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# Disruptive Photon Technologies for Chemical Dynamics

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Received Xth XXXXXXXXXXXX 20XX, Accepted Xth XXXXXXXXXXXX 20XX

First published on the web Xth XXXXXXXXXXXX 200X

DOI: 10.1039/c000000x

A perspective of new and emerging technologies for chemical dynamics is given, with an emphasis on the use of X-ray sources that generate sub-picosecond pulses. The two classes of experimental techniques used for time-resolved measurements of chemical processes and their effects are spectroscopy and imaging, where the latter includes microscopy, diffractive imaging, and crystallography. X-ray free-electron lasers have brought new impetus to the field, allowing not only temporal and spatial resolution at atomic time and length scales, but also bringing a new way to overcome limitations due to perturbation of the sample by the X-ray probe by out-running radiation damage. Associated instrumentation and methods are being developed to take advantage of the new opportunities of these sources. Once these methods of observational science have been mastered it should be possible to use the new tools to directly control those chemical processes.

## 1 Introduction

Although several years in the preparation by its organisers, this Faraday Discussions meeting on “Emerging Photon Technologies for Chemical Dynamics” was very timely. X-ray free-electron lasers (FELs) are now a reality and have been operating for several years, enough to give a sense of the capabilities and opportunities these sources open up. In addition the field of attosecond science, driven by advanced laser technologies and techniques, is fast developing and allowing the investigation of the electron dynamics that ultimately influences chemistry at longer timescales. The brightness of X-ray sources have followed an exponential growth over time. From the first parasitic use of synchrotron radiation to today's FELs represents 22 orders of magnitude in peak brightness over 40 years, or a doubling every 6.5 months. Like all exponential trends this cannot continue indefinitely, but hopefully high-brightness sources will become cheaper, more plentiful and more accessible, and the science that will flow from them will build upon some of the work discussed here.

There has been a rapid progress of the field of chemical dynamics, or related fields that could be referred to as femto-chemistry, time-resolved chemistry, and structural dynamics. This can be attributed to the newly-available photon technologies, as was emphasised in the meeting. The speed of development can

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be highlighted by the fact that in a previous Faraday Discussions on the related topic of “Time-Resolved Chemistry: From Structure to Function” that was held twelve years ago, FELs got barely a mention, and in his concluding remarks John Meurig Thomas noted that synchrotron sources were finally revealing their utility for time-resolved studies<sup>1</sup>. This was certainly not an oversight, since at that time X-ray FELs were still in the planning stage and it was by no means clear that amplification of X-ray pulses could be achieved. As it turned out, the performance of FELs far exceeded even the most optimistic predictions. The rapid adoption of FEL sources, following the only-recent application of synchrotron radiation to time-resolved studies, is certainly not surprising given that they produce pulses with a billion times higher peak brightness than synchrotron facilities (1000 times shorter pulses with 1 million times more photons per pulse for a similar bandwidth). With pulse durations that can be tuned from about 1 fs to 100 fs, these sources are truly matched to the timescales of atomic processes (with X-ray wavelengths that access inter-atomic length scales), allowing a broad range of explorations in femto-chemistry. Other technological developments have fuelled the field, including the alignment of molecules by polarised laser beams<sup>2</sup>, the mapping of ejected particle kinetic energy and momentum by so-called velocity map imaging<sup>3</sup> and reaction microscopy<sup>4</sup>, the generation of short wavelength attosecond pulses by high-harmonic generation<sup>5</sup> and terahertz radiation from high-intensity laser pulses, new spectroscopies such as angular-resolved photoemission spectroscopy<sup>6</sup>, multidimensional spectroscopies<sup>7,8</sup>, optical - X-ray pulse cross correlation and streaking to determine relative arrival times and pulse durations to few femtoseconds<sup>9,10</sup>, and new pixel detectors<sup>11–13</sup> and sample handling methods<sup>14–16</sup>. These innovations have given researchers a rich new toolbox that is currently being applied to gain fundamental insights into chemical dynamics in simple model systems and offer ways to exert control of interactions and molecular processes.

## 2 Time-resolved imaging and spectroscopy

The study of chemical dynamics using photons falls into the two broad methodologies of time-resolved structure determination based on X-ray scattering (often referred to as “making the molecular movie”)<sup>17</sup> and following energetics, by spectroscopy<sup>18</sup>. The birth of these techniques can be attributed to William Lawrence Bragg and his father William Henry Bragg, respectively, about 100 years ago. William Bragg’s spectrometer, now on display in the Faraday Museum of the Royal Institution, was used to analyse crystals, reveal characteristic fluorescence from anode materials, and to indicate the wave nature of X-rays. X-ray fluorescence and absorption spectroscopies were initially used to establish the atomic theory and determine the atomic composition of materials. With the development of intense and tunable synchrotron radiation, spectroscopy became more powerful and applicable on micrometer length scales. X-rays probe atomic core shells, which gives element specific measurements in complex systems. Near an absorption edge, shifts of the edge or changes in strengths of pre-edge peaks (due to core to valence shell transitions) measure coordination chemistry, which can also be revealed by shifts of fluorescence energies. Lighter elements predominantly emit photoelectrons, which also reveal fine spectral in-

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formation about the chemical environment. At photon energies tens of electron volts above the absorption edge of a particular atomic species the extended X-ray absorption fine structure is the result of interference of photoelectrons scattering from neighbouring atoms. Three-dimensional structural information can be obtained if the molecular system is fixed in space (e.g. in a crystal) and the absorption spectrum is measured as a function of orientation. This is the inverse mode of photoelectron holography. Angular resolved photoemission spectroscopy resolves the single-particle spectral function in energy and momentum, giving insight into the electronic structure of solids, also in three dimensions. Inelastic X-ray scattering, utilising spectrometers of meV resolution, provides details of the excitations of the atomic lattice. Circularly polarised X-rays can access the angular momentum of electrons and separate spin and orbital components.

Following Lawrence Bragg's initial insights, three-dimensional images of molecules can be synthesised from Fourier components that are measured in a diffraction experiment. This approach requires solution of the well-known phase problem, and the history of X-ray structure determination follows a series of breakthroughs to derive diffraction phases, including the Patterson method, direct methods based on atomicity of matter, isomorphous replacement, molecular replacement (which could be thought of as treating a known part of the structure as a holographic reference), and anomalous diffraction. Macromolecular crystallography is a particularly important technique, and today almost 80% of all protein structures utilise synchrotron radiation at dedicated beamlines. This being the international year of crystallography there are many excellent recent reviews of this history<sup>19–21</sup>. The methodology of image synthesis has also been applied to non-crystalline samples, by using coherent X-ray beams to measure the continuous diffraction pattern<sup>22–24</sup>. Isolated objects of compact support result in a diffraction pattern that is band limited and can be completely measured if sampled sufficiently finely. This has opened up another phasing method where real-space and Fourier-space constraints are iteratively enforced until convergence is reached<sup>25</sup>. Images of matter are more readily obtained directly using an X-ray microscope, although spatial resolution is limited to tens of nanometres by the performance of high-resolution diffractive zone-plate lenses<sup>26</sup>. The method of ptychography overcomes the resolution limit of nano-fabricated lenses by combining scanning and coherent diffraction<sup>27</sup>. A particular attraction of X-ray microscopy is that the spectroscopic modalities mentioned above can be used to provide the contrast mechanism for image formation, and the resulting rich high-dimensional spectro-micrographs can be analysed to extract spatial and chemical features at the tens of nanometre scale as was presented by Chris Jacobsen<sup>28</sup> at this meeting. By measuring spectra in a spatially resolved manner, real inhomogeneous materials and systems, such as catalysts or biological cells, can be measured and understood in terms of functional units rather than as an average over the entire sample. Jacobsen's method goes beyond principle component analysis and cluster analysis and demonstrates the power of applying physically-meaningful constraints such as sparsity and positivity. This approach would no doubt be equally useful applied the time domain (e.g. time-resolved crystallography<sup>29,30</sup>) as in the frequency domain.

The extension of X-ray spectroscopy and imaging into the time domain has predominantly been carried out using pulsed X-ray sources synchronised with a

preceding laser pulse to excite the sample. This “pump-probe” scheme can in principle be carried out with all the techniques mentioned above and thus builds upon the long history and development of those methods, as well as techniques in laser science and optical spectroscopy. Until recently, the available pulsed X-ray sources, including synchrotrons and laser-produced plasmas, were rather weak (that is, of low peak brightness). For time resolution better than nanoseconds this required an experiment design that was able to combine stroboscopic measurements with samples that could be rapidly replenished or brought back to the ground state. Measurements often took many days or weeks to complete. Now, with X-ray FELs we are witnessing a new chapter. With a billion-fold improvement in peak brightness, FELs are a disruptive new technology that opens up new types of time-resolved experiments. Since the opening of the first hard X-ray FEL, the Linac Coherent Light Source, in 2009<sup>31</sup> we have seen new explorations in non-linear atomic physics<sup>32,33</sup> and non-linear optics<sup>34</sup>; gas diffraction<sup>35–38</sup>; imaging of phonons in nanocrystals<sup>39</sup>; diffraction measurements of materials at extreme departures from equilibrium<sup>40</sup>; and time-resolved serial femtosecond crystallography<sup>41–43</sup>.

Since this meeting dealt with the topic of photon technologies, there was limited discussion on the use of short electron pulses for obtaining spectral and structural information. The million-times larger atomic scattering potential for electrons over that of X-rays means that electron diffraction is extremely well suited for dilute systems, allowing experiments in the lab on diffraction from laser-aligned molecules<sup>44</sup> that are certainly more impressive than the LCLS experiments reported at this meeting<sup>35,38</sup>. As pointed out in the meeting by John Spence, short electron pulses may not outrun damage effects (see below) as effectively as X-ray pulses do, but this may not necessarily be required. For samples in the liquid or solid state there are also issues of multiple and inelastic scattering of the strongly interacting electrons, requiring energy filtering of the scattered electrons. These technologies are well developed and available in electron microscopes, and perhaps will be implemented with short-pulse electron instrumentation. Element specificity is achieved at higher contrast by X-ray absorption as by electron energy loss measurements. It is expected that, just as with static measurements, the extensions of imaging and spectroscopy into the ultrafast time regime will rely upon the complementarity of these methodologies.

### 3 The perfect probe?

The ideal probe should have no influence on the state of the sample, yet radiation damage often limits the collection of atomic-resolution information in scattering and imaging experiments, and the generation of space charge at high intensities reduces the resolution of photoelectron spectra. The atomic scattering cross sections in the X-ray regime are considerably smaller than the absorption cross sections, resulting in the unfortunate situation that for every scattered photon of 8 keV energy, for example, about 250 keV of energy is absorbed in the sample. Perturbation of the sample can be avoided by working at as low dose as possible, which requires samples that give strong enough signal above noise at low dose. Large crystals amplify diffraction intensities and data can be collected in a regime where there are fewer absorbed photons than molecules in the crystal.

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Such an approach can even be applied to single molecule diffraction with X-ray pulses when the molecules are aligned and signals can be accumulated over many pulses, each with a fresh sample. Stephan Stern described experiments where the number of accumulated scattered photons in the entire detector frame was much less than one per pulse<sup>38</sup>.

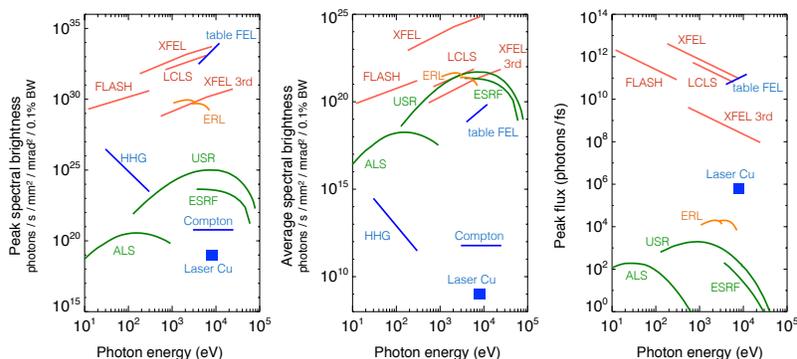
One of the initial motivations to build X-ray FELs was to use short pulses to outrun the effects of radiation damage. The proposal<sup>45</sup> was that with short enough pulses you could obtain the “perfect probe”—one that is non-perturbing but which gives measurable signals from dilute or weakly scattering objects. When the first soft X-ray FEL, FLASH, turned on (then called the Tesla Test Facility) the initial quest was to understand the interaction of matter with intense pulses and determine how true this desired outcome was, starting with model systems such as atomic clusters<sup>46</sup> and nanostructures<sup>47,48</sup>. Those initial experiments were guided by theory and simulations, such as molecular dynamics<sup>45</sup> and hydrodynamics<sup>49</sup> that were applied significantly beyond the regimes that they were initially developed. The interaction starts with photoabsorption and ejection of a photoelectron. The excited atom may relax by filling the core hole by decay of an electron of a higher orbital, accompanied by either emission of a photon (fluorescence) or Auger decay. At the high intensities of focused X-ray FEL pulses there may be more absorbed photons than atoms in the sample, giving rise to a sequence of photon absorption and relaxation leading to higher and higher charge states with a shifting of the absorption edge to higher energies. If the X-ray dose rate is high enough, such that the X-ray intensity is higher than the inverse of the photoabsorption cross section divided by the decay time, then a second core-shell ionisation can occur prior to relaxation, leading to a hollow atom that frustrates further absorption. Such effects were observed in some of the very first experiments carried out at the LCLS<sup>32</sup> and provided the data needed to develop the theory of atomic interactions at high dose rate<sup>50</sup>. We now have validated theoretical tools, such as the XATOM toolkit<sup>50</sup> to determine the fate of isolated atoms in high-intensity X-ray beams.

Molecules are certainly more complicated than isolated atoms, and electronic damage and nuclear motion will be strongly influenced by ionisation by free electrons. In large enough condensed systems there will be a cascade of collisional ionisations that could last about 100 fs and ionise more than 100 atoms from just one photoabsorption event<sup>51,52</sup>. On timescales as short as 5 fs charges from neighbouring atoms can quench the development of high charge states of heavy atoms in a molecule<sup>53</sup>. Robert Moshhammer described a series of elegant experiments that examined differences between isolated iodine atoms and I<sub>2</sub> molecules, by changing the order of an infrared fragmentation pulse and an XUV probe pulse impinging on a beam of I<sub>2</sub> molecules<sup>54</sup>. Even in this simple system there are significant differences in the yield of charged iodine ions for atoms or molecules. Nora Berrah reported on recent measurements to investigate such processes in C<sub>60</sub> molecules, using soft X-ray pulses at LCLS<sup>55,56</sup>. This is a model system for more complicated biomolecules, but also connects to studies of graphene<sup>57</sup> and nanotubes, as well as atomic clusters. The experiments measured the charge states of atomic and molecular fragments that result from the absorption of an average of 180 photons per molecule at the highest intensities. The measurements were compared with XMDYN simulations, which combines classical molecular

dynamics with cross sections modelled by XATOM, and effects such as molecular Auger decay<sup>55</sup>. The remarkable agreement between experiment and model is a significant advance and shows that the dynamics of the explosion is dominated by secondary ionisation by trapped photo- and Auger electrons. This highlights the effect of the sample environment on the interaction with the intense pulse and should give crucial guidance for optimising pulse parameters for imaging and spectroscopy experiments.

So far, the knowledge obtained by the latest experiments largely agree with the predictions of Neutze *et al.*<sup>45</sup> that pulses of 10 fs or less are required for “diffraction before destruction” at molecular resolution. It appears that the perfect probe is obtained in the limit of the pulse duration tending to zero, or highest intensity (with a short enough duration pulse). Higher intensity results in a faster explosion, but gives overall more scattered photons before loss of the structure under investigation<sup>58,59</sup>. Sub-femtosecond pulses should outrun even most electronic processes<sup>50</sup>, and perhaps even allow photoelectron spectroscopy at high dose. Perhaps more general than “diffraction before destruction” we can refer to spectroscopic or other measurements in a “detection before destruction” regime, as pointed out by Majed Chergui. Since electronic damage precedes nuclear motion, spectroscopic information will be perturbed at pulses with lower fluences (i.e. lower dose) than those that can out-run nuclear motion. One particular limit is that which every atom has been collisionally ionised by the end of the pulse, which implies that less than about 1% of atoms are photoionized (depending on the photon energy and if the system is large enough to trap all photoelectrons). Under this condition, most photons that interact with atoms will do so with neutral atoms; that is, atoms that have not absorbed a photon nor collisionally ionised. The probability of a fluorescence photon being emitted by a perturbed atom, or an elastic scattering event from a perturbed atom, will thus be small, given that the measurement is integrated over the pulse and the sample is initially neutral. The dose for this condition has been estimated at about 400 MGy for protein crystals measured with 100 fs pulses<sup>60</sup>, considerably higher than the 30 MGy safe dose that can be tolerated with steady-state exposures at a synchrotron<sup>61,62</sup>. Metal centres in proteins are much more sensitive to the effects of X-ray exposure, and with slow synchrotron exposures they are reduced at much lower doses of only kGy, by capture of solvated electrons<sup>63</sup>. It has been argued that no structure in the protein data bank of a redox protein has been measured in its un-reduced state, prior to the use of X-ray FELs. Kern *et al.*<sup>64</sup> have taken advantage of X-ray FEL pulses to measure X-ray emission spectra of Mn in photoexcited photosystem II micro-crystals, simultaneous with diffraction measurements. The maximum dose was 150 kGy, and the Mn K spectrum in the ground state was identical to spectra of unreduced photosystem II acquired at low dose under cryogenic conditions. This strategy of combining multiple probes in time-resolved experiments gives a much greater understanding and cross validation in experiments. Bressler reported on measurements of aqueous iron(II)tris(bipyridine),  $[\text{Fe}(\text{bpy})_3]^{2+}$ , at a storage ring (the Advanced Photon Source) and an FEL (the LCLS) that carry out X-ray emission or absorption spectroscopies simultaneously with wide-angle X-ray solution scattering<sup>65</sup>.

Even though the full effects and limits of the influence of high-intensity X-ray probe on the sample have not been fully established, this has not precluded the



**Fig. 1** Three comparisons of X-ray sources as a function of photon energy: (left) peak spectral brightness, (centre) average spectral brightness, and (right) peak flux. These plots only give partial comparisons. For example, the table-top FELs will have pulses of broader bandwidth and would have 20 times higher peak brightness (not spectral brightness) compared with linac FELs. USR = ultimate storage ring, ALS = undulator with 2 GeV electron energy, ESRF = undulator with 7 GeV electron energy, table FEL = table-top FEL<sup>73</sup>, laser Cu = Max Born Institute laser-driven plasma source with Cu target<sup>77</sup>.

application of short-duration FEL pulses to time-resolved measurements, especially using replenishable samples. Examples using the pump-probe methodology on photostimulated systems include time-resolved crystallography of photosystem II<sup>42,43</sup> and time-resolved wide-angle X-ray solution scattering revealing the protein quake after excitation of a reaction centre<sup>66</sup>. One of the leading model systems for X-ray time-resolved studies and for gaining insights into chemical dynamics is the metal-to-ligand charge transfer system  $[\text{Fe}(\text{bpy})_3]^{2+}$  mentioned above. Recent time-resolved photoemission spectroscopy carried out on this system at LCLS revealed the presence of an intermediate triplet state, revealed to sub-picosecond resolution<sup>67</sup>.

#### 4 New technologies for chemical dynamics

X-ray FELs are by no means the only source available to the field of chemical dynamics. Majed Chergui summarised the properties of pulsed X-ray sources, including laser-induced plasma sources, high harmonic generation sources, storage rings and insertion devices (including slicing sources), table-top accelerators, and energy recovery linacs (ERLs). These have a wide range of peak and average brightness values, pulse durations, available photon energy ranges, bandwidths, spatial and temporal coherence, polarisation states, pulse stability, and repetition rates. This is a large parameter space, and different techniques and scientific questions emphasise different source properties. Any graphical comparison of sources therefore fails to illustrate how appropriate a source may be for a particular application, but we do so anyway, in Fig. 1.

What are the pulse specifications needed for ultrafast X-ray studies? As discussed above, most time-resolved X-ray experiments are carried out by employ-

ing the pump-probe method, which requires a high degree of synchronisation between the excitation pulse (usually a laser pulse in the IR to UV spectrum) and the probe. Other excitation schemes are possible, such as temperature jumps or fast mixing of samples, but laser pulses offer the fastest and most controlled way of inducing the dynamics to be studied. The achievable temporal resolution obviously depends on the durations of the pump and probe pulses, as well as the uncertainty in the delay between those pulses. The feasibility of a time-resolved measurement depends if adequate pump-induced signal can be measured, which requires a large enough fraction of the sample to be photoexcited (yet without bleaching or damaging the sample) and a strong enough probe to give a measurement. By repeating measurements, and ensuring that the sample is either refreshed or brought back to the ground state between pump-probe cycles, the signal for a given time delay can be accumulated. In the words of Christian Bressler, what is important in such an experiment is the total number of photons collected, which is dictated by the pulse energy, repetition rate, and the duration of the entire experiment.

A temporal resolution of about 10 fs (the femto-chemical time-scale) is required to follow the dynamics of chemical pathways and capture elusive transition states, and thus the ideal X-ray pulse duration should not exceed this value. With compact laser-driven sources, such as the plasma X-ray source at the Max Born Institute<sup>68</sup>, a low degree of jitter between pump and probe is achieved by the fact that both pulses are ultimately derived from the same laser. At kilometre-long FEL facilities, the jitter between pump and probe is on the order of 100 fs but it is possible to approach a time resolution of a few femtoseconds by determining the relative arrival times of the two pulses on a shot by shot basis and appropriately sorting the data *post facto*<sup>10</sup>. Seeding schemes, such as carried out at the FERMI soft-X-ray FEL give inherently lower jitter between pump and probe arrivals<sup>69</sup>. At the LCLS it is possible to generate pairs of X-ray pulses with a well defined and arbitrary delay and different photon energies<sup>70</sup>. In the Discussions there was the opinion that pulses even shorter than 10 fs (and even into the attosecond regime) would certainly be advantageous, not only because such pulses more closely approach the “perfect probe” mentioned above, but to measure electronic processes on their inherent timescales<sup>71</sup>.

As faster timescales are accessed, the corresponding length scales are reduced, requiring wavelengths shorter than 1 Å for scattering measurements. Mike Miniti and colleagues demonstrated that atomic resolution in X-ray molecule diffraction could in principle be achieved at 20 keV photon energy, from the third harmonic of the LCLS undulator<sup>35</sup>. Michael Woerner suggested that pulses of 200 keV photon energy would open up the ability to measure not only charge density, but also spin density maps at high resolution.

Spatial resolution at the atomic scale can still be realised with soft X-ray sources by obtaining this information from photoelectrons, whose de Broglie wavelengths are certainly short enough to resolve interatomic spacings. This is particularly relevant for attosecond pulses generated from high-harmonics in gases, solids, or relativistic plasmas that produce pulses with photon energies below about 1 keV, which can ionise inner-shell electrons of the lighter elements. Daniel Rolles presented experiments carried out at the LCLS (and the synchrotron facility PETRA III) on photoelectron diffraction of laser-aligned

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molecules, showing the feasibility to obtain three-dimensional structural information of the molecular environment around a target atom, with a photon energy of about 735 eV<sup>72</sup>.

As sources approach attosecond durations, as achievable by high-harmonic generation and possibly by inverse Compton scattering by THz accelerated electron pulses<sup>73</sup>, we must consider the effect of increased bandwidth and longitudinal coherence due to diffraction limits. For example, consider a sample of width  $w$  diffracting to a resolution  $d$  with a wavelength  $\lambda$ . The waves scattering from extreme points of the sample (separated by  $w$ ) will interfere at the far field with a path difference of  $\Delta = w \sin 2\theta \approx w\lambda/d$ . For  $w = 300$  nm,  $d = 0.1$  nm,  $\lambda = 0.1$  nm, the path difference is  $\Delta = 300$  nm, or 0.66 fs. How does interference occur if the pulse is shorter than this delay between scattered waves? The simple answer is that the pulse can be considered to be synthesised by a broad and continuous spectrum of Fourier frequencies. Particular 3D spatial frequencies of the sample will selectively diffract these pulse frequencies according to Bragg's law<sup>74</sup>. This is nicely illustrated in Laue diffraction by a pink beam from a protein crystal<sup>75</sup> where a particular Bragg order will select a particular part of the pink spectrum. The pulse arriving at the detector in a particular diffraction order or detector pixel will therefore be longer than the attosecond incident pulse. This begs the question as to what is the actual interaction time and achievable temporal resolution of the measurement<sup>76</sup>.

An intriguing application of diffraction of attosecond pulses was given by John Spence<sup>74</sup> who suggests that under certain conditions two different wavelengths out of the diffraction limited spectrum of an attosecond pulse will diffract to different Bragg orders at a common  $2\theta$  angle. These two diffraction orders will overlap on the detector. The interference of these two frequencies beat at their difference frequency and hence the relative phase of the two orders can be determined if the pulse duration is less than that beat frequency.

Michael Woerner's source produces 100 fs duration pulses with  $6.8 \times 10^7$  photons per pulse from a  $10 \mu\text{m}$  diameter source at a repetition rate of 1 kHz and a photon energy of 8.06 keV (from a Cu target)<sup>77</sup>. With a suitably well-diffracting sample, a powder of NaBH<sub>4</sub> ionic crystals in this case, Woerner reports that it is possible to collect datasets in several days of continuous operation. This is obviously longer than would be required at an X-ray FEL, but the stability and reliability of the source and the fact it is a laboratory source, allows such a strategy. It also highlights the fact that the sample properties are a key consideration in dynamics experiments (as for static measurements). That is, given short duration pulses, source brightness may be traded for diffraction strength of the sample, and high repetition rate (or available measurement time) for pulse energy. For well-ordered and non-dilute samples, this would argue that the appropriate source metric is average brightness. Thus, an energy recovery linac source, generating pulses at a megahertz repetition rate, may offer advantages for spectroscopic or scattering experiments from certain systems. The high repetition rate of the European XFEL (27,000 pulses delivered per second) gives the possibility to achieve in 1 minute what would take almost four hours at LCLS operating at 120 Hz. Such capability enables the measurement of rare or unusual events, such as crystal nucleation or a short-lived intermediate state. X-ray FELs produce ordered light (spatially coherent pulses with extremely high pho-

ton degeneracy) that enables the study of dilute systems such as laser-aligned molecules and weakly scattering protein nanocrystals, or the search for short-range order and local symmetry in complex or amorphous samples<sup>78,79</sup>. The diffracting strength of such dilute systems is easily  $10^{-12}$  times the strength of a perfect microscopic crystals: e.g. a  $10\ \mu\text{m}$  wide crystal of  $10\ \text{\AA}$  unit cell length contains  $10^{12}$  unit cells, which highlights the great range of sample diffracting strengths and the need for sources of spanning this range.

The experiment is more than the source, and experiments with high-peak-brightness sources require a corresponding capability in refreshing or replenishing the sample and high dynamic-range detectors that can match the source in frame rate. The sample environment ideally should provide a geometry where both the pump and probe interact uniformly with the sample in a common volume. Liquid-jet injectors have been very successful used at X-ray FELs for delivering a new sample on every pulse<sup>14,15</sup>, and John Spence showed latest developments in using this fast-flow technology for mixing samples moments before X-ray exposure<sup>74</sup>. Pulsed gas jets were used in many of the experiments reported at this Faraday Discussion, and can provide densities high enough for ion spectroscopies<sup>72</sup> and diffraction<sup>38</sup>. Gas cells provide fresh sample by diffusion and can give a longer interaction length with the X-ray beam, to give higher signals, but this can complicate the scattering geometry<sup>35</sup>. Laser-induced alignment of gas molecules<sup>2</sup> can also be categorised as a sample delivery and preparation technique, even though the study of rotational dynamics of complex systems is itself a vibrant field of chemical dynamics<sup>80</sup>. Laser alignment is improved by cooling the molecules to a rotational temperature of about 1 K and selecting low-energy quantum states using an electrostatic deflector, as was used for initial experiments of diffractive imaging of aligned diiodobenzonitrile molecules<sup>38</sup>.

Most chemical reactions are not accessible via initiation of a laser pulse or temperature jump. Spence presented a mixing apparatus for obtaining time-resolved measurements of chemical reactions on timescales of microseconds<sup>74</sup>. This may be faster than can be achieved by the freezing of intermediates, e.g. in trapped-state crystallography<sup>81</sup> due to the fact that we can now obtain information from small crystals—giving short times for mixing by diffusion<sup>82</sup>. The jet has an inner bore capillary, carrying one reagent such as protein nanocrystals in solution, that can be slid telescopically inside another capillary in which the second reagent solution flows. These solutions mix, and the mixing time before probing is controlled by the distance from the exit of the inner capillary to the interaction region, and the flow speed. The apparatus could also be used to study the dynamics of protein folding.

It is a well-known problem that whenever source capabilities are improved there is a deficiency of detectors that can fully exploit those capabilities. Thankfully, X-ray FEL facilities anticipated the need for high frame-rate pixellated detectors and there are several detectors in use such as the Cornell-SLAC pixel array detector<sup>12</sup> and the pnCCD<sup>11</sup> that have millions of pixels and frame rates higher than 120 Hz. For the European XFEL, which will operate in bursts of 2,700 pulses at 4.5 MHz, 10 times per second, the challenge is even greater, and developments are taking place to handle this extreme pulse pattern. One such development is the Adaptive Gain Integrating Pixel Detector<sup>13</sup>. Each pixel has analogue storage for 352 frames that can be addressed in less than the 220 ns be-

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tween pulses and which can all be digitised and read out in less than the  $\approx 100$  ms between pulse trains. Thus, 3,520 frames per second can be stored. It is possible to overwrite any of the frames within the pulse train, which means that for low sample concentrations where not every shot hits a sample it is possible to achieve higher effective frame rates if a suitable veto signal can be created. Initial AGIPD systems have reached a dynamic range of  $10^4$  and single-photon sensitivity<sup>83</sup>.

The new detector technologies described here may also have a profound effect on time-resolved experiments at synchrotron radiation facilities and other pulsed sources. Since the AGIPD detector can measure  $10^4$  photons per pixel at  $5 \times 10^6$  frames per second, it can record  $5 \times 10^{10}$  photons / pixel / second, which matches the intensity of the direct beam at many synchrotron beamlines. This capability opens up new possibilities for time-resolved experiments with  $\approx 100$  ps synchrotron bunches and rapidly performing delay scans from a single pump followed by a series of pulses. Similarly, advanced detectors developed for synchrotron radiation, such as the Pilatus, are finding a lot of use in laboratory sources, such as Michael Woerner's plasma source. The photon-counting Pilatus cannot count above a single count over the duration of a femtosecond pulse. Thus, even with a plasma source the fast-frame integrating detectors developed for XFELs may be even better suited in cases where there can be more than a single photon per pixel per frame as can occur in Bragg peaks.

The improved source and detector capabilities at synchrotron facilities may speed up data collection in methods such as ptychography<sup>84</sup> and scanning transmission X-ray microscopy<sup>28</sup> to the point that the pulse structure of the storage ring will be noticeable. Indeed, these facilities are being applied for time-resolved studies at high repetition rates, and strategies such as photon time-stamping<sup>85,86</sup> to make use of all X-ray pulses, given that laser pump pulses cannot usually be delivered at megahertz repetition rates.

## 5 Outlook

Accelerator-driven sources offer many possible pulse parameters and configurations, and can be optimised for high peak brightness (e.g. X-ray FELs), high average brightness (e.g. ERLs and synchrotrons), pulse duration, pulse stability, and so on. While some parameters can be agreed upon as needed for a broad range of femto-chemical dynamics studies, the potential experiments and directions in chemical dynamics means that no single source will meet all needs. As pointed out by Nora Berrah<sup>55</sup>, there is a legitimate question as to whether large-scale facilities are worth the cost, especially since linac-driven sources can only serve a limited number of experiments at a time. The counterpoint is that the cost of not building sources that open up new exploratory science could be far greater to society in the long run. One of the key issues to capitalising on the exciting new opportunities offered by these disruptive new sources is their limited access. This can impact the science that is carried out, because of the low tolerance for failure and the avoidance for allowing difficult and risky experiments. The field therefore needs complementary sources that can guide the development and help prepare experiments. It also needs more facilities world wide and methods for multiplexing or efficiently sharing the beam. The SFX User Consortium<sup>87</sup> at the European XFEL, for example, proposes to collect nanocrystal diffraction data in

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a parasitic fashion, as part of the SPB/SFX beamline<sup>88</sup>.

As pointed out in the introduction, the drive for higher peak brightness can not continue indefinitely, and Gwyn Williams pointed out in this Faraday Discussion that X-ray brightness depends on the peak current that can be achieved in the radiating electron bunch, which is fundamentally limited by space charge in the relativistic bunch<sup>89</sup>, even given the amplification that occurs in an FEL. However, this situation is similar to power limits in optical laser amplifiers<sup>90</sup> and the way to overcome those limits has been through chirped pulse amplification<sup>91</sup>. Thus, in a similar way, it should be feasible to increase the power (and hence brightness) of X-ray pulses with chirped electron bunches of high-charge but limited peak current and then compress the resulting chirped X-ray pulse using X-ray optics<sup>92,93</sup>. This may give factors of 10 or 100 increase in peak brightness.

It has been a glorious century of X-ray science, celebrated this year by the International Year of Crystallography. The focus of the last 102 years has been on determining static structures at atomic detail, and only recently has it been possible to observe the dynamics of those structures with the types of tools discussed at this meeting. Many of these tools, such as X-ray FELs, bring large increases of capabilities which we are still coming to grips with, and may overturn many of the limitations and requirements that have long faced the investigation of matter at atomic scales. Once we have mastered observing chemistry at its fundamental length and time scales of atoms and electronic transitions, it should be possible to control those structures and processes, which is the dream of coherent control. In such a way, it may be possible to influence the course of complex catalytic reactions to mimic the light-induced steps of photosynthesis or peptide bond-formation in a ribosome, or to drive chemical reactions to specific products. It is clear that in this period of rapid source developments it will take some time to establish the most efficient, useful, and accurate methods to meet such goals. Such was the case in fully harnessing radiation from storage rings, and some of the pioneers of those days happily still play a significant role today, and actively participated in these Discussions.

## Acknowledgements

I acknowledge support through the European Research Council through the grant SYG 2013-609920 - AXSIS “Frontiers in Attosecond X-ray Science: Imaging and Spectroscopy.”

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