity loss due to the rapid reduction of photoionisation cross-section with increasing photon energy it is essential for the incident beam to impinge the sample at a grazing angle. However, this arrangement

significantly elongates the beam footprint which adversely affects the momentum resolution of the electron analyser. On I09 this situation will be improved by the reduction in horizontal beam size with the Diamond-II upgrade, leading to a nearly threefold increase in the analyser signal.

On beamline I05, maintaining a tuneable source down to low photon energies (~18-20 eV) is essential and can be achieved by installing new low-power APPLE-Knot insertion devices. There is also an opportunity to revisit the optimal energy range and look at the potential to integrate a low photon energy laser system for additional and complementary high-resolution ARPES. Furthermore, the current focussing optics for nano-ARPES are based on Fresnel zone plates that would benefit from an increase in the coherent flux within the small spot to fill the optic.

References

- Fert, A., Cros, V. & Sampaio, J. Skyrmions on the track. *Nature Nanotechnology* **8**, 152–156 (2013).
- Fert, A., Reyren, N. & Cros, V. Magnetic skyrmions: Advances in physics and potential applications. *Nature Reviews Materials* **2**, 17031 (2017).
- Chang, C. Z. *et al.* Experimental observation of the quantum anomalous Hall effect in a magnetic topological insulator. *Science* (80-.). **340**, 167–170 (2013).
- Nayak, C., Simon, S. H., Stern, A., Freedman, M. & Das Sarma, S. Non-Abelian anyons and topological quantum computation. *Rev. Mod. Phys.* **80**, 1083–1159 (2008).
- He, Q. L. *et al.* Chiral Majorana fermion modes in a quantum anomalous Hall insulator–superconductor structure. *Science* (80-.). **357**, 294–299 (2017).
- Zhang, P. *et al.* Observation of topological superconductivity on the surface of an iron-based superconductor. *Science* (80-.). **360**, 182–186 (2018).
- Rajamathi, C. R. *et al.* Weyl Semimetals as Hydrogen Evolution Catalysts. *Adv. Mater.* **29**, 1–6 (2017).
- Le Tacon, M. *et al.* Inelastic X-ray scattering in YBa₂Cu₃O_{6.6} reveals giant phonon anomalies and elastic central peak due to charge-density-wave formation. *Nat. Phys.* **10**, 52–58 (2013).
- Ghiringhelli, G. *et al.* Long-range incommensurate charge fluctuations in (Y,Nd)Ba₂Cu₃O_{6+x}. *Science* (80-.). **337**, 821–825 (2012).
- Chang, J. *et al.* Direct observation of competition between superconductivity and charge density wave order in YBa₂Cu₃O_{6.67}. *Nat. Phys.* **8**, 871–876 (2012).
- Comin, R. *et al.* Broken translational and rotational symmetry via charge stripe order in underdoped YBa₂Cu₃O_{6+y}. *Science* (80-.). **347**, 1335 (2015).
- Achkar, A. J. *et al.* Superconductivity: Nematicity in stripe-ordered cuprates probed via resonant x-ray scattering. *Science* (80-.). **351**, 576–578 (2016).
- Farhan, A. *et al.* Exploring hyper-cubic energy landscapes in thermally active finite artificial spin-ice systems. *Nat. Phys.* **9**, 375–382 (2013).
- Konings, S. *et al.* Magnetic domain fluctuations in an antiferromagnetic film observed with coherent resonant soft x-ray scattering. *Phys. Rev. Lett.* **106**, 1–4 (2011).
- Shpyrko, O. G. *et al.* Direct measurement of antiferromagnetic domain fluctuations. *Nature* **447**, 68–71 (2007).
- Fratini, M. *et al.* Scale-free structural organization of oxygen interstitials in La₂CuO_{4+y}. *Nature* **466**, 841–844 (2010).
- Campi, G. *et al.* Inhomogeneity of charge-density-wave order and quenched disorder in a high-Tc superconductor. *Nature* **525**, 359–362 (2015).
- Dagotto, E. Complexity in Strongly Correlated Electronic Systems - ProQuest. *Science* (80-.). **309**, 257–262 (2005).
- Qazilbash, M. M. *et al.* Mott Transition in VO₂ Revealed by Infrared Spectroscopy and Nano-Imaging. *Science* (80-.). **318**, 1750 (2007).
- Braicovich, L. *et al.* Magnetic excitations and phase separation in the underdoped La_{2-x}Sr_xCuO₄ superconductor measured by resonant inelastic X-Ray scattering. *Phys. Rev. Lett.* **104**, 077002 (2010).
- Schlappa, J. *et al.* Spin-orbital separation in the quasi-one-dimensional Mott insulator Sr₂CuO₃. *Nature* **485**, 82–85 (2012).
- Fabbris, G. *et al.* Doping Dependence of Collective Spin and Orbital Excitations in the Spin-1 Quantum Antiferromagnet La_{2-x}Sr_xNiO₄ Observed by X Rays. *Phys. Rev. Lett.* **118**, (2017).
- Zhou, K. J. *et al.* Persistent high-energy spin excitations in iron-pnictide superconductors. *Nat. Commun.* **4**, 1470 (2013).
- Chaix, L. *et al.* Dispersive charge density wave excitations in Bi₂Sr₂CaCu₂O_{8+δ}. *Nat. Phys.* **13**, 952–956 (2017).
- Strocov, V. N. Concept of a spectrometer for resonant inelastic X-ray scattering with parallel detection in incoming and outgoing photon energies. *J. Synchrotron Rad.* **17**, 103–106 (2010).
- Chen, X. M. *et al.* Remarkable Stability of Charge Density Wave Order in La_{1.875}Ba_{0.125}CuO₄. *Phys. Rev. Lett.* **117**, 167001 (2016).
- Morley, S. A. *et al.* Vogel-Fulcher-Tammann freezing of a thermally fluctuating artificial spin ice probed by x-ray photon correlation spectroscopy. *Phys. Rev. B* **95**, 3–9 (2017).
- Bramwell, S. T. *et al.* Measurement of the charge and current of magnetic monopoles in spin ice. *Nature* **461**, 956–959 (2009).
- Tabata, Y. *et al.* Kagomé ice state in the dipolar Spin Ice Dy₂Ti₂O₇. *Phys. Rev. Lett.* **97**, 257205 (2006).
- Pappas, C. *et al.* Chiral paramagnetic skyrmion-like phase in MnSi. *Phys. Rev. Lett.* **102**, 197202 (2009).
- Gutfleisch, O. *et al.* Magnetic materials and devices for the 21st century: Stronger, lighter, and more energy efficient. *Advanced Materials* **23**, 821–842 (2011).
- Fernández-Pacheco, A. *et al.* Three-dimensional nanomagnetism. *Nat. Commun.* **8**, 15756 (2017).
- McCray, W. P. How spintronics went from the lab to the iPod. *Nature Nanotechnology* **4**, 2–4 (2009).
- Curie, P. Lois expérimentales du magnétisme. Propriétés magnétiques des corps à diverses températures. *Ann Chim Phys.* **5**, 289–405 (1895).
- Weiss, P. L'hypothèse du champ moléculaire et la propriété ferromagnétique. *J. Phys. Théorique Appliquée* **6**, 661–690 (1907).
- Bitter, F. On inhomogeneities in the magnetization of ferromagnetic materials [1]. *Physical Review* **38**, 1903–1905 (1931).

37. Donnelly, C. *et al.* Three-dimensional magnetization structures revealed with X-ray vector nanotomography. *Nature* **547**, 328–331 (2017).
38. Brown, W. F. Virtues and weaknesses of the domain concept. *Rev. Mod. Phys.* **17**, 15–19 (1945).
39. Shtrikman, S. & Treves, D. On the resolution of brown's paradox. *J. Appl. Phys.* **31**, S72–S73 (1960).
40. Pavel, C. C. *et al.* Substitution strategies for reducing the use of rare earths in wind turbines. *Resour. Policy* **52**, 349–357 (2017).
41. Ryu, K.-S., Thomas, L., Yang, S.-H. & Parkin, S. Chiral spin torque at magnetic domain walls. *Nat. Nanotechnol.* **8**, 527–533 (2013).
42. Chmiel, F. P. *et al.* Observation of magnetic vortex pairs at room temperature in a planar α -Fe₂O₃/Co heterostructure. *Nat. Mater.* **17**, 581–585 (2018).
43. Wadley, P. *et al.* Spintronics: Electrical switching of an antiferromagnet. *Science (80-)*. **351**, 587–590 (2016).
44. Bodnar, S. Y. *et al.* Writing and reading antiferromagnetic Mn₂Au by Néel spin-orbit torques and large anisotropic magnetoresistance. *Nat. Commun.* **9**, 348 (2018).
45. Šmejkal, L., Železný, J., Sinova, J. & Jungwirth, T. Electric Control of Dirac Quasiparticles by Spin-Orbit Torque in an Antiferromagnet. *Phys. Rev. Lett.* **118**, 1–5 (2017).
46. Šmejkal, L., Mokrousov, Y., Yan, B. & MacDonald, A. H. Topological antiferromagnetic spintronics. *Nature Physics* **14**, 242–251 (2018).
47. Parkin, S. S. P., Hayashi, M. & Thomas, L. Magnetic domain-wall racetrack memory. *Science* **320**, 190–194 (2008).
48. Holler, M. *et al.* High-resolution non-destructive three-dimensional imaging of integrated circuits. *Nature* **543**, 402–406 (2017).
49. Heron, J. T. *et al.* Deterministic switching of ferromagnetism at room temperature using an electric field. *Nature* **516**, 370–373 (2014).
50. Vecchini, C. *et al.* Magnetically induced femtoscale strain modulations in HoMn₂O₅. *Phys. Rev. B - Condens. Matter Mater. Phys.* **89**, 125114 (2014).
51. Walker, H. C. *et al.* Femtoscale magnetically induced lattice distortions in multiferroic TbMnO₃. *Science (80-)*. **333**, 1273–1276 (2011).
52. Johnson, R. D. *et al.* X-Ray imaging and multiferroic coupling of cycloidal magnetic domains in ferroelectric monodomain BiFeO₃. *Phys. Rev. Lett.* **110**, 1–5 (2013).
53. Waterfield Price, N. *et al.* Coherent Magnetoelastic Domains in Multiferroic BiFeO₃ Films. *Phys. Rev. Lett.* **117**, 1–5 (2016).
54. Newton, M. C., Parsons, A., Wagner, U. & Rau, C. Coherent x-ray diffraction imaging of photo-induced structural changes in BiFeO₃ nanocrystals. *New J. Phys.* **18**, 093003 (2016).
55. Vecchini, C. *et al.* Magnetically induced femtoscale strain modulations in HoMn₂O₅. *Phys. Rev. B - Condens. Matter Mater. Phys.* **89**, 125114 (2014).
56. Walker, H. C. *et al.* Femtoscale magnetically induced lattice distortions in multiferroic TbMnO₃. *Science (80-)*. **333**, 1273–1276 (2011).
57. Wilkins, S. B. *et al.* Nature of the magnetic order and origin of induced ferroelectricity in TbMnO₃. *Phys. Rev. Lett.* **103**, 207602 (2009).
58. Beale, T. A. W. *et al.* Antiferromagnetically spin polarized oxygen observed in magnetoelectric TbMn₂O₅. *Phys. Rev. Lett.* **105**, 3–6 (2010).
59. Farokhipoor, S. *et al.* Artificial chemical and magnetic structure at the domain walls of an epitaxial oxide. *Nature* **515**, 379–383 (2014).
60. Wilkins, S. B., Hatton, P. D., Roper, M. D., Prabhakaran, D. & Boothroyd, A. T. Soft X-Ray Resonant Magnetic Diffraction. *Phys. Rev. Lett.* **90**, 4 (2003).
61. Akinwande, D., Petrone, N. & Hone, J. Two-dimensional flexible nanoelectronics. *Nature Communications* **5**, 5678 (2014).
62. Rycerz, A., Tworzydło, J. & Beenakker, C. W. J. Valley filter and valley valve in graphene. *Nat. Phys.* **3**, 172–175 (2007).
63. Mak, K. F., McGill, K. L., Park, J. & McEuen, P. L. The valley Hall effect in MoS₂ transistors. *Science (80-)*. (2014). doi:10.1126/science.1250140
64. Lee, J., Wang, Z., Xie, H., Mak, K. F. & Shan, J. Valley magnetoelectricity in single-layer MoS₂. *Nat. Mater.* **16**, 887–891 (2017).
65. Gong, C. *et al.* Discovery of intrinsic ferromagnetism in two-dimensional van der Waals crystals. *Nature* **546**, 265–269 (2017).
66. Huang, B. *et al.* Layer-dependent ferromagnetism in a van der Waals crystal down to the monolayer limit. *Nature* **546**, 270–273 (2017).
67. Kern, J. *et al.* Nanoscale Positioning of Single-Photon Emitters in Atomically Thin WSe₂. *Adv. Mater.* **28**, 7101–7105 (2016).
68. Britnell, L. *et al.* Strong light-matter interactions in heterostructures of atomically thin films. *Science (80-)*. **340**, 1311 (2013).
69. Riley, J. M. *et al.* Direct observation of spin-polarized bulk bands in an inversion-symmetric semiconductor. *Nat. Phys.* **10**, 835–839 (2014).
70. Kane, C. L. & Mele, E. J. Z₂ Topological Order and the Quantum Spin Hall Effect. *Phys. Rev. Lett.* **95**, 146802 (2005).
71. König, M. *et al.* Quantum spin hall insulator state in HgTe quantum wells. *Science* **318**, 766–70 (2007).
72. Hsieh, D. *et al.* A topological Dirac insulator in a quantum spin Hall phase. *Nature* **452**, 970–974 (2008).
73. Peng, H. *et al.* Aharonov-Bohm interference in topological insulator nanoribbons. *Nat. Mater.* **9**, 225–9 (2010).
74. Arango, Y. C. *et al.* Quantum Transport and Nano Angle-resolved Photoemission Spectroscopy on the Topological Surface States of Single Sb₂Te₃ Nanowires. *Sci. Rep.* **6**, 29493 (2016).
75. Fu, L. & Kane, C. L. Superconducting Proximity Effect and Majorana Fermions at the Surface of a Topological Insulator. *Phys. Rev. Lett.* **100**, 096407 (2008).
76. Collins, G. P. Computing with Quantum Knots. *Sci. Am.* **294**, 56–63 (2006).
77. Xu, S. Y. *et al.* Discovery of a Weyl fermion state with Fermi arcs in niobium arsenide. *Nat. Phys.* **11**, 748–754 (2015).
78. Xu, S.-Y. *et al.* Experimental discovery of a topological Weyl semimetal state in TaP. *Sci. Adv.* **1**, e1501092–e1501092 (2015).
79. Qi, X.-L. & Zhang, S.-C. The quantum spin Hall effect and topological insulators. *Phys. Today* **63**, 33–38 (2010).
80. Fei, Z. *et al.* Edge conduction in monolayer WTe₂. *Nat. Phys.* **13**, 677–682 (2017).
81. Qian, X., Liu, J., Fu, L. & Li, J. Solid state theory. Quantum spin Hall effect in two-dimensional transition metal dichalcogenides. *Science* **346**, 1344–7 (2014).

7.5. Advanced Material Engineering and Processing

7.5.1. Introduction

Advanced Materials and Manufacturing was identified as a key to the UK's technology strategy in both the BEIS's Eight Great Technologies and Industrial Strategy reports.¹

² Emphasis has been placed on areas of UK strength such as advanced composites, high-performance alloys, low-energy electronics and telecommunications, materials for energy and nano-materials for health. Diamond-II will be a transformative technology driving progress in these key areas.

Diamond is already actively supporting many of the EPSRC's Future Manufacturing Hubs including Additive Manufacturing (AM) of metallic components for high added-value applications in aerospace and engineering, which is working with 17 Industrial collaborators including Rolls-Royce, Johnson Matthey and Renishaw - all companies with a strong UK base. The potential for additive manufacturing (AM) is huge (estimated to generate >£3.5bn GVA and to support 60,000 jobs by 2025 in the UK³), but only if the physics and mechanisms underlying the processes can be understood

The scope of engineering research is also changing with materials such as polymers increasingly changing the engineering landscape with broad impact on every aspect of modern life. Synthetic fabrics, food safety through protective films, energy for transportation, medical devices, 3D printed devices, flexible low-cost electronics, building blocks for medicines and the necessary coatings and lubricants for large-scale production, transportation, and manufacturing are just some examples of the non-traditional engineering research already active at Diamond. Global environmental concerns with respect to pollution and sustainability are creating new challenges for the polymer industry aimed at biodegradability, development of alternate feedstocks for production of plastic, epoxies and other performance polymers and energy efficiency. These challenges drive the "green chemistry" trend that seeks 'to promote innovative chemical technologies that reduce or eliminate the use of generation of hazardous substances in the design, manufacture, and use of chemical products.

Central to advanced materials design is an approach connecting modelling, processing, structure, properties and technological performance, which increasingly requires multiscale approaches and tools that can enable a bottom-up design to tailor properties at the chemical, nanostructural, and microstructural level. For example, in the nuclear industry the reactor pressure vessel (RPV) of a nuclear reactor provides containment of the reactor core. During service, the low alloy RPV steel used for light water

reactors degrades. Understanding and predicting the degradation phenomena using a combination of modelling and experiment underpins plant lifetime extension as the RPV cannot be economically replaced. In the aerospace, nuclear or medical device industry understanding material properties and the physics governing any changes that occur across the product life cycle is critical to being able to develop new materials and/or manufacturing processes. This is particularly important when it is not possible to test under representative service conditions.

Our ability to understand material physics and link experiment and modelling is in many areas limited by our ability to fully probe the critical length and times scales of material processes. A gap exists between the nanoscale region in which many processes occur and the microscale region that we currently spatially probe using Diamond instruments. In the time domain, current experiments at Diamond to study systems in *operando* make a compromise between time resolution, penetrating depth of the X-rays and signal-to-noise. Diamond-II will bridge these gaps by providing: more intense, smaller beams to probe the changes in composition and structure across surfaces and interfaces that are typically only a few μm in size (oxides, corrosion, welds); high resolution chemical and structural probing of defects and precipitates; higher signal to noise enabling rapid measurements; phase contrast to examine bubbles, cracks and voids; and new imaging and coherent diffraction techniques to provide nano and microscale strain under real operating conditions. *In-operando* studies at process timescales with Diamond-II will help drive the next generation of materials, engineering and process development.

7.5.2. New Materials and processes

Increasing the operating temperature is a key factor to improve the efficiency of aero-engines and industrial gas turbines and has driven the development of nickel-based alloys that can operate at the elevated temperatures required, due to their microstructure and resulting high creep-resistance. Typical Ni-based superalloys contain nickel, aluminium and/or titanium as well as many other additions that are used to optimise the alloy microstructure and the resulting mechanical properties. They are engineered using specific processing routes (e.g. directional solidification) and possess excellent mechanical properties mainly linked to the high-volume fraction of precipitates with specific properties (phase, shape and size).

The precipitates in these alloys are in the range of 100 nm to 1 micron⁴ (Figure 1). Processing (this example uses an external magnetic field) can influence their size and overall structure and they are also known to evolve during high temperature operation due to elemental redistribution⁵.

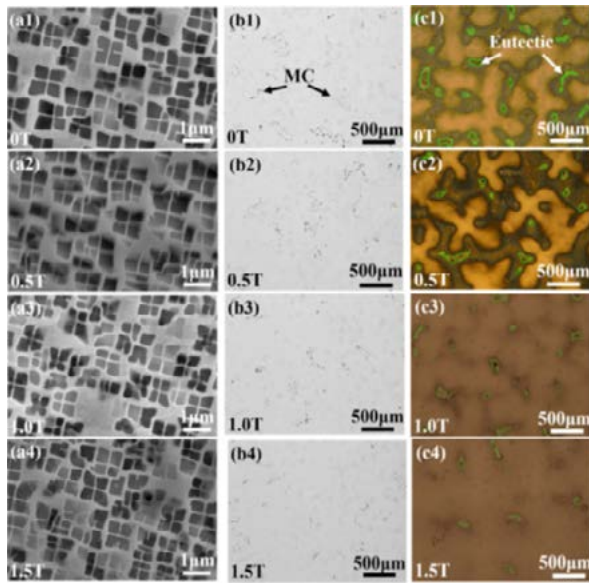


Figure 1. The nanoscale to microscale structures are clearly shown with the growth of the precipitation phases in the superalloy influenced using external magnetic fields (a1~a5) γ' precipitation at the dendrite core. (b1~b5) carbides. (c1~c5) γ/γ' eutectic phases (indicated with the green line by hand for the clear presentation). Adapted from Ref.⁴. <https://creativecommons.org/licenses/by/4.0/>.

Our ability to optimise the material is limited by our ability to observe and study the structural and chemical properties at these critical sub-micron to micron length scales.

Electron microscopy (SEM, EBSD etc.) of extracted sections is currently the most common method used for microstructural investigations but offers a limited field of view (FOV) and restricted sample conditions (*ex situ*, thin 2D sections). X-ray studies have been restricted to larger scale imaging of overall dendrite structures but the opportunities for nano-focussed spot sizes with Diamond-II will allow for highly efficient projection-based nano-tomography and high spatial resolution scanning probe diffraction, which can bridge the resolution gap between SEM's and X-rays, increasing the FOV and 3D information provided at this scale. An additional advantage from the coherence-based imaging that Diamond-II brings is that we directly measure the phase shift produced by the sample which provides a measure of the refractive index. The refractive index of a compound material is directly proportional to its electron density distribution (away from the absorption edges). This provides quantitative density measurements that can be matched to known materials, weighed or segmented, greatly increasing the depth of information available.

Additive Manufacturing

Additive manufacturing offers huge opportunities to tailor material strength and composition and incorporate structural features to improve function. However, in AM the high and rapid thermal transients created by the focussed laser create microstructures, residual stress states and defects that are vastly different from those created

through traditional manufacturing routes. These produce unpredictable and sub-optimal properties. The melting, flow, chemical reactions and phase formation happen within a few milliseconds of formation and high residual stresses can distort a part's geometry and leave crystal defects. The formation of microscale voids or chemical inhomogeneity in the material can cause parts to fail unpredictably.

AM processes require further study and optimisation in the near future. Rather than simply optimising existing processes, we will need to design new classes of materials that build on our understanding of these advanced processes, requiring characterisation (ideally *in situ* and *operando*) of the nano and microstructure, which govern the final properties of the material. As an example of the rapid progress in this area, 3D printed structures using hybrid organic–inorganic materials with 100 nm resolution have recently been demonstrated, showing the feasibility of nano-architected structures⁶ (Figure 2). High-speed X-ray imaging is already playing a part in this, but the significant improvements in phase contrast, micro-diffraction and nano-tomography with Diamond-II will provide the spatial and temporal resolution needed to match and understand the processes involved^{7–9}.

Chemical and Polymer Manufacturing

Chemical manufacturing is seeking to reduce the use of volatile organic compounds with alternative such as low temperature ionic liquids. Ionic liquids are formed from an array of non-covalent chemical interactions (e.g. van der Waals, charged, dipole and hydrogen bonding interactions) and can be readily tuneable through selective choice of ions. Room temperature ionic liquids (RTILs) can be made from renewable feedstocks with the added benefit of energy efficiency by promoting chemistry at lower reaction temperatures. Recent synchrotron-based studies of ionic liquids using X-ray reflectivity and GI-SAXS have revealed basic insights into how ionic liquids order at interfaces¹⁰. However, how the ionic liquids function in chemical processes remains to be determined, as this aforementioned study is one of the very first systematic studies of ionic liquids probed at the sub-nanometer scales.

Other areas of polymer film production present great challenges, for example through blown-film extrusion occurring at speeds of up to 9 meters per second where the material experiences temperature decreases at rates greater than 100 degrees per second. These films likely acquire their material properties from the distribution of vertical and horizontal strains introduced during annealing. Polymeric film production has largely been a trial-and-error process and it was only recently that structural insight was obtained from a first SAXS measurements at a synchrotron¹¹. Sub-microsecond, time-resolved SAXS, WAXS and reflectivity studies will be critical to the future

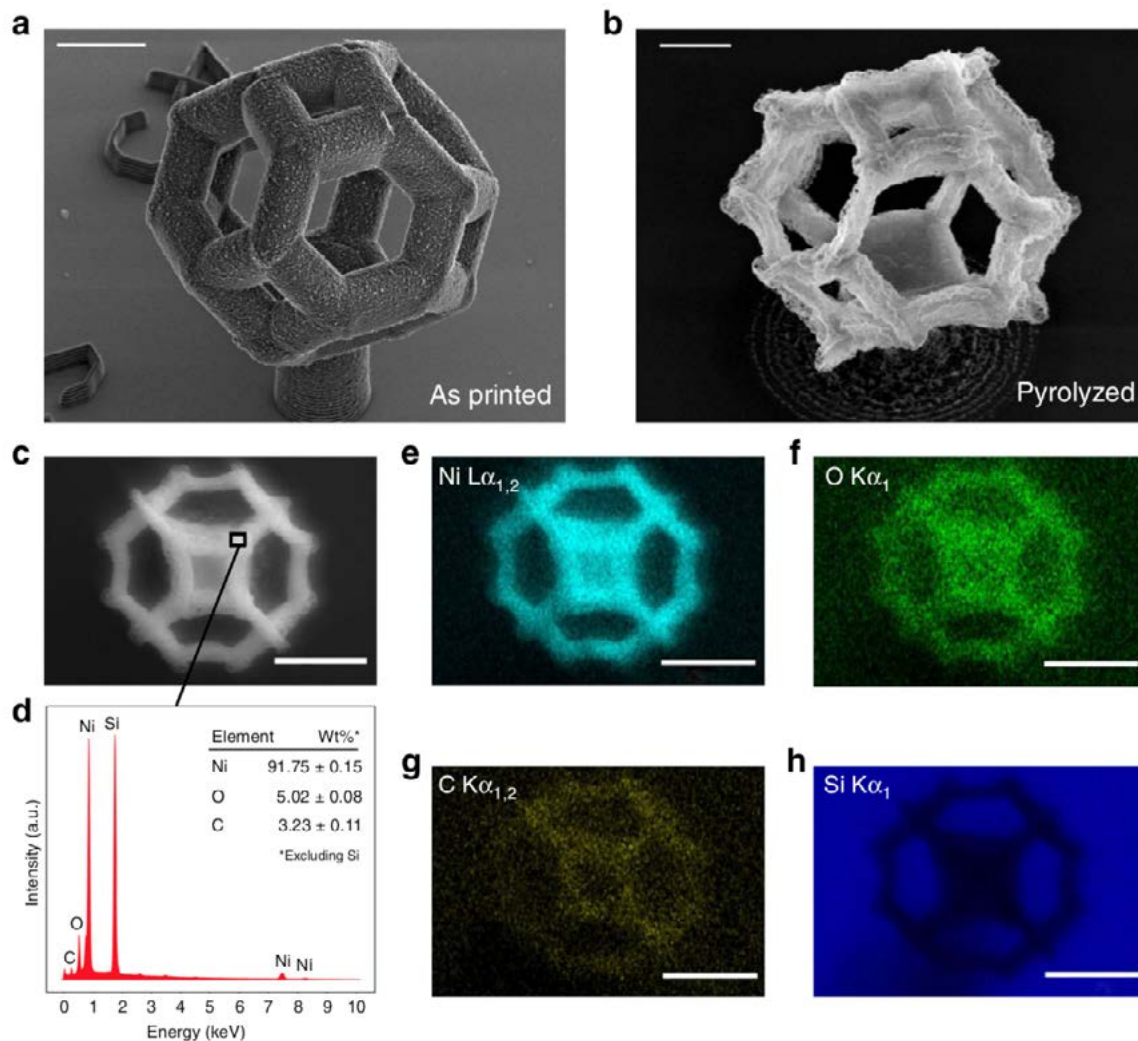


Figure 2 3D printed structures with 100 nm resolution created using lithography techniques and Ni-containing hybrid organic–inorganic materials are the first demonstration of nano-architecture AM. Scale bars are 5 μm for a, 1 μm for b and 2 μm for c, e–h.⁶

<https://creativecommons.org/licenses/by/4.0/>. Adapted from Ref.⁶

developments of these materials and processes and this will only be possible through the brightness gains in Diamond-II.

7.5.3. Materials *In-operando* and Ex-situ: Impact of Irradiation, Friction, Corrosion, Stress and Strain

Irradiated Materials

Understanding structural change due to radiation and in operation is a major challenge for the nuclear industry, against a back drop of ageing plants and the desire for life extension, future waste encapsulation and to design materials with surety of long-term fitness for purpose. Radiation damage tends to increase the strength and impair the toughness of steel, such that the mechanical properties of the pressure vessel or near-core components change throughout plant life. Helium bubble formation due to alpha-decay in a material can fill cavities within

the metal matrix created by displacement damage. These cavities can eventually grow into voids that lead to dimensional instability in the material, which causes degradation of mechanical properties. High sensitivity phase-contrast imaging possible with Diamond-II has the potential to show regions of negative contrast elucidating bubble-formation mechanisms at work in a range of systems including glass encapsulants, fuel surrogates and waste slurries/sludges. Understanding of pore connectivity and dynamics upon radiation/chemical insult is also key for both waste encapsulation (e.g. geopolymers) and fuel cladding.

Beamline I12 has already been used to perform pioneering imaging and diffraction work on corrosion of uranium as encapsulated for long-term disposal^{12–14}. Such work has a vital strategic importance in preparing the safety case for a long-term nuclear waste storage facility. Public confidence must be secured by demonstrating that processes which might happen in storage have been thoroughly investigated. Uranium and uranium compounds are

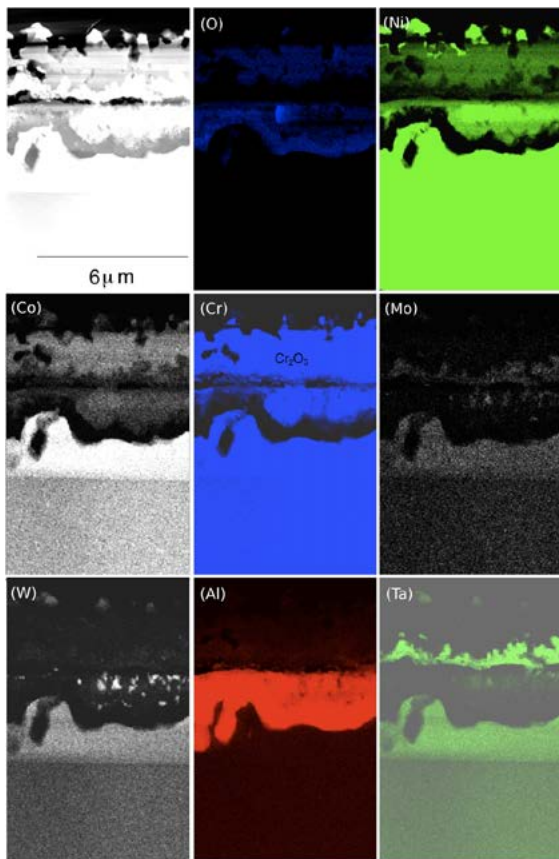


Figure 3 Oxide surface interface from a single-crystal nickel-based superalloy heated at 1000°C for 100 hours. The oxide layer shows structural and compositional variations over the scale of a few μm (e.g. Al_2O_3 phase formation). Adapted from Ref.¹⁷. Reprinted from *Acta Materialia*, 59, Sato, A. et al., *Oxidation of nickel-based single-crystal superalloys for industrial gas turbine applications.*, 225–240, Copyright (2011), with permission from Elsevier.

highly absorbing of X-rays, limiting the scope of current experiments. Diamond-II at 3.5 GeV is calculated to offer 112 up to 3.5 times more flux at 115 keV, just below the uranium absorption edge. Shorter scan times for tomography and diffraction will enable more samples to be studied in a visit and offer better time resolution for *in situ* experiments.

Corrosion and surface processes

The corrosion of materials represents a global burden in terms of financial costs (~£2 trillion, 3.4% global GDP¹⁵), environmental and human health risks, and the long-term sustainability of materials use/re-use. Many of the unmet challenges of designing and managing systems to control degradation result from a lack of mechanistic understanding of the processes, which is linked to a paucity of *in situ* experimental data replicating real world conditions. These challenges cut across sectors, including oil and gas, nuclear, transportation, aerospace, renewables, and nanotechnology.

Structured coatings can minimise materials deterioration and corrosion by impeding ion diffusion, for example,

but this understanding has only come from extracting and modelling the coating using nano-tomography¹⁶. In operation, oxidation and corrosion are important modes of damage and understanding these surface interactions and the role of coatings that occur over the micron length scale is equally as important as the bulk structure¹⁷. (Figure 3). Zirconium alloys are universally used as fuel cladding and support structures in Pressurised Water Reactors but suffer from aqueous corrosion in service¹⁸. Understanding and controlling the re-distribution of alloying elements in the metal from second phase particles after exposure to high neutron fluxes in a reactor is crucial to modifying the corrosion kinetics.

Stress corrosion cracks can develop from micron-scale corrosion pits and these cracks can cause catastrophic failure of aluminium airframes or titanium pipework, but the pit-to-crack transition is poorly understood.

While corrosion and oxidation processes cover a range of length scales, studies to date have been limited to bulk processes or imaging /scanning probe experiments over a defined region. Challenging environments, rapid surface dynamic and the electrochemical nature of the processes mean that real time, *in situ* experimentation is required—and combined information on phases formed, morphology evolution and chemistry at surfaces and interfaces is critical¹⁹.

The Diamond-II upgrade will bring increased flux to allow better depth penetration (enabling better environment representation without mass transport limitations). The increased speed of scanning probes will open their use for real time imaging of corrosion attack, providing observation of droplet shapes (which controls electrochemical reaction rates), identification of salts and corrosion products with micro-diffraction and chemical state mapping providing input to corrosion prediction models. In terms of surface dynamics, high energy enabled rapid tomography and diffraction measurements on DIAD *during* reactions would provide – for the first time – direct insights into the formation of surface passive films. This information is critical to the long-term prediction of materials behaviour.

Stress and Strain

DIAD's unique offer of simultaneous diffraction and tomography opens the door to novel investigation of some of the most challenging and timely engineering topics such as welding and thermal shock. Such phenomena are fundamentally time-dependent, and the high temporal resolution offered by the increase in photon flux in Diamond-II will enable key information, not currently obtainable, to be recorded on DIAD. For example, identification of the temperature at which the delta ferrite phase forms during the welding of metallic systems, within a few milliseconds, can help prove or disprove models that are used to predict the behaviour of the material in these

processes. In his review of fracture mechanics, Phil Withers outlined the critical importance of combining imaging and diffraction, particularly where stress or the occurrence of phase transformations need to be related to structural changes or degradation²⁰. The 70-fold increase in flux on DIAD, coupled with the reduced spot size, will provide significant improvements in the spatial and temporal scales that can be studied.

Diamond has the infrastructure on I12 to implement 3D-XRD, a diffraction technique presently available at only a few synchrotrons worldwide. The technique enables the crystallography, stress state, position and volume of individual grains to be measured. Unique studies have been made in recent years to monitor neighbourhood effects during deformation of engineering alloys and phase transformations of polycrystalline materials. The capability to monitor individual crystals and their crystal environment is critical for understanding micro-scale kinetic and mechanical detail to explain macroscale behaviour. Variations on 3D-XRD are also being developed on the nano-probe beamline, I14, to extract strain from grains in thin film coatings. Experiments using 3D-XRD are typically slow and limit the studies that can be performed. To measure all crystals in the probed volume requires diffraction pattern acquisition at fine angular increments as the sample is rotated through 360° or in a raster-pattern in

2D about a rocking curve. Increased brightness and high-energy photons will significantly enhance the capability of this technique, enabling materials to be measured in dynamic environments, therefore extending the feasibility of 3D in-situ studies of crystalline materials.

One of the biggest gains for Diamond-II is in coherent imaging techniques. Coherent Diffractive Imaging (CDI) and Bragg Ptychography are still relatively young characterisation techniques but can be used to examine strain on the nanometre, and in some cases, sub-nanometre scale in 3D. These techniques have evolved very rapidly from studies on isolated nanoparticles to studies probing strain in electronic devices (Figure 4), dislocations in operating devices, damage and strain induced from focussed ion beam processing and strain in extended nanowire structures^{21–24}. The application of coherent diffraction to material science is, to date, relatively limited due to the available coherent flux, processing complexity and experimental setups required. While Diamond-II can improve spatial resolution, the biggest gains for material science from the increased coherent flux, improved focussing and new instrumentation will be a move towards *in operando* experiments, allowing us to routinely image the changes in individual grains in novel materials and alloys under conditions that allow us to understand and influence real world systems.

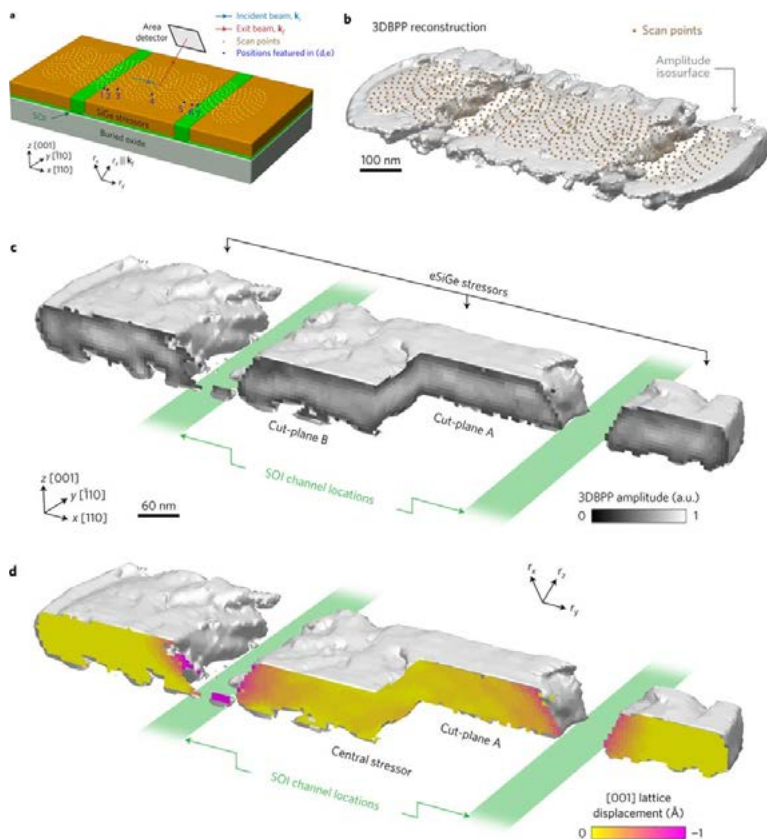


Figure 4 – Coherent diffraction patterns measured at the 004 SiGe Bragg peak **a** SiGe on Silicon on insulator (SOI) structure showing angstrom scale strain measurements, **a** SiGe on SOI structure, **b–d**, The isosurface of the amplitude of the resulting reconstruction (**b**), showing gaps at the positions of the SOI channels. The internal structure of the SiGe material in the field of view is revealed by way of cuts through the isosurface depicting the amplitude of the reconstruction, which is closely related to the material density (**c**), as well as the crystal lattice displacement along the [001] direction (**d**), which is derived from the phase of the reconstruction. Adapted from Ref.²⁴. Reprinted by permission from Copyright Clearance Center: Springer Nature, Nature Materials, High resolution three-dimensional structural microscopy by single-angle Bragg ptychography, Hruszkewycz, S.O. et al., Copyright (2017).

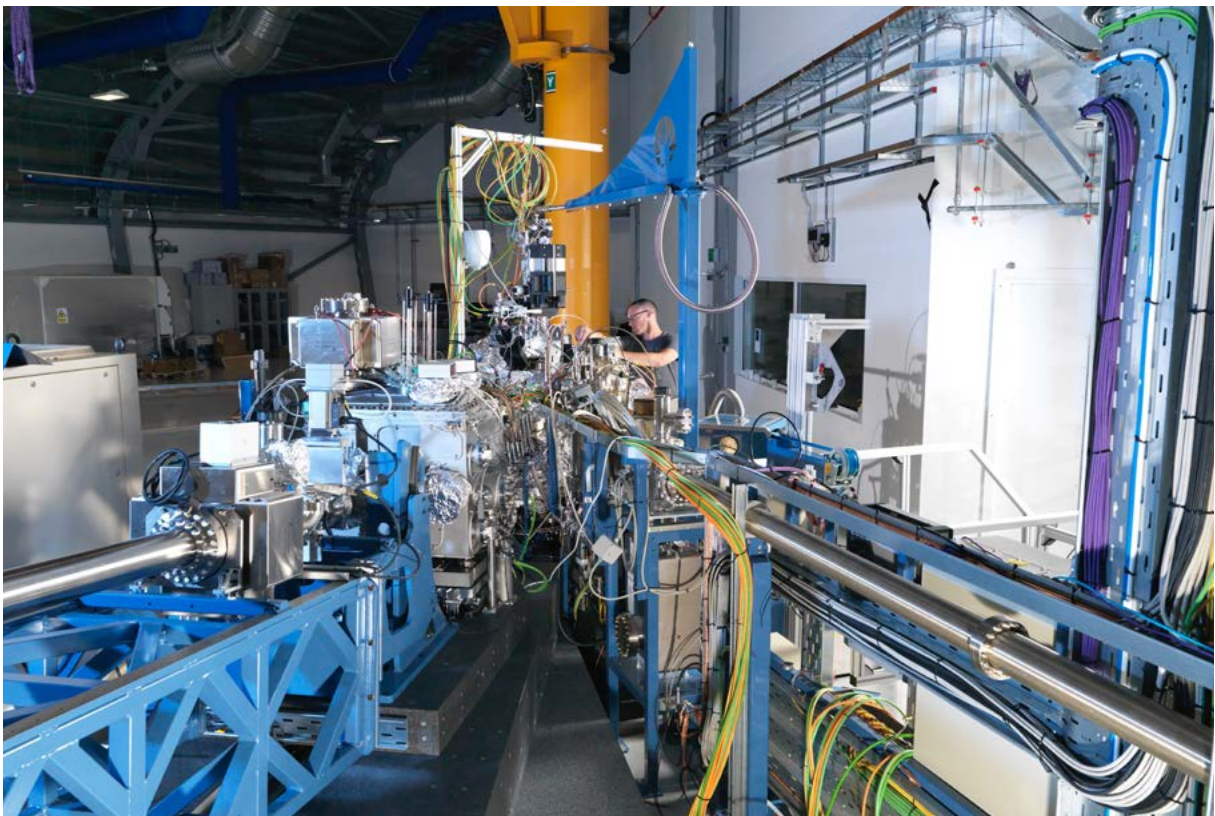
Friction

One of the biggest challenges for industry is friction and wear - materials consumption, energy waste and increasing operational costs. In the automotive industry, reducing engine friction and increasing the performance of fuels, particularly biofuels, in various conditions is one of the key components in reducing emissions and reaching UK targets for biofuel usage but a number of basic challenges exist. In cold weather, molecules in fuels can crystallize, forming waxes that then block fuel filters to the engine. The growing use of biofuels complicates the search for a solution; as biofuels are made from living sources, each fuel sample's molecular structure is different, making it difficult to find a common solution that works across fuels. Infineum, a leading formulator, manufacturer and marketer of petroleum additives, for fuels and lubricants has used Diamond to conduct real-time molecular-level examinations of the crystallisation process and to examine the interaction between fuel additives and metals, looking for ways to reduce friction in engines and improve performance²⁵. Studies of how lubricants flow, layer and form films are crucial to future development and a critical but central component of the research consists in monitoring these systems *in-operando* under a range of different conditions (e.g. a sudden temperature drop, or gradual fall over time with varying rates) with time scales, chemical sensitivities and spatial resolutions significantly improved with Diamond-II. As for other cases reviewed in this section, the use of phase contrast to highlight subtle imaging changes in light materials, combined with a greatly

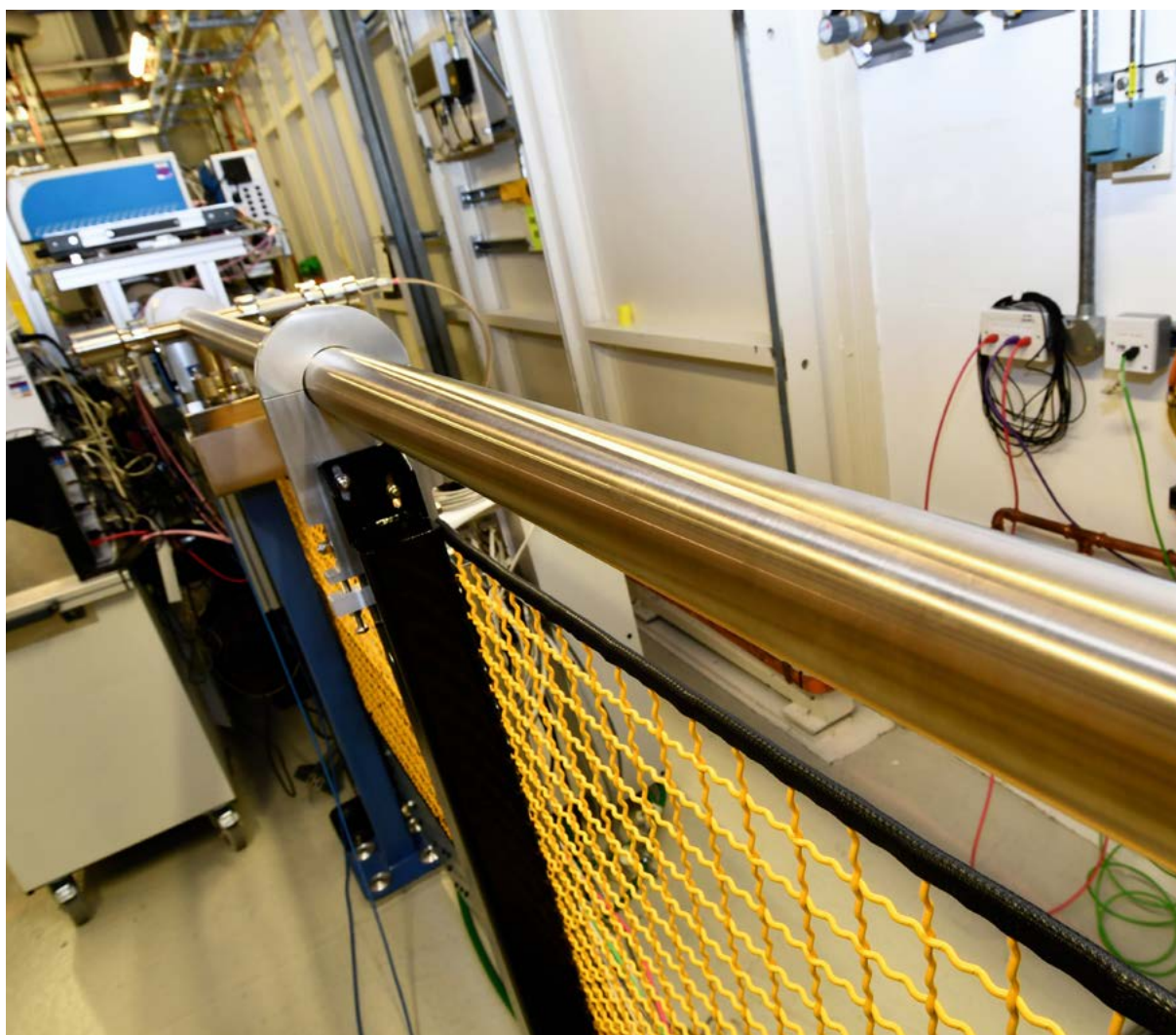
improved time resolution offered by a more routine use of pink beam imaging techniques, will offer step changes in our ability to probe these materials.

References

1. Willetts, D. *Eight great technologies*. (2013). doi:ISBN: 978-1-907689-40-6
2. UK Government. Green Paper January 2017. (2017).
3. AM_UK. Additive manufacturing UK 2018-25. (2018).
4. Ren, W. *et al.* Improvement in creep life of a nickel-based single-crystal superalloy via composition homogeneity on the multiscales by magnetic-field-assisted directional solidification. *Sci. Rep.* **8**, 1–17 (2018).
5. Connor, L. D. *et al.* *In situ* study of sigma phase formation in Cr–Co–Ni ternary alloys at 800°C using the long duration experiment facility at Diamond Light Source. *J. Synchrotron Rad.* **25**, 1371–1378 (2018).
6. Vyatskikh, A. *et al.* Additive manufacturing of 3D nano-architected metals. *Nat. Commun.* **9**, 593 (2018).
7. Leung, C. L. A. *et al.* *In situ* X-ray imaging of defect and molten pool dynamics in laser additive manufacturing. *Nat. Commun.* **9**, 1–9 (2018).
8. Martin, J. H. *et al.* 3D printing of high-strength aluminium alloys. *Nature* **549**, 365–369 (2017).
9. Escano, L. I. *et al.* Revealing particle-scale powder spreading dynamics in powder-bed-based additive manufacturing process by high-speed x-ray imaging. *Sci. Rep.* **8**, 15079 (2018).
10. Haddad, J. *et al.* Surface structure evolution in a homologous series of ionic liquids. *PNAS* **1**, (2018).



11. Troisi, E. M., van Drongelen, M., Caelers, H. J. M., Portale, G. & Peters, G. W. M. Structure evolution during film blowing: An experimental study using in-situ small angle X-ray scattering. *Eur. Polym. J.* **74**, 190–208 (2016).
12. Stitt, C. A. *et al.* In-situ, time resolved monitoring of uranium in BFS:OPC grout. Part 2: Corrosion in water. *Sci. Rep.* **8**, 1–12 (2018).
13. Stitt, C. A. *et al.* An investigation on the persistence of uranium hydride during storage of simulant nuclear waste packages. *PLoS One* **10**, 1–13 (2015).
14. Stitt, C. A. *et al.* In-situ, time resolved monitoring of uranium in BFS:OPC grout. Part 2: Corrosion in water. *Sci. Rep.* **8**, 1–9 (2018).
15. NACE. NACE 2016 Impact Study. (2016).
16. Guizar-Sicairos, M. *et al.* Three-dimensional structure analysis and percolation properties of a barrier marine coating. *Sci. Rep.* **3**, 1–5 (2013).
17. Sato, A., Chiu, Y. L. & Reed, R. C. Oxidation of nickel-based single-crystal superalloys for industrial gas turbine applications. *Acta Mater.* **59**, 225–240 (2011).
18. Annand, K., Nord, M., MacLaren, I. & Gass, M. The corrosion of Zr(Fe, Cr)₂ and Zr₂Fe secondary phase particles in Zircaloy-4 under 350 °C pressurised water conditions. *Corros. Sci.* **128**, 213–223 (2017).
19. Rayment, T. *et al.* Characterisation of salt films on dissolving metal surfaces in artificial corrosion pits via *in situ* synchrotron X-ray diffraction. *Electrochem. commun.* **10**, 855–858 (2008).
20. Withers, P. J. Fracture mechanics by synchrotron X-ray microscopy. *Philos. Trans. A* (2015).
21. Hofmann, F. *et al.* 3D lattice distortions and defect structures in ion-implanted nano-crystals. *Sci. Rep.* **7**, 1–10 (2017).
22. Robinson, I. & Harder, R. Coherent X-ray diffraction imaging of strain at the nanoscale. *Nat. Mater.* **8**, 291–298 (2009).
23. Hill, M. O. *et al.* Measuring Three-Dimensional Strain and Structural Defects in a Single InGaAs Nanowire Using Coherent X-ray Multiangle Bragg Projection Ptychography. *Nano Lett.* **18**, 811–819 (2018).
24. Hruszkewycz, S. O. *et al.* High-resolution three-dimensional structural microscopy by single-angle Bragg ptychography. *Nat. Mater.* **16**, 244–251 (2017).
25. Lewtas, Prof. Ken, I. U. L. Case study: Controlling Crystallisation in Fuels and Biofuels. Available at: <https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-Infineum-oil-additives.html>.



7.6. Earth, environment & planetary science

One of the most important measures of our future success as Earth and Environmental scientists will be our ability to help global societies and economies identify and implement effective solutions to environmental problems. Key to this challenge is our ability to understand natural and perturbed (anthropogenic) systems, so that we can predict their behaviour, mitigate against their failure, and even be able to optimise their outputs for socio-economic benefits. This has direct relevance to the 2013 IPCC report on climate change¹ (see example in Section 1.1.1). Rapid technological developments in observational science now allow us to globally monitor physical properties on daily to hourly timeframes, and manipulate this data in real time, providing unprecedented snapshots of the Earth system. This data is used to develop increasingly sophisticated Earth system models that can describe global processes, but in order to predict the response of the Earth system to current and future environmental change, these models must be underpinned by an understanding of the fundamental mechanisms, and interconnect the physics, chemistry, biology and geology of our planet. In this respect, Earth and Environmental science is still in its infancy, but work in this area is directly relevant to the UK government Grand Challenge on Clean Growth². To keep pace with observational technology we require ever more advanced analytical instrumentation capable of investigating the entire range of Earth and environmental materials (fluids, biological, atmospheric and geological), at the smallest scales, in multiple dimensions, and in real time. For example, understanding the atomic structure and chemical nature of nuclear waste has direct relevance to understanding the long-term efficacy of a geological repository. An estimated 500 million people live close enough to volcanoes to be affected by them when they erupt³ and many cities have developed on the fertile land often found in the vicinity of volcanoes. Developing a fundamental understanding of magma properties and behaviour can provide inputs to modelling and forecasting of volcanic activity, which aids in the development of risk-based assessments of these natural hazards.

The use of synchrotron research in the Earth, Environmental & Planetary Sciences has grown substantially over the past few years and continues to do so at all synchrotron facilities. This has been largely driven by the integration of environmental cells that can mimic physical parameters (humidity, fluid, temperature, pressure, etc.) integration with X-ray methods, which has permitted probing processes in geoscience and environment science under realistic chemical conditions (e.g. temperatures up to 1200°C, confining pressures up to multi-GPa)⁴ in real time. Third-generation facilities in particular have allowed spectroscopy, diffraction and imaging to address challenges from a wide range of fundamental and applied

geoscience areas: from understanding volcanic eruptions to modelling the sub-surface flow of hydrocarbons; from quantifying mineral growth to maintaining soil sustainability; and from planetary formation mechanisms to the best storage strategies for nuclear waste. The range of questions we can answer will only increase as the Diamond-II upgrade delivers simultaneous advances in temporal, spatial and chemical resolution, allowing analysis of more complex heterogeneous materials. At one end of the research spectrum, Diamond-II will offer high energy and temporal resolution sufficient to constrain reactive pore and grain scale processes under realistic geological conditions, while at the other it will enable better multidimensional chemical and elemental mapping across the key range of compositional ranges, and to integrate transmission and diffraction-based imaging modalities. Bringing quantitative understanding of microscale processes into our understanding of our macroscale observations has always been a challenge in Earth and environmental science, and this is exactly the transformative understanding that Diamond-II will provide.

7.6.1. Understanding global environmental issues: the organic carbon paradox

Central to understanding a range of Earth and Environmental systems is our ability to determine the mechanisms and processes that control the abundance and distribution of elements in the atmosphere, hydrosphere and lithosphere. This grand challenge is fundamental to understanding and predicting the global cycling of macro and micro nutrients and how these cycles will respond to current and future land use and climate change. Soil remediation and management to maintain healthy soil structure, enhance water retention and prevent reduction in productivity are key challenges across the globe. This is especially true with the increase in extreme weather events driven by climate change and the migration of populations to expanding urban centres in developing nations. Soil and crop productivity and resilience is intrinsically linked to the porosity, permeability and nutrient availability⁵ – and understanding the mechanisms by which these factors can be enhanced or reduced is a key challenge for maintaining food and environmental security and mitigating the effects of climate change. (UN Sustainable Development Goals⁶, Global Challenges Research Fund (GRCF), the DEFRA 25 year plan to improve the environment which includes improved management of soils⁷, and others.)

Our efforts to understand the reactivity and cycling of organic carbon are of profound importance for the Earth system because, in the oceans and on land, the conversion of atmospheric carbon dioxide into photosynthetic biomass, and the stabilisation of this biomass, leads to the preservation of organic carbon in marine sediments.

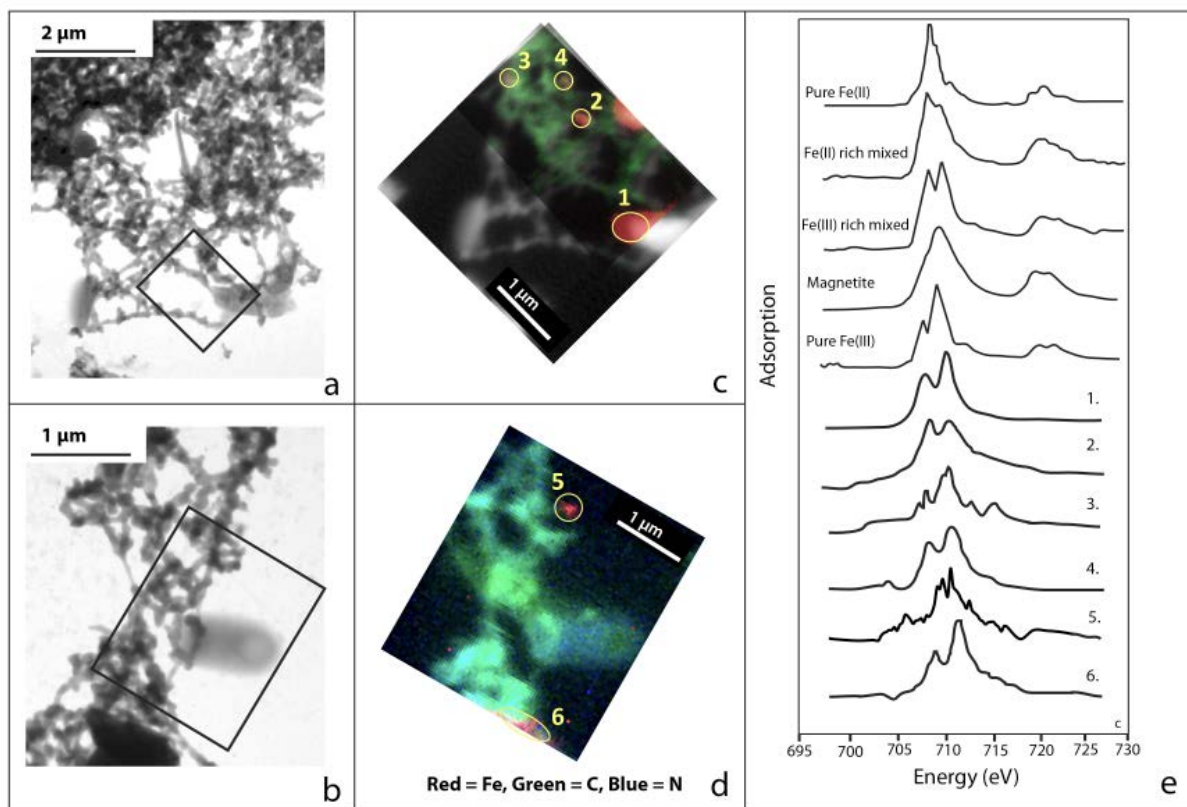


Figure 1: TEM images of web-like organic fibrils (a) and bacterial cells and organic fibrils (b), show darker 'inclusions', investigated using SXM on beamline I08. The XRF maps of these organic structures shows carbon-rich (green), nitrogen-rich region (blue) and iron-rich (red) regions (c, d). The NEXAFS spectra of Fe-rich regions were compared with spectra of Fe particles from the Southern Ocean¹¹, showing that Fe(III) oxides are associated with organic matter (e). Copyright Diamond Light Source.

This regulates global climate⁸, and the preservation of organic carbon in terrestrial soils, ensures soil health and fertility for global agricultural production⁹. Indeed, understanding the organic carbon cycle constitutes one of the biggest challenges in Earth and Environmental sciences and encompasses one of the oldest paradoxes in modern biogeochemistry. In essence, the stabilisation of highly degradable organic carbon biomass in the face of almost ubiquitous microbial decomposition is central to regulating global climate and agriculture. The fact that any organic carbon survives to be preserved is profoundly puzzling.

A recent example from Hirst *et al.*¹⁰ illustrates how understanding organic carbon (C) and its interaction with iron at the nanoscale can underpin our knowledge of biogeochemical cycle from terrestrial systems to the ocean. Reactive iron (Fe)-bearing mineral particles trap organic C in soils and continental shelves, yet the amount of reactive Fe and how it reacts with organic C in large Arctic rivers is poorly understood. Using a transmission electron microscope and the Scanning Transmission X-ray Microscopy beamline (I08) at Diamond Light Source, the size, mineralogy, and form of Fe particles and their association with organic matter in samples obtained from a representative Arctic river basin were characterised. X-ray Absorption Near Edge Structure (XANES) spectroscopy

and X-ray Fluorescence (XRF) mapping at I08 confirmed that Fe is transported as particles and colloids in the Lena River, and that 70% of these particles are composed of poorly crystalline ferrihydrite, which is a reactive form of Fe (Figure 1). Distinguishing between C and Fe at nanoscale resolution, the ferrihydrite was revealed to be in the form of discrete particles within networks of organic C, and transported by attachment to the surface of larger organic matter (>0.7 μm) and clay particles. These important insights into the reactivity of Fe-bearing particles in the Lena River basin, and information about how well Fe traps and transports organic C, show that the Lena River supplies reactive Fe to the ocean, a significant proportion of which is already associated with organic C. These results confirm that Fe-bearing particles contribute towards natural C sequestration on the continental shelf.

Traditional approaches to understanding how and why organic C becomes stabilised and preserved in sediments and soils provide only limited information. Organic C in its preserved form is unhydrolysable, which on the one hand almost certainly helps it escape microbial decomposition, but on the other hand means that even our most advanced wet chemical techniques struggle to separate the organic carbon material into its smaller component parts for aqueous chemical analysis¹². This 'molecularly uncharacterised carbon' has also largely eluded our

most advanced solid state characterisation techniques, including those currently available at Diamond, because without chemical separation it is present in dilute to ultra-dilute concentrations that are often below current detection limits. It is also chemically chelated with a host of porewater ions that can complicate target element detection and specificity, and it is physiochemically intermixed on the nanoscale with sediment and soil minerals that appear to control its reactivity. These relationships cannot be investigated currently at sufficient spatial and dimensional resolution. Moreover, the material can undergo chemical fractionation and transformation that cannot be investigated at present on sufficiently fast timescales¹³.

Moving forward, Diamond-II presents a unique opportunity to shed new light on the reactivity and cycling of organic carbon and determine what controls organic C stabilisation and preservation. Specifically, an increase in photon flux coupled with higher brightness will allow the study of ultra-dilute organic carbon concentrations typical to sediment and soil samples, while a smaller spot size coupled with increased brightness will enable elemental mapping with super high spatial resolution. In addition, the enhanced coherence of Diamond-II will be a step change for ptychography and Transmission X-ray Microscopy (TXM) using phase contrast imaging, capable of locating organic C in the presence of porewater ions and mapping in 3D its intimate association with nanoscale minerals. We are already targeting sub-10 nm resolution with ptychography and aim for sub-5 nm with a much faster data collection time on Diamond-II (<1 min) for a similar field of view of 60x60x60 μm^3 . As shown in Dobson *et al.*⁵ this will enable advanced 2D and 3D mapping of the components e.g. pore water, mineral particles and organic matter within soils and how they are associated with each other.

A several fold increase in brightness will also allow for much faster raster scanning, offering the possibility of monitoring chemical fractionation and transformation of organic carbon in real time. Together these advances will overcome the primary barriers to investigating organic carbon in natural samples and will revolutionise our understanding of its reactivity and cycling in real environmental systems. Furthermore, enhanced ring properties could be used to facilitate photon hungry techniques like X-ray Raman, providing complimentary *in situ* investigation of organic carbon embedded in mineral matrices, and high energy resolution (HR) XANES. HR-XANES measurements are possible at much lower concentrations than EXAFS and might provide additional insights in a fraction of the measurement time, and so could be ideally suited to investigating organic C speciation and reactivity.

Diamond-II will provide a new set of next generation tools to finally unravel a profoundly puzzling paradox, in which, highly degradable organic C becomes stabilised and

preserved, and ultimately helps maintain our habitable planet. If we can better understand organic C stabilisation and preservation then not only can we better understand the global Earth system, but we can make more informed efforts to enhance the sequestration of organic carbon in sediments and soils, thus helping to mitigate climate change and increase agricultural production for a more sustainable planet¹⁴. This aim is embodied in the Paris 2015 Climate Conference which saw the launch of the "4 per 1000" initiative¹⁵ which aims to improve the amount of available carbon in soils by 0.4% per year.

7.6.2. Nuclear waste remediation

A key problem facing the UK is the decommissioning and clean-up of all civil nuclear licensed sites and the implementation of geological disposal of highly active wastes¹⁶⁻¹⁹. The estimated cost of UK nuclear decommissioning is circa £120 billion over 100 years, with geological disposal of wastes costing circa £14 billion over a further 100 years. In the mind of many people, this is entwined with the commitment of the UK government to the building of new reactors and our need to handle future waste. Therefore, central to the success of this task will be "a joined-up approach to nuclear R&D across government, industry and academia which [...] benefit(s) the UK economy and ensures the security of supply" and "to establish UK industry as a global leader in waste management and decommissioning"²⁰. There is a key responsibility to deliver policies with respect to legacy wastes²¹, with the ultimate goal of management of waste through a geological disposal facility (GDF). Indeed the launch of the GDF site selection process opened in Dec 18²². A research area of national priority for the UK is therefore facilitating the development of approaches for implementing safe, cost-effective environmental clean-up, decommissioning and waste disposal of existing and future nuclear sites and facilities²³.

Answering many basic science questions is fundamental to developing new solutions for nuclear waste remediation, management and understanding of how radionuclides interact with materials in the environment. At Diamond, crystallographic, spectroscopic and imaging techniques are used for such research and will strongly benefit from the proposed upgrade, with the availability of greater brightness/flux, a wider range of energies (>25 keV for 2nd row absorption edges and penetration of sample cells) and smaller beam sizes all being utilised. For all techniques (crystallography, spectroscopy and imaging), one of the significant advantages would be the ability to analyse smaller samples with lower (i.e. environmentally relevant) concentrations of higher activity materials, including transuranic radionuclides, on a wide range of beamlines. These could include spent nuclear fuels, vitrified high level waste, and plutonium, or legacy samples brought from the storage ponds or effluent

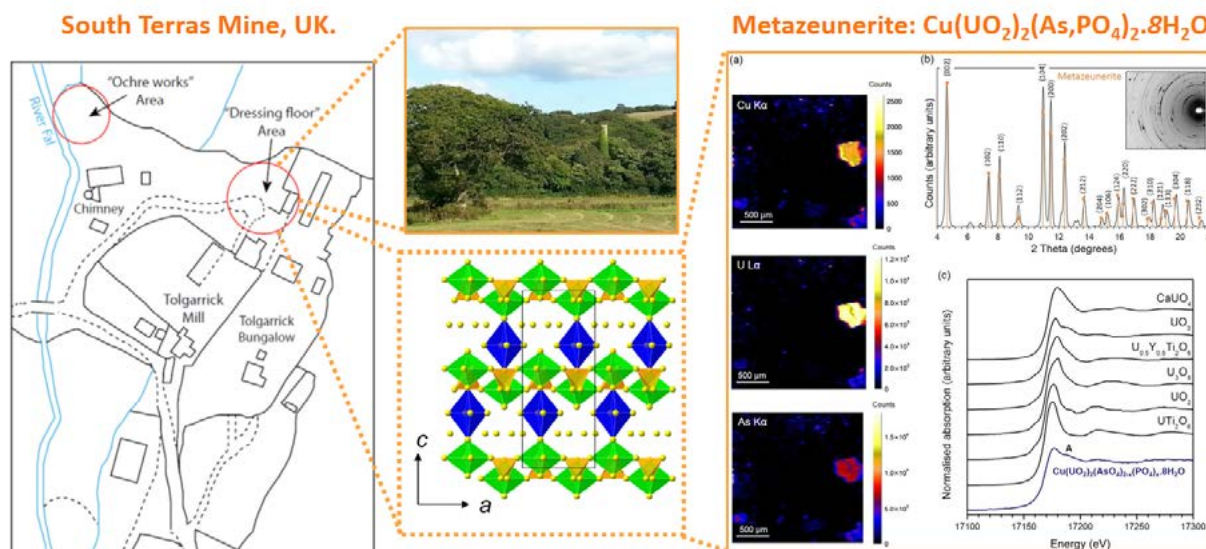


Figure 2: Understanding the speciation and migration of uranium at Marie Curie's radium mine – South Terras, UK. Microfocus XAS/XRD revealed arsenic as the unlikely hero: weathering of local arsenic and uranium rich mineralogy, under oxidising conditions, promotes formation of a novel metazeunerite – meteteorbenite solid solution, which is the solubility limiting phase²⁴.

Corkhill, C. L. et al. Multi-scale investigation of uranium attenuation by arsenic at an abandoned uranium mine, South Terras. *npj Mater. Degrad.* 1, 19 (2017) <https://creativecommons.org/licenses/by/4.0/>.

treatment facilities at Sellafield in order to analyse the effect of radiation damage (e.g. powder X-ray diffraction (XRD) and pair distribution function analysis) and to determine radionuclide speciation (X-ray spectroscopy).

X-ray Absorption Spectroscopy (XAS) techniques are powerful tools providing critical quantification of radionuclide speciation and local environment, which control solubility, sorption and precipitation behaviour in natural systems (e.g. repository far-field processes), see Figure 2, and nuclear fuel cycle processes (e.g. third phase formation in nuclear fuel reprocessing and effluent treatment). The increased brightness at hard and soft X-ray wavelengths, and a smaller probe size, will permit investigation of elements (e.g. Pu) of fundamental importance to the safe handling of spent nuclear fuel. On I14, the Hard X-ray nanoprobe beamline, the increased flux density will allow study of extremely active materials as only a tiny amount of material (1-10 μm particles) will be necessary. Also, Diamond-II will deliver enhanced capability to collect EXAFS on radionuclides at concentrations below 100 ppm on I20, and the development of soft X-ray Emission Spectroscopy (XES) to quantify the oxidation state of actinide elements will permit XAS/XES M-edge studies of the electronic and chemical structure of transuranic and Rh/Pd alloy particles in spent nuclear fuel and associated with geological materials, which are critical to maintaining favourable geochemical conditions, and hence low actinide solubility in the repository. Likewise, determination of the speciation and partitioning of Ru, iodine and transuranic elements in spent nuclear fuel, enabled by the higher energy of Diamond-II, will allow us to understand the release of these volatile elements in nuclear fuel reprocessing and accidents, as major contributors to the

dose uptake by workers and populations. The increased brightness of Diamond-II will also enable exploitation of XAS techniques to speciation of trace radionuclides with powerful applications, in contaminated land and nuclear forensics/security to detect and attribute forensic signatures in trace element speciation, for which large data sets are desirable but limited by sample throughput. The enhanced brightness will also enable more routine exploitation of XES techniques, and application to dilute systems, to identify radionuclide co-ordinated ligands from analysis of valence-to-core emission, with wide application to the nuclear fuel cycle and radiopharmaceuticals.

7.6.3. Understanding global environmental issues: atmospheric pollution

Atmospheric aerosols are known to be the source of the largest uncertainty when assessing the man-made contribution to climate change. They are key to the Earth's climate as well as to urban air quality, with nearly all atmospheric aerosols containing organic compounds that often contain both hydrophilic and hydrophobic parts. However, the nature of how these compounds are arranged within an aerosol droplet remains unknown. Fine particulate matter ($\text{PM}_{2.5}$) is one of the five damaging air pollutants targeted in the UK's Clean Air Strategy 2018²⁵ with ambitious national emission reduction commitments for $\text{PM}_{2.5}$ against the 2005 baseline of 30% by 2020, and 46% by 2030 underlining the urgent need for a better understanding of the processes impacting on atmospheric residence times of particulates.

Emissions from cooking have been estimated to contribute nearly 10% to the UK total anthropogenic emissions of $PM_{2.5}$; these small particles are particularly relevant for human health since they can enter the lungs. Very recent studies in Chinese cities point to substantially higher proportions of meat cooking emissions of up to 50% of $PM_{2.5}$ (Dr Nemitz, private communication, 2018). Furthermore, biodiesels (such as Fatty Acid Methyl Esters or 'FAME') are composed of surface-active molecules with very similar properties that are likely to have an increasing impact on urban air quality given the rising additions of biodiesel into mineral diesel products. A recent article by Pfrang *et al.*²⁶ demonstrates that complex 3D self-assembly occurs, affecting the particles' optical properties and hence atmospheric properties. Using an ultrasonic levitation system, microdroplets were suspended and Small-Angle X-ray Scattering (SAXS) and Raman measured as the fatty acids in proxies for atmospheric aerosols self-assembled into highly ordered three-dimensional nanostructures. By changing the environment, atmospherically-relevant reactions and changes occurred (Figure 3) that have potential implications for radiative calculations, residence times of such systems and other key aerosol characteristics. This study used droplets with sizes larger than $30\ \mu m$; an improved I22 on Diamond-II would allow these studies to be carried out on aerosols in the atmospheric prevalent range of $0.1\text{-}2.5\ \mu m$ (the "accumulation mode" of atmospheric aerosols), currently inaccessible, but key both for understanding atmospheric processes as well as for establishing human health implications. This would also lead to nano-scale structure analysis of levitated sub-micron particles with applications far beyond atmospheric sciences (e.g. droplet drying processes, nanomaterial development or catalysis).

Magma crystallisation is a fundamental process driving volcanic eruptions and controlling the style of volcanic activity. Recent studies have followed the *in situ* crystallisation of basaltic magma by 4D X-ray tomography on I12 which is opening an entirely new frontier in experimental petrology and volcanological research²⁷. The

researchers measured the nucleation and growth kinetics of crystals in experiments that simulate natural lava, helping to improve our understanding of these flows. The experiments were conducted using a high-temperature environmental cell with a beamline capable of fast X-ray microtomography. This study provides the first realistic constraint on the timescales of magmatic crystal nucleation and growth and therefore the flow behaviour of basaltic lava flows. The research is a major milestone and helps in assessing volcanic eruption hazard and in mitigating the risk of eruptions.

Other ongoing work on I12 to capture bubble growth dynamics and multi-phase flow mechanics will also be greatly enhanced by the increased $\sim 3\times$ flux and higher energy range (improving temporal resolution, data quality, and allowing imaging of larger sample sizes) that will be enabled by Diamond-II. Magmatic evolution, the mobility of many other sub-surface fluids and fluid-rock interactions are critical to both resource management (ore formation and metal extraction, petroleum exploitation, carbon capture, aquifer management, pollutant transport) and our built environment. These occur in both natural and anthropogenic settings, leading to the dissolution, precipitation, rearrangement and recrystallisation of both inorganic and organic components. In natural environments, these interactions can result from both diagenesis and weathering. At longer and larger scales fluid rock interactions can influence the development of the stresses fields driving fault propagation and slip i.e. earthquakes. Syntectonic veins have been commonly used to assess the composition and source of fluids involved in fault zone activity and a study by Lacroix *et al.*²⁸ used SIMS (Secondary Ion Mass Spectrometry) to study the veins at the micron level. Anthropogenic activities, such as mineral extraction^{29,30}, drilling for oil and gas extraction³¹, geothermal energy, CO_2 sequestration³² and the long-term storage of nuclear waste, must also exploit or mitigate fluid rock interactions in the subsurface system. It is the changes in rock properties and migration of species and

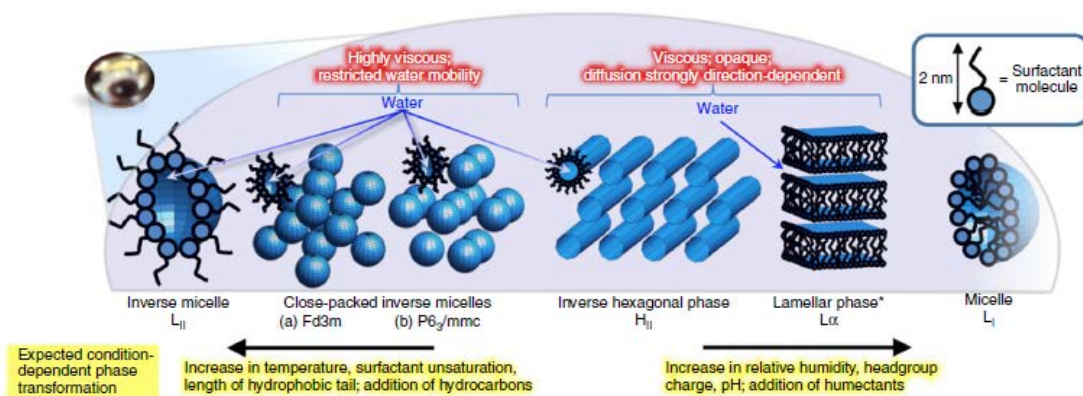


Figure 3: Complex 3D self-assembly of surfactant molecules in proxies for atmospheric aerosols. Lyotropic phases formed; impact on key properties of atmospheric aerosols (highlighted in red); and proposed condition-dependent phase changes (yellow). Copyright Diamond Light Source.

Diamond-II: Advancing physical sciences

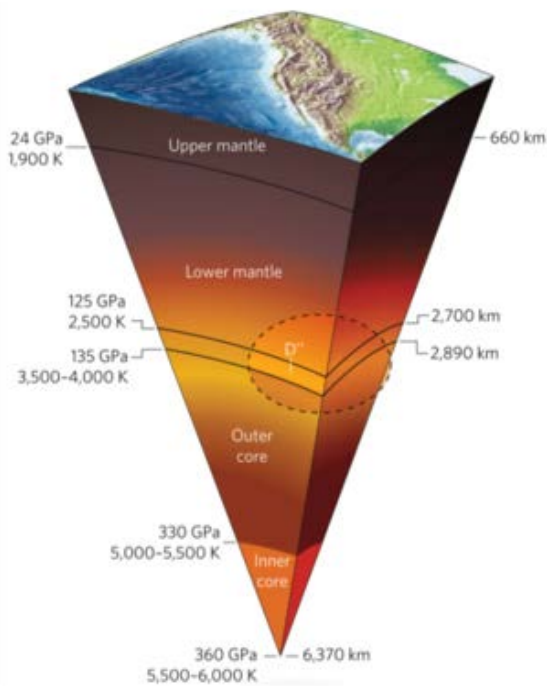


Figure 4: Cross-section through the Earth's interior showing the expected pressure-temperature range²⁵. Reprinted by permission from Copyright Clearance Center: SpringerNature, *Nature, Mineralogy at the extremes*, Duffy, T. S., Copyright (2008). Adapted from Ref.²⁵

elements within the fluids that requires understanding if prediction, exploitation or mediation/mitigation can be achieved. Diamond-II with its higher machine energy of 3.5 GeV will deliver improved flux in the high energies necessary for penetrating high density rock materials with *in situ* pressure/flow cells, allowing pseudo simultaneous diffraction contrast tomography and traditional transmission, possibly with K-edge specificity (depending on the system) to see deformation, then fracture and fluid locations/evolution at a few micron resolution and in real time as the system evolves.

For deep Earth and planetary science, X-ray diffraction combined with the diamond-anvil cell (DAC) has played a crucial role in unravelling the crystal structure of matter compressed to extreme pressures and recently also to high temperatures. Only the DAC with its optical transparent windows enables samples to be heated with powerful lasers up to temperatures of 6000 K at multi-Mbar pressure (1 Mbar = 100 GPa) and allows the elucidation of structural properties of mineralogical relevant samples at pressure and temperature conditions prevailing deep inside the Earth (Figure 4). The observation of the "post-perovskite" structure of $(\text{Mg,Fe})\text{SiO}_3$ – the major mineral of the Earth's lower mantle – at 125 GPa and 2000 K³³ was a turning point in understanding the structure and

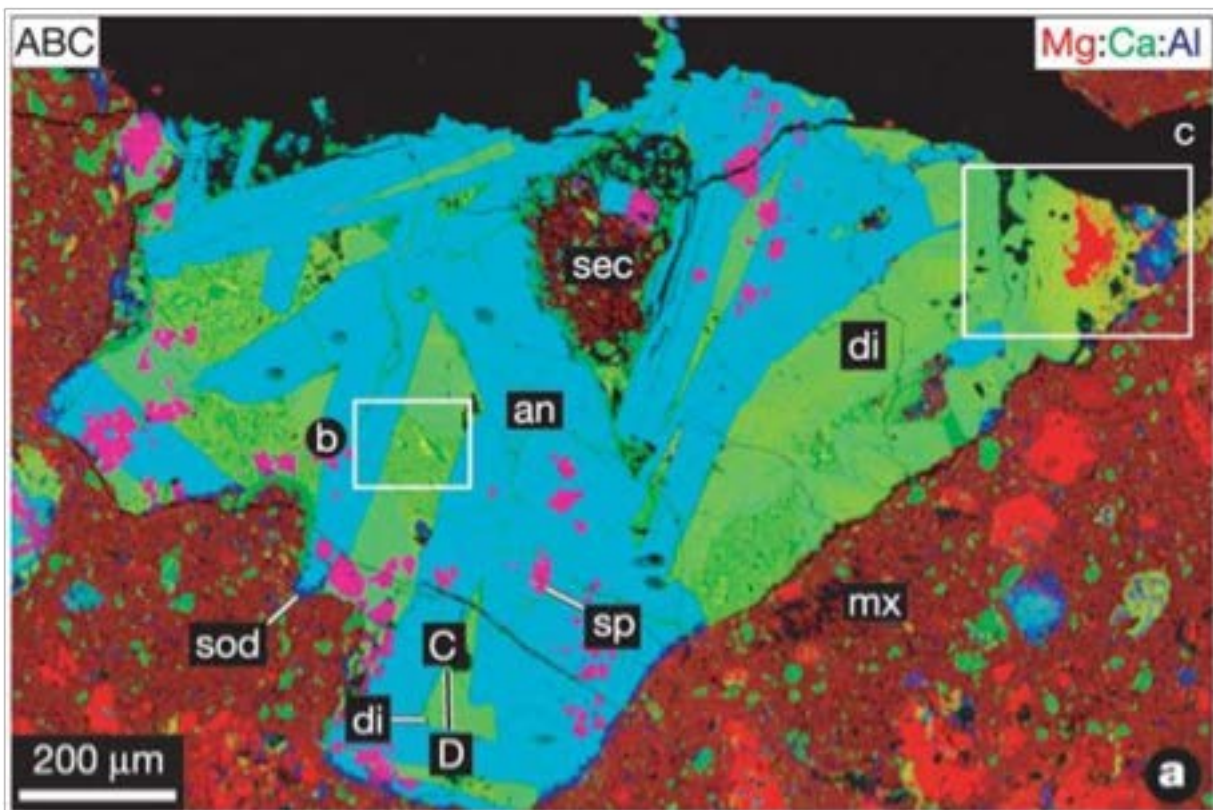


Figure 5: Combined elemental map in Mg (red), Ca (green) and Al K α (blue) X-rays. The CAI consists of coarse-grained, anorthite laths partly replaced by sodalite and nepheline, coarse-grained Al-Ti-diopside enclosing spinel grains, and interstitial material composed of fine-grained Al-diopside and melilite replaced by grossular, monticellite and wollastonite. A relict olivine-low-Ca pyroxene fragment occurs in the right portion of the CAI in the boxed area; it is surrounded by a halo of high-Ca pyroxene²⁷. Reprinted by permission from Copyright Clearance Center: SpringerNature, *Nature, Chronology of the early Solar System from chondrule-bearing calcium-aluminium-rich inclusions*, Krot, A.N. et al., Copyright (2005). Adapted from Ref.²⁷

dynamics of the deep Earth³⁴. Even more than ten years after the discovery of the (metastable) post-perovskite structure, simple questions such as the driving force for this structural transition have not yet been answered and unfolding the relationship between geophysics and the deep Earth and its constituents has just started. Similarly, structural changes and metallisation of the ices (H₂O and methane) and gases (H₂) likely to happen at pressure and temperature conditions inside giant planets, as well as the structures of minerals and iron that probably are the main constituent of extrasolar planets, are questions that can be addressed with Diamond-II.

In order to investigate *in situ* pressure-induced changes of structural or physical properties (typical sample dimensions are less than 30 µm), high-energy X-rays with beam sizes in the micrometre range and below are required. Diamond-II will provide high-energy X-rays with the low emittance needed to penetrate through the millimetre-sized diamond walls of the DAC and to generate measurable signals from the minute samples. *In situ* studies at extreme pressure and temperature conditions will make it possible to explore the *terra incognita* in Earth and Planetary Sciences to explore the structural, mechanical, chemical and electronic properties of relevant minerals, alloys and metals.

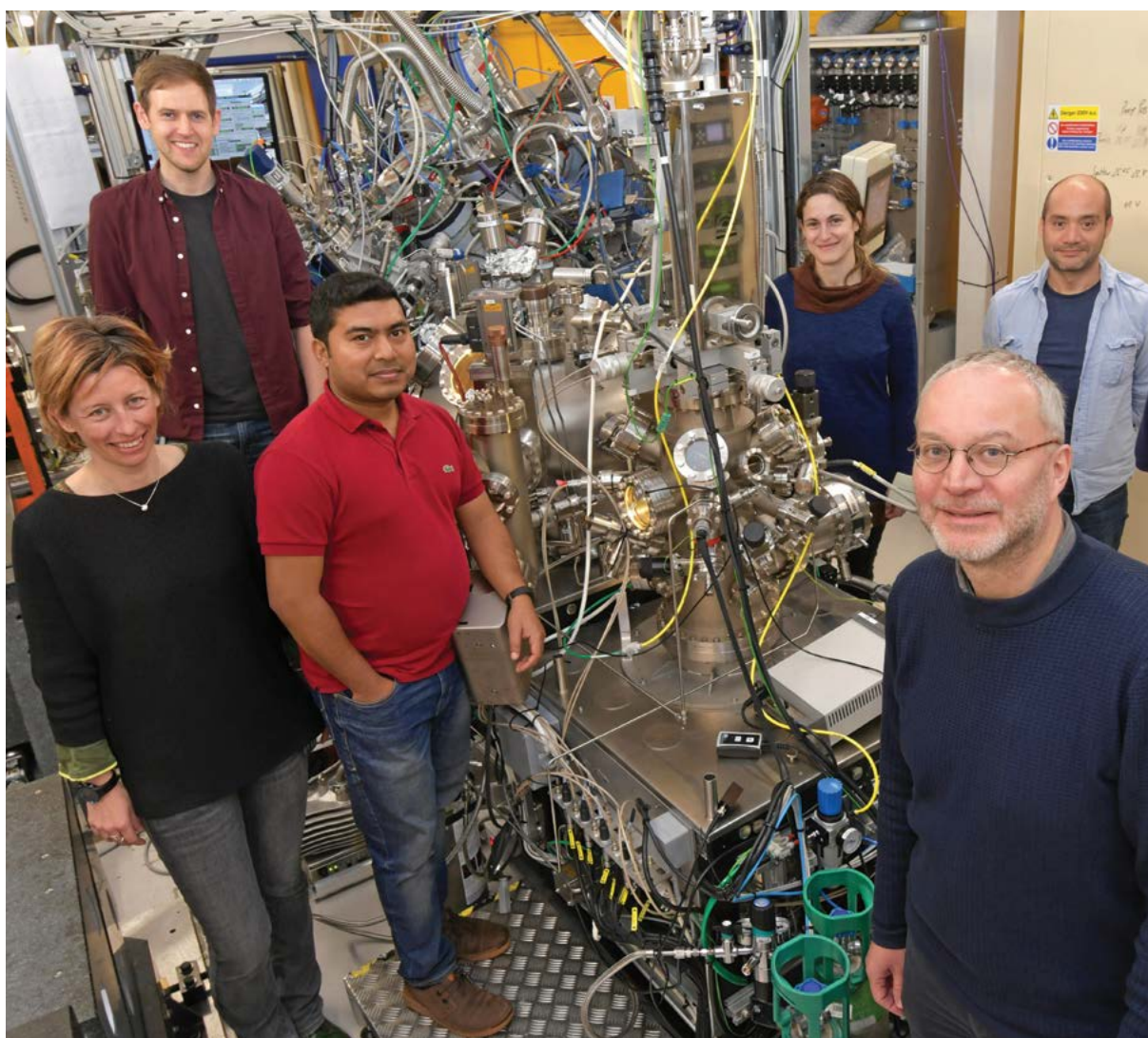
Finally, with a number of space missions collecting dust particles, and returning to Earth in the early to late 2020s³⁵⁻⁴⁰ the timing for these to be examined at Diamond-II is perfect. Using the improved flux of I14 for XRF and Near Edge X-ray Absorption Fine Structures (NEXAFS) analysis of pre-biotic organic matter from comets and asteroids has implications for understanding the early formation of life, and hydration processes in carbonaceous chondrites have major implications for models of solar system formation. Chondrules and calcium aluminium inclusions (CAI's) are the first materials to condense from the Solar Nebula and mapping them using X-ray and electron methods can give greater insights into their structure (Figure 5) and history and will benefit from higher flux at mid-range energies 20-40 keV and diffraction tomography.

References

1. Sabine, C. *et al.* Carbon and Other Biogeochemical Cycles. In: *Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change Coordinating Lead Authors: Lead Authors: Contribu.* (Peter, 2013).
2. The Grand Challenges. Available at: <https://www.gov.uk/government/publications/industrial-strategy-the-grand-challenges/industrial-strategy-the-grand-challenges#clean-growth>.
3. 'Geology for Society' outlines the importance of geology to our society. (2014).
4. Philippe, J. *et al.* Rotating tomography Paris–Edinburgh cell: a novel portable press for micro-tomographic 4-D imaging at extreme pressure/temperature/stress conditions. *High Press. Res.* **36**, 512–532 (2016).
5. Dobson, K. J. *et al.* 4-D imaging of sub-second dynamics in pore-scale processes using real-time synchrotron X-ray tomography. *Solid Earth* **7**, 1059–1073 (2016).
6. Support Sustainable Soil Management | UN Global Compact. Available at: <https://www.unglobalcompact.org/take-action/action/sustainable-soil-management>. (Accessed: 3rd January 2019)
7. *The National Adaptation Programme and the Third Strategy for Climate Adaptation Reporting Making the country resilient to a changing climate.* (2018).
8. Berner, R. a. Fuels and Atmospheric Composition. *Nature* **426**, 323–326 (2003).
9. Schmidt, M. W. I. *et al.* Persistence of soil organic matter as an ecosystem property. *Nature* **478**, 49–56 (2011).
10. Hirst, C. *et al.* Characterisation of Fe-bearing particles and colloids in the Lena River basin, NE Russia. *Geochim. Cosmochim. Acta* **213**, 553–573 (2017).
11. von der Heyden, B. P., Roychoudhury, A. N., Mtshali, T. N., Tyliczszak, T. & Myneni, S. C. B. Chemically and geographically distinct solid-phase iron pools in the Southern Ocean. *Science* **338**, 1199–201 (2012).
12. Burdige, D. J. Preservation of organic matter in marine sediments: Controls, mechanisms, and an imbalance in sediment organic carbon budgets? *Chem. Rev.* **107**, 467–485 (2007).
13. Hedges, J. I. *et al.* The molecularly uncharacterized component of nonliving organic matter in natural environments. *Org. Geochem.* **31**, 945–958 (2000).
14. Couradeau, E. *et al.* In Situ X-Ray Tomography Imaging of Soil Water and Cyanobacteria From Biological Soil Crusts Undergoing Desiccation. *Front. Environ. Sci.* **6**, 65 (2018).
15. Welcome to the '4 per 1000' Initiative | 4p1000. Available at: <https://www.4p1000.org/>. (Accessed: 19th October 2018)
16. NIRAB. UK Nuclear Innovation and Research Programme Recommendations. **NIRAB-75-1**, (2016).
17. BIS. Long-term Nuclear Energy Strategy. (2013).
18. BIS. Nuclear Industrial Vision Statement. (2013).
19. BIS. Nuclear Energy Research and Development Roadmap: Future Pathways. 128 (2013).
20. BIS. *The UK's Nuclear Future.* (2013).
21. NDA. *Strategy - effective from April 2016.* **2011**, (2016).
22. *CONSULTATION: National Policy Statement For Geological Disposal Infrastructure Implementing Geological Disposal.* (2018).
23. EPSRC. EPSRC Independent Review of Fission and Fusion EPSRC Independent Review of Fission and Fusion. (2016).
24. Corkhill, C. L. *et al.* Multi-scale investigation of uranium attenuation by arsenic at an abandoned uranium mine, South Terras. *npj Mater. Degrad.* **1**, 19 (2017).
25. Air quality: draft Clean Air Strategy 2018. Available at: <https://consult.defra.gov.uk/environmental-quality/clean-air-strategy-consultation/>. (Accessed: 2nd January 2019)
26. Pfrang, C. *et al.* Complex three-dimensional self-assembly in proxies for atmospheric aerosols. *Nat. Commun.* **8**, 1724 (2017).
27. Polacci, M. *et al.* Crystallisation in basaltic magmas revealed via *in situ* 4D synchrotron X-ray microtomography. *Sci. Rep.* **8**, 8377 (2018).

Diamond-II: Advancing physical sciences

28. Lacroix, B., Baumgartner, L. P., Bouvier, A. S., Kempton, P. D. & Vennemann, T. Multi fluid-flow record during episodic mode I opening: A microstructural and SIMS study (Cotiella Thrust Fault, Pyrenees). *Earth Planet. Sci. Lett.* **503**, 37–46 (2018).
29. Dobson, K. *et al.* Insights into Ferric Leaching of Low Grade Metal Sulfide-Containing ores in an Unsaturated Ore Bed Using X-ray Computed Tomography. *Minerals* **7**, 85 (2017).
30. Lamy-Chappuis, B., Yardley, B. W. D., He, S., Zu, Y. & Xie, J. A test of the effectiveness of pore scale fluid flow simulations and constitutive equations for modelling the effects of mineral dissolution on rock permeability. *Chem. Geol.* **483**, 501–510 (2018).
31. Saif, T., Lin, Q., Singh, K., Bijeljic, B. & Blunt, M. J. Dynamic imaging of oil shale pyrolysis using synchrotron X-ray microtomography. *Geophys. Res. Lett.* **43**, 6799–6807 (2016).
32. Callow, B., Falcon-Suarez, I., Ahmed, S. & Matter, J. Assessing the carbon sequestration potential of basalt using X-ray micro-CT and rock mechanics. *Int. J. Greenh. Gas Control* **70**, 146–156 (2018).
33. Murakami, M. Post-Perovskite Phase Transition in MgSiO₃. *Science (80-.)*. **304**, 855–858 (2004).
34. Duffy, T. S. Mineralogy at the extremes. *Nature* **451**, 269–270 (2008).
35. Zolensky, M. (NASA). CosmoELEMENTS. *Elements* **12**, 159–160 (2016).
36. JAXA Hayabusa2 Project. Available at: <http://www.hayabusa2.jaxa.jp/en/>. (Accessed: 19th November 2018)
37. Overview - Mars 2020 Rover. Available at: <https://mars.nasa.gov/mars2020/mission/overview/>. (Accessed: 19th November 2018)
38. ExoMars / Space Science / Our Activities / ESA. Available at: http://www.esa.int/Our_Activities/Space_Science/ExoMars. (Accessed: 19th November 2018)
39. Future Chinese Lunar Missions. Available at: https://nssdc.gsfc.nasa.gov/planetary/lunar/cnsa_moon_future.html. (Accessed: 19th November 2018)
40. Russian Moon exploration program. Available at: <http://www.iki.rssi.ru/eng/moon.htm>. (Accessed: 19th November 2018)
41. Krot, A. N., Yurimoto, H., Hutcheon, I. D. & MacPherson, G. J. Chronology of the early Solar System from chondrule-bearing calcium-aluminium-rich inclusions. *Nature* **434**, 998–1001 (2005).



Appendix 1

Diamond's beamlines: current operational status April 2019		
Beamline Name and Number	Main Techniques	Energy / Wavelength Range
I02-1 - Versatile MX micro (VMXm)	Micro- and nano-focus in vacuum cryo-macromolecular crystallography (VMXm)	7 - 28 keV
I02-2 - Versatile MX <i>in situ</i> (VMXi)	<i>In situ</i> microfocus macromolecular crystallography, Serial Synchrotron Crystallography	10 - 25 keV
I03 - MX	Macromolecular crystallography (MX), Multiwavelength Anomalous Diffraction (MAD)	5 - 25 keV
I04 - Microfocus MX	MX, MAD	6 - 18 keV
I04-1 - Monochromatic MX	MX, XChem fragment screening	13.53 keV (fixed wavelength)
I05 - ARPES	Angle-Resolved PhotoEmission Spectroscopy (ARPES) and nano-ARPES	18 - 240 eV; 500 eV
I06 - Nanoscience	X-ray Absorption Spectroscopy (XAS), X-ray photoemission microscopy and X-ray magnetic circular and linear dichroism	80eV - 2200eV
I07 - Surface and Interface Diffraction	Surface X-ray diffraction, Grazing Incidence X-ray Diffraction (GIXD), Grazing Incidence Small Angle X-ray Scattering (GISAXS), X-ray Reflectivity (XRR)	6 - 30 keV
B07 - VERSOX: Versatile Soft X-ray	Ambient Pressure XPS and NEXAFS	250 - 2800 eV
	NEXAFS and High-Throughput XPS	50 - 2200 eV
I08 - Scanning X-ray Microscopy	Scanning X-ray microscopy, NEXAFS/ XANES, X-ray fluorescence	I08 branch: 250 eV - 4.4 keV
		J08 - Soft and Tender X-ray Ptychography branch: 250 - 2000 eV
I09 - Atomic and Electronic Structure of Surfaces and Interfaces	XPS (including HAXPES), X-ray Standing Waves (XSW), Near Edge X-ray Absorption Fine Structure (NEXAFS), energy-scanned photoelectron diffraction	Hard X-rays: 2.1 - 18+ keV Soft X-rays: 0.1 - 2.1 keV (currently 0.1 - 1.9 keV)
I10 - BLADE: Beamline for Advanced Dichroism Experiments	Soft X-ray resonant scattering, XAS and X-ray magnetic circular and linear dichroism	Circular: 400-1600eV; Linear Horizontal: 250-1600eV; Linear Vertical: 480-1600eV
I11 - High Resolution Powder Diffraction	X-ray powder diffraction	6 - 25(30) keV (0.5 - 2.1 Å)
DIAD: Dual Imaging and Diffraction	Simultaneous imaging and diffraction	8 - 38 keV
I12 - JEEP: Joint Engineering, Environmental and Processing	Time-resolved imaging and tomography (phase- and attenuation-contrast), time-resolved powder diffraction, single crystal diffraction, diffuse scattering, energy dispersive X-ray diffraction (EDXD), high-energy small angle X-ray scattering (under development)	53 keV - 150 keV monochromatic or continuous white beam
I13 - X-ray Imaging and Coherence	Phase contrast imaging, tomography, full-field microscopy (under commissioning), coherent diffraction and imaging (CXRD, CDI), ptychography and photocorrelation spectroscopy (XPCS) (under commissioning), innovative microscopy and imaging	Imaging branch: 8 - 30keV
		Coherence branch: 7 - 20keV
I14 - Hard X-ray Nanoprobe	Scanning X-ray fluorescence, X-ray spectroscopy, ptychography and transmission diffraction	5 - 23 keV
I15 - Extreme Conditions	Powder diffraction, single crystal diffraction	Monochromatic and focused 20 - 80 keV White beam
I15-1 - XPDF	X-ray Pair Distribution Function (XPDF)	40, 65, and 76 keV
I16 - Materials and Magnetism	Resonant and magnetic single crystal diffraction, fundamental X-ray physics	2.5 - 15 keV

Appendix 1

Diamond's beamlines

B16 - Test beamline	Diffraction, imaging and tomography, topography, reflectometry	4 - 20 keV monochromatic focused 4 - 45 keV monochromatic unfocused White beam
I18 - Microfocus Spectroscopy	Micro XAS, micro Extended X-ray Absorption Fine Structure (EXAFS), micro fluorescence tomography, micro XRD	2.05 - 20.5 keV
B18 - Core XAS	X-ray Absorption Spectroscopy (XAS)	2.05 - 35 keV
I19 - Small-Molecule Single-Crystal Diffraction	Small-molecule single-crystal diffraction	5 to 25 keV / 0.5 to 2.5 Å
I20 - LOLA: Versatile X-ray Spectroscopy	X-ray Absorption Spectroscopy (XAS), X-ray Emission Spectroscopy (XES) and Energy Dispersive EXAFS (EDE)	Dispersive branch: 6 - 26 keV Scanning branch: 4 - 20 keV
I21 - Inelastic X-ray Scattering	Resonant Inelastic X-ray Scattering (RIXS), X-ray Absorption Spectroscopy (XAS)	Currently 250 - 1500 eV (to be upgraded to 250 - 3000 eV)
B21 - High Throughput SAXS	BioSAXS, solution state small angle X-ray scattering	8 - 15 keV (set to 13.1 keV by default)
I22 - Small Angle Scattering and Diffraction	Small angle X-ray scattering and diffraction: SAXS, WAXS, USAXS, GISAXS. Micro-focus.	7 - 20 keV
B22 - MIRIAM: Multimode InfraRed Imaging And Microspectroscopy	IR micro- & nano-spectroscopy, IR imaging, THz spectroscopy	nanoFTIR : 4000-900 cm ⁻¹ (2.5-11 μm) microFTIR: 10,000-100 cm ⁻¹ (1-100 μm) Spectroscopy (FTIR): 10,000-10 cm ⁻¹ (1-1000 μm) Imaging (FPA): 10,000-900 cm ⁻¹ (1-11 μm)
I23 - Long Wavelength MX	Long wavelength macromolecular crystallography	3 - 8 keV (1.5 - 4.1 Å)
B23 - Circular Dichroism	Circular Dichroism (CD)	125-500 nm & 165-650 nm for CD Imaging at 50 μm resolution, 96-cell High-Throughput CD (HTCD) and High-Pressure CD up to 200 MPa
I24 - Microfocus and Serial MX	Macromolecular crystallography, MAD, Serial Crystallography	6.5 - 25.0 keV
B24 - Cryo Transmission X-ray Microscopy (TXM)	Full field X-ray imaging	200eV - 2600eV

Electron Microscopes

Microscope	Main Capabilities	Accelerating Voltages
Titan Krios I	Cryo-EM, Cryo-ET	80, 120, 200, 300 kV
Titan Krios II	Cryo-EM, Cryo-ET	80, 120, 200, 300 kV
Titan Krios III	Cryo-EM, Cryo-ET	80, 120, 200, 300 kV
Titan Krios IV	Cryo-EM, Cryo-ET	80, 120, 200, 300 kV
Titan Krios V	Cryo-EM, Cryo-ET	80, 120, 200, 300 kV
Talos Arctica	Cryo-EM, Cryo-ET	200 kV
Glacios	Cryo-EM, Cryo-ET	200 kV
Scios	Cryo-SEM, Cryo-FIB	3 to 30 kV
Aquilos	Cryo-SEM, Cryo-FIB	3 to 30 kV
JEOL ARM200F	Atomic scale STEM imaging, EELS, EDX, electron diffraction	80, 200 kV
JEOL ARM300F	Atomic scale TEM and STEM imaging, electron diffraction, 4D-STEM, EDX	30, 60, 80, 160, 200, 300 kV

Appendix 2

Diamond-II Workshop: Crystallography
3 - 4 Sept 2018Monday 3rd September 2018

10:00 - 10:20	Registration / Coffee	
10:20 - 10:30	Welcome & Diamond-II introduction	Andy Dent
10:30 - 10:50	Overview I11	Chiu Tang
10:50 - 11:10	Overview I15	Heribert Wilhelm
11:10 - 11:30	Overview I15-1	Phil Chater
11:30 - 11:50	Overview I19	Dave Allan
11:50 - 12:10	"Diamond-II: Implications of machine upgrade"	Ian Martin
12:10 - 12:30	"Nano-focussing at Diamond"	Paul Quinn
12:30 - 13:30	Lunch	
Energy Materials (Chair: Phil Chater)		
13:30 - 14:00	"What do we need to know to understand functional Materials?"	John Claridge (Liverpool)
14:00 - 14:30	"Porous materials for energy and environmental applications"	Sihai Yang (Manchester)
14:30 - 15:00	"From Solar Cells to Magnetic Skyrmions - a Research Journey through Diffraction studies of Energy Materials"	Peter Hatton (Durham)
15:00 - 15:30	Coffee Break	
Chemistry & Materials Discovery (Chair: Dave Allan)		
15:30 - 16:00	TBA	Edman Tsang (Oxford)
16:00 - 16:30	"From Fundamentals to Flow: Structural Evolution In and Into the Solid State"	Chick Wilson (Bath)
16:30 - 17:00	"Opportunities for small molecule crystallography – When your home source is at its limit"	Christian Lehmann (Mühlheim, Germany)
17:00 - 17:15	Coffee Break	
17:15 - 18:00	Discussion	
18:30 - 21:00	Dinner	

Tuesday 4th September 2018

08:45 - 09:00	Summary of day 1	Heribert Wilhelm
Quantum & Material Processes (Chair: Heribert Wilhelm)		
09:00 - 09:30	"Time-resolved Photocrystallography: State-of-the-Art and Future Possibilities"	Paul Raithby (Bath)
09:30 - 10:00	"Interrogating dynamical phase transitions and crystal structures for exoplanet equation of state investigations"	Peter Norreys (Oxford)
10:00 - 10:30	"A New Generation of Extreme Conditions Science on Diamond-II"	Malcolm McMahon (Edinburgh)
10:30 - 11:00	Coffee Break	
Earth & Environment (Chair: Chui Tang)		
11:00 - 11:30	"Structural studies of materials for radionuclide uptake"	Joe Hriljac (Birmingham)
11:30 - 12:00	"Shining a light on drug discovery and development"	Cheryl Doherty (Pfizer)
12:00 - 12:30	"The role of macromolecules in controlling CaCO ₃ crystallisation during biomineralisation"	Fabio Nudelman (Edinburgh)
12:30 - 13:30	Lunch	
13:30 - 15:00	Discussion	
15:00	End of Workshop	

Appendix 2

Firstname	Lastname	Organisation	Job Role
Phoebe	Allan	University of Birmingham	Academic Staff
Dave	Allan	Diamond Light Source	
Christine	Beavers	LBL	
Thomas	Bennett	University of Cambridge	Research Fellow
Anna	Bogush	University College London (UCL)	Post Doctoral Researcher/PDRA (or equivalent)
Samuel	Booth	University of Glasgow	Post Doctoral Researcher/PDRA (or equivalent)
Marie	Camilleri	University of Malta	Student
Simon	Cassidy	University of Oxford	Post Doctoral Researcher/PDRA (or equivalent)
Phil	Chater	Diamond Light Source	
Tianyi	Chen	University of Oxford	Doctoral Research Student e.g. PhD
John	Claridge	University of Liverpool	Academic Staff
Jeremy	Cockcroft	University College London (UCL)	Academic Staff
Dominik	Daisenberger	Diamond Light Source	
Sarah	Day	Diamond Light Source	
Andy	Dent	Diamond Light Source	Deputy Director - Physical Sciences
Maria	Diaz-Lopez	Science and Technology Facilities Council (STFC)	Post Doctoral Researcher/PDRA (or equivalent)
Stephen	Dodsworth	University of Sheffield	Doctoral Research Student e.g. PhD
Cheryl	Doherty	Pfizer	
Timothy	Easun	Cardiff University	Academic Staff
Anton	Goetzee-Barral	University of Leeds	Research Fellow
Matthias	Gutmann	Rutherford Appleton Laboratory	Academic Staff
Lauren	Hatcher	University of Bath	Research Fellow
Peter D	Hatton	Durham University	Academic Staff
Guanze	He	University of Oxford	Doctoral Research Student e.g. PhD
Joe	Hriljac	University of Birmingham	Academic Staff
Stephen	Hull	STFC	ISIS Crystallography Group Leader
Saurabh	Kabra	Science and Technology Facilities Council (STFC)	UK Research Council Staff
Dean	Keeble	Diamond Light Source	
David	Keen	Rutherford Appleton Laboratory	UK Research Council Staff
Annette	Kleppe	Diamond Light Source	
Ewelina	Kosior	Diamond Light Source	Senior Support Scientist
Christian	Lehmann	Max-Planck-Institut für Kohlenforschung	Academic Staff
Hauke	Marquardt	University of Oxford	
Ian	Martin	Diamond Light Source	
Malcolm	McMahon	University of Edinburgh	Academic Staff
Jiawei	Mi	University of Hull	Academic Staff
Saumya	Mukherjee	Diamond Light Source	Postdoctoral Research Associate
Claire	Murray	Diamond Light Source	
Subhasisa	Nath	Coventry University	Post Doctoral Researcher/PDRA (or equivalent)
Peter	Norreys	University of Oxford	
Fabio	Nudelman	University of Edinburgh	Academic Staff
Ahu	Parry	Imperial College London	Teaching Fellow
Shaojun	Qi	University of Birmingham	Research Fellow
Paul	Quinn	Diamond Light Source	
Paul	Raithby	University of Bath	Academic Staff

Thomas	Roseveare	University of Sheffield	Post Doctoral Researcher/PDRA (or equivalent)
Elizabeth	Shotton	Diamond Light Source	Head of Industrial Liaison
Chiu	Tang	Diamond Light Source	Principal Beamline Scientist I11
Stephen	Thompson	Diamond Light Source	Senior Beamline Scientist I11
Amber	Thompson	University of Oxford	
Edman	Tsang	University of Oxford	
Liana	Vella-Zarb	University of Malta	Academic Staff
Armin	Wagner	Diamond Light Source	Principal Beamline Scientist I23
Mark	Warren	Diamond Light Source	
Shi	Wei		
Heribert	Wilhelm	Diamond Light Source	Science Group Leader - Crystallography Group
Chick	Wilson	University of Bath	Academic Staff
Chao	Xu	University of Cambridge	Research associate
Sihai	Yang	University of Manchester	Academic Staff

Diamond-II Workshop: MX & Soft Condensed Matter 10 - 11 Sept 2018

Day 1: MX Workshop - 10th September

09:45 Registration

Session 1: Opportunities of the Diamond-II upgrade for MX beamlines

10:30	D-II and Grand Challenges	Dave Stuart (DLS, Oxford)
10:55	D-II Impact for MX beamlines	Dave Hall (DLS)
11:20	XChem and beamline move	Frank von Delft (DLS, Oxford)
11:45	Bang for your buck - getting the best data with D-II	Gwynndaf Evans (DLS)
12:10	Lunch	
13:10	The future of cryo-samples - automation and streamlining	Katherine McAuley (DLS)
13:35	Future of phasing and exploiting tuneability	Armin Wagner (DLS)
14:00	Discussion	
14:30	Coffee	

Session 2: Serial crystallography and time resolved experiments

15:00	Introduction to Serial crystallography	Robin Owen (DLS)
15:15	Opportunities for rapid and time resolved serial crystallography	Mike Hough (University of Essex)
15:40	What does D-II mean for the XFEL-Hub	Allen Orville (DLS)
16:05	MX at SLS and SwissFEL	Meitian Wang (Paul Scherrer Institut)
16:30	Discussion	
17:00	Coffee	

Session 3: Structural biology needs for the future

17:25	Elucidating mechanism of biotechnologically relevant enzymes, the need for time resolved approaches	Colin Levy (University of Manchester)
17:50	What do we want? More (much more) of the same please!	Susan Lea (University of Oxford)
18:15	Discussion	
19:00	Dinner	

Appendix 2

Day 1: Soft Condensed Matter Workshop - 10th September

09:45	Registration	
10:30	SCM beam line introduction	Rob Rambo (DLS)
10:45	I22	Nick Terrill (DLS)
11:05	B23	Giuliano Siligardi (DLS)
11:25	B22	Gianfelice Cinque (DLS)
11:45	B21	Nathan Cowieson (DLS)
12:05	Lunch	
13:00	SAXS tomography	TBA
13:20	CD MMP for imaging	Bart Kahr (NYU)
13:40	nano IR tomography	Luca Quaroni (Jagiellonian University, Poland)
14:00	THZ MOF	Jin-Chong Tan (University of Oxford)
14:20	Discussion	
14:50	Coffee	
15:20	Applications of Microfluidics on I22	TBA
15:40	Applications of Microfluidics on B23	Jerome Charmet (Warwick University)
16:00	Applications of Microfluidics on B22	Russel Howe (Aberdeen University)
16:20	SOLEIL microfluidics	Benedikt Lassalle (SOLEIL)
16:40	Discussion	
17:10	Coffee	
17:30	XFMS	Peter Stockley (Lees U)/Sayan Gupta (ALS)
17:50	TBA	
18:10	B22 <i>In situ</i> time-resolved electrochemistry and correlated IR molecular analysis (faster and signal-to-noise)	Kylie Vincent (University of Oxford)
18:30	IR imaging and correlative studies	Rohit Bhargava
18:50	Discussion	
19:00	Dinner	

Day 2: Joint MX and Soft Condensed Matter Workshop - 11th September

Session 1: High throughput methods and drug discovery

09:00	High-Throughput Methods and Drug Discovery Introduction	Dave Brown (University of Kent)
09:10	MPS1 inhibitors and the molecular basis of resistance to MPS1 inhibition	Rob van Montfort (ICR)
09:35	Drug Discovery an industrial perspective	Dave Brown on behalf of Rob Cooke (Heptares)
10:00	Protein Engineering/Ligand Screening SAXS	Greg Hura (ALS, Berkeley)
10:25	Coffee	
10:55	CD based screening method	Lorenzo Di Bari (Pisa U.)
11:20	High-throughput GI-SAXS	Alex Hexemer(ALS, Berkeley)
11:45	Discussion	
12:15	Lunch	

Session 2: Data deluge

13:15	Data handling at Diamond	Andrew Richards (DLS)
-------	--------------------------	-----------------------

13:40	Data analysis for integrated biology at Diamond	Alun Ashton (DLS)
14:05	Data mining science	Alex Hexemer (ALS, Berkeley)
14:30	Discussion	
15:00	Coffee	
Session 3: Broader topics		
15:30	X-ray crystallography of large complexes in the age of cryo-EM	Ashwin Chari (Max Planck, Gottingen)
15:55	The ESRF upgrade - impact on MX and SAXS for users	Jean Susini (ESRF)
16:20	Mono and Pink beam SSX and Life Science with APS-U	Bob Fischetti (APS, Chicago)
16:45	Discussions and Conclusions	

MX Attendees

Firstname	Lastname	Organisation	Job Role
Pierre	Aller	Diamond Light Source	Beamline Scientist
Alun	Ashton	Diamond Light Source	Group Leader - Data Analysis Software
Danny	Axford	Diamond Light Source	Beamline Scientist I24
Arnaud	Basle	Newcastle University	Post Doctoral Researcher/PDRA (or equivalent)
Jose	Brandao-Neto	Diamond Light Source	Senior Beamline Scientist I04.1
Stephen	Carr	Research Complex at Harwell	Post Doctoral Researcher/PDRA (or equivalent)
Ashwin	Chari	Max Planck Institute for biophysical chemistry	Group leader
Ian	Clifton	University of Oxford	Academic Staff
Nora	Cronin	Institute of Cancer Research	Academic Staff
Alexandre	Dias	Diamond Light Source	Senior Industrial Liaison Scientist - X-Ray Spectroscopy
Jing	Dong	Astex Pharmaceuticals	Post Doctoral Researcher/PDRA (or equivalent)
Alice	Douangamath	Diamond Light Source	Senior Support Scientist I04.1
Louise	Dunnett	University of Essex	Doctoral Research Student e.g. PhD
Kamel	El Omari	Diamond Light Source	Beamline Scientist BLI23
Gwyndaf	Evans	Diamond Light Source	Principal Beamline Scientist VMXm - Research Fellow
Susan Kathleen	Fetics	Trinity College, Dublin	Post Doctoral Researcher/PDRA (or equivalent)
Robert	Fischetti	Argonne National Laboratory	Life Science Adviser and GMCA Group Leader
Ralf	Flaig	Diamond Light Source	Principal Beamline Scientist - I04
Markus	Gerstel	Diamond Light Source	Data Analysis Scientist
Richard	Gildea	Diamond Light Source	Data Analysis Scientist (MX)
Jonathan	Grimes	University of Oxford	Academic Staff
Dave	Hall	Diamond Light Source	Science Group Leader - MX
Karl	Harlos	University of Oxford	Academic Staff
Mike	Hough	University of Essex	Academic Staff
Ronan	Keegan	Research Complex at Harwell	Academic Staff
Hossein	Khosroabadi	SESAME	Academic Staff

Appendix 2

Tobias	Krojer	University of Oxford	Academic Staff
Pauline	Lang	University of Oxford	Masters Research Student
David	Lawson	John Innes Centre	Academic Staff
Susan	Lea	University of Oxford	Academic Staff
Colin	Levy	University of Manchester	Post Doctoral Researcher/PDRA (or equivalent)
Edward	Lowe	University of Oxford	Academic Staff
Anka	Lucic	King's College London	Masters Research Student
Sarah	Macdonell	Diamond Light Source	Head of Beamline Systems Engineering
Marco	Mazzorana	Diamond Light Source	Senior Support Scientist I04
Katherine	McAuley	Diamond Light Source	Principal Beamline Scientist I03
Michael	McDonough	University of Oxford	Post Doctoral Researcher/PDRA (or equivalent)
Marc	Morgan	Imperial College London	Academic Staff
Vitaliy	Mykhaylyk	Diamond Light Source	Beamline Scientist I23
Allen	Orville	Diamond Light Source	Principal Scientist XFEL Hub
Robin	Owen	Diamond Light Source	Principal Beamline Scientist I24
Neil	Paterson	Diamond Light Source	Beamline Scientist I03
Ehmke	Pohl	Durham University	Academic Staff
Ailsa	Powell	Diamond Light Source	Industrial Liaison Scientist - X Chem
Andrew	Richards	Diamond Light Source	Head of Scientific Computing
Pierre	Rizkallah	Cardiff University	Academic Staff
Juan	Sanchez-Weatherby	Diamond Light Source	Senior Beamline Scientist I02
James	Sandy	Diamond Light Source	Senior Support Scientist I02
Kaushik	Sarkar	UCB	Research Scientist
Elizabeth	Shotton	Diamond Light Source	Head of Industrial Liaison
Jean	Susini	ESRF	Director of Research
Jennifer	Swarbrick	BBSRC	Strategy and Policy Officer
Leah	Taylor Kearney	Chemistry	Student
Jose	Trincao	Diamond Light Source	Senior Beamline Scientist VMX
Rob	van Montfort	Institute of Cancer Research	Academic Staff
Melanie	Vollmar	Diamond Light Source	Post Doctoral Research Associate-VMXm
Frank	von Delft	Diamond Light Source	Principal Beamline Scientist I04-1
Armin	Wagner	Diamond Light Source	Principal Beamline Scientist I23
Meitian	Wang	Paul Scherrer Institute	
Mark	Williams	Diamond Light Source	Automation Scientist
Benjamin	Williams	Diamond Light Source	Post Doctoral Research Associate CSMD
Graeme	Winter	Diamond Light Source	Senior Software Scientist
Maximilian	Wranik	SGC	

Soft Condensed Matter Attendees

Firstname	Lastname	Organisation	Job Role
John	Barker	Evotec	
Liz	Blackburn	University of Edinburgh	Post Doctoral Researcher/PDRA (or equivalent)
John	Brazier	University of Reading	Academic Staff
Nicholas	Brooks	Imperial College London	Academic Staff
Andrew	Burnett	University of Leeds	Research Fellow
Valeria	Castelletto	University of Reading	Government funded Staff
Ka Lung Andrew	Chan	King's College London	Academic Staff

Diamond-II: Advancing Science

Jerome	Charmet	University of Warwick	Academic Staff
Gianfelice	Cinque	Diamond Light Source	Principal Beamline Scientist B22
Nathan	Cowieson	Diamond Light Source	Principal Beamline Scientist B21
Joanna	Denbigh	University of Salford	Academic Staff
Calliope	Dendrou	University of Oxford	Academic Staff
Charlotte	Edwards-Gayle	University of Reading	Doctoral Research Student e.g. PhD
Mark	Frogley	Diamond Light Source	Senior Beamline Scientist B22
Peter	Gardner	University of Manchester	Academic Staff
Ian	Hamley	University of Reading	Academic Staff
Alexander	Hexemer	LBNL	
Peter	Huggard	Rutherford Appleton Laboratory	UK Research Council Staff
Charlotte	Hughes	Diamond Light Source	Support Scientist B23
Ashley	Hughes	Diamond Light Source	Post Doctoral Research Associate (RIF)
Greg	Hura	UC Santa Cruz and LBNL	Research Scientist
Rohanah	Hussain	Diamond Light Source	Senior Beamline Scientist B23
Katsuaki	Inoue	Diamond Light Source	Senior Beamline Scientist B21
Robert	Jacobs	University of Oxford	Academic Staff
Tamas	Javorfi	Diamond Light Source	Senior Support Scientist B23
Ashley	King	Natural History Museum	Research Fellow
Nigel	Kirby	Australian Synchrotron	Government funded Staff
Benedikt	Lassalle	Synchrotron Soleil	Research Fellow
Ioannis	Lekkas	Diamond Light Source	Senior Support Scientist
Longfei	Lin	University of Manchester	Post Doctoral Researcher/PDRA (or equivalent)
Michael	Lockhart	University of Manchester	Post Doctoral Researcher/PDRA (or equivalent)
Ivalina	Minova	University of St Andrews	
Geoffrey	Moggridge	University of Cambridge	Academic Staff
Azura	Mohd Noor	University of Sheffield	Doctoral Research Student e.g. PhD
Dan	Pantos	University of Bath	Academic Staff
Claire	Pizzezy	Diamond Light Source	Deputy Head of Industrial Liaison
Luca	Quaroni	Jagiellonian University	Research Fellow
Robert	Rambo	Diamond Light Source	Science Group Leader - Soft Condensed Matter
Sion	Richards	Rutherford Appleton Laboratory	Doctoral Research Student e.g. PhD
Tara	Schiller	University of Warwick	Assistant professor
Giuliano	Siligardi	Diamond Light Source	Principal Beamline Scientist B23
Andy	Smith	Diamond Light Source	Beamline Scientist I22
Peter	Stockley	University of Leeds	Professor of Biological Chemistry
Eugen	Stulz	University of Southampton	Academic Staff
Jin-Chong	Tan	University of Oxford	Academic Staff
Alexander	Tansell	Cardiff University	Doctoral Research Student e.g. PhD
Nicholas	Terrill	Diamond Light Source	Principal Beamline Scientist I22
Mark	Tully	ESRF	
Arwen	Tyler	University of Leeds	Academic Staff
Matt	Veale	Science and Technology Facilities Council (STFC)	UK Research Council Staff
Jessica	Wade	Imperial College London	Post Doctoral Researcher/PDRA (or equivalent)
Martin	Walsh	Diamond Light Source	Deputy Director - Life Sciences
Magda	Wolna	Diamond Light Source	Support Scientist

Appendix 2

Diamond-II Workshop: Structures & Surfaces 13 Sept 2018

Thursday 13th September 2018

09:30 - 10:00	Registration / Coffee	
10:00 - 10:15	Introduction & Aims of Workshop	Chris Nicklin
10:15 - 10:40	Diamond-II Layout and Performance	Marco Apollonio
10:40 - 11:00	Outline Case for the Structures & Surfaces Group Discussion on Technical Issues, Initial Science Case	Chris Nicklin
11:00 - 12:00	Session 1: Non-UHV Studies Mary Ryan, Bridget Murphy, Ethan Crumlin	Chair – tbc
12:00 - 12:30	Discussion	
12:30 - 13:30	Lunch	
13:30 - 14:45	Session 2: Electronic Structure Phil King, Ralph Claessen, Louis Piper	Chair – Andrew Thomas
14:45 - 15:15	Discussion	
15:15 - 15:45	Coffee Break	
15:45 - 16:45	Session 3: Surface Science, Spectroscopy and Electrochemistry Geoff Thornton, Phil Woodruff	Chair – tbc
16:45 - 17:30	Discussion	
17:30 - 17:45	Summary of the Day & Closing Remarks	
17:45	Close of Workshop	

Structures & Surfaces Attendees

Firstname	Lastname	Organisation	Job Role
Efren Alberto	Andablo Reyes		
Marco	Apollonio	Diamond Light Source	Accelerator Physicist
Roger	Bennett	University of Reading	Academic Staff
Cephise	Cacho	Diamond Light Source	Principal Beamline Scientist I05
Francesco	Carla	Diamond Light Source	Principal Beamline Scientist I07
Jiahao	Chen	University of Oxford	Doctoral Research Student e.g. PhD
Ralph	Claessen	University of Wuerzburg	Research Fellow
Ethan	Crumlin	LBNL	Scientist
Andy	Dent	Diamond Light Source	Deputy Director - Physical Sciences
David	Duncan	Diamond Light Source	Beamline Scientist I09
Andrew	Evans	Aberystwyth University	Academic Staff
David	Grinter	Diamond Light Source	Beamline Scientist BLB07
Georg	Held	Diamond Light Source	Principal Beamline Scientist B07
Paul	Howes	University of Leicester	Academic Staff
Hadeel	Hussain	Diamond Light Source	
Mark	Jackman	AstraZeneca	Senior Scientist
Rob	Jones	University of Nottingham	
Timur	Kim	Diamond Light Source	Senior Beamline Scientist BLI05
Philip	King	University of St Andrews	Academic Staff
Andreas Ejdrup	Lauritzen	University of Oxford	Doctoral Research Student e.g. PhD
Tien-Lin	Lee	Diamond Light Source	Principal Beamline Scientist I09

Kevin	Lovelock	University of Reading	Academic Staff
Bridget	Murphy	University of Kiel	Academic Staff
Chris	Nicklin	Diamond Light Source	Science Group Leader - Surfaces Group
Giancarlo	Panaccione	IOM-CNR TASC Laboratory	Academic Staff
Louis	Piper	Binghamton University	Academic Staff
Rob	Rambo	Diamond Light Source	
Jonathan	Rawle	Diamond Light Source	Senior Support Scientist I07
Anna	Regoutz	Imperial College London	Research Fellow
Moritz	Riede	University of Oxford	Academic Staff
Mary	Ryan	Imperial College London	
Frank	Schreiber	University of Tuebingen	Academic Staff
Sven	Schroeder	University of Leeds	Academic Staff
Vladyslav	Solokha	Johannes Kepler University Linz	Doctoral Research Student e.g. PhD
Karen	Syres	University of Central Lancashire	Academic Staff
Nuria	Tapia Ruiz	Lancaster University	Academic Staff
Andrew	Thomas	University of Manchester	Academic Staff
Geoff	Thornton	University College London (UCL)	Academic Staff
Ophelie	Torres	University of Leeds	PhD Student
Federica	Venturini	Diamond Light Source	Senior Beamline Scientist BLB07
Robert	Weatherup	University of Manchester	Academic Staff
Phil	Woodruff	University of Warwick	Academic Staff

Diamond-II Workshop: Quantum Materials 13 Sept 2018

09.30 Coffee and Registration

10.00 Introduction and Opening Comments
Andy Dent, *Diamond Light Source*

10.10 Diamond-II and the Magnetic Materials Group
Sarnjeet Dhesi, *Diamond Light Source*

Session 1 : The Diamond-II Machine Upgrade (Chair: Steve Collins)

10.20 Diamond-II layout and performance
Riccardo Bartolini, *Diamond Light Source*

Session 2 : Excitations and Dynamics (Chair: Kejin Zhou)

10.45 Soft x-ray spectroscopy beamline: before and after the EBS ESRF upgrade.
Nick Brookes, *ESRF*

11.10 Ultrahigh-Resolution Resonant Inelastic Soft X-ray Scattering for Quantum Materials.
Di-Jing Huang, *NSRRC*

11.35 Statics and dynamics of Néel skyrmions in chiral magnetic multilayers
Christopher Marrows, *University of Leeds*

12.00 Discussion

12.30 - Lunch

Session 3 : Magnetic Imaging (Chair: Sarnjeet Dhesi)

13.30 Magnetoelectric imaging of multiferroic heterostructures
Massimo Ghidini, *University of Cambridge*

13.55 Domain walls in magnetic nanowires
Thomas Moore, *University of Leeds*

14:20 Imaging the electrical control of antiferromagnetic domains and domain walls in CuMnAs
Peter Wadley, *University of Nottingham*

Appendix 2

14.45 Imaging Vortex/Meron Pairs in a planar α -Fe₂O₃/Co Heterostructure
Noah-Waterfield Price, *University of Oxford*

15.05 Discussion

15.30 - Coffee

Session 4 : Magnetic Scattering (Chair: Paul Steadman)

16.00 Resonant X-Ray Dichroism Extinction Effect - Measurement of Chirality and Beyond
Shilei Zhang, *University of Oxford*

16.25 Magnetisation dynamics in nanostructures and devices
Stuart Cavill, *University of York*

16.50 Diamond-II for hard x-ray resonant and magnetic scattering
Steve Collins, *Diamond Light Source*

17.15 Discussion

17.45 - Close of workshop

Quantum Materials Attendees

Firstname	Lastname	Organisation	Job Role
Michael Lloyd	Baker	University of Manchester	Academic Staff
Riccardo	Bartolini	Diamond Light Source	Head of Accelerator Physics - Research Fellow
Peter	Bencok	Diamond Light Source	Senior Beamline Scientist I10
Alessandro	Bombardi	Diamond Light Source	Senior Beamline Scientist I16
Neil	Bourne	University of Manchester	
Nicholas	Brookes	ESRF	beamline Responsible
Stuart	Cavill	University of York	Academic Staff
Steve	Collins	Diamond Light Source	Scientific Training & Education Co-ordinator
Sarnjeet	Dhesi	Diamond Light Source	Diamond Staff
Kevin	Edmonds	University of Nottingham	Academic Staff
Raymond	Fan	Diamond Light Source	Senior Support Scientist I10
Thomas	Forrest	Diamond Light Source	Senior Support Scientist BLI06
Mirian	Garcia-Fernandez	Diamond Light Source	Senior Support Scientist BLI21
Massimo	Ghidini	University of Cambridge	Academic Staff
T P A	Hase	University of Warwick	Academic Staff
Thorsten	Hesjedal	University of Oxford	Academic Staff
Di-Jing	Huang	NSRRC	Academic Staff
Francesco	Maccherozzi	Diamond Light Source	Beamline Scientist I06
Tuhin	Maity	University of Cambridge	Marie-Curie Postdoctoral Fellow
Christopher	Marrows	University of Leeds	Academic Staff
Thomas	Moore	University of Leeds	Academic Staff
Saumya	Mukherjee	Diamond Light Source	Post Doctoral Research Associate
Gareth	Nisbet	Diamond Light Source	Beamline Scientist I16
Andrew	Princep	University of Oxford	Post Doctoral Researcher/PDRA (or equivalent)
Sonka	Reimers	University of Nottingham	Doctoral Research Student e.g. PhD
Cecilia	Sanchez Hanke	Diamond Light Source	Scientific Operations Coordinator
Paul	Seller	Science and Technology Facilities Council (STFC)	UK Research Council Staff
Paul	Steadman	Diamond Light Source	Principal Beamline Scientist I10
Gerrit	van der Laan	Diamond Light Source	Diamond Senior Fellow

Peter	Wadley	University of Nottingham	Post Doctoral Researcher/PDRA (or equivalent)
Andrew	Walters	Diamond Light Source	Beamline Scientist
Noah	Waterfield-Price	University of Oxford	Doctoral Research Student e.g. PhD
Shilei	Zhang	University of Oxford	Academic Staff
Kejin	Zhou	Diamond Light Source	Principal Beamline Scientist I21

Diamond-II Workshop: Imaging 18 - 19 Sept 2018

Day 1: Tuesday 18th September 2018

Overview of the Diamond-II science case in these areas and purpose of the day

10:30 - 10:40	Paul Quinn/Martin Walsh, Diamond	Welcome and Introduction
10:40 - 11:00	Riccardo Bartolini, Diamond	Diamond-II
11:00 - 11:30	Paul Quinn, Diamond	Current facilities and science case for physical sciences

Ptychography and Scanning probes at low emittance sources

11:30 - 12:00	Volker Rose, APS	Towards sub-10 nm Microscopy enabled through the Upgrade of the Advanced Photon Source
---------------	------------------	----------------------------------------------------------------------------------------

12:00 - 13:00 **LUNCH**

User Community Talks: Session 1

13:00 - 13:30	Stephen Price, Finden	Advances in multimodal tomography: Spatially and temporally resolved catalyst imaging
13:30 - 14:00	Marcus Newton, Southampton	Bragg Coherent Imaging of Structural Dynamics in Nanomaterials
14:00 - 14:30	Chris Jones, Bristol	Going to higher brightness - advantages for <i>in situ</i> analysis of nuclear materials at Diamond

14:30 - 15:00 **Open Discussion 1**

15:00 - 15:30 **COFFEE**

Full field and fast imaging - Engineering

15:30 - 16:00	Francesco De Carlo, APS	X-ray full-field imaging at the Advanced Photon Source: Opportunities with the APS Upgrade
---------------	-------------------------	--------------------------------------------------------------------------------------------

User Community Talks: Session 2

16:00 - 16:30	Peter Lee, UCL	Capturing ultra-fast phenomena during the processing of advanced materials.
16:30 - 17:00	Richard Abel, Imperial	Multi-modal imaging in bone (osteoporosis) and eye (glaucoma) disease research
17:00 - 17:30	Biao Cai, Birmingham	4D Imaging of Directional Solidification Under Magnetic Field

17:30 - 18:00 **Open Discussion 2**

18:30 - 20:30 **DINNER**

Day 2: Wednesday 19th September 2018

Life Science: Overview

09:15 - 09:30	Intro Paul Quinn/Martin Walsh	Current facilities and science case for life science
09:30 - 10:00	Colin Nave, Diamond	X-ray imaging for biology: An overview and the damage done
10:00 - 10:30	Ian Robinson, BNL	
10:30 - 11:00	Adrian Mancuso, XFEL	Biological Imaging at XFELs: Some observations, a way forward and where does Diamond-II fit in?
11:00 - 11:30	COFFEE	

Appendix 2

Coherence for biological and soft matter imaging

11:30 - 12:00	Sarah Shahmoradian, PSI	Cryo ptychographic X-ray computed tomography (cryo-PXCT) for biological applications: nanoscale 3D imaging with quantitative contrast
12:00 - 12:30	Sylvain Bohic, Inserm/ESRF	Hard X-ray fluorescence nanoimaging of metal ions in cells
12:30 - 13:00	Andrew Parnell, Sheffield	Using morphology to understand structural colour in nature
13:00 - 14:00	LUNCH	
14:00 - 14:30	James Everett, Keele	Probing metals in neurodegenerative diseases using X-ray spectromicroscopy

Bio-imaging II

14:30 - 15:00	Helen Saibil, Birkbeck	Correlative video microscopy, fluorescence, EM and soft X-ray tomography studies of biological machinery
15:00 - 15:30	Carolyn Larabell, LBNL	CT scans of biological cells at 35 nm resolution with soft X-ray tomography
15:30 - 16:30	Open Discussion 4 - New opportunities for multiscale imaging at Diamond-II & wrap up	

Imaging Attendees

Firstname	Lastname	Organisation	Job Role
Richard	Abel	Imperial College London	
Mark	Basham	Diamond Light Source	
Darren	Batey	Diamond Light Source	
Sylvain	Bohic	ESRF	
Sylvia	Britto	Diamond Light Source	Post Doctoral Research Associate I18
Biao	Cai	University of Manchester	Research Student
Enrico	Castroflorio	MRC Harwell	Post Doctoral Researcher/PDRA (or equivalent)
Silvia	Cipiccia	Diamond Light Source	
David	Collins	University of Birmingham	Academic Staff
Thomas	Connolley	Diamond Light Source	Principal Beamline Scientist (JEEP) I12
Leigh	Connor	Diamond Light Source	Senior Industrial Scientist Engineering & Diffraction
Silvia	corrochano	MRC	Senior Investigator Scientist
Fred	Currell	University of Manchester	Academic Staff
Maedeh	Darzi	Institute for Research in Fundamental Science	Masters Research Student
Francesco	Di Carlo	APS	
Ian	Dobbie	University of Oxford	
Katherine	Dobson	University of Manchester	Post Doc
Kate	Dobson	University of Durham	
Tiarnan	Doherty	University of Cambridge	Doctoral Research Student e.g. PhD
Liz	Duke	Diamond Light Source	
Maud	Dumoux	Diamond Light Source	Senior Support Scientist - Mammalian Cell Culture Research Associate
David	Eastwood	University of Manchester	
Gwyndaf	Evans	Diamond Light Source	
James	Everett	University of Keele	
Jonathan	Grimes	University of Oxford	Academic Staff
Dave	Hall	Diamond Light Source	Science Group Leader - MX
Maria	Harkiolaki	Diamond Light Source	Acting - Principal Beamline Scientist
Nicola	Harrington	Diamond Light Source	Scientific Liaison Officer

Diamond-II: Advancing Science

Rohanah	Hussain	Diamond Light Source	
Sally	Irvine	Diamond Light Source	
Christopher	Jones	University of Bristol	Post Doctoral Researcher/PDRA (or equivalent)
Burkhard	Kaulich	Diamond Light Source	Principal Beamline Scientist I08
Daniil	Kazantsev	Diamond Light Source	
Angus	Kirkland	University of Oxford	Academic Staff
Ewelina	Kosior	Diamond Light Source	Senior Support Scientist
Ilias	Kounatidis	Diamond Light Source	Post Doctoral Researcher/PDRA (or equivalent)
Carolyn	Larabell	University of California, San Francisco	Professor
Petrina	Lau	MRC Harwell	Postdoc. fellow
Laura	Leay	The University of Manchester	Nuclear Engineering Innovation Fellow
Peter	Lee	UCL	
Enzo	Liotti	University of Oxford	Post Doctoral Researcher/PDRA (or equivalent)
Joshua	Lobo	Diamond Light Source	
Nouf	Mahmoud	Al Zaytoonah University of Jordan	assistant professor
Adrian	Mancuso	European XFEL	Leading Scientist SPB/SFX Instrument
Christopher	Mitchell	University of Ulster at Coleraine	Academic Staff
Colin	Nave	Diamond Light Source	Life Sciences Consultant
Marcus	Newton	University of Southampton	Academic Staff
Julia	Parker	Diamond Light Source	Senior Beamline Scientist I14
Andy	Parnell	University of Sheffield	Academic Staff
Aaron	Parsons	Diamond Light Source	
Caroline	Peacock	University of Leeds	Academic Staff
Stephen	Price	Finden	
Christoph	Rau	Diamond Light Source	Principal Beamline Scientist I13
Sion	Richards	Rutherford Appleton Laboratory	Doctoral Research Student e.g. PhD
Ian	Robinson	UCL	
Volker	Rose	APS	
Helen	Saibil	Birkbeck, University of London	Academic Staff
Cecilia	Sanchez Hanke	Diamond Light Source	Scientific Operations Coordinator
Sarah	Shahmoradian	Paul Scherrer Institute	Principal Investigator
Xiaowen	Shi	Diamond Light Source	
Elizabeth	Shotton	Diamond Light Source	Head of Industrial Liaison
Giuliano	Siligardi	Diamond Light Source	
Matthew	Spink	Diamond Light Source	
Samuel	Stranks	University of Cambridge	Academic Staff
Amber	Vater	STFC	Programme Manager
Dirk	Visser	Loughborough University	Academic Staff
Nghia	Vo	Diamond Light Source	
Nicola	Wadeson	Diamond Light Source	
Matthew	Wilson	Rutherford Appleton Laboratory	UK Research Council Staff
Jenny	Woods	University of Manchester	Academic Staff
Zhengyi	Yang	Diamond Light Source	
Morfo	Zembyla	University of Leeds	PhD

Diamond-II Workshop: Spectroscopy 18 - 19 Sept 2018

Tuesday 18th September

- 13:00 - 13:10 Laurent Chapon
Welcome
- 13:10 - 13:30 Riccardo Bartolini
Machine upgrade
- 13:30 - 14:00 Sofia Diaz-Moreno
Diamond-II: Opportunities for Spectroscopy
- Session I - Bioscience (Session Chair: Konstantin Ignatyev)**
- 14:00 - 14:25 Paul Walton, The University of York
Multi-spectroscopic characterisation of Cu active sites in oxygenase enzymes
- 14:25 - 14:50 Joanna Collingwood, The University of Warwick
Understanding the metallomics of neurodegeneration through spectro-microscopy
- 14:50 - 15:15 David Leys, The University of Manchester
Unravelling enzyme mechanism guides biotechnological application
- 15:15 - 15:45 Coffee
- 15:45 - 16:15 Discussion
Discussion Leader: Allen Orville

Session II - Energy Materials and Systems (Session Chair: Giannantonio Cibin)

- 16:15 - 16:40 Stephen Skinner, Imperial College London
Probing solid oxide electrode interfaces – towards in-operando understanding of cell lifetime
- 16:40 - 17:00 Andrea Russell, University of Southampton
X-ray Emission Spectroscopy studies of electrocatalysts
- 17:00 - 18:00 Discussion
Discussion leader: Alan Chadwick
- 18:30 - 20:30 Dinner

Wednesday 19th September

Session III - Chemistry and Materials Discovery (Session Chair: Sofia Diaz-Moreno)

- 09:00 - 09:25 Chris Hardacre, The University of Manchester
Current state of the art X-ray spectroscopy and new challenges
- 09:25 - 09:50 James Anderson, University of Aberdeen
Advances and opportunities for real time monitoring of catalysts and surfaces
- 09:50 - 10:15 Andy Beale, UCL
Real-time operando studies of supported catalysts
- 10:15 - 10:45 Coffee break
- 10:45 - 11:10 Matthias Bauer, Universitat Paderborn
X-ray emission and high energy resolution absorption spectroscopy: New developments in inorganic chemistry and catalysis
- 11:10 - 11:35 Sven Schroeder, University of Leeds
Perspectives for Core-Level Spectroscopy: Beyond Absorption Measurements
- 11:35 - 12:15 Discussion
Discussion leader: John Evans
- 12:15 - 13:15 Lunch

Session IV Earth and Environment (Session Chair: Fred Mosselmans)

- 13:15 - 13:40 Sam Shaw, The University of Manchester
Further directions for X-ray spectroscopy in Earth and Environmental Science
- 13:40 - 14:05 Neil Hyatt, University of Sheffield
Underpinning UK radioactive waste management with X-ray spectroscopy
- 14:05 - 14:35 Discussion
Discussion leader: Bhoopesh Mishra
- 14:35 - 15:00 Coffee Break
- 15:00 - 15:30 Summary and wrap up

Spectroscopy Attendees

Firstname	Lastname	Organisation	Job Role
Monica	Amboage	Diamond Light Source	Senior Beamline Scientist BLI20
James	Anderson	University of Aberdeen	Academic Staff
Tohru	Araki	Diamond Light Source	Senior Beamline Scientist I08
Alun	Ashton	Diamond Light Source	Group Leader - Data Analysis Software
Andrew	Barrow	rolls-royce	Technical Specialist - Materials
Matthias	Bauer	University of Paderborn	Research Fellow
Andy	Beale	University College London (UCL)	Academic Staff
Thomas	Bennett	University of Cambridge	Research Fellow
Anna	Bogush	University College London (UCL)	Post Doctoral Researcher/PDRA (or equivalent)
Samuel	Booth	University of Glasgow	Post Doctoral Researcher/PDRA (or equivalent)
Marcello	Borri	STFC	
Neil	Bourne	University of Manchester	Academic Staff
Daniel	Bowron	Science and Technology Facilities Council (STFC)	UK Research Council Staff
Sylvia	Britto	Diamond Light Source	Post Doctoral Research Associate I18
Alan	Chadwick	University of Kent	Academic Staff
Jennifer	Channell	EPSRC-UKRI	Portfolio Manager
Giannantonio	Cibin	Diamond Light Source	Principal Beamline Scientist BLB18
Paul	Collier	Johnson Matthey	Industry/Business Person
Jo	Collingwood	University of Warwick	Academic Staff
Andy	Dent	Diamond Light Source	Deputy Director - Physical Sciences
Maria	Diaz-Lopez	Science and Technology Facilities Council (STFC)	Post Doctoral Researcher/PDRA (or equivalent)
Sofia	Diaz-Moreno	Diamond Light Source	Science Group Leader - Spectroscopy Group
Baran	Eren	Weizmann Institute of Science	Academic Staff
R J	Errington	Newcastle University	Academic Staff
John	Evans	Diamond Light Source	Consultant
Tina	Geraki	Diamond Light Source	Beamline Scientist I18
Diego	Gianolio	Diamond Light Source	Beamline Scientist B18
Sergio	Gonzalez-Cortes	University of Oxford	Post Doctoral Researcher/PDRA (or equivalent)
Shaoliang	Guan	Cardiff University	Post Doctoral Researcher/PDRA (or equivalent)
Christopher	Hardacre	University of Manchester	Academic Staff
Shusaku	Hayama	Diamond Light Source	Senior Beamline Scientist BLI20
Ian	Horswell	Diamond Light Source	Senior Electronics Engineer
Karen	Hudson-Edwards	University of Exeter	Academic Staff
Neil	Hyatt	University of Sheffield	Government funded Staff
Tim	Hyde	Johnson Matthey	
Konstantin	Ignatyev	Diamond Light Source	Principal Beamline Scientist I18
Anna	Kroner	Diamond Light Source	Senior Industrial Liaison Scientist - X-Ray Spectroscopy
David	Leys	Manchester Institute of Biotechnology	Academic Staff
Enzo	Liotti	University of Oxford	Post Doctoral Researcher/PDRA (or equivalent)
Alastair	Lough	University of Southampton	Doctoral Research Student e.g. PhD

Appendix 2

Kevin	Lovelock	University of Reading	Academic Staff
Grazia	Malta	Cardiff Catalysis Institute	Doctoral Research Student e.g. PhD
Bhoopesh	Mishra	University of Leeds	Academic Staff
Oliver	Moore	University of Leeds	Post Doctoral Researcher/PDRA (or equivalent)
Fred	Mosselmans	Diamond Light Source	Principal Beamline Scientist I20
Saumya	Mukherjee	Diamond Light Source	Post Doctoral Research Associate
Allen	Orville	Diamond Light Source	Principal Scientist XFEL Hub
Christopher	Parlett	ASTON UNIVERSITY	Post Doctoral Researcher/PDRA (or equivalent)
Caroline	Peacock	University of Leeds	Academic Staff
Anna	Peacock	University of Birmingham	Academic Staff
Silvia	Ramos	University of Kent	Academic Staff
Andrea E	Russell	University of Southampton	Academic Staff
Cecilia	Sanchez Hanke	Diamond Light Source	Scientific Operations Coordinator
Gopinathan	Sankar	University College London (UCL)	Academic Staff
Andrei	Sapelkin	Queen Mary, University of London	Academic Staff
Paul	Schofield	Natural History Museum	Academic Staff
Sven	Schroeder	University of Leeds	Academic Staff
Stewart	Scott	Diamond Light Source	Head of Beamline Systems Engineering
Sam	Shaw	University of Manchester	Academic Staff
Stephen	Skinner	Imperial College London	Academic Staff
Małgorzata	Swadzba-Kwasny	Queen's University of Belfast	Academic Staff
Moniek	Tromp	University of Groningen	Academic Staff
Amber	Vater	STFC	Programme Manager
Matt	Veale	Science and Technology Facilities Council (STFC)	UK Research Council Staff
Kylie	Vincent	University of Oxford	Academic Staff
Paul	Walton	University of York	Academic Staff
Robert	Weatherup	University of Manchester	Academic Staff
Peter	Wells	University of Southampton	Academic Staff
Matthew	Wilson	Rutherford Appleton Laboratory	UK Research Council Staff
Pu	Zhao	University of Oxford	Post Doctoral Researcher/PDRA (or equivalent)

Acknowledgements

The science case was written by the following Diamond staff:

Isabelle Boscaro-Clarke	Gwyndaf Evans	Rob Rambo
Laurent Chapon	Dave Hall	Dave Stuart
Andy Dent	Andrew Harrison	Martin Walsh
Sarnjeet Dhesi	Chris Nicklin	Heribert Wilhelm
Sofia Diaz-Moreno	Paul Quinn	

Produced by: Isabelle Boscaro-Clarke, François Cesmat, Sarah Tridgell

With external contributions in the following areas from:

Integrated structural biology

Jonathan Grimes	University of Oxford
Susan Lea	University of Oxford
Jim Naismith	Research Complex at Harwell & Rosalind Franklin Institute
Ray Owens	Research Complex at Harwell

Biotechnology & biological systems

Richard Abel	Imperial College London
Nick Brooks	Imperial College London
Geoff Moggridge	University of Cambridge
Andrew Parnell	University of Sheffield

Health & well-being

Sylvain Bohic	ESRF
Dave Brown	University of Kent, Charles Rivers Ltd & CCP4
Gillian Burgess	Vertex Pharmaceuticals
Joanna Collingwood	University of Warwick
Peter Sadler	University of Warwick
Tara Schiller	University of Warwick
Neil Telling	Keele University

Energy

Alan Chadwick	University of Kent
Matthew Fuchter	Imperial College London
Georg Mehl	University of Hull
Silvia Ramos	University of Kent
Andrea Russell	University of Southampton

Acknowledgements

Paul Shearing	University College London
Stephen Skinner	Imperial College London
Sam Stranks	University of Cambridge
Goran Ungar	University of Sheffield

Quantum materials

Felix Baumberger	University of Geneva
Kevin Edmonds	University of Nottingham
Massimo Ghidini	University of Cambridge
Peter Hatton	Durham University
Stephen Hayden	University of Bristol
Philip King	University of St Andrews
Danny Mannix	ESS Lund
Chris Marrows	University of Leeds
Des McMorrow	University College London
Paolo Radaelli	University of Oxford
Pete Wadley	University of Nottingham

Chemistry

Andrew Beale	University College London
Thomas Bennett	University of Cambridge
Daniel Bowron	ISIS Neutron and Muon Source
Richard Catlow	University College London
Christopher Hardacre	University of Manchester
Graham Hutchings	Cardiff University
David Keen	ISIS Neutron and Muon Source
Tim Lodge	University of Minnesota
Stephen Price	Finden Ltd
Robert Raja	University of Southampton
Martin Schroeder	University of Manchester
Paul Walton	University of York
Chick Wilson	University of Bath
Sihai Yang	University of Manchester

Engineering materials & processing

Biao Cai	University of Birmingham
David Collins	University of Birmingham
Fred Currell	University of Manchester
Peter Dowding	Infineum
Jonathan Hyde	National Nuclear Laboratory
Laura Leay	University of Manchester
Peter Lee	University College London
Mary Ryan	Imperial College London

Earth, environment & planetary science

Kate Dobson	Durham University
Joe Hriljac	University of Birmingham
Neil Hyatt	University of Sheffield
Malcolm McMahon	University of Edinburgh
Peter Norreys	University of Oxford
Caroline Peacock	University of Leeds
Sam Shaw	University of Manchester

And with internal scientific contributions from:

Lucia Alianelli	Michael Drakopoulos	Robin Owen
Dave Allan	Ralf Flaig	Christoph Rau
Christine Beavers	Tina Geraki	Kawal Sawhney
Cephise Cacho	Maria Harkiolaki	Giuliano Siligardi
Francesco Carla	Shu Hayama	Paul Steadman
Phil Chater	Georg Held	Chiu Tang
Giannantonio Cibir	Konstantin Ignatyev	Nick Terrill
Gianfelice Cinque	Burkhard Kaulich	Frank von Delft
Steve Collins	Tien-Lin Lee	Armin Wagner
Thomas Connolley	Katherine McAuley	Hongchang Wang
Leigh Connor	Fred Mosselmans	Kejin Zhou
Nathan Cowieson	Allen Orville	

With thanks to all the Diamond staff that helped in the preparation of this document.





Diamond Light Source Ltd
Harwell Science & Innovation Campus
Didcot, Oxfordshire OX11 0DE
Tel: +44 (0)1235 778 639
Fax: +44 (0)1235 778 499
www.diamond.ac.uk

