SCIENCE CASE FOR
A NEW LIGHT SOURCE (NLS)

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EXECUTIVE SUMMARY

Seeing inside matter, to capture the nanoscopic motions that determine macroscopic properties and function, is the revolutionary goal that will be made possible by NLS. The light source capabilities available from NLS will enable new scientific frontiers to be explored. These include:

- **IMAGING NANOSCALE STRUCTURES.**
  Instantaneous images of nanoscale objects can be recorded at any desired instant allowing, for example, nanometer scale resolution of sub-cellular structures in living systems.

- **CAPTURING FLUCTUATING AND RAPIDLY EVOLVING SYSTEMS.**
  Rapid intrinsic evolution and fluctuations in the positions of the constituents within matter can be characterized.

- **STRUCTURAL DYNAMICS UNDERLYING PHYSICAL AND CHEMICAL CHANGES.**
  The structural dynamics governing physical, chemical and biochemical processes can be followed by using laser pump- X-ray probe techniques.

- **ULTRA-FAST DYNAMICS IN MULTI-ELECTRON SYSTEMS.**
  New approaches to measuring the multi-electron quantum dynamics, that are present in all complex matter, will become possible.

These are unique areas of research that are in significant measure distinct from those enabled by other international facilities (e.g. LCLS, XFEL) where programmes such as single molecule atomic scale imaging, time-resolved crystallography and the effects of shocks upon a lattice are better studied. The emphasis for NLS will be in enabling ultra-fast measurement that requires an array of synchronised light sources spanning a very wide spectral range from THz to soft X-ray.

The drivers behind this programme are basic science that will emerge from the new capability. There is an excellent coupling to the basic science and technology needed to address key societal challenges such as Energy, Healthcare and Nanotechnology.

To enable these scientific advances the NLS Facility will require:

Photon energies tuneable over the range from THz/IR through to soft X-rays (to ~ 1.5 keV in the fundamental /7.5 keV in harmonics)

Two-colours (i.e. UV/Vis or IR/THz synchronised with soft X-ray pulses)

Ultra-fast pulses with duration down to sub-femtosecond range

High temporal and transverse coherence

This combination of light source requirements forms the science-led demand for a novel facility capability. These appear to be achievable parameters through a combination of linac based FELs and advanced conventional laser technology. A technical design study is now needed to allow this science case to be coupled to a facility solution.

In this document we will present a justification of the case for the groundbreaking new science enabled by NLS and a summary of capabilities required for this science that define a unique, and realisable, UK New Light Source Facility. A number of example research areas, that couple to current UK interests and strengths, and so could be tackled in the early years of the facility are highlighted to illustrate the kind of new opportunities enabled by NLS.

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1. OVERVIEW OF CASE

1.1 INTRODUCTION

Across a broad range of disciplines, the scientific community is currently frustrated by its inability to observe directly the ultrafast dynamics of matter on the nanoscale. We can at present only observe relatively slow motion changes to structure, or infer dynamical effects via indirect measurements. In short, we are presently blind to structural changes occurring on the sub-picosecond timescale (we can infer but not see). Yet many critically important processes evolve on the femtosecond timescale and at the molecular and sub-cellular level, requiring nanometre scale resolution. In this document we will discuss the scientific case for a new light source facility that would permit us to see ultra-fast dynamics on the nanoscale. The key tools to enable this breakthrough are advanced conventional lasers and free electron lasers (FELs).

The properties of the light from the next generation of photon sources, i.e. free electron lasers, are dramatically different from those of storage rings and conventional lasers. Storage ring synchrotron radiation has enormous spectral coverage and can deliver a high photon fluence (photons per second) up to hard X-rays (10's keV). This has allowed these sources to be the dominant tool for crystallography, X-ray spectroscopy and many other areas of X-ray science for the last four decades. Nevertheless these sources have low peak brightness, especially if a narrow spectral bandwidth or a short pulse is selected. With advanced pulse slicing, these sources can provide sub-picosecond temporal resolution but only with tiny flux which severely limits the utility for measuring rapid changes. Conventional lasers have advanced hugely in recent years and can produce extremely short pulses (~5 fs) at very high brightness but these capabilities are limited to UV/visible/near IR range.

Free electron lasers have the potential to deliver across an exceptional spectral range (<10 meV to multiple-keV) narrow bandwidth (~0.1% of photon energy) radiation with very energetic (millijoule) short pulses (~50 fs duration), and therefore exceptionally bright (10^{12} photons per 50 fs pulse) fully coherent radiation. A FEL undulator produces a very bright pulse at the fundamental frequency, but also bright pulses at three and five times that frequency (the harmonics) with photon number dropping by a factor ~100 at each frequency step. This is a vastly larger spectral range than covered by conventional lasers and the pulses are typically a thousand times shorter and millions of times brighter than a storage ring can provide. FELs are likely to have a revolutionary impact on the science we do with light, potentially as profound as the revolution created by the laser and the synchrotron.

We concentrate here on identifying and developing those scientific objectives for which a new UK facility with unique capabilities would be the optimal tool. This does not mean that some of these objectives are not possible, at least in part, using other international facilities (e.g. LCLS or XFEL). It would be unnecessarily limiting in planning a new UK light source facility to consider solely that science that could not be done elsewhere. Nevertheless we believe a facility with correctly chosen capability can be developed that can undertake an exceptionally exciting programme ranging across the sciences that contains a major component of objectives that are unique or simply better done there than anywhere else.

The science that is made possible by the availability of ultra-short, high brightness, pulses in the THz to soft X-ray range is summarised in figure 1. The processes of interest, i.e. valence/core electron dynamics, chemical dynamics, dynamics in condensed matter systems, and dense plasmas, are plotted in terms of the time and spatial resolution scales of the measurements required to capture them. Included also are the timescales in which high resolution "snapshots" must be recorded in order to ensure distortion free images from coherent diffraction imaging of nanoscale objects. The message is that to measure all of these fundamental processes, many for the first time, pulses as short as 10 fs or less are needed. The high spatial resolution is only possible if short wavelengths are used, in most cases utilising soft X-ray excitation near atomic absorption edges (in the 200 eV – 7 keV range) to

capture local spatial relationships, but in some cases direct scattering (diffraction) signals can be used to obtain the spatial resolution.

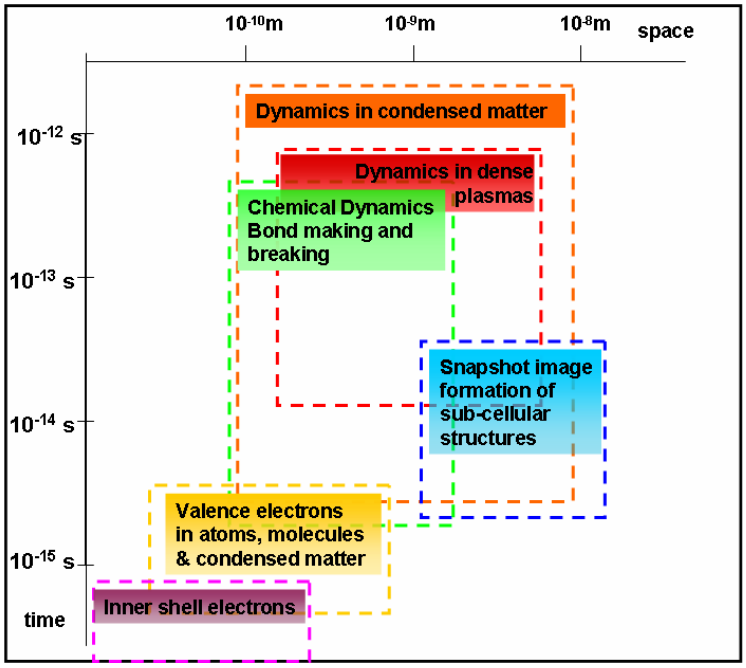

Figure1. The new science areas that will be enabled by an ultra-fast, high brightness, soft X-ray to THz light source

We put forward the following major themes for the scientific impacts of NLS which we will then develop in more detail in the next sections. They collectively encompass a new capability for seeing and controlling the nanoscale motions of the constituents of matter. We believe that the science and technology that will emerge from this capability will be revolutionary.

1.2 A. IMAGING NANOSCALE STRUCTURES

The high coherence and brightness of the FEL in the soft X-ray range will enable the exploitation of new imaging methodologies: e.g., coherent diffraction imaging and X-ray holography. The short wavelength limit of the FEL fundamental is anticipated to be below 1 nm so covering the "water window" (~4.36 – 2.38 nm) , which is the wavelength range used to achieve penetration and contrast in "live" biological samples. Radiation damage by such high fluxes will be a serious consideration with living systems and flash imaging, cryo-preservation and other approaches are being considered. Recent work at FLASH has shown that images can be captured before the deleterious events of damage occur provided the pulse is short enough and bright enough but only one shot is possible. Flash imaging has the potential for a new level of understanding of sub-cellular and macromolecule organisation within cells, and should complement information gained by optical and electron microscopy. Moreover for non-biological objects, because the fundamental is bright enough to capture a full image in a single shot of <100 fs duration, the motion within nanoscale objects might be followed stroboscopically using a sequence of mutually delayed pulses split from a common pulse or in a repetitive measurement following a sequence of identically prepared samples with increasing delay after the preparation step. The proposed NLS wavelength range also covers the most important edges for the study of complex condensed matter systems, i.e. the transition metal *L* edges, which access the physics of 3d valence electrons, and oxygen *K* edge for the physics of 2p shells. The New Light Source would be ideally used to image complex electronic, magnetic and orbital structures, both statically and dynamically, down to 1 nm resolution. A key application will be to make stopwatch images of fluctuating magnetic, orbitally-ordered and electronic domains, polaronic states and even single Cooper pairs. Secondly, evolving structures around individual charge or spin carriers in functioning devices could be studied on an ultra-fast timescale.

This theme is anticipated to have high impact in the following areas **life sciences, medicine, nano-technology.**

It requires a machine optimised for a fundamental in the soft X rays, including the water window. The use of higher harmonics into the near 5 keV region would allow imaging of the distribution of specific atoms at the nanoscale. Equal pulse spacing at a moderate repetition rate (>100 Hz) is suitable for getting the best from sample handling and detector technology. A machine with these capabilities is optimal for this scientific application.

1.2 B. CAPTURING FLUCTUATING AND RAPIDLY EVOLVING SYSTEMS

Many material systems have intrinsically fast fluctuations of their nanoscopic structure. For example in liquids, glasses, magnetic materials at moments around a phase change all show rapid fluctuations in structure and changes in the correlation between neighbouring particles. It is known that these can be followed over longer timescales using X-ray speckle and time-resolved X-ray speckle techniques. A FEL with a short wavelength reach from 1-7 keV (including harmonics) and ultra-fast bright pulses will allow such changes to be tracked at unprecedented timescales potentially leading to breakthroughs of our understanding of condensed matter, in bulk or in nanoscale systems. Likewise use of X-ray Thompson scattering is the ideal method to explore the properties of dense plasmas as they approach the strongly coupled condition which is of enormous importance to our understanding of warm dense matter that occurs in many situations (e.g. giant planet interiors, solid systems evolving rapidly into the plasma state, laser fusion plasmas).

This theme is anticipated to have high impact in the following areas **nanotechnology, ultra-fast solid state and magnetic devices, energy from fusion.**

A wide spectral range and high transverse coherence are essential source requirements. A set of many repeated measurements is often required to obtain good S/N so optimised pulse stability must be sought. High spectral resolution for Thomson scattering to measure the ion acoustic feature is required.

1.2 C. STRUCTURAL DYNAMICS UNDERLYING PHYSICAL AND CHEMICAL CHANGES

Understanding the mechanism of physical, chemical and biological change at the microscopic scale is critical for a broad range of science and technology. A common goal is to develop this understanding to the point where it becomes possible to tailor functionality through material design, or by the application of electric, magnetic or optical fields. Chemical and physical changes involve the coupled flow of both charge and energy within the system due to electronic and nuclear motions. These processes may be triggered by e.g. the thermal fluctuations in the surrounding environment or by the absorption of light by a chromophore. Such processes, and the various processes which precede or compete with them, typically occur on the timescale of nuclear motion which is in the femtosecond regime. We anticipate a step function in our ability to *directly* monitor structural dynamics at the molecular level through the availability of femtosecond light pulses with X-ray wavelengths. The NLS will greatly extend the range of techniques we can use to both initiate and probe these processes. By use of visible/UV or IR/THz light of short pulse duration we can trigger these events ourselves (a sort of ultra-fast “Bunsen burner”). Having triggered these events we can then follow them structurally using e.g. X-ray absorption techniques (XAS) or spectroscopically in the IR/visible. A combination of a tuneable soft-X-ray FEL synchronised to a IR/THz FEL or a UV/Vis ultra-fast laser will enable the structural changes to be followed in a vast range of physical and chemical processes. This will revolutionize our understanding of mechanisms in, for example, solution phase chemistry in enzyme and surface catalysis and DNA photo-induced radiation damage. A variant of this method that would use a moderate energy electron beam to initiate “change” in non-photosensitive molecular samples and materials (radiolysis) can be readily combined with the soft X-ray probe capability,

Moreover the moderate energy electrons may prove of great utility of a structural probe of laser or FEL induced changes in a new regime of relativistic electron diffraction.

> It is expected that this theme will have a revolutionary impact upon **materials technology, biochemistry, drug discovery, cancer/health, catalysis, sustainable use of resources.**

A source providing tuneable high brightness soft X-ray to allow XAS across *K* and *L* edges of a majority of elements is essential as XAS is the primary tool for capturing the structural information. An adequate rep-rate is important to enable all measurements with good S/N and is essential to permit PES free from space-charge distortions. High spectral resolution is also very important in PES. To achieve the best temporal resolution in pump-probe measurements a minimum jitter between lasers/electron beams and the FEL is needed.

1.2 D. ULTRA-FAST DYNAMICS IN MULTI-ELECTRON SYSTEMS

Recent work using existing laser based HHG (high harmonic generation) methods has established the possibility to probe directly the ultra-fast electron dynamics in atoms and small molecules. Extension to more complex systems requires the wider spectrum of photon energies and far higher fluxes available from a FEL source. Examples of the capabilities that are only now becoming possible are the measurement of hole dynamics in molecules and condensed matter (expected to happen in 10^{-15} to 10^{-17} s), direct measurements of electron dynamics and damping in plasmons (of increasing interest to frontier technological applications of nanoplasmonics), and observing the photoelectric effect from multi-electron states in real time. There is the new potential for measuring ultra-fast electron dynamics through the non-linear response which is only possible if high brightness sub-fs pulses are available. Understanding ultra-fast electron dynamics lie at the heart of material response to electromagnetic fields and so the outcomes may lead to a better understanding of the interaction of large molecules with light and to new generations of optical and electro-optical devices and ultrafast semiconductor and nanofabricated components.

> This will have a high impact on areas such as **nanotechnology, quantum control, advanced materials, light harvesting.**

The research needs appropriate ultra-fast conventional lasers and pulse slicing for high brightness sub-fs pulses for X-ray pump- X-ray probe; phase-locking to an external IR laser for correlated electron studies is also required.

1.3 MAPPING TO SOCIETAL DEMANDS

There is a strong recognition that science and technology must rise to a number of pressing current societal challenges related, for example, to environmental sustainability, energy supply, healthcare and advanced information technology. NLS, although driven by the needs of the new basic science outlined above, is well suited to make major contributions to all these challenges by providing fundamental understanding of matter and processes that will lead directly to radical improvements through design and verification of, for example, better materials, molecules and catalysts.

This connection between new basic science and the sustainable energy agenda was eloquently expressed in the 2007 Basic Energy Sciences Report for the Department of Energy in the USA which was prepared by a team of eminent scientists. They captured the contribution that science must make to the long term Energy agenda in terms of five grand challenges:

> ***How do we control material processes at the level of electrons?***
> ***How do we design and perfect atom- and energy-efficient synthesis of revolutionary new forms of matter with tailored properties?***
> ***How do remarkable properties of matter emerge from complex correlations of the atomic or electronic constituents and how can we control these properties?***

How can we master energy and information on the nanoscale to create new technologies with capabilities rivalling those of living things?
How do we characterize and control matter away— especially very far away —from equilibrium?

The new science enabled by NLS maps excellently to these challenges.

Likewise the high brightness soft X-ray and THz radiation will enable potentially revolutionary new imaging methodologies that will permit e.g. living cells to be imaged at close to the nm resolution limit, and human tissue to be imaged that yields new medical detail. This will potentially have a major impact upon medical research and healthcare.

1.4. FACILITY CAPABILITIES

1.4.1 Relationship to other facilities

It is fully part of the UK strategy to use the other existing machines (a number of longer wavelength FELS such as FELIX and the FLASH VUV FEL), several hard X-ray FELS in construction (e.g. LCLS, Stanford operational summer 2009; SCSS, Spring 8 operational 2011; and XFEL, Hamburg operational 2014) and a number of other projects in the planning stage. The UK has strong links to FELIX, FLASH, XFEL and LCLS and these facilities can satisfy a significant range of national scientific objectives in this area. In particular LCLS and XFEL provide high brightness hard X-rays that may enable the exciting possibility of single molecule atomic scale diffractive imaging that will reveal the detailed structure of macromolecules not amenable to crystallization. LCLS will be the earliest machine to come on line, as it is exploiting an already existing LINAC, and it is in this context that as part of an overall strategy STFC has committed funds for a partnership with LCLS which is intended to enable UK users to gain access as early as 2009. On a longer timescale, XFEL (which will use superconducting accelerator technology), will provide access to far higher repetition rate hard X-rays and STFC is also committed to supporting this project, with UK in-kind contributions already at an advanced planning stage. STFC's Photon Science Research Institute (PSRI) has been formed to promote activity with these international partners and to nurture the UK community in this field. Exciting as hard X-ray science is, there are many other compelling scientific directions available for which a soft X-ray optimised facility is ideal. It is our position that this is the scientific area where NLS should concentrate and this will allow many original scientific opportunities. If that soft X-ray facility has a two-colour capability for pump-probe studies, possibilities of high temporal coherence and very short pulses, then the machine will be unique and optimal for tackling a wide range of new science which we discuss in detail below. Whilst FLASH (and the planned FLASH II) are also likely to develop two-colour and seeding capabilities the wavelength range of that facility will remain more limited than NLS.

1.4.2 Unique capabilities for NLS

We concentrate on identifying and developing those scientific objectives for which a new facility, with unique capabilities going beyond the existing array of international facilities, would be able to tackle. In particular two colour capability with IR/THz and visible sources tightly synchronised to a soft X-ray tuneable FEL (reaching up to >7 keV at the 5th harmonic) will be a powerful combination not well matched by any existing source. The spectral coverage of this tuneable X-ray source will access all the *K* edges of the elements up to iron plus the *L* edges of the majority of atoms, this will permit dynamic structure determination for a vast range of solids, liquids and molecules inaccessible otherwise. Moreover femtosecond time-resolved X-ray diffraction for atom scale determination will be permitted at the highest photon energies still at a flux (~ 10^{10} photon/s) much higher than storage ring pulse slicing.

A further combination of capabilities that are exceptionally important to achieve a unique programme includes seeding (with HHG) and pulse slicing. Both require synchronised external lasers and with

present technology this puts constraints on the time structure of the machine. LCLS will have a 120 Hz repetition rate and this readily permits seeding and slicing to be implemented, a higher repetition rate is a significant advantage in a significant range of experiments. XFEL will have a 10 Hz repetition rate of macro-pulses each containing up to 3000 pulses at a temporal separation of 200 ns. This makes it very hard to seed or slice the machine at the full repetition rate. In contrast a machine with even pulse spacing and a moderately high repetition rate (~100 Hz to 10 kHz) will be optimally suited to seeding and slicing and so will be ideal for application where temporal coherence, tight synchronisation to external lasers and sub-fs pulses are essential.

We summarise in figure 2 the photon energy and pulse duration capabilities required for NLS (red quadrilateral) in order to deliver the desired science. It can be seen that to deliver this science NLS would need to access a wider range of this parameter space than, for example, the current FLASH facility or the planned XFEL. First it must be noted that NLS should encompass an exceptionally wide spectral range. This would be achieved by using the FEL fundamental and harmonic radiation (region with diagonal stripes) from undulators to reach to > 7keV. IR/THz undulators would ensure the low photon energy range, whilst the deep ultra-violet (UV) to mid-infrared (IR) would be covered by ultra-fast lasers. Second it must be understood that the highest scientific impact is made possible by availability of near transform limited pulses (where energy and time spread are close to the uncertainty limit) that can be created by using techniques of pulse-slicing and seeding. Extreme ultra-fast measurements will require pulses down to 1 fs (or shorter pulses). There are also a broad class of measurements, which are currently not possible because sources with high spectral brightness don't exist, where high energy resolution and somewhat lower temporal resolution are required it is anticipated that a combination of seeding alone or seeding and spectral selection can generate transform limited pulses of 100 fs – 1 ps.

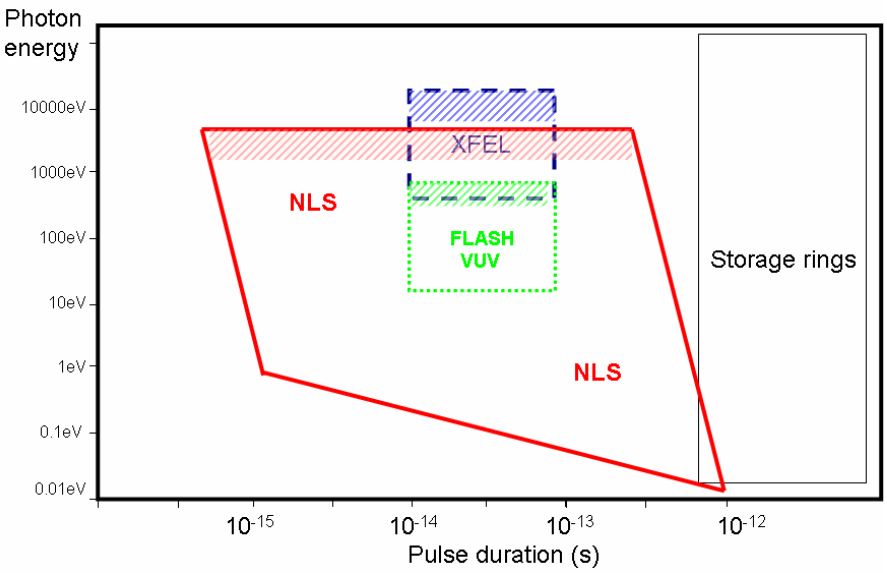

Figure 2. The coverage required from NLS to deliver the science in this case is shown (red quadrilateral) in terms of the pulse duration and photon energy (region covered by FEL harmonics shown with diagonal stripes), this coverage will enable the science illustrated in figure 1. The current coverage of storage rings (with pulse slicing), FLASH and the planned performance for XFEL are also shown.

2 KEY SCIENCE DRIVERS

The choice of the four themes for the science drivers around which the case is organised is an effective way to explain the uniqueness of the science. The themes form an interlinked, and overlapping, set which conveniently encompasses almost all of the important new science accessible to NLS.

Imaging of nanoscale structure with X-rays, whilst not an entirely new direction, will benefit hugely from the high coherence, brightness, repetition rate and short pulses of free electron lasers. Whilst hard X-ray single molecule imaging awaits the hard X-ray FEL machines for proof of principle experiments, there are already some very positive results supporting the concept of intense soft X-rays applied to imaging nanoscale objects. Nature is full of systems with a structure that rapidly evolves and/ or fluctuates, e.g. condensed matter systems close to a phase change, liquids and dense plasmas. Hitherto it has not been possible to capture these over all the important timescales. A new light source will provide a profound insight into this aspect of matter. Directed change, e.g. chemical reactions or triggered phase changes, which involve dynamical structural changes over all possible timescales are another area of great importance. A unique capability of two or more synchronized and tuneable colours across the entire THz to soft X-ray range will enable the structural dynamics to be fully elucidated for the first time in a multitude of physical, chemical and biochemical systems. Finally electron dynamics require soft X-ray pulses of sub-femtosecond timescale and so up to now have only been directly measured in a tiny set of systems. A combination of FEL and laser based sources will extend our understanding of the fundamentals of the electron dynamics across the whole range of complex matter.

2.1 IMAGING NANOSCALE STRUCTURES

'Imaging is fundamental in all biological and biomedical research and the essence of cell biology' [1]'. X-ray crystallography can give us the atomic structures of macromolecules. Electron microscopy has been a most important tool for imaging at the sub-cellular level and at the molecular level but demands thin specimens (< 0.5 μm thick). In optical microscopy, tracking the location and interactions of proteins inside cells using genetically encodable fluorescent proteins has been enormously successful but does not image the shapes of the macromolecular complexes, but pinpoints the source of fluorescence. Soft X-ray microscopy methods using Fresnel zone plate lenses as objectives are now delivering images to ~20 nm resolution. Such methods are starting to be applied to monitor dynamic events in cells. Because of the importance of visualisation in biology, new imaging methods raise great interest. The possibility of using X-ray imaging to achieve resolutions of the order of 1-2 nm raises exciting possibilities when combined with other imaging technologies. In order to achieve a resolution approaching 1 nm, at which natural and fabricated nano-objects and cells and sub-cellular structures can be resolved, short wavelengths (soft X-ray light) are needed. For biological specimens it is advantageous to work within the "water window" (4.36 to 2.28 nm) between the absorption edges of carbon (284 eV) and oxygen (543 eV) to get both high penetration through the aqueous matter and contrast against water for organic compounds of biological interest. A high brightness, short pulsed, soft X-ray source can make a significant impact in imaging of biological and non-biological objects. Furthermore, the ultrafast pulses will allow dynamics imaging of nanoscale objects by taking a sufficiently short "snap shot" or a series of "snap shots.

2.1.1 Imaging at cellular and sub-cellular scale

Recent progress, made with the existing free electron laser (FLASH) at DESY (figure 3), has laid the basis for these new imaging technologies in the life sciences. Here a living cell has been imaged by soft X-ray flash coherent diffraction imaging. The resolution is limited by the wavelength of the radiation of FLASH (13.5 nm). Shorter wavelengths should allow large macromolecular assemblies to be resolved. Understanding the relationship between macromolecular structure and function at the cellular level requires understanding macromolecular complexes, their assembly as a function of cellular activity, and their regulation. This information is key to developing our understanding of

fundamental cellular processes that are critical in development growth, homeostasis and disease. Flash imaging of cells by soft X-ray diffraction imaging should provide resolutions that will allow assemblies of macromolecules and their location with respect to cellular processes to be identified and should give information that will be complementary to that of the other technologies. Outlined here is a selection of molecular assemblies and cellular processes that are at the focus of research council/major charity priorities of research into ageing, disease, immunity and therapy.

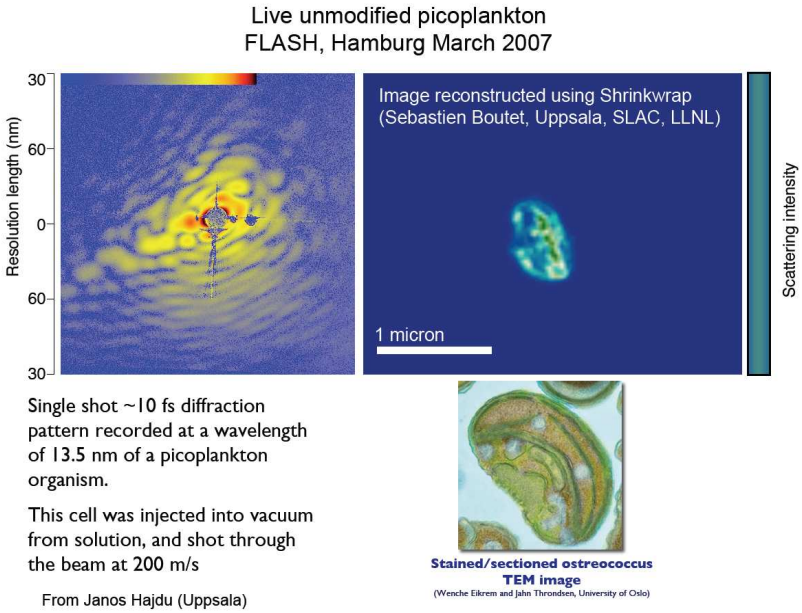

Figure 3. (left) Single shot ~10 fs diffraction pattern recorded at a wavelength of 13.5 nm of a picoplankton organism. This cell was injected into vacuum from solution, and shot through the beam at 200 m/s. (right) Image reconstructed using Shrinkwrap algorithm.

(a) The mitotic spindle. The mechanisms of cell division by which a cell duplicates its chromosomes and then distributes these to two identical daughter cells have been informed by a combination of cell biology and biochemistry with structural information from protein crystallography, electron microscopy and optical microscopy. But profound questions of the molecular organisation remain. The mitotic spindle is at the heart of this organisation. In animal cells the centrosomes (an assembly of two orthogonal centrioles composed of at least four different proteins) extend microtubule filaments that end in attachment to the kinetochores (an assembly of >45 proteins) located at the centromeres of the chromosomes. Cell division does not take place until each chromosome is attached via the microtubules to the two opposite poles of the mitotic spindle. It is possible to arrest cells at different stages of cell division. Imaging at these different stages should allow the composition and structure of each of the complexes to be studied, allowing insight into assembly and disassembly processes.

(b) The nuclear envelope of all eukaryotes is perforated by large multi-protein complexes known as nuclear pore complexes (NPC). They form aqueous channels that are the gateways for all molecular traffic between the nucleus and the cytoplasm. Their recent structural elucidation has relied on a number of synergistic imaging and reconstruction techniques. The central pore is believed to be able to change in size from 10 to 26 nm. The traffic through the NPC is highly regulated and specific, yet very efficient, with hundreds of translocation events per second. How NPCs mediate this massive macromolecular flux is debated. A clear picture of the molecular organisation and dynamics of the NPC is one of the basic requirements that is still lacking to resolve the transport mechanism. Snap shot imaging of these large assemblies as they act as transporters using coherent X-ray sources may allow us to understand how and to what extent rearrangements of the NPC can modify its transport properties, as this could provide the cell with an important mechanism to respond to new physiological requirements.

(c) The active movement of the kinesin molecular motors supports several cellular functions including mitosis, meiosis and transport of cargo such as axonal transport. A large body of structural, biochemical and biophysical evidence shows that Kinesin-1 has just one binding site per tubulin dimer, and that the motor takes 8-nm steps from one tubulin dimer to the adjacent one in a direction parallel to the protofilaments. Since the isolated motor domain of Kinesin-1 can hydrolyze up to 100 ATP molecules per second, it is likely that each step corresponds to one cycle of the ATPase reaction. The step size is 8 nm, corresponding to the axial distance between microtubule heterodimer subunits, and is independent of ATP concentration and load. The mechanical substeps should be amenable to direct imaging techniques available at a new light source.

How is such imaging to be achieved? A FEL source would have the capability to enable significant advances in single shot imaging due to the exceptionally high peak brightness and ultra-short pulse duration of the soft X-rays. Single-shot (flash) coherent diffraction imaging (CDI) relies on collecting a diffraction pattern with a single high brightness short pulse of X-rays. The assumption is that the radiation damage will modify or destroy the sample but that the diffraction pattern can be recorded before these events occur. Phases can be retrieved from the over-sampled diffraction pattern and hence the image reconstructed. The theoretical calculations in 2000 [2], which showed that this should be possible, have had a profound influence on the field. CDI is already practical with the coherence available from present-day 3rd generation sources of synchrotron radiation for imaging of the structure of nanoparticles and imaging the strain fields within [3, 4]. Experimental verification of coherent flash-diffraction imaging has been achieved [5] and this work has been followed by time-resolved structural studies with femtosecond time-delay X-ray holography [6]. Significantly it was shown that the photons are scattered before the shock wave of damage is propagated through the specimen, allowing image formation from the diffraction pattern.

In recent theoretical work [7], Bergh et al. have analysed the interactions of an intense X-ray pulse with a living cell, using a non-equilibrium population kinetics plasma code in which radiation transfer as a function of pulse length, wavelength and flux is incorporated, to model radiation damage and hydrodynamic expansion. The results (Figure 4) show that resolutions approaching 1 nm could be reached on micron sized living cells in diffraction-limited geometries at different wavelengths. Interestingly the shortest wavelengths or the highest intensities do not give the highest resolution on non-reproducible biological objects where averaging is not possible. These calculations suggest that a highly coherent source of soft X-ray wavelength (eg ~600 eV) with 10-20 fs pulses with fluxes of the order of 10^{11}-10^{12} photons per μm^2 could deliver the capabilities for these new imaging methods. A key requirement that is not yet fully solved will be to obtain 3D information in order to resolve complexes within the crowded environment of the cell. Some 3D information may be obtained from a single diffraction pattern by numerically propagating the complex-valued wave front [7]. The possibility to split the single intense pulse to obtain three simultaneous projections of a sample from a single radiation pulse has been proposed that would allow some degree of tomographic imaging (Schmidt, KE et al. Submitted). A further crucial step in following cellular function in real time will be in developing capabilities to trigger events in specimens and then record images from a number of identically prepared specimens in a series of time steps. Combination of these methods with those of light microscopy will provide new insights into cellular organisation.

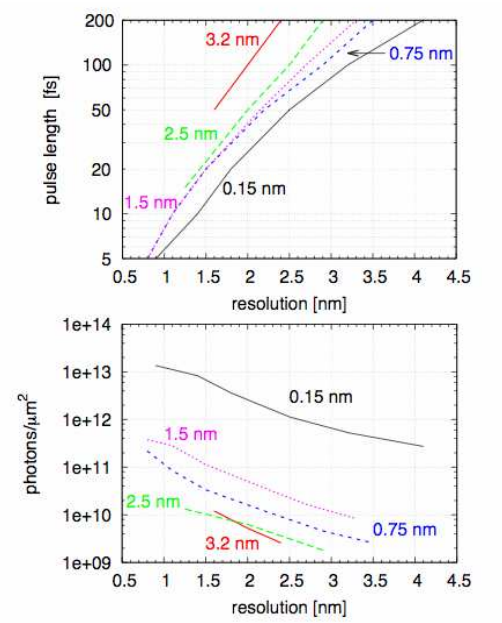

Figure 4. Expected resolution for a micron-sized living cell as a function of pulse parameters (wavelengths, pulse length, integrated intensity). (a): Achievable resolution as a function of pulse length at different wavelengths. These curves are cut at the diffraction limited resolution for soft X-rays. (b): Number of photons per μm that would be needed in the pulse to achieve a selected resolution in (a). Reference [7] Bergh et al.

Contrast agents can be employed, but there are advantages of using pure phase contrast for biological material. A key feature will be to develop specific labelling methods (e.g. [8]) so that individual proteins can be tagged, as has been developed so effectively for light microscopy. In cryo-EM similar approaches to proteomics are being developed [9, 10].

There are several strategies for presentation of the sample in the beam that include mounting on a support film, injection by mechanisms similar to those used in mass spectrometry and the 'serial crystallography' method of creating a stream of droplets flying through the X-ray beam, which may be ordered by external forces to provide a semi-crystalline view [11]. With a single shot only a 2D view of the sample is available. If the assemblies are identical (e.g. viruses) many images for all views may be collected and merged to form a single 3D image. The "dose-fractionation" theorem [12] indicates that the allowed dose can be spread over multiple views to gain 3D information with the same dose as needed in 2D. However this is only applicable for assemblies that are identical. For structures which are not identical from particle to particle, such as living cells, and where radiation damage permits only a single shot, other strategies need to be developed for a 3D image as described above.

2.1.2 Imaging of nanoscale systems for science and technology

The methods just outlined for biological imaging carry straight over to imaging non-biological condensed matter systems. One of the key challenges in X-ray scattering/spectroscopy in condensed matter is to be able to determine the structure and dynamics of *individual objects* on nanometre scale. Typical questions to be answered are:

- How do bond lengths, coordination, electronic and magnetic structure vary between core and shell in a particular nanoparticle?
- Can we see an individual Cooper pairs or polaronic states in general and image the texture of lattice distortions, orbital and spin structure as well as the electronic properties.
- Can we image charge or spin carriers within individual electronic devices as they function at the nanoscale.

Continuous and quasi-continuous beams cannot be used for scattering from isolated objects. Over-illumination, necessary to collect sufficient number of scattered photons, results in damage. The concept of Flash Imaging with FEL's, where a single, ultrashort scattering pulse captures the structure of an isolated object before this is destroyed, is of great interest for this set of problems.

Hard condensed matter is more radiation-resistant than biological matter, while heavier constituent atoms imply longer times for the structure to be destroyed (phonon frequencies and speeds of sound are lower). With the same "inertial confinement" concept, one could not only measure atomic structures, but also electronic and magnetic properties of isolated objects. This would require soft X-ray probes, which have the advantage of stronger scattering cross sections.

2.1.3 THz studies of living tissue and THz signatures for disease

The availability of bright coherent THz radiation alongside the soft X-rays is likely to provide a number of important additional science opportunities (see below for the pump-probe science). Here near field imaging techniques are looking promising achieving resolution better than $\lambda/100$ and so despite the long wavelength of the radiation it may be possible to obtain spatial resolutions in the 100's of nanometre range. Direct use of THz radiation for imaging has already been developed towards commercial scanners for medical applications; however the basic science behind the contrast mechanism that provides useful medical information is not yet understood. Very bright THz radiation will permit essential quantitative studies to be carried out to establish a proper basis for the use of THz radiation in medical imaging.

There is a pressing need for fundamental work to establish the chemical origin of the THz fingerprint in intra-operative THz imaging of cancer patients, in order to establish the relevant protocols e.g. range of frequencies for use in applications such as sentinel node mapping during cancer surgery. Although skin cancer is the obvious immediate application of THz technology it also has potential for diagnosis of other diseases by recording signals using endoscopic techniques. Commercial companies (Teraview) are already marketing instruments that can be used to diagnose skin cancers. However the current power levels available with laboratory sources do not make it possible to determine the origin of the contrast mechanism in these applications.

2.2 CAPTURING FLUCTUATING AND RAPIDLY EVOLVING SYSTEMS

Many natural systems undergo intrinsic rapid structural evolution and fluctuations in the constituent parts, either at the atomic scale or larger scales e.g. of magnetic zones or grains. This is obvious when we considered matter in the liquid state where a non-static structure must be anticipated, but extends also to situations as diverse as domain fluctuations of correlated electronic materials, dynamics in glass transitions and in high density plasmas. A variety of scattering techniques e.g. XPCS (X-ray photon correlation spectroscopy) and X-ray Thomson scattering are available. To capture the full fluctuation spectrum or to measure the properties of a rapidly evolving system requires high brightness, short pulses so the full scattering information can be gained in a single instant. NLS will have the temporal structure and wavelength range (1-6 keV) high coherence and brightness ideal for these studies in many different systems, accompanied by synchronisation to other external sources (e.g. high magnetic fields).

2.2.1 Fluctuating nanosystems

A variety of related soft X-ray scattering techniques i.e. coherent speckle patterns/photon correlation/holography can be used to provide information on the spatial fluctuations of the structures within nano-particles. At present photon correlation techniques can access very slow dynamics. In principle, with short pulses and fast repetition rates one can access faster and faster dynamics. Current X-ray photon correlation (XPCS) measurements suffer from difficulties with beam coherence, but nonetheless provide access to dynamics on the timescale from μs to 10's of ks. The X-ray wavelengths provide access to dynamics at non-zero momentum transfer values, and with tunable

sources, element specific information. A pulsed X-ray laser would enhance coherence significantly. Methods for ultrafast XPCS have been proposed that split a pulse and introduce a delay to allow very short timescales (potentially as to ps timescales) to be measured. With this, dynamics could be measured in the same setup over the entire range of timescales (ps – ks). This would allow us to investigate the links between small atomic fluctuations and larger scale motions in e.g. proteins and polymer chains, something which to date can only be done by considering different time regimes in isolation. With a tunable X-ray laser this could be done for different elements (the soft X-ray regime covers the most interesting elements). With some work on X-ray optic elements, polarization analysis could also be introduced to enhance magnetization contrast.

The dream would be to be able to study ultrafast switching at the picosecond scale. Ideally, one would like to reconstruct the *intermediate scattering function*, but photon correlation loose phase information between t and $t+\Delta t$. This problem has been addressed by the so-called **heterodyne mixing** technique, in which the undisturbed beam is used as a reference to reconstruct phase information.

Other methods for exploiting the coherence of the beam include photon echo, which would also allow access to very short timescales, and probe both driven and internal dynamics, and more crucially, perhaps, their interactions. If appropriate pumps can be designed, normally weak features can be boosted, such as orbital ordering in manganites.

2.2.2 States of high density plasma

A diffuse plasma, like a gas, will display only weak correlation in the positions of the constituent charged particles (electrons and ions). At high density, approaching that of solids, the ions can become partially or fully ordered due to the strong Coulombic interaction. Whilst the solid extreme is relatively well understood the partially correlated state, often referred to as warm dense matter (WDM), remain a great challenge to theoretical description. This state is especially important as it is traversed by all plasmas created initially from heating solids (e.g. laser or X-ray produced plasmas) and moreover is a common constituent of astrophysical objects. Understanding the basic properties of WDM is of key relevance to Inertial Confinement Fusion research, and thus has direct links with the energy agenda. This is potentially strategically important for the UK, given, for example, that we lead the HiPER project.

Warm dense matter is thus an intriguing and largely unexplored state of matter that can be roughly described as midway between condensed and plasma states (see figure 5). Matter in this regime is ‘strongly-coupled’, that is to say the Coulomb energies are comparable to the thermal energies. This makes WDM notoriously difficult to model, as the thermal component of the energy cannot be looked upon as a perturbation to the inter-atomic forces (as in a solid), or vice versa (as in a low density gas or plasma). As a result accurate equations of state (EOS) – the relationship of density, temperature, pressure, and energy density for the system of interest – which normally permit prediction of the state of a system and its evolution, are largely unknown in this region (for example, at solid densities and temperatures of a few eV, several credible theories differ by up to a factor of two in their prediction of pressure).

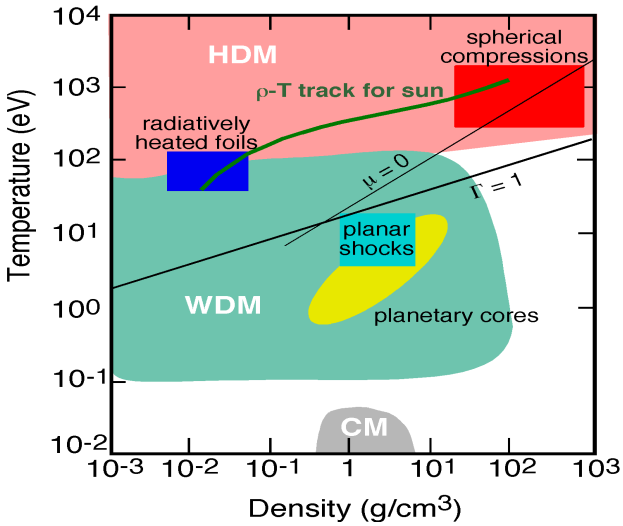

Figure 5. A density – temperature plot shows the different regimes pertinent to high energy density matter. Condensed matter (CM) lies at the bottom centre (low temperature, solid density), whilst hot dense plasmas (HDM) are at the top (high temperature, range of density). The region of greatest challenge to understanding in plasma physics, warm dense matter (WDM), lies at high density and relatively low temperature

The most powerful probe of plasma state, including electron and ion temperature, electron density, velocity distribution and collisional damping rates come from light scattering (Thomson scattering). Examination of the optical scattered spectrum has been a powerful tool for diagnosis of lower density plasmas. As the density increases towards that of a solid, however, the plasma becomes opaque in the optical domain and the plasma will only be transparent in the X-ray range. Thus X-ray Thomson scattering is required to examine the detailed state of a high density plasma. For this a short pulse (sub-ps) of very bright X-rays are essential to capture the often very rapidly evolving plasma. A soft X-ray FEL is ideally suited for this purpose. Moreover the high longitudinal coherence of the beam will permit X-ray interferometry, phase contrast and holographic imaging measurements of fast evolving dense plasmas. This will contribute not only to our knowledge of the EOS in WDM but also allow the direct study of shocks, instabilities, jet formation and turbulence.

Furthermore it has also been problematic in the past to produce WDM uniformly (i.e. with minimal gradients in temperature and density) in the laboratory. The soft X-rays have the potential to overcome these problems owing to the relatively long absorption length of the radiation compared with visible light – indeed it is important to note that WDM will inevitably be produced in many 4th generation light source experiments - the radiation is so intense that its interaction with solid matter will (unless undertaken at grazing angles of incidence) automatically produce WDM. For this reason alone WDM research will be an integral part of any new light source project, including the NLS. This 'automatic' WDM production will be isochoric, with energy initially deposited in the electrons, with subsequent thermalization via electron-ion coupling on picosecond timescales.

Spectroscopy of plasmas on NLS, whether in the non-perturbing or perturbing mode, will be a key diagnostic of plasma parameters. Unique possibilities will exist which will both extend and complement the efforts on strongly coupled plasmas outlined above. In the non-perturbing mode (where we observe the WDM produced by the X-ray beam irradiating a solid, foam, or gas-phase target), the emission line intensity, position and shape of NLS-produced plasmas may be effected by strong coupling. Secondly, an intense X-ray source will act as a unique perturbing-pump for laser-produced plasmas which will test our understanding of several basic features of the radiative properties of strongly-coupled plasmas; for example, the capacity to model the full kinetics of even the simplest systems (i.e bare, hydrogenic, and helium-like ions). Such experiments are impossible with current laser-plasma based soft X-ray lasers, as they do not have sufficient intensity for the pump rate to greatly exceed the spontaneous emission rates. Importantly, a monochromated intense soft X-ray source will be sufficiently narrow-band to pump within the line-width of a Stark-broadened bound-bound profile. Subsequent observation of the line shape of the emitted radiation will test the

normal assumption of complete frequency re-distribution within the line. This assumption can be invalidated by ion-field fluctuations and inelastic collisions, and measuring the detailed redistribution of population after pumping can therefore provide crucial information on the rate of the relevant plasma processes.

2.3. STRUCTURAL DYNAMICS UNDERLYING PHYSICAL AND CHEMICAL CHANGE

Ultra-fast events in nature are often accompanied by equally fast structural and electronic changes. To understand the mechanism behind, e.g. chemical reactions, ultra-fast magnetization, phonon triggered changes in electronic structure, photon induced processes in solids and at surfaces, we need to be able to measure these changes in real time. This requires us to make measurements in the 10 ps to 10 fs range in order to capture all the timescales of motion associated with changes in any complex matter system. To succeed in this new endeavor we need to be able to; (1) trigger the event of interest, (2) follow it with a probe sensitive to structural and electronic change. For most problems the dominant interest is in local changes around the active site and here soft X-ray methods (e.g. X-ray absorption and emission spectroscopy, and X-ray photoemission) provide an ideal tool. The trigger can be made via a variety of means e.g. controlled "thermal" excitation of lattice/vibrational modes, photoexcitation of electronic states with a resonant laser, and electron beam excitation of system (radiolysis). Of critical importance is that the pump (event trigger) and probe pulses are sufficiently well synchronized to permit temporal resolution approaching the 10 fs limit. It is essential that any new light source will provide an array of pump-probe capabilities that will collectively resolve the ultra-fast structure and dynamics in a wide range of processes.

2.3.1 THz-visible pump – X-ray probe of condensed phase systems

We consider first the measurement of ultrafast structural dynamics and photo-control in complex matter. The use of light to control the macroscopic properties of solids [13] has recently emerged as a new approach to investigate the underlying ordering principles of condensed matter (e.g. by measuring elementary interactions between various microscopic degrees of freedom) and develop new means of controlling the functionality of solids on the ultrafast timescale. Applications are many, from optical switching at Tbit rates to magnetization control on the ultrafast timescale.

How do many degrees of freedom synchronize dynamically to bring about an ultrafast phase transition? How can we control this behaviour? Why are highly-correlated electron systems soft against photo-excitation? What other forms of impulsive stimulation could be used? Is it possible to photo-initiate new interesting functionalities? Can we photo-induce superconductivity? All these questions are extremely difficult to tackle theoretically, since they involve highly non-equilibrium dynamical states, for which our understanding of even basic statistical mechanics is very limited.

Excite-probe geometries, involving visible or THz [14] "pump" events, and X-ray pulses that interrogate atomic [15,16,17] and electronic structure along its stimulated, dynamic pathway should be used. One would wish to use femtosecond or even attosecond X-ray probes to capture the microscopic properties of matter along ultrafast photo-controlled pathways. Among the probe methods we will employ are XPS/ARPES and XAS.

A powerful X-ray probe technique, available from a seeded FEL, is inelastic X-ray scattering (IXS) which probes the dynamics of condensed matter systems in the energy domain. A photon-in, photon-out technique, it offers a momentum-resolved, bulk-sensitive probe of excitations from 1 meV up to 10's of eV and with momentum transfers from 0.1 $Å^{-1}$ to 10 $Å^{-1}$. In particular, it suffers from none of the limitations of ARPES, which is restricted in application to cleave-able conductors. Furthermore, IXS has a very clean, well-understood cross-section. At the best synchrotron sources today, the flux on the sample is 3×10^{10} photons s^{-1} in a band pass of 6 meV. This is sufficient to measure phonons, which have relatively large cross-sections, but is inadequate for measuring any electronic excitations (at these resolutions). This is extremely unfortunate, since many of the most interesting questions in condensed matter revolve around understanding electronic response functions

on these energy and momentum scales, and could in principle be addressed with this powerful technique.

A transform-limited, seeded FEL offers a tremendous gain for this field. Here, the energy bandpass is inversely related to the pulse duration. For a 100 fs pulse, it is ~10 meV. This would be sufficient for many experiments and would eliminate the need for any upstream optics. Time-averaged fluxes in excess of 10^{15} photons s^{-1} are needed for these measurements, which would represent a gain of *five orders of magnitude* over existing instruments. This would transform the applicability of the technique and would have enormous scientific impact.

Measurements of electronic excitations with these kind of resolutions (few meV, pulse lengths of >100 fs) would be transformative. Examples of excitations that one cannot currently study include electronic gaps (e.g. superconducting gaps, charge-density-wave gaps), collective excitations (so-called "orbitons", particle-hole excitations, "holons") and more exotic excitations (the pseudogap in high-Tc superconductors, new modes predicted for broken gauge symmetries in high-Tc superconductors [18]).

To take one example, measurements of the superconducting gap are in principle possible with this technique. However, at SPring-8 today, calculated cross-sections [19] translate into count rates of 10^{-3}-10^{-2} cps – well below the observable threshold. At a seeded FEL, these same experiments would have count rates of 10^{2}-10^{3} cps, and become feasible for the first time.

Similarly, the pseudogap in high-Tc superconductors remains one of the great mysteries of these materials, with the general belief that it is an electronic continuum of some kind. IXS measurements at an FEL could probe the energy and momentum dependence of this continuum and reveal a great deal about its nature. Other fruitful areas of inelastic scattering study would include non-equilibrium dynamics, possibly interrogating transient intermediates of a system driven by external stimulation.

2.3.2 THz-visible/UV pump – X-ray probe of chemical processes

NLS will provide an exceptional capability to trigger chemical reactions using synchronised THz-visible/UV pump fields and tunable soft X-ray probing of geometry and electronic character. The use of soft X-ray techniques for structural and electronic interrogation of matter in all phases is well established with conventional synchrotron sources, and their extension to ultrafast timescales will open entirely new windows into the realm of atomic motion, electronic structure rearrangements and thereby chemical dynamics [20].

X-ray absorption spectroscopy (XAS) provides a powerful probe of both local geometry and oxidation state of an atomic species within chemical systems. X-ray emission spectroscopy (XES) and X-ray photoelectron spectroscopy (XPS) also provide an atom-specific probe of electronic structure and site geometry, and in general provide complementary information to that of XAS techniques. A key advantage of these techniques is that they are structurally incisive and so it is possible to probe a specific species in the presence of a complicated mixture of chemical reagents, products and transition states. Combining XAS and XES can also deliver spin-selective information, and a key development that will be enabled by a suitable X-ray source at the NLS will be correlated XAS-XES spectroscopy.

In XES the atomic sensitivity arises from the creation of a core hole during the absorption process and the fact that this core hole can only be filled by valence electrons in the proximity of the excited atom [21]. The final state of the X-ray emission process is a valence hole state similar to the final state in valence band photoemission but here the valence electronic structure is projected onto a specific atom. Another essential aspect of the spectroscopy is that the polarization of the incident radiation and the direction of the emitted radiation allow directional sensitivity, providing a direct measure of the molecular orbital symmetry.

In XPS a core electron is ionized and the binding energy and photoelectron angular distribution provides a direct measure of the local chemical surrounding. XPS can probe local chemical states of individual atoms embedded in molecules, in bulk, and at interfaces, properties that are relevant to physics, materials science and chemistry. Furthermore the tunability of the photon energy allows atom and site specific enhancement of the signal through the photon energy dependence of the photoionization cross-section.

Time-resolved XPS is a particularly appealing extension to the study of isolated gas phase molecular systems where time-resolved valence-shell photoelectron spectroscopy has emerged as a general tool for molecular processes [22] due to sensitivity to both electronic and nuclear motions. Extension of valence and core photoelectron spectroscopy to ultra-fast timescales with few-fs X-ray pulses will enable very fast chemical events to be followed which are typically complicated by the breakdown of the Born-Oppenheimer picture as the flow of charge and energy in the molecule becomes strongly coupled at regions of configuration space such as conical intersections. Time and angle resolved XPS, and allied methods, suffer from space charge distortion unless the photoelectron density is strictly controlled (e.g. by limiting flux or sample density) and often this compels the use of a high repetition rate source to achieve acceptable signal.

The use of precisely synthesized optical fields for the control of chemical [23] and even biological [24] systems has emerged as a powerful application of femtosecond laser technology. Despite the advances made in this field over the past decade, to date the precision with which these processes have been controlled has been limited by the available probing techniques provided by conventional lasers. The combination of optical lasers with time-resolved X-ray probing will therefore open many new opportunities for highly efficient coherent control strategies. It is also anticipated that the availability of high intensity IR radiation will allow for conformational selection and control of large molecular systems, as well as the control of molecular orientation and alignment of isolated gas phase molecules leading to enhancement of the information content of subsequent X-ray structural probing.

A tuneable and scanable source of femtosecond X-ray pulses with high flux ($>10^{12}$ photon/s) in the 0.1-7.5 keV range is therefore a key requirement for access to the X-ray absorption edges of a wide range of chemically important elements (see periodic table in figure 6 for *K* and *L* edge energies). The use of EXAFS requires access to *K* edges of atoms, or *L* edges above 2 keV. While low lying edges (at around 0.5 – 1.5 keV) are good probes of geometric and electronic structure of light molecular species (for example at the surface of a catalyst), XAS and XES above 2-5 keV also have the advantage of being good probes of bulk material. With the high photon energy limit anticipated to reach ~7.5 keV (e.g. 5th harmonic of a 1.5 keV FEL) time-resolved X-ray diffraction studies are also likely to be of importance.

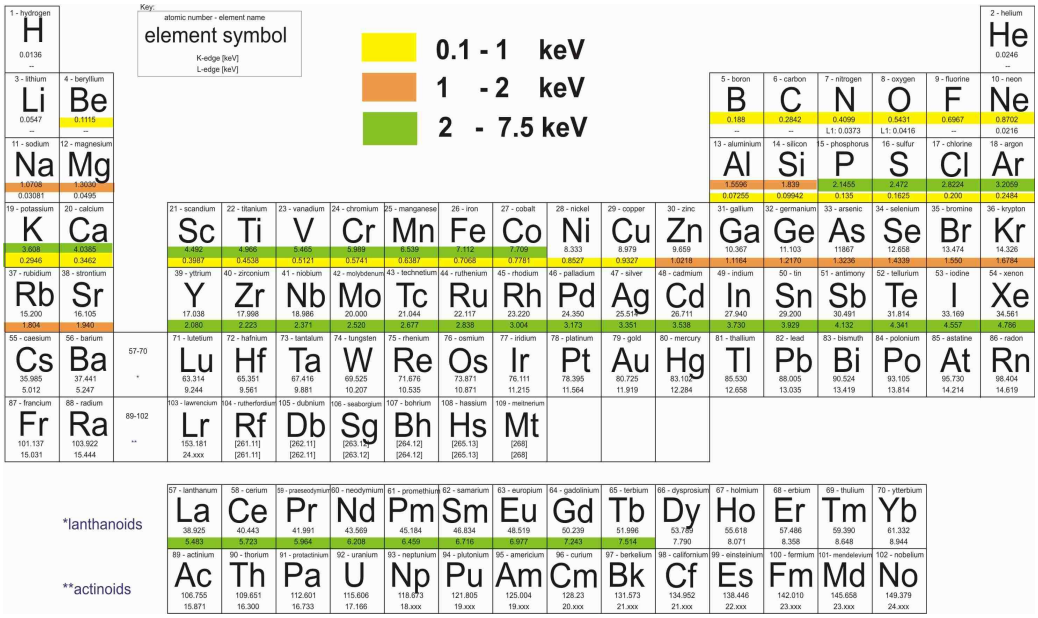

Figure 6. Periodic table showing the energies of the K (green) and L (yellow) edges of the elements. We can see for instance that the K and L edges of Fe can be accessed if the 5th harmonic reaches above 7keV.

2.3.3 THz to visible vibrational spectroscopy – chemistry and the life sciences applications

When combined with X-ray techniques, vibrational spectroscopy provides an important complementary probe of structural dynamics. Whilst the fine structure detected in XAS/XES provides geometrical information and is especially sensitive to heavy neighbouring atoms, infra-red (IR) and Raman vibrational spectroscopy can identify functional groups, light elements such as hydrogen, and, in some cases, the local symmetry.

A major challenge across chemical science is to understand molecular reorganisation in complex environments in terms of both intra-molecular and environment dynamics. The reorganisation of the environment of a molecule influences processes by solvation perturbations and outer-sphere molecular co-ordination and often dictates transition states, chemical outcomes, and product state distributions. However, these problems are technologically challenging. Current laser technology provides time-resolved IR capability [25], but with limited spectral coverage; currently the region below ~ 800 cm^{-1} is inaccessible. Extension of the spectral coverage to provide a full temporally resolved 4000 – 1 cm^{-1} spectrum would allow for example the study of hindered rotations or vibrational structure of solvent molecules which influence solvent reorganisation dynamics in liquids, the direct probing of metal-carbon and metal-metal atom motions in surface science problems, and identification of key biologically active radical species during radical migration during DNA strand breaks. Accessing the complete vibrational spectrum and being able to relate mode-to-mode dynamics in 2D and multi-time dimensions would open up a complete way of investigating molecular dynamics. Raman techniques, such as time-resolved resonance Raman, offer a complementary and powerful probe of vibrational dynamics. A key requirement of the NLS is to be able to employ these techniques as the probe process in pump-probe measurements, and this will require synchronized deep IR sub-picosecond pulses.

The relevant frequencies for promoting motions of biological macromolecules lie in the far-IR/THz, so highly intense broadband IR/THz radiation should provide the ideal source for a new generation of non-damaging macromolecular dynamics experiments. Combinations of pump-probe studies (e.g. THz pump, IR or UV/vis probe) are required to assess the role of promoting motions in biological responses, such as catalysis. Near infrared and THz pump probe experiments will monitor the rate of relaxation and localization of energy within biological chromophores, the protein scaffold and between protein-protein complexes. The rate change can then be measured in the presence of pre-pumping or post probing THz radiation. Low temperatures will be used to obtain defined THz spectral

features and pulse shaping will be investigated as a means to drive and optimize mode enhanced energy transfer in biological macromolecules. THz pump followed by UV/vis probing will address the role of promoting motions in biological catalysis through direct analysis of the chemical rate process.

2D-IR: Infrared spectroscopy is an important diagnostic tool in the life sciences. IR measures vibration-vibration coupling. It provides structural analysis for extremely small or rare samples and can detect structural changes on a ps or fs timescale. NMR for structure determination was revolutionised by 2D methods. 2D-Infrared spectroscopy is an optical analogue of 2D NMR. Coherent multidimensional spectroscopy has considerable benefits and avoids the problems of peak overlap in the spectra of complex macromolecules [26]. With time-resolved multi-pulse coherent spectroscopy it has been possible to measure vibration/vibration cross-couplings on the ps timescale. This has been applied to a range of coupled vibrations in protein molecules and has allowed identification of individual proteins based on their unique amino acid composition from signals of four amino acids. The method is not limited by protein size and it can in principal detect post-translational modifications (e.g. phosphorylation), or protein responses such as light activated isomerisation between the ground state and intermediate states of the photo-response cycle of bacteriorhodopsin.

With a brighter source, the method could be extended to time-resolved structural analysis to follow ligand/protein interactions through dipole/dipole coupling (r^{-3} dependence). This would extend the technique to allow measurement of coupling of short and long-range interactions from the present estimate of 4-5 Å limit to the 16-20 Å range. With bright IR radiation the method could also be extended to a wider range of applications utilizing high intensity, broad tuneable radiation, and shorter pulses (~1 ps) to explore collective protein motions and conformational changes. The extension of triply resonant 2D-IR to THz wavelengths will make it possible to explore global collective protein motions and to study hydrogen bond dynamics and coupling. A combination of wavelengths is particularly powerful for coherent two-dimensional methods allowing THz-THz mode couplings, THz-mid IR couplings and triply resonant (vibration-vibration-electron) couplings to be studied. The technique requires two independently tuneable IR sources coupled with a synchronized visible/UV tuneable laser source.

2.3.4 Electron beam excitation and probing

Pulse radiolysis as a trigger and soft X-ray probes of structural change will also be an important avenue of research. A pulsed electron beam is a complementary and powerful method for the generation of chemical intermediates and excited states which has made a major impact in areas as diverse as geochemistry [27], nanoscience [28], ionic liquids [29] and radiation damage of DNA [30]. Its principal difference from laser initiation is that the primary excitation step involves interaction of electrons with the media and does *not* rely on the absorption by a chromophore of the laser light of a particular wavelength. Other advantages of using high energy electrons to generate transient species include:

(a) Direct relevance to kinetics in radiation tracks and spurs influencing overall radiation chemical processes, in particular applied to changes during the nuclear cycle. This has particular application to all stages of the nuclear power cycle, including waste remediation and management, spent fuel processing, deep geological disposal etc.

(b) Specific generation of excited triplet states [31] of polymers and other advanced materials – these states are of importance in light emitting electrophosphorescent devices and photovoltaic devices, yet frequently are optically inaccessible.

(c) Specific generation and study of charged species for determining charge mobility on the nanoscale in molecular electronic devices, artificial solar energy conversion systems and radiation damage of biomolecules. Pulse radiolysis provides a unique method for specifically generating and studying the behaviour of positive and negative charges separately [32]. NLS would enable the introduction of vibrational state, and potentially diffraction, probing which will provide, for the

first time, information on both the spatial aspects and the detailed mechanisms of the holes and electrons migration before recombination.

(d) Characterization of chemical and biological intermediates stemming from oxidation/reduction reactions, including triggering enzymatic activity through heteroleptic bond cleavage [33], and resolving catalytic pathways in natural enzymes [34]. Metalloenzymes are of particular interest as currently information on the detailed dynamics of primary processes is missing. Examples include triggering enzymatic activity through bond cleavage.

The coupling of picosecond and sub-picosecond electron pulses (~ 5-10 MeV) as a trigger for chemical change with the structural probe techniques described above would represent a unique capability internationally. In particular, compared to existing pulse radiolysis facilities worldwide [35] (of which none exist in the UK), this would give the NLS a leading edge in terms of both structural sensitivity and time resolution. The combination of XUV pulses and pulsed radiolysis at the same facility will allow direct comparison of optically induced dynamics with those of radiolysis, a potential key international defining feature for the NLS.

The pulsed electron beam, synchronised to the NLS light sources, offers a further potentially high impact possibility. A complementary technique to X-ray diffraction for measuring structural dynamics is offered by electron diffraction. Time-resolved studies in which electron diffraction/microscopy is used as the structural probe are now well established, and typically employ electrons with non-relativistic energies of around 100 keV [36]. In comparison with X-ray diffraction, electron diffraction has several advantageous features: (1) scattering cross sections for electrons are typically 4-6 orders of magnitude larger due to the Coulombic interaction with both the nuclei and electrons in the target; (2) the inelastic: elastic scattering cross section for electrons is lower for electrons than for X-rays; and (3) the energy deposited into the target per inelastic collision is lower for electrons than X-ray photons. At these low electron energies, the temporal resolution is, however, typically limited to ~1 ps by velocity mismatch between laser and electron pulses, space charge repulsion and the initial electron velocity spread.

The shortcomings and limitations of conventional pulsed electron diffraction may be alleviated by employing the ~5 MeV relativistic energy electrons from the aforementioned beam, for which the space-charge repulsion can be significantly reduced allowing for significantly higher bunch charges and preservation of short bunch durations. In fact, it is anticipated that bunch charges may be achieved that are sufficient to record single-shot images. In addition, relativistic electron bunches travel close to the speed of light removing issues of velocity mismatch with the pump laser pulse through the sample under study. Electron diffraction with relativistic electrons therefore presents an opportunity to extend time-resolved electron diffraction and microscopy measurements into the < 100 fs domain, representing a step function in capability with application across the physical and life sciences. Recently, diffraction of relativistic electrons (5.4 MeV energy) from aluminium foil has been achieved at SLAC [37] demonstrating the feasibility of this approach. Further development of the technique is nonetheless required in order to implement fully time-resolved measurements, and the challenges associated with the small diffraction angles will need further work. Nonetheless, the provision of a relativistic electron beamline synchronized to the other light sources at the NLS will represent an internationally unique capability for ultrafast structural dynamics measurements for all phases of matter.

2.4 ULTRA-FAST ELECTRON DYNAMICS

Electrons play an essential role in determining the structure and dynamics of matter by mediating the bonding between atoms and governing the optical, electrical and magnetic properties. The dynamics of bound state electrons in matter are tremendously fast with timescales from a few femtoseconds down to a few attosecond duration. Electrons in valence, conduction or inner shell states are invariably strongly correlated to one another through the Coulomb interaction and spin statistics. Moreover inherently quantum properties, such as entanglement, play a vital role in the multi-electron

states of all matter. NLS will be bright and short wavelength enough to drive a new class of simultaneously multi-electron and multi-photon non-linear interactions. These interactions are essential to understand in all applications of high brightness short wavelength light with matter (e.g. in single shot diffractive imaging) but also may unlock a new understanding of multi-electron dynamics in complex matter. Our present understanding of the dynamical response of multi-electron states to a rapid change (e.g. high frequency external field, sudden removal or excitation of an electron) is very limited. Recently measurement methods have begun to address the question of attosecond electron dynamics. These methods, based upon high harmonic generation (HHG) from lasers, are very limited by the spectral range and photon flux (~10^6 photons/pulse and ~10^{10} photons/second) of these light sources. We need the capability to extend the previous studies based upon HHG by using a combination of improved HHG, relativistic HHG and by applying pulse slicing in a FEL. By this latter means the photon fluence could be increased to > 10^{15} photon/second so permitting massive improvements in the measured signal. This will also provide a greatly enhanced flux to > 10^{11} photons/pulse so making possible, for the first time, non-linear interactions. The wide spectral range will allow access to the states of interest in all matter and not just a few test systems as is presently the case.

2.4.1 Short Pulse High Intensity X-ray Interaction Physics

The interaction of matter with strong high frequency soft X-ray fields is a new physical regime which is fundamentally different to that accessed with strong visible/NIR fields (see figure 7). This frequency regime is poorly understood and involves highly correlated multi-electron multi-photon interactions. In part this arises because the external field frequency is too high to be effectively screened by the outer electrons so the fields can couple with several electrons simultaneously. This is in contrast to interaction with UV/Vis/NIR light, where the interaction with the light field intrinsically only involves a single electron, and is well studied and understood. All measurements made with high intensity short pulse soft X-ray FELs will encounter the complexities associated with this new regime of interaction.

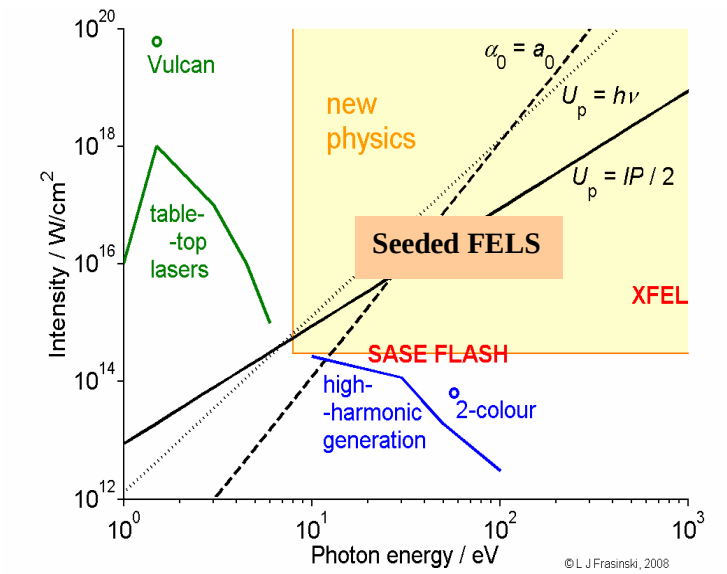

Figure 7. Strong field physics enters a new regime for high frequency fields. There is special interest in the soft X-ray range (10eV- 1keV) where the fields couple efficiently to multi-electron – multi-photon processes in matter.

An understanding of the fundamentals of high intensity soft X-ray-matter interaction physics will be crucial in all the FEL based measurements on complex systems of relevance to condensed matter, material, chemical, nano- and bio- sciences. We anticipate that new ultrafast measurement techniques will emerge from understanding this regime – for example, coherent non-linear multi-dimensional X-ray spectroscopic techniques [38] and non-linear optical based X-ray temporal gating have been proposed.

2.4.2 Revealing Correlated Ultra-Fast Electron Dynamics

A powerful approach to studying ultrafast electron dynamics in matter is through following the relaxation dynamics of a system after instantaneous removal of an electron, or in other words, observing the "hole dynamics". In this approach, an electron is first rapidly removed from a bound valence or inner shell state (with a short pump pulse) and the evolution of the remaining electrons into new states observed using a photoionisation probe. This approach requires either attosecond pulses as both pump and probe, or, alternatively, another fast event may be used as the pump (e.g. strong field ionisation).

The use of strong field soft X-ray pulses as a probe of electronic dynamics will allow us to directly observe for the first time correlated electron dynamics. At present, our understanding of the way in which electron motions are correlated in matter is indirectly inferred through measurement of the single electron response of matter to light. The multi-electron nature of the response of matter to high intensity soft X-ray fields will allow an entirely new view of the way in which the ultrafast motions of electrons in matter are correlated. Since all complex matter involves multi-electron states, correlated electronic motion underpins the nature of matter at the quantum scale. Though there is a vast knowledge of equilibrium electronic structure, based on established theoretical tools (e.g. DFT), our understanding of the dynamics of these systems is in its infancy, having only been studied through the response of individual electrons. The correlations of the many electrons induced by Coulomb interactions are strong and rapidly changing (on the sub-femtosecond timescale), and the role of quantum correlations (e.g. entanglement) is largely unexplored. The ability to study this fundamental feature of complex matter may underpin a new generation of optical, data storage and logic devices based upon ultrafast semiconductor and nanofabricated components.

2.4.3 Tools for Attosecond Science

An X-ray free-electron laser operating in the Self Amplified Spontaneous Emission (SASE) mode of operation, as proposed at e.g. LCLS and XFEL, generates radiation pulses of limited temporal coherence consisting of a series of phase uncorrelated spikes within an envelope duration approximately that of the electron bunch (10-100fs). The FLASH Free Electron Laser operating in the Self Amplified Spontaneous Emission high-gain amplifier regime is currently the world leader in the field and is able to generate ~10 fs pulses of ~50 μJ at wavelength of 13.7 nm, and following a recent upgrade to a 1 GeV electron beam has achieved lasing to saturation at 6.5 nm. If we anticipate a soft X-ray FEL (20 eV to a few keV where we expect the electron correlation physics to be most interesting) with pulses of ~10 fs we can be confident that it is already sufficient for new studies of non-linear interaction (1.1) and other time-resolved structural studies (see other sections). Nevertheless to extract the maximum information on multi-electron dynamics attosecond pulses, full coherence with probe lasers, will ultimately be needed. Therefore part of the science programme must involve proving the necessary pulse slicing/seeding techniques for 20 eV to few keV FELs. In the meantime HHG (high harmonic generation) and relativistic HHG (RHHG) can be used to permit attosecond domain studies to be conducted from the start, although with much lower flux and lower rep-rate than a FEL source. Further RHHG may provide an appropriate seed source for keV range FELs.

3. FACILITY CAPABILITY

3.1 CAPABILITY REQUIRED FOR SCIENCE DRIVERS

To satisfy the scientific objectives set out above there are a number of core capabilities that the facility must be able to provide:

- **High brightness (up to 10^{12} photons/pulse) pulsed coherent light source coverage from THz to ~1.5 keV (with less bright harmonics to 7.5 keV)**
- **Much of the science benefits from 1-10 kHz repetition rate (or higher)**
- **Even pulse spacing for optimized data collection and for efficient synchronization to external lasers (including for seeding and slicing)**
- **Photon source capable of smooth tuning across the entire spectral range**
- **Pulse durations down to ~20 fs for soft X-ray applications with sub-femtosecond capability required for attosecond science**
- **Soft X-ray linewidths of 0.1% of bandwidth, with the possibility to reduce this in the future**
- **Two-colour capability for pump probe experiments with synchronisation jitter better than 10fs. For example, Colour 1: THz- UV (pump)/ Colour 2: VUV-7 keV (probe)**
- **High degree of transverse and temporal coherence.**
- **Synchronised auxiliary devices e.g. high power lasers, pulsed electron beam, high magnetic field facilities**

It is anticipated that, where appropriate, conventional lasers should be employed, e.g in the range 0.4-5 eV where this technology has exceptional capability. Most applications will require this in synchronization with a FEL or require multi-colours from the FELs e.g. a IR/THz and a soft X-ray FEL driven in series from the same LINAC.

Electron beam modulation and seeding are essential to achieving the full NLS scientific mission. Modulation of the electron beam by a laser immediately before the FEL undulator can prepare the electrons so only a small portion of the electron pulse radiates in very short X-ray pulses. In this way pulse durations in the soft X-ray range of ~1 fs with a few μJ energy are feasible. There are possibilities to shorten the pulse length even further which will be explored in a second stage.

To overcome the intrinsic jitter and fluctuations inherent to the SASE process seeding by the highly coherent short wavelength light produced by high harmonic generation has been identified, and recently demonstrated [39], as the best strategy to radically improve the coherence and synchronization properties of a FEL. This will be essential to achieving the conditions needed for a wide range of the NLS science objectives. Conventional HHG has been shown to be efficient for photon energies approaching 400 eV and so we can anticipate seeding being effective for FELs at up to 10 kHz operating towards those photon energies. For shorter wavelength seeding down to 1 keV or higher energy relativistic HHG now looks very promising and with the likely improvement of high power ultra-fast lasers anticipated to push the average power limit from 1 kW towards 10 kW over the next decade or so this may well provide seeding capability across the full energy range of the FEL. This would correspond in the FEL harmonics to exceptional coherence and synchronization properties up to >5 keV.

It must be recognized from the start that there will need to be provision for a range of additional equipment and facilities that are essential to the NLS science. These obviously include a suite of lasers synchronized to the FEL which form an integral part of the light source. Moreover, to realize the full potential of NLS, other large equipment must be included in the facility such as the pulsed electron beam, high field magnets and possibly a high power long pulse laser. Likewise essential

facilities for sample preparation (e.g. tissue culture, crystal growth,) and handling will need to be available from the start of operation.

3.2 BASELINE SPECIFICATION AND UPGRADE PATH FOR A NEW LIGHT SOURCE

For a facility of this scale there are advantages, in terms of a manageable cost profile and exploiting technological advances as they emerge, in taking a staged approach to the construction of the facility. A Stage 1 baseline specification that we envisage should be available from day one of the facility operation is:

- **High brightness (up to 10^{12} photons/pulse) pulsed coherent light source coverage from THz to ~1keV (with harmonics to ~5 keV)**
- **~1kHz repetition rate with even pulse spacing**
- **Photon source capable of smooth tuning across most of the spectral range**
- **Pulse durations down to ~20 fs**
- **Two-colour capability for pump probe experiments with synchronistaion jitter better than 10fs. For example, Colour 1: THz- IR (pump)/ Colour 2: 100 eV-5 keV (probe)**
- **High degree of transverse coherence**
- **High degree of temporal coherence up to 400 eV, extending to >1 keV as seeding sources improve**
- **Synchronised to short pulsed lasers**

This baseline specification is sufficient to enable the majority of the science outlined in this case.

Additional capabilities, such as extending the seeding photon energy range and implementing pulse slicing, where the technology and cost present no significant barriers to progress could then be established within the routine facility development schedule. In addition to incremental improvements and developments, on for example seeding and pulse slicing, more substantial future up-grade routes should be kept in mind from the start.

A Stage 2 upgrade could then tackle the increase of the photon energy to the 1.5 keV photon limit and beyond, increased repetition rate (to 10 kHz or higher), and implementation of advanced pulse slicing techniques that couldn't be up-graded through routine facility development. An energy up-grade will be a relatively costly and disruptive step as it entails adding additional accelerator modules to increase the primary electron beam energy. Provision of a tunnel long enough to accommodate an increase in the linac length is a requirement. Increasing the repetition rate above 10 kHz would be feasible if a higher repetition rate gun is developed (not yet available but it is predicted to be possible in future) and a CW superconducting linac were adopted. It will not be possible to increase the repetition rate above ~500Hz if a non-superconducting technology is adopted. At the end of Stage 2 the facility would have all of the capabilities required for the science drivers identified in this report (if the high repetition rate is available – see additional note).

The potential for a Stage 3 up-grade to further enhance the facility should also be considered, perhaps waiting for technological advances that may make higher repetition rate or photon energy cheaper and more feasible than using current technology. Extending the spectral coverage of the FEL fundamental to higher photon energies (>2 keV) is a potential future aspiration. This would usually require either the increase of the linac energy (by adding acceleration modules) or a reduction in the undulator gap. It is desirable to retain the option of a potentially strategically important upgrade route to a UK hard X-ray (~8 keV) machine in the case that single macromolecular imaging were to become as successful as current protein crystallography. Adding extra undulators to be served by electron bunches switched from the main linac path could take advantage of a higher repetition rate to increase the number of beamlines and end stations to deliver more science. This would be moderately expensive but would be potentially very beneficial. Adding a second soft X-ray FEL served by the same electron bunch synchronized to the main FEL is also desirable to enable two-colour X-ray experiments. This will be a

technical challenge as the effect of the first FEL on the electron bunch will be to degrade it significantly. In the meantime a second soft X-ray field can be provided by HHG from a synchronized laser.

4. HIGHLIGHTS OF INITIAL SCIENCE OBJECTIVES FOR NLS

In the following section we discuss a number of example science projects that may form the highlights of research on NLS for the first three to five years of operation. Most would be achievable, at least in part, with a facility with the Stage 1 baseline specification. They have been selected as each has a coupling to significant UK expertise and current activity, these topics emerged strongly from the community consultation. They capture some of the excitement and opportunities NLS can provide. They do not comprehensively explore all of the NLS potential but rather serve as a sample of the science we believe is achievable.

We caution that the projects that follow should only be regarded as examples of potential experiments that could be carried out and not concrete experimental proposals. At this early stage, before a facility specification has been determined, it is impossible to "design" an experiment so these examples must be treated only as sketches. Also the science will continue to evolve in the period (at least five years) before first light so it would indeed be a surprise if what follows were a complete list of first research projects. In any event if NLS is built a peer reviewed system to call for and competitively select proposals will be in place so there will be every opportunity for new ideas to emerge.

4.1 NANOSCALE IMAGING

4.1.1 Development of Sub-Cellular Imaging

Imaging of cells is an exciting opportunity for the NLS using radiation in the soft X-ray region. Recent calculations show that resolutions approaching 1-2 nm could be reached on micron sized living cells in diffraction-limited geometries with radiation wavelengths between 1.5 nm and 4.8 nm and intensities around $10^{10} – 10^{11}$ photons per μm^2 and pulse length 20-50 fs [7]. It is anticipated that NLS will deliver these specifications (and superior). For non-reproducible particles such as living cells, uniformity cannot be assumed and radiation damage demands that information has to be obtained from a single shot. More work is needed to develop the methods to deliver high resolution and to deliver 3D images. We anticipate that considerable advantages will result from using the NLS as it is well matched to address the soft X-ray region for cellular imaging, while the other new sources (e.g. LCLS and XFEL) develop the capabilities for hard X-ray imaging at the molecular level.

Important proof of principal experiments to test X-ray imaging on the fs timescale for biological specimens have been successfully completed in the work of Janos Hajdu (Uppsala) and Henry Chapman (DESY) [5,6] and unpublished results (figure 3), which were described at the NLS life sciences workshop. Their work uses the principle that scattering can be recorded before X-ray damage occurs, provided that the X-ray pulse is short enough. The first biological specimen, photosynthetic picoplankton, mounted on a solid silicon nitride support had been imaged with a 10 fs pulse of wavelength 13.5 nm. A novel spray mechanism for injecting the specimen into the beam has been developed. Image reconstruction of micro-organisms with 7 nm radiation has so far been achieved. The results from FLASH, operating in the VUV wavelength region, are an impressive start. The soft X-rays available from NLS will be of immediate utility in extending these concepts into the water window. Radiation damage is the primary factor limiting the CDI experiment in biological samples. If only one copy of a sample is available, an approach to avoid this limit is to collect the data very rapidly, faster than the timescale of the atomic vibrations, roughly 10 fs, as described above. Depth penetration could be as great as 20 μm. By exploiting the appropriate wavelengths, as indicated by Bergh et al [7] a resolution approaching 2 nm for realistic intensities and pulse duration appears feasible.

NLS will be engaged initially in proof of principle experiments with test objects fabricated to test these resolution predictions. Nevertheless the goal even in the early stages will be to extend these investigations to interesting biological problems. There are a range of sub-cellular features and processes of current biological interest that would be accessible to study (see section 2 for other examples). Thus for an individual cell it might be possible to image, for example, the mitotic spindle as it forms during mitosis with details of the centrosomes and their microtubule organising functions,

of the kinetochores and their attachment to chromosomes and microtubules, and the events leading to the separation of sister chromatids through breaking of cohesin; or the organisation of protein complexes on the surface of mitochondria and events associated with cellular mitochondrial energy and apoptotic functions; or the structure of intact membranes and their associated proteins at different functional states say in response to hormonal and neuronal stimulation.

Optical microscopy has advanced spectacularly through the power of the fluorescence confocal microscope and recent developments to overcome the diffraction limit on resolution. In special circumstances resolutions of ~30 nm have been obtained with living cells but more commonly resolution is limited to 100 nm. These advances are having immediate applications to medicine. For example at the workshop, work was described [40, 41, 42] in which sites of protein interactions associated with cytoskeleton remodelling on specific membrane protrusion structures in the cell periphery had been mapped between Cdc42 (a GTP activated protein) and PAK1 (p21 activated kinase 1) in response to GTP. These events could be correlated in real time as an immune cell probed a series of cancer cells. In vivo imaging has allowed the longitudinal tracking of cancer cells in the mouse and endoscopy imaging of many important complexes such as CXCR4 complexes and PKC/ezrin interactions. The detection of image traits associated with cancer invasion, derived from patient cancer tissue microarrays, could provide a diagnostic marker for metastasis. In these studies there is a requirement to extend the resolution so as to be able to visualise the precise subcellular location of the protein complexes. By combining high resolution X-ray images of cells (initially flash-frozen but eventually live) at defined time points with images from live cells using optical microscopy such understanding could be achieved. This is an exciting early challenge for NLS that will harness the already flourishing expertise in the UK biomedical imaging community.

4.1.2 Imaging nanocrystals

Strain field dynamics in nanocrystals can be studied with the NLS using a vacuum backscattering geometry with a direct-detection pixel detector surrounding the incident beam. For example, backscattering of the Au(111) Bragg reflection requires a photon energy of 2630 eV, which is achievable at NLS. Coherent diffraction patterns of Au or other nanocrystals, mounted as grown on a substrate, could be collected in a single shot and inverted to real-space images of the crystals using suitable iterative phasing methods. Focussing of the beam using a Fresnel zone plate would allow access to relatively small crystals in the range of 100 – 500 nm, where dynamical effects would not distort the diffraction pattern too seriously (although this would require testing).

As shown previously [3], the amplitude of such real-space images corresponds to the shape of the crystal, while the phase represents a projection of the internal displacements from the ideal lattice, which is highly sensitive to strain within the particle. Lattice displacements of a small fraction of an atomic spacing are routinely visible.

The new opportunity at NLS concerns pump-probe experiments of single-shot diffraction patterns following laser excitation of the nanocrystals. Laser-induced melt fronts could be followed comfortably as it would take 100 ps to traverse a 100 nm particle. The initial stages of the build-up of the melt front would be visualised as a strain field or a region of reduced density. Laser induced mixing, phase transitions and shape changes would all be accessible.

4.2 FLUCTUATING AND RAPIDLY EVOLVING SYSTEMS

4.2.1 Complex correlations and fluctuations in solids

Some of the most difficult questions in modern condensed matter physics are related to the physics of complex solids. These are highly non-linear systems in which the choice of ground state is dictated by a subtle balance between the energetics of multiple degrees of freedom. The free energy landscape is then a very rugged terrain with multiple competing local minima, and an enormous degeneracy of states on similar energy scales. These are reminiscent of “glassy” or “liquid” states and exhibit very

large sensitivity to external stimulation, leading to spectacular phenomena like colossal magneto-resistance, where a change in resistivity of nearly ten orders of magnitude may be triggered by the application of a moderate magnetic field. Some have compared this behaviour to the spectacular response of chaotic systems to even subtle changes of the boundary or initial conditions. Quantum mechanical coherence is also known to survive up to high temperatures in these systems, giving rise to superconductivity well above 100 K and indeed on a similar energy scale as room temperature. These are the problems that are very challenging to the physics community, and remain by and large unanswered.

Beyond academic interest, there is also true potential for a revolution in technology, leading to a world where magnetic storage would become orders of magnitudes denser and faster, where high critical magnetic fields from room-temperature superconductors would lead to frictionless mechanics, levitation transport and where energy transport without resistance would become possible.

In this context, it is imperative to understand the type of physics that stabilizes particular states, controls switching between competing ones, or which mediates condensation of Cooper pairs in high-Tc superconductors. One would like to know the type and size of ordering domains that form, their dynamics and the multiplicity of order parameters. All these phenomena are extremely hard to describe with conventional theories of phase transitions.

Multiple pulse experiments that combine holographic imaging with photon correlation spectroscopies would teach us about such complex correlations and fluctuations. For instance in the colossal magneotresistive anti-ferro to ferro-magnetic transition, an orbital-melting transition, an insulator-metal transition and a structural transition all coexist and dominate the physics. Can we separate the fluctuations in each degree of freedom as an external parameter is slowly varied? Can we extend static diffraction experiments from atomic, orbital, spin and charge lattices (all demonstrated with 3rd generation synchrotrons) and bring this methodology to a combination of holographic imaging and X-ray Photon Correlation Spectroscopy? Currently some seed experiments are being performed at the FLASH facility in Hamburg [43], and a new generation of these will become possible with new sources. The anticipated capabilities of NLS would be a very good match to the requirements of such research and would significantly extend beyond the FLASH capability in terms of the wavelength reach. We see that the UK can be at the forefront in this area.

4.2.2 Thomson scattering from X-ray produced plasmas

There is an early opportunity to use a soft X-ray FEL to create and probe the formation and properties of WDM. Thin foils of solid density can be isochorically heated by the NLS beam to produce, warm (10 – 100 eV) matter. The possibility of uniform heating throughout the foil thickness and the very short time of the interaction will set up the ideal situation to track the plasma conditions as they evolve through the WDM state. This could then be probed by harmonics of the NLS beam of higher photon energy via Thomson scattering, to provide information on temperature, density, ionization state, and structure, as well as electron-ion equilibration times. Alternatively, the NLS fundamental pulse would be split into two different beams with different polarizations, one to produce the isochorically heated WDM, and the other to probe the system. By using polarization analysers, we will be able to collect the scattering signal from the probe beam only. There is even the possibility of X-ray diffraction probing at the fifth harmonic. The thickness of foils amenable to isochoric heating in this way will depend strongly on material and the NLS wavelength - ideally, for uniform heating (as a function of distance), the foil should be less than of order 0.2 absorption depths of the radiation in question - e.g. for Al about 0.6 μm for 1.0 keV radiation (Al is a good material at modest temperatures, as up to 10 eV it has a constant number of free electrons at solid density). The 3-5 keV probe radiation (in 3rd and 5th harmonic) is particularly suited to scatter from coupled electron plasma modes, as the spatial scale-length of the plasmons is comparable to the X-ray wavelength. In an inelastic scattering experiments, plasmons as well as ion acoustic modes (phonons) exchange energy with the probe photons, and the scattered radiation shows characteristic resonances in its frequency spectrum. These indeed describe the full microscopic dielectric response of the WDM state. The UK

already has world-leading capability to perform experiments in this area, albeit using the present, severely non-optimal sources.

A powerful new approach to dense plasma measurements, use of a relativistic electron beam to probe a plasma created by the soft X-rays, can be pursued by NLS. Electrons scatter from charge fluctuations, thus the scattering signal is directly correlated to the charge-charge response function, which is different from the density-density correlation function probed with X-rays, and provides a means to investigate the dynamics of micro-field distribution in WDM. In addition, electron energy loss spectroscopy is a powerful technique to measure the stopping power and the integrated static structure in strongly coupled non ideal systems. This has particular relevance for the understanding of energy deposition in WDM states that occurs in inertial fusion energy experiments. The approach suggested for the NLS is a pump-probe experimental configuration where the X-ray FEL beam or a synchronized optical laser is used to produce the WDM state and the electron beam is employed as a probe. By using the relativistic 1-10 MeV electrons generated in a RF photocathode gun and accelerated through compact linac optics, the spatial broadening of the pulse due to Coulomb repulsion can be minimized and time resolution <500 fs can be achieved. To achieve the highest contrast spatial resolution, the linac should be operated at ~1-2 kA in a focused ~50 μm diameter electron beam.

4.2.3 X-ray spectroscopy and opacity experiments

An important initial objective for soft X-ray spectroscopy with the NLS would be in the area of the creation and observation of hollow ions. These states are automatically produced when atoms are illuminated by intense X-rays and are an intrinsic feature when NLS interacts with matter. There will be considerable overlap here with the experimental goals of the atomic physics community, who wish to observe hollow atoms and ions produced in, for example, the interaction of the NLS beam with a gas-jet target. The interesting point here is to use hollow ions as a powerful new diagnostic of the conditions within dense plasmas. If the NLS irradiates a plasma (produced, for example, by optical laser-matter interactions), then the hollow-ion X-ray and XUV spectra provide a unique diagnostic of the ionic state and plasma conditions – the details of the complex recombination K-shell spectra depend on the occupancy (or otherwise) of the *L*, *M* (etc) shells, which of course is dictated by the temperature and density within the plasma.

Coupling of a 10 Hz optical system to the NLS will also allow us to obtain detailed opacity measurements of dense plasmas produced by the optical system. Such experiments have, in the past, produced limited information due to the technical difficulties in obtaining bright X-ray back-lighters to probe dense matter (that said, the information that has been gained has often proved invaluable - e.g. opacity measurements of hot-iron plasmas, made with laser-plasma sources, led to revisions in opacity tables and calculations that had an impact on the prediction of the behaviour of Cepheid variables, and in turn the Hubble constant). The high brightness monochromatic NLS beam should eliminate many of the problems normally encountered in such experiments.

4.2.4 High density matter

As well as isochoric heating, a further exploration of the parameter space of hot, dense plasmas could be achieved if the NLS is coupled with a high-power relatively high repetition rate nanosecond laser. Diode-pumped systems are now being in existence that can produce 100 J, 1 nsec output at 10 Hz. It is more than likely that 1 kJ modules of such systems, required for the HiPER project, will be available on the NLS construction timescale. To our knowledge no other 4th generation source has plans to couple technologies in this way, and such a step would set the NLS apart from many of its competitors.

With such a nanosecond laser system one could pre-compress (by laser irradiation) foils, that are then probed with the NLS beam (with similar X-ray photon energies to those stated above). We note that a nanosecond optical laser is a requirement for such experiments, as the typical compression (shock)

velocities in matter are on the 10^4 ms^{-1} timescale, requiring of order several hundred ps to traverse a few micron thick foil when shocking it, and longer if one wishes to keep it off-Hugoniot via ramp compression. At high laser irradiances, and fast rise times, ($>10^{14}$ $W.cm^{-2}$) highly compressed hot plasmas can be produced, which greatly extend the parameter space from those simply produced by isochoric heating. These can once more be probed with the NLS via Thomson scattering.

Molecular-dissociation, partial ionization, strong coupling, nonlinear transport, and indeterminate quantum statistics make the matter produced in this way very complicated but is a state that any solid must pass through en route to becoming a plasma. As noted above, matter of this type is of relevance to the physics of planetary interiors, being similar in nature (in terms of densities, temperatures, and coupling parameters) to those found towards the centre of the giant planets. Such conditions also prevail within inertial confinement fusion pellets during the implosion phase, and accurate prediction of capsule trajectories relies heavily on a detailed knowledge of the EOS in this regime. Thomson scattering allows direct measurement of the structure factor of such systems, which is closely related to the pressure. Details of the Thomson spectra (plasmon modes) are also sensitive to the electron-ion collision time - which is also unknown in this regime owing to the difficulties in calculating Coulomb logarithms. Measurement of this timescale is crucial for an understanding of all transport properties of such plasmas.

4.3 STRUCTURAL DYNAMICS UNDERLYING PHYSICAL AND CHEMICAL CHANGES

4.3.1 Bulk Fermi-surface dynamics from time-resolved high-energy ARPES

Mapping the temporal evolution of the electronic structure of condensed matter systems is an exciting new possibility enabled by NLS. Angularly resolved photoelectron spectroscopy (ARPES) studies of the equilibrium near-surface electronic structure of complex materials such as the high-temperature superconductors have shaped our understanding of correlated electron systems. A new FEL source with sufficiently high flux per unit bandwidth in the near-keV region provides a prime opportunity for transforming ARPES to accessing non-equilibrium electronic states with sensitivity to bulk properties of solids.

This offers exciting prospects for the study of relaxation phenomena, electronically driven phase transitions or novel photo-induced states. Bulk sensitivity would result from longer escape depth of energetic photo-electrons. The decrease in photoemission cross section could be compensated by gain in average flux. Time resolution would result from a pump-probe scheme exploiting the shorter pulse duration of FEL sources. Due severe space charge distortion of the ARPES spectra only relatively small numbers of photoelectrons per shot are tolerable and so to accumulate good quality data a high repetition rate is needed. A 1-10 kHz initial repetition rate of the FEL would be sufficient for early studies, but future work will be extended if the repetition rate is increased to >10 kHz.

4.3.2 Determination of mechanism in chemical catalysis

Use of pump-probe techniques employing a range of IR/visible pump and X-ray probe photon energies marks a step function change in ability to measure catalytic reaction dynamics. The use of X-ray techniques such as XAFS, XANES, XES and XPS will be the key enabling probe technologies of catalytic processes both in heterogeneous and homogeneous systems. Catalysis is one example of the application of NLS to complex chemical reactions, including solution phase chemical dynamics, where we believe it will have a very broad impact.

Over the past two decades, laser and synchrotron techniques have allowed for the measurement of static active site structures and atomic architectures under catalytic conditions. These measurements, when combined with computational models, have advanced understanding of catalysis significantly. However, while current computer models are able to offer predictions of key chemical intermediate and transition state structures, we currently lack the experimental ability to resolve the dynamic structural changes that occur on the ps and fs timescales associated with chemical reaction, and so

only static pictures of structures averaged over a multitude of molecular processes are obtained. As a result we know little about the structure of transients, and virtually nothing about the charge and energy transfer occurring during the primary steps of catalytic reactions. In order to advance catalysis design further it is necessary to develop new techniques for probing catalytic reaction dynamics on the femtosecond timescale in order to allow for true mechanistic measurements to be made. Such advances, when combined with advanced models enabled by upcoming advances in petascale computing, will allow for new models of catalytic mechanism and improved catalytic design.

A fundamental aspect of catalysis is that many reactions are thermally driven at around room temperature, and this motivates a desire to carry out pump-probe studies with a pump closely mimicking thermal activation. Short pulse radiation in the 1-20 THz region provides a potentially useful resource for mimicking thermal initiation of catalytic processes through broadband impulsive excitation. A deep IR/THz pump source tuned to excite the substrate phonons, metal-adsorbate modes or adsorbate internal modes could also be used in heterogeneous catalysis to allow direct investigation of the each region on the overall reaction mechanism. This would enable rational catalyst design to be achieved by identifying which modes of a system promote a desired reaction, and by maximising the number of relevant active sites. Surface photoreactions can also be driven by a visible or near-infrared pulse to excite hot electrons in the substrate, which may thermalize and couple to the adsorbate within the first picosecond. Alternatively, the hot electron bath may excite phonons within a few picoseconds and these phonons, in turn, can couple to the adsorbate and initiate a reaction. Importantly, the pump-probe experiments will not just involve the use of structural/electronic probes such as EXAFS but also surface IR to detect adsorbed species and using the time resolutions available combined with gas phase measurements of the products formed provide information regarding spectators and reactive intermediates on the surface. The correlation of the transient timescales using a range of techniques is very powerful and the NLS has the potential to provide significant input and a step change in our understanding.

Homogeneous catalyst systems are typically single site materials and thus ideal molecules on which to probe reaction mechanisms in detail and, in this case, provide an understanding of the true active state of the catalyst by using spectroscopic probes with timescales shorter than that of a typical molecular vibration. Visible and UV pulses may be used to photoinitiate a process via electronic excitation, or by multi-photon excitation with IR radiation in the solvent transmission window. Direct monitoring of the products at high time resolutions in the liquid phase may not be possible in this case; however, X-ray and IR/Raman will be used to examine the changes in the coordination sphere as a function of time following the NLS pump.

Nanoscale imaging would also be of significant benefit to heterogeneous catalysis, in particular where the imaging can be performed under reaction conditions. In-situ high resolution transmission electron microscopy has been pioneered by Haldor Topsøe and is very powerful but is limited to gas phase reactions and then only at low pressures. As stated for biological systems, if resolutions approaching 1-2 nm could be achieved in the X-ray region, this provides the possibility to image supported metal clusters under realistic pressures for gas phase reactions as well under liquid phase conditions for the first time. Metal particle sizes of this dimension are typical for many oxide and carbon supported materials but often the shape of the particle is not well understood. Given that the shape, as well as the size, determines the proportion and type of defect sites present, an understanding of the metal particle profile is of significant importance. Where this technique may be very powerful is for carbon supported materials utilised in organic solvents. These materials are often used for liquid phase fine and pharmaceutical chemical transformations, such as selective oxidation and hydrogenation reactions, and imaging would provide morphological changes of the metal with the support and the solvent being effectively invisible to the probe. Furthermore, in-situ spectroscopy, such as EXAFS, combined with the spatial resolution in this regime would provide important correlated information concerning the local and long range environment as a function of the reaction conditions and an in depth understanding of how catalysts work in both the liquid and gas phases.

There is a myriad of reactions in both heterogeneous and homogeneous catalysis where this information is of critical importance, but there is clearly a need to make a relatively simple initial choice of system for study. Supported Au catalysts have shown a remarkable activity in a variety of industrially-important low-temperature oxidation reactions, such as the oxidation of CO [44]. Despite extensive investigations of powder and model catalysts the mechanism by which molecular oxygen is activated in these reactions is not understood. Gold single crystals are inactive towards oxygen unless energy is provided to break the O-O double bond. Activation of O_2 on the gold particles has been observed for TiO_2 and Al_2O_3 supports. On the other hand, for reducible supports (such as TiO_2) it has been suggested that this step proceeds on the support, which then provides active oxygen to the gold cluster. This view is supported by the low reactivity of bulk gold towards O_2. DFT calculations [45] predict two oxygen activation pathways for gold supported on oxides: (i) an activation on the gold cluster and (ii) activation on the support oxide. However, experimental data elucidating O_2 activation over these catalysts is scarce, and there is an urgent need to disentangle both the individual and cooperative roles played by gold, the adsorbates (including reactants and spectator species), and the support materials. Pump-probe spectroscopy with combined XAS and IR probes will allow the reaction mechanism to be established, distinguishing between the alternative proposed schemes illustrated in Figure 8. Combined access to the Au M edges (~2200 eV), the O *K* edge (~500 eV) and the C *K* edge (~300 eV) will be required to probe individual pathways within the network of elementary reactions. Especially where putative "oxidised" Au species are proposed, the XANES-type information available at the Au $M_{4,5}$ edges will be particularly important. Initial activation of the physisorbed oxygen (which initiates reaction) can be achieved by either electron or VUV photon irradiation [46]. We anticipate a temporal resolution of some tens of ps will be achieved in initial experiments of this type, moving to some hundreds of fs as the experiments are optimised.

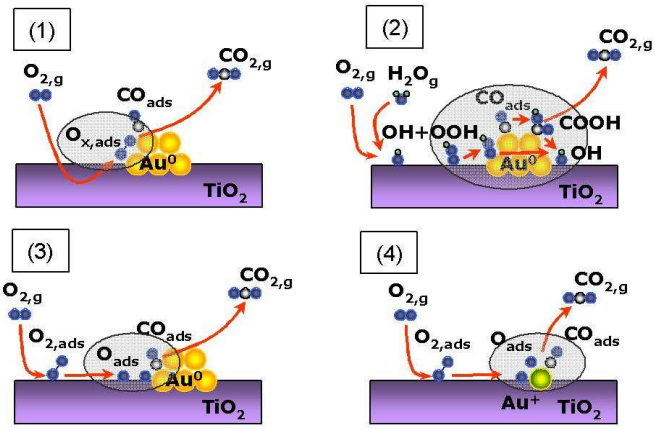

Figure 8 (1) Current mechanistic understanding of the reaction sequence leading from molecular O_2 to its dissociation and/or reaction with CO to CO_2 over supported Au. Note that the nature of the reactive oxygen species remains unspecified as $O_{x,ads}$ (2) Thermodynamically plausible, but experimentally unverified, sequence of elementary reactions leading from the adsorption of O_2 to CO_2 in the presence of moisture. (3) Langmuir-Hinshelwood type reaction of O_2 with CO. Experimentally not verified. (4) Alternative reaction scheme to (3) but involving a cationic Au species as the active site. Experimentally not verified. Reproduced with the permission of Sven Schroeder.

4.3.3 Chemical dynamics in isolated molecules

Understanding the structure and dynamics of isolated molecules has been key to developing an understanding of chemical reaction dynamics. Techniques for studying gas phase samples are appealing as it allows for the removal of environmental effects in order to study nascent molecular properties.

Time-resolved photoelectron spectroscopy (TRPES) has emerged as a powerful and general technique for studying the flow of charge and energy in molecular systems [22], revealing important information regarding the non-Born-Oppenheimer coupling of nuclear and electronic motions governing excited

state dynamics. The NLS will allow an important extension of this technique to allow the ejection of inner shell electrons which will provide critical new insight into molecular structural dynamics. In TRPES measurements performed to date, it is the valence electrons which are both implicated in the neutral dynamics following pump excitation, and also ionized in the probe step. As such, although valence ionization does carry the fingerprint of the nuclear dynamics, it is logical to also consider ionization of inner valence and core electrons which would be made possible by the availability of femtosecond probe pulses at > 100 eV. Such experiments would yield complementary information regarding nuclear motion to conventional valence ionization, since the core level ionization thresholds of constituent atoms depend sensitively upon the chemical environment within the molecule. While chemical shifts are reflected in the binding energies of core electrons, far more detail about the molecular structure is available from the photoelectron angular distribution (PAD) following core level ionization. The photoelectron angular distribution is a diffraction pattern created by the electron wave as it leaves the molecule and scatters off the molecular potential – core electron ionization in a sense "illuminates the molecule from within". Such techniques have also been shown to be sensitive to chirality [47], and provide a way of probing the dynamics of enantiomerically selective processes.

X-ray photoionisation may also serve as the pump process, initiating a chemical rearrangement. For example carbon *K* shell ionization of acetylene at 310 eV triggers a fast rearrangement of the resulting acetylene ion to the vinylidene ion, which is expected to occur on a sub 100 fs timescale, and competes with Auger decay [48]. Time-resolved probing of such nuclear rearrangements upon core shell ionization is presently challenging, but is enabled by the NLS through the availability of femtosecond XUV pump and probe pulses. The potential of using X-ray ionization to probe the time evolution of electron correlation in molecular systems is also possible with the capabilities provided by the NLS (see section on Ultra-fast Electron Dynamics).

Measurements made on gas phase samples typically suffer a reduction in information due to averaging over the random orientations in the sample. In recent years, molecular axis alignment and orientation using strong non-resonant IR laser fields has been demonstrated, and offers a general route to avoiding the orientational averaging. The extension of these techniques to larger molecular systems requires intense IR and THz radiation at wavelengths beyond those currently available from conventional lasers, and will require the ability to deliver polarization tuneable pulse sequences on target. The provision of this capability in conjunction with the X-ray capability of NLS offers exciting new prospects for highly refined structural measurements. Furthermore, the IR may be exploited for conformational control and selection in extended molecular systems which would otherwise be present in all thermally accessible conformations. In this regard IR double resonance and hole-burning are expected to be of great utility for conformational selection. The possibility of using high intensity deep IR fields to provide internal forces to molecules in order to control conformation is an exciting and largely unexplored area which will be enabled through the NLS capabilities.

Finally we note that with recent advances in cluster production, helium droplet encapsulation [49], and electrospray techniques it is now possible to systematically study intermolecular interactions in gas phase systems, and use size controlled clustering to mimic inner salvation shells. Also, advances in microjet and microfluidic technologies now allow for gas phase techniques to be applied to gas-liquid interfacial problems [50]. The time-resolved techniques for structural dynamics of gas phase molecular systems described above will be directly applicable to these richer and more complex systems, and the high photon flux of the NLS is a key advantage here as such extended molecular systems are often exceptionally dilute due to their preparation methods.

4.3.4 Pump-probe studies of the dynamics in biological macromolecules.

The following examples of research into biomolecule and biochemical ultra-fast dynamics are all enabled by the capabilities of NLS to provide high brightness photons in the THz/FIR or X-ray range. There is a strong coupling of each example to activity within the UK research community. The examples given below are based on ongoing work where the extension to a faster and brighter long

wavelength source would require some innovation in instrumentation but could be implemented relatively easily based on existing technology.

(a) Enzyme catalysis Structural, kinetic and mutational data over the last 40 years have provided an understanding of enzyme catalysis for many systems based on transition state theory. Chemists now seek a more detailed explanation, for example, of the time-resolved events by which a hydrogen or hydride ion may be transferred by tunnelling mechanisms at rates (~ 2 x 10^6 s^{-1}) that seem faster than allowed by the current static structures of enzymes. There is a need for sub-ps high power THz radiation to promote molecular motions in macromolecules followed by probes in visible or IR to understand how conformational dynamics map to chemistry in enzyme catalysis [51]. Accurate measurements of spectra will provide information on the lifetime of promoting vibrations and yield insight into energy transfer processes. Careful synchronisation of the THz pump with initiation of H-transfer catalysis, possibly through light activated catalysts as already used, would be required.

If an electron beam were available for pulsed radiolysis new opportunities are opened up in studying enzyme catalysis. Metalloenzymes are of particular interest, whilst structures with atomic scale resolution of hydrogenase, light harvesting systems and photocentres are now available detailed dynamics are still missing. Electro-injection or removal can be achieved using radiation chemical methodology and complements results obtained from photoinduced measurements. The spatial and temporal resolution of the oxidation/reduction steps are needed to unravel the dynamics of the structural changes necessary for the catalytic action. These will be best achieved by combining pulse radiolytic pump with time-resolved EXAFS probes, which will also enable the study of systems containing spectroscopically silent metal ions such as zinc proteins.

(b) Identification of the transient intermediates in DNA damage. Living organisms regularly encounter ionizing events that could promote DNA damage, mutation and the onset of oncogenic transformations. Whilst only a few of these events result in irreversible damage they do nonetheless represent a threat. The chemical processes involved in DNA damage and repair stretch across the time domains from femto-seconds to seconds. Time-resolved vibrational spectroscopy allows a direct structural probe in solution to investigate the nature of the excited states, the inter- and intra-relaxation times leading to chemical modification of nucleic acid bases, (e.g different tautomers, pyrimidine dimer formation, radical formation) following DNA irradiation by UV light. Pump-probe measurements in which UV photo-excitation was followed by time-resolved infrared spectroscopy have provided an in depth understanding of the photo-excited states using both model compounds and DNA with time resolutions in the ps range [52,53,54,55]. However such studies are limited by the wavelengths obtainable from the laser sources. There is a need to access sub 1000 cm^{-1} region to understand the role of low-lying modes and to translate the complex vibrational fingerprints into definable structures. The experiments require a fully tuneable source of high intensity with frequencies 10-4000 cm^{-1} (in a single shot).

(c) Structure and conformational responses in the extra-cellular matrix The glycosaminoglycans, e.g., heparan sulfate, hyaluronic acid, are components of the extracellular matrix and contribute to the regulation of cell/cell communication and signalling. Little is known of their overall conformation and how their conformations respond to stimuli. Spectroscopic methods have been applied to study the extracellular matrix using synchrotron CD and vibrational spectroscopy with IR, UV. Vibrational CD (in the infra-red region) has been used to probe for structure fingerprints and conformational response of effector proteins during their activation by the sugars [56,57]. Further progress in the field requires sources with high peak power because of the low concentration of the macromolecules in physiological conditions (μg/ml).

4.3.5 Laboratory astro-chemistry

A major motivation for laboratory astro-chemistry at the NLS is the ability to measure the spectroscopy and dynamics of short-lived chemical intermediates. Accurate measurements of absolute cross sections of spectroscopic transitions in both stable and transient (free radical) species will allow

accurate modelling of the chemistry [58] and of a wide range of physical parameters, including density, temperature, elemental abundances, and the freeze out of molecules on to dust grains in both stellar and interstellar mediums. The availability of soft X-rays and pulse radiolysis for creation of transient species with synchronized THz/IR/UV-visible spectroscopic techniques presents a key opportunity to remove the reliance on purely computed parameters in current astrophysical models.

The importance of gas-grain chemistry to chemical evolution in the inter-stellar medium has become clear in recent years and provides motivation for understanding the primary chemistry of ion-grain chemistry, and its interplay with gas phase ion-molecule chemistry. Combining ion beam sources with X-ray and IR structural probing will allow for a new class of measurements to be made examining the chemistry occurring when the surface of dust grains and single nanoparticles are irradiated with ions.

A key question that the NLS will also be able to address is the origin of the primary asymmetry in biological molecules. All biologically relevant amino acids are left handed while the sugars that form the energy source and constructional material in many biological systems are right handed. Already numerous experiments are showing us that photon- and low energy electron-induced processes in simple ice mixtures can result in the formation of pre-biotic molecules. But this chemistry is achiral – it does not introduce a handedness into the reaction products. A range of mechanisms have been suggested that could result in the necessary enantiomeric excess that include photodestruction of specific enantiomers by circularly polarized VUV/XUV in the gas phase or in the icy mantle, and the enantiospecific electron induced desorption from particles following irradiation with circularly polarized UV radiation to produce spin polarized electron emission from the substrate surface. The combination of X-ray, IR, and optical laser based probing with synchronized circularly polarized VUV pumping will allow the chemical mechanisms giving rise to this primary chiral asymmetry to be elucidated.

4.4 ULTRA-FAST ELECTRON DYNAMICS

4.4.1 X-ray interaction physics

Cross sections for the non-linear response of matter to high intensity soft X-rays can be systematically measured by NLS in atoms, molecules and clusters. NLS can greatly improve on existing studies (e.g. at FLASH) by delivering a wider photon energy range (e.g. 20 eV- 500 eV) and by improved shot to shot stability of energy and temporal profile through seeding across this energy range. Few femtosecond soft X-ray pulses will allow new understanding of the ultrafast response of many electron systems to high intensity high-frequency light. Photon energies in the range from 20 eV to a keV are of interest for these measurements (for harder photons multi-photon cross-sections are likely to be vanishingly small and the linear processes will dominate). Extension of the NLS to provide sub-femtosecond pulses which approach the timescales of electron motions will further refine our understanding.

Developing an understanding of the ultrafast electronic dynamics occurring upon interaction with short-pulse high intensity X-ray pulses is a key area where the NLS will further international efforts towards the goal of single molecule and time-resolved measurement. There is currently considerable international activity focussed towards the long-term and high profile goal of imaging the static and dynamic structure of single molecules via X-ray diffraction. Other methods to achieve the measurement of structural dynamics, including time-resolved photoelectron techniques and time-resolved X-ray absorption (e.g. EXAFS) are dealt with elsewhere in this report. Although these are powerful techniques for elucidating local structural dynamics of a part of a complex system it is anticipated that time-resolved X-ray diffraction will give complete global structural and dynamical information. For the successful realization of the single molecule X-ray imaging concept, freezing the motion of nuclei is critical since the high X-ray fluxes cause massive structural disruption. Currently it is posited that pulses less than 10 fs are sufficient to achieve this – but sub-femtosecond electron dynamics may also be critically important as X-rays must scatter from the bound electrons to provide the images. Indeed, since severe multi-electron ionization results in electrons with 100’s of eV energy,

it is anticipated that electrons will leave the target on attosecond timescales. The subsequent decay dynamics of the remaining highly perturbed electrons (through e.g. Auger decay, autoionization) is poorly understood, but critically important for the realization of this technique. The availability at NLS of a ~10 fs, 50 eV- 7.5 keV FEL source will allow this problem to be addressed directly, through studies of the photoelectrons and fragmentation of large molecules, clusters and nanostructures.

4.4.2 Measuring multi-electron dynamics

It is anticipated that NLS will provide the capability, through the HHG sources and the possibility of intense sub-fs soft X-ray pulses from the FEL, to make completely new types of measurements that uncover ultra-fast electron dynamics. These fall into three categories: (a) following hole dynamics in matter formed by near instantaneous photoionization, (b) directly measuring electron correlation in multi-electron systems by measuring the signatures in two-photon, soft X-ray ionized, photoelectrons, and (c) real time tracking of coherently excited electron motions induced by controlling laser fields.

A powerful approach to studying ultrafast electron dynamics in matter is through following the relaxation dynamics of a system following removal of an electron, or in other words, observing the "hole dynamics". In this approach, an electron is first rapidly removed from a bound valence or inner shell state (with a short pump pulse) and the evolution of the remaining electrons into new states observed using a photoionisation probe. This approach requires either attosecond pulses as both pump and probe, or, alternatively, another fast event may be used as the pump (e.g. strong field ionisation). Recent work using existing HHG methods has established this methodology for atomic samples, but extension to more complex systems requires the wider spectrum of photon energies and fluxes available from a FEL source. Examples of the sort of thing that is of current interest are the measurement of hole dynamics in molecules and condensed matter (expected to happen in $10^{-15} – 10^{-17}$ s), electron dynamics and damping in plasmons (of increasing interest to frontier technological applications of nanoplasmonics), and observing the photoelectric effect from multi-electron states in real time. These topics lie at the heart of material response to electromagnetic fields and so the outcomes may lead to a better understanding of the interaction of large molecules and other extended systems with light and to new generations of optical and electro-optical devices and ultrafast semiconductor and nanofabricated components.

Fundamental understanding of electron correlation can be gained by working in the soft X-ray regime in which we are able to preserve the electron coherence in direct multi-photon double ionisation induced by a strong X-ray field. Phase sensitive measurements of single electron wavepackets are presently an emerging tool using high intensity visible lasers, and the NLS will build on this ability by combining short pulse XUV and strong-field conventional laser physics to achieve phase and amplitude measurement of two-electron wavepackets. For example, an XUV pump can induce a multi-photon double ionisation of a free atom or a molecule creating a two-electron wavepacket. A pair of such wavepackets can be created in the presence of a mid-IR coherent dressing field by using two slightly delayed replicas of the XUV pulses. The mid-IR field induces a controllable momentum shear between the wavepackets. This results in modulations of the wavepacket interference as a function of the pump-probe delay from which the amplitudes and phases can be extracted. Standard coincidence techniques can be used to record phase and amplitude correlations on two-electron energy maps, although a high repetition rate (> 1 kHz) will be required to ensure good map statistics. Pump-probe coherence can be maintained by deriving the mid-IR beam from the laser used to modulate the electrons for the required pulse slicing to produce the XUV pulse and controlling its stability relatively to the FEL radiation path. From such measurements the original state can be recovered, including its coherence and electron correlations. This will be a huge step in our ability to measure electronic dynamics and will provide unprecedented insights into complex systems, where there may be multiple states and couplings at play, and provide a handle for optimising their control.

Coherent control of material processes (physical and chemical) relies upon the generation and manipulation of electronic quantum coherence through interaction with electromagnetic fields. Since electronic excitation is typically used to mediate the control, even if the end result is control of a

nuclear coordinate, future improvements in the engineering of coherent control schemes will require an ability to manipulate and measure on timescales shorter than the optical oscillations (i.e. sub-fs). "Instantaneous" probes in the soft X-ray with pulse durations much shorter than the electron coherence periods (i.e. driving laser periods) will allow observation of the evolving electronic coherence through ionization, or the measurement of scattered radiation. This will require sub-femtosecond soft X-ray pulses synchronised to shaped control laser fields with a precision of ~50 as which will require pulse slicing. With this ability we anticipate a step function change in our ability to design optimal laser fields for coherent control, with major potential benefits to nanofabrication and pharmaceutical syntheses.

4.4.3 Attosecond photon source science

NLS would provide the facilities required to investigate the science to develop true sub-femtosecond and fully coherent soft X-ray FEL. Those discussed below need to have features anticipated in the initial machine design but all constitute rather straightforward up-grades when they are to be implemented.

The simplest method to reduce the poor temporal coherence of the SASE output is to seed the FEL amplifier with a resonant seed source. It has been shown via simulations, using conservative estimates for seed pulse energies from HHG sources, that this is feasible for wavelengths >10 nm to generate pulse lengths ~40 fs. These results concur with recent experiments demonstrating the principle at 160 nm. This method gives significantly improved temporal coherence, close to the transform limit, and the potential for short pulse generation with FEL output having approximately the same duration as the seed or the FEL cooperation length, whichever is longer. It can be anticipated that there will be a phase relationship between the seed input and output fields of the FEL and, for seed sources such as HHG and RHHG that require a long wavelength drive laser, that a phase relationship also exists between the drive laser and FEL output. The repetition rate is limited to that of the seed source which for current HHG sources is ~10 kHz. There is a clear synergy in the development of HHG-RHHG and FEL sources. As the former improve in spectral reach, peak power, duration and repetition rate, so the simpler are the FEL systems required to achieve target output parameters, and the greater the range of target output parameters become achievable.

Several techniques have been identified that may shorten the pulse durations yet further into the attosecond regime. The most important class of ideas use the pre-modulation of the electron bunch energy by a carrier envelope phase-locked high power IR laser (typically an 800 nm Ti:Sapphire) before the bunch enters the radiator undulator. The resonant FEL wavelength is correlated to this energy modulation, and it is expected to be possible to selectively filter or amplify a narrow wavelength band to generate short pulses with widths of a fraction of the modulation period. The energy modulation also allows short regions of the electron bunch to be correlated to a specific method that preferentially lases at a given electron energy. The above techniques generate single attosecond pulses (there may be smaller satellite pulses about the main pulse) of typical duration ~100-300 as at a target wavelength of $\lambda_1 \approx 1$Å. For these electron energy pre-modulation methods, it is expected that output at longer wavelengths will typically longer pulse lengths, but even at 10 nm these will be ~1 fs.

5 THE CONSULTATION PROCESS

We have been successful in engaging a wide cross-section of the UK scientific community in constructing this case. A full account of this process may be found in appendix 2. Altogether more than 300 individuals have attended NLS meetings. Advice was sought from many who were unable to attend and was received from a good proportion. An e-mailing list of over 900 was used as the primary means for first contact. A dedicated website www.newlightsource.org was set up in March.

Additionally the NLS science team has taken the opportunity to contact, visit and discuss with a large number of scientists in the UK and internationally. Jon Marangos has visited LCLS, XFEL, FLASH, LBL, BESSY, SOLEIL and MAX Lab (Lund) in the course of the consultation. Contacts with Italian and Japanese activities have also been developed. Further details of the international participation in workshops and working groups are given below.

An important early step was to ensure the engagement of the groups of people who had led the two earlier UK FEL activities; the 4GLS project and the Sapphire proposal. We believe we have successfully engaged with these groups through the composition of the NLS team and the working groups as well as through the participation in the workshops.

It is not possible to claim that all potentially interested parties have responded. We have had to operate within tight time constraints imposed by STFC and this may have been a limit to engagement with some. At the time of writing, it is only six months since the consultation process was launched (beginning of April) and in practice the engagement activities had to be confined to the period from mid-April to beginning of July to coincide with the university summer terms. Many individuals, although expressing interest and support for the project, were unable to attend any meetings due to work commitments. Nevertheless we do not believe that that the scope or completeness of this initial science case has been seriously compromised by the short timescale. Nevertheless in phase II it is the intention to significantly widen contact to engage additional groups (e.g. biomedical researchers).

We are enormously grateful to all of those who contributed to the construction of this science case including many individuals both within and external to the working groups. Space in the present document does not permit us to list by name all who participated, but we hope shortly to make available a compilation of all contributors.

Below we give the list of meetings and workshops organized:

NLS Launch, 11th April 2008, Royal Society London

Electron Dynamics/Attosecond Science, 13th May 2008, Imperial College London

High Energy Density Science, 20th May 2008, Rutherford Appleton Laboratory

Condensed Matter, 21st May 2008, Rutherford Appleton Laboratory

Chemical Science, 22-23rd May 2008, Daresbury Laboratory

Advanced Photon Sources, 3rd-4th June 2008, Daresbury Laboratory

Life Sciences, 19th June 2008, Diamond Light Source

International Engagement

NLS is at too early a stage to have sought yet any formal international partnerships or even endorsements. Nevertheless we have been gratified by the enthusiasm and support received by many

leading international experts who have participated in the consultation process including giving talks at the various meetings and participating in the working groups:

Roger Falcone (LBNL/Berkeley, USA)
Marc Vrakking (AMOLF/ Netherlands)
Richard Lee (LLNL, USA)
Hermann Durr (BESSY, Germany)
Fulvio Parmigiana (FERMI@Elettra, Italy)
Andreas Wolf (MPI Kernphyik, Germany)
Christian Bressler (Lausanne, Switzerland)
Bettina Kuske (BESSY, Germany)
Alexander Zholents (LBNL, USA)
Holger Schlard (FLASH, Germany)
Misha Ivanov (NRC, Canada)
Marie-Emmanuelle Couprie (SOLEIL, France)
Paul Emma (LCLS/Stanford, USA)
John Costello (DCU, Ireland)
John Singleton (Los Alamos, USA)
Alexey Kimel (Nijmegen, Netherlands)
Michael Gensch (DESY, Germany)
Vitali Averbukh (MPIKS, Germany)
Filipe Maia (Uppsala, Sweden)
Josef Feldhaus (FLASH, Germany)
Sven Reiche (UCLA, USA)
Luca Poletto (Padova, Italy)
Janos Hajdu (Uppsala/Stanford)

They have helped stimulate and develop the ideas expressed in this case and we look forward to a strong collaboration with these and other leading international experts. Collaboration and partnership with international bodies will strengthen and deepen if and when there is a concrete proposal tabled.

Research Council Engagement

In addition to STFC we have by now had the opportunity to discuss our plans and ideas with EPSRC, BBSRC and MRC. We have received constructive comment and general interest and support from all of these Research Councils. It can only be as the project advances to a more concrete form that we can expect to identify specific areas and mechanisms of deeper involvement with these bodies. At this stage we can report that a constructive engagement has begun and we look forward to developing this further in the coming months.

Engagement with other research councils (NERC), Research Charities (Wellcome, Cancer UK), learned societies is anticipated to begin in the next phase of the project. It awaits the STFC to endorse the next phase of the project before this will be a profitable exercise.

Industry Engagement

It is likewise too soon to begin a full consultation with industry, this is anticipated to begin if the project goes to the second phase. Certain interested parties (including participants in the Industrial Advisory Panel of 4GLS) have already been approached for their views and some useful feedback already received.

6. ECONOMIC BENEFITS OF NLS

Although early in the process we can already identify a number of key technology areas where the science that NLS could produce will provide significant benefit. These include:

- **Catalysis – the revolutionary improvement likely in understanding of the mechanisms of catalysis will benefit the chemical industry**
- **Radiochemistry – unprecedented time-resolved measurement of mechanism of damage mechanisms will result in improved materials for nuclear industry**
- **Biomedical imaging capabilities – new methods will be developed using the high brightness coherent short wavelength radiation that may impact medical research, diagnosis and therapy**
- **Condensed phase dynamics – better understanding of structural dynamics in strongly correlated will benefit for example high speed magnetic recording technology**
- **Accelerator technology – impetus provided to advanced accelerator technology will benefit next generation of compact accelerators e.g. for therapy applications in hospitals**

The NLS project can provide a direct coupling to economic activity in a number of ways. Firstly, as just elucidated, improved understanding of the fast structural changes that underpin high technology (nanotechnology, biotechnology, advanced materials, catalysis etc) will lead to long term benefits to UK industry. Secondly NLS will provide UK industry with access to advanced high brightness X-rays for myriad applications. Further NLS will provide a flow of highly trained manpower with skills in some of the most advanced areas of technology and measurement.

There are also direct benefits to industry through the engagement with industry as contractor and supplier. NLS will stimulate UK/EU industry through procurement of high technology components and systems both during construction and throughout operational lifetime

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APPENDIX 1

Glossary and Common Abbreviations

ARPES	Angularly Resolved Photoelectron Spectroscopy
CDI	Coherent Diffraction Imaging
EM	Electron Microscopy
EOS	Equation of State
eV/keV	Electron volt/ kilo electron volt
FEL	Free Electron Laser
FLASH	Free electron LASer Hamburg
HHG	High Harmonic Generation
IR	Infra-red
IXS	Inelastic X-ray Scattering
LCLS	Linac Coherent Light Source (Stanford)
LINAC	Linear Accelerator
NLS	New Light Source
PAD	Photoelectron Angular Distribution (see ARPES)
PES	Photoelectron Spectroscopy
SASE	Self Amplified Spontaneous Emission
Soft X-ray	No universally accepted definition- taken here to encompass the range 100eV-5keV
THz	Terahertz
WDM	Warm dense matter
XANES	Near Edge X-ray Absorption Fine Structure
XAS	X-ray Absorption Spectroscopy
XES	X-ray Emission Spectroscopy
XFEL	X-ray Free Electron Laser Project (DESY, Hamburg)
XPCS	X-ray photon correlation spectroscopy
XPES/XPS	X-ray Photoelectron Spectroscopy (see PES)
XUV	Extreme Ultra-Violet (10-100eV)

Useful Conversions

Photon energy E= 1 keV	**Wavelength λ=1.24nm**	**$E \propto 1/\lambda$**
5fs pulse duration Δt	**~ 0.4eV energy spread ΔE ***	**$\Delta E \propto 1/\Delta t$**
ϖ 10 cm^{-1}	**ν 0.3 THz**	**$\varpi \propto \nu$**
	*** transform limited pulse**	

APPENDIX II

New Light Source Consultation Process

The first phase of the NLS project was to determine, through wide consultation, the key long-term scientific objectives for the UK light source strategy and establish the light source capability we need to implement that strategy.

This consultation aimed to reach existing users of UK light source facilities (DIAMOND, CLF, SRS), supporters of recent proposals (4GLS, Sapphire) and the science community in general.

Consultation Process

The consultation process included the following:

- A project launch, 11th April 2008, Royal Society London, 113 attendees excluding meeting administration, advertised by email to STFC and DLS lists and on the STFC web
- A series of workshops in five key science areas during May and June, convened by co-ordinators drawn from the science community, advertised by email to STFC and DLS lists, by flyers to university departments and on the STFC web. These were informal meetings with significant time for discussion and debate.
- Working groups in each of these science areas to further consult within their specialisms and to collate the community views, distilling key drivers and requirements (through June-August). Membership was by invitation to leading UK scientists in each field and international experts
- Individual input was sought via an email invitation on STFC and DLS lists; this input could be either to the project leader, science area co-ordinators, or via a web-based form
- Meetings with Research Council representatives (July)
- Additionally, a workshop on Advanced Photon Sources, bringing together experts to discuss the technological capabilities and limitations of both the conventional laser and accelerator based light sources on which it may be based

Analysis of input

Method	**Registrations**
Attendance at Launch (11th April)	122
Registered general interest on web (available ~21st March)	33
Attendance at workshops	
Ultrafast Electron Dynamics and Attosec Science; 13th May 2008	74
High Energy Density Science; 20th May 2008	69
Condensed matter; 21st May 2008	50
Chemical science	62
Advanced Photon Sources	81
Life sciences	51
Total persons	**317**

Membership working groups

Condensed matter (co-ordinator Andrea Cavalleri)

Andrea Cavelleri	Oxford, STFC
Ian Robinson	UCL, DLS
Gabriel Aeppli	UCL
Elizabeth Blackburn	Birmingham
Gerrit van der Laan	STFC
Paolo Radaelli	STFC
Felix Baumberger	St, Andrews
Peter Hatton	Durham

Chemical science (co-ordinators Jonathan Underwood and Wendy Flavell)

Jonathan Underwood	UCL
Wendy Flavell	Manchester
Jon Marangos	Imperial
Justin Wark	Oxford
Peter Barker	UCL
Majed Chergui	EPFL
Anders Nilsson	SLAC
Helen Fielding	UCL
Ivan Powis	Nottingham
Gopinathan Sankar	RI
Martin McCoustra	Heriot Watt
Julia Weinstein	Sheffield
John Evans	Southampton
Sven Schroeder	Manchester
Christian Bressler	EPFL
Mike Towrie	STFC

Ultra fast (co-ordinator Jon Marangos)

Jon Marangos	Imperial
Jonathan Underwood	UCL
John Tisch	Imperial
Matt Zepff	QUB
Will Bryan	Swansea
Leszek Frasinski	Reading/Imperial
Ian Walmsley	Oxford
Brian McNeil	Strathclyde
Riccardo Bartolini	DLS
(Justin Wark)	Oxford

HEDS (co-ordinator Justin Wark)

Justin Wark	Oxford
Steve Rose	Imperial
Roger Evans	Imperial
Dave Riley	QUB
Gianluca Gregori	Oxford
Malcolm McMahon	Edinburgh
Nigel Woolsey	York
Greg Tallents	York
Dirk Gerricke	Warwick
Dick Lee	LLNL

Life Science (co-ordinators Louise Johnson, Peter Weightman)

Louise Johnson	DLS/Oxford
Peter Weightman	Liverpool
Tony Parker	STFC
David Klug	Imperial

Nigel Scrutton	Manchester
Tony Ng	Kings
Colin Nave	STFC/Diamond
Donna Lammie	Cardiff
Tim Wess	Cardiff
Alan Michette	Kings

UK distribution of involvement

The distribution of the persons showing interest across the HEIs and institutes is shown overleaf. The types of institutes involved are shown below left with 32 UK HEIs represented. The table on the right shows the total persons, the numbers from 'project delivery' institutes, the numbers of non-UK people, giving a remainder of 179 people from UK HEIs.

HEIs	32
Facilities	2
accelerator institutes	2
other	7
RCs	2
total institutions	45

total	**317**
STFC	71
DLS	25
RCs	2
Cockcroft and Adams	2
NWDA	1
overseas (mostly speake	37
remaining	**179**