FEMTOPHYSICS

Double vision

Andrea Cavalleri

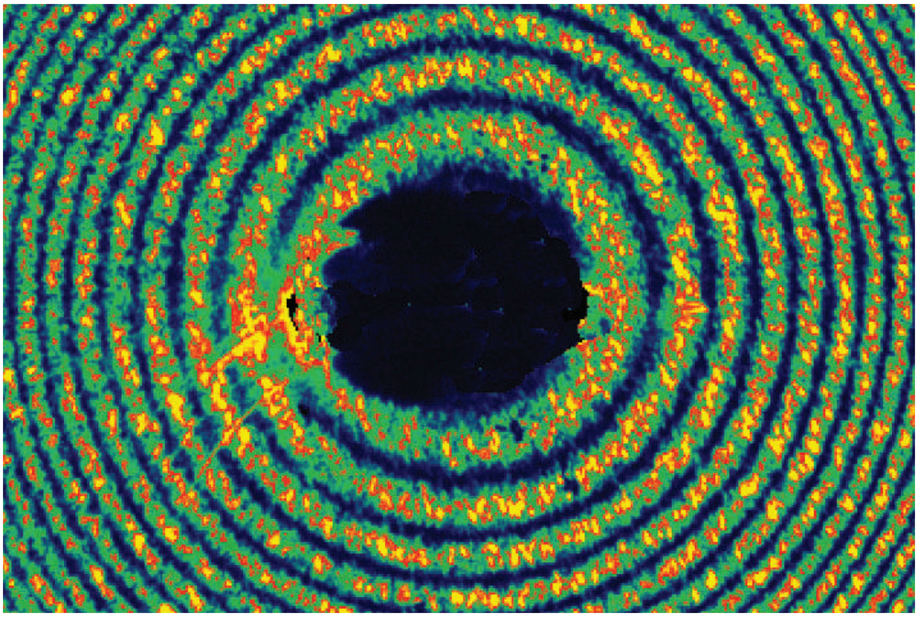
By cunningly diffracting X-rays twice from an exploding nanometre-scale sphere, holographic images can be made of a tiny system evolving at lightning speed. The technique could be used to picture atomic dynamics.

On page 676 of this issue[1], Chapman *et al.* demonstrate how coherent, ultrafast X-ray pulses from a free-electron laser[2] can be used to yield a series of femtosecond-resolved holographic images of an evolving nanometre-scale object. This exquisite resolution in both time and space brings us closer to a long-sought-after goal — the ability to observe atomic-scale processes as they happen.

The femtosecond (10^{-15} s) is the natural timescale of atomic motions. Optical pulses of femtosecond duration thus allow us a glimpse of the evolution of chemical reactions, phase transitions and other elementary atomic interactions — processes that could otherwise be followed only indirectly. Traditional time-resolved optical techniques operating at near-visible wavelengths can often only establish how fast many of these phenomena occur, being blind to what exactly is happening. This is because they are only sensitive to spectroscopic signatures that are difficult to interpret without knowledge of the atomic structures that produced them. Ideally, these structures should also be sampled on the femtosecond timescale.

This frontier territory has recently been conquered with a first generation of X-ray and electron sources, including both 'tabletop' equipment[3,4] and accelerator-based techniques[5]. Measurements of femtosecond atomic-structural dynamics have thus become possible[6–8]. But the ultimate goal — the determination of all atomic positions of a solid or a molecule with the same sort of time resolution — requires short pulses of X-rays or electrons to be combined with other advanced crystallographic concepts and techniques.

Specifically, optical imaging requires the 'inversion' of a pattern of light scattered (diffracted) from an object. This diffraction pattern is related to the shape of an object through a mathematical operation known as a Fourier transformation, which encodes the image in propagation directions and phases of the electromagnetic field. To obtain an image, one must be able to invert the Fourier transformation. Lenses do precisely that: they can, in fact, be thought of as physical computers that perform an inversion by recombining different rays at a given distance and making them interfere to form a magnified or demagnified replica of the object.



H. N. CHAPMAN *ET AL.*

Figure 1 | Nano-explosion. A typical two-pass coherent diffraction pattern encoding shape and evolution of an object, as used by Chapman *et al.*[1] for their nanometre-scale, femtosecond holographic imaging.

Where lenses do not exist or are hard to make, as is the case at X-ray wavelengths, the best one can do is record the diffraction pattern on a screen. This is a destructive process that throws away half of the necessary information — that contained in the phase of the electromagnetic field. Alternative methods must then be developed to fully recover an object's shape. For example, by measuring the diffraction pattern on the screen with sufficiently high spatial resolution, and making assumptions about the size of the object[9], trial-and-error numerical methods to invert the Fourier transformation can be applied[10,11].

An alternative approach is to add a second, reference light wave to the field scattered from the object, which allows an image to be recovered from scratch — the technique known as holography[12]. But holography is only feasible if one has a well-behaved X-ray beam to start with. The quality of an optical beam is usually quantified in terms of coherence, which is a measure of the volume over which the electromagnetic field oscillates in lock-step with itself. Free-electron lasers, in which coherent light is produced by amplification through a beam of relativistic electrons, are the first sources devised that are both coherent and generate ultrashort pulses in the X-ray regime. This opens up new possibilities for structure determination based on holography, interferometry or coherent diffraction, as well as for studies that investigate the femtosecond dynamics of matter in new ways.

Chapman *et al.*[1] combine an imaginative experimental geometry with cutting-edge multilayer mirror technology and special imaging algorithms to achieve time-resolved holography. They use this to monitor the X-ray-induced explosion of a microscopic object. An X-ray pulse first impinges onto a tiny sphere, diffracting from it and initiating its explosion. The pulse then travels to a multilayer mirror behind the sphere, hitting it almost at a right angle. Next, it is reflected back and diffracts from the sphere again after a given time delay (see Fig. 1 on page 676).

Because of the backing mirror's slight tilt, the reflected pulse follows a slightly different path from the beam that originally interacted with the sphere. The two diffraction patterns — one from the unperturbed sphere, one from the exploding sphere — overlap on a screen and interfere (Fig. 1). The first pattern is always the same, whereas the second varies with the time delay, which can be controlled by the distance between the object and the backing mirror. The interference pattern encodes both the shape of the exploding object and the time delay between the two pulses. The pulse thus acts as a reference beam to itself, permitting a true hologram of the evolving object to be constructed.

Owing to the relatively long wavelength used in this experiment (32.5 nm), it was only possible to probe scales of tens of nanometres. But all the conceptual ingredients are in place, and we can afford to dream of what will become possible when the wavelength is reduced. Most straightforwardly, experiments of this type will become the key towards realizing one of the most ambitious *gedanken* applications of X-ray free-electron lasers — the imaging of single molecules with very high photon doses. This technique would beat the disruption of the molecule initiated by the flux of incident X-rays by taking all the structural information in one ultrashort burst[13,14].

As X-ray wavelengths are decreased towards the final goal of 1 ångstrom (10^{-10} m), the size of the objects that can be imaged decreases towards the atomic scale. At the same time, however, structures also become shorter-lived, and the constraints on the pulse duration more stringent. For this reason, the jury is still out on whether single-molecule imaging using free-electron lasers will work for the smallest timescales.

To perform holography of the disruption process with the necessary time resolution, shorter distances between the object and backing reflector will be required — less than 1 μm for the necessary resolution of near 5 femtoseconds. To achieve this, the imaged object will probably have to be deposited directly on the multilayer mirror, and different grazing-incidence angles used to tune the time delay.

Femtosecond holography could also be used in other fields. In condensed-matter physics, more and more experiments have demonstrated static imaging using lensless techniques[15,16]. The free-electron laser at DESY in Hamburg used by Chapman *et al.*[1] is now operating at a wavelength near 6 nm, and also at a secondary wavelength near 2 nm. These wavelengths are close to some important X-ray absorption edges that are often used for X-ray studies of solids[17].

In experiments probing condensed matter, one will want to use geometries different from the scheme used by Chapman and colleagues[1]. Of interest will be a dynamic behaviour that is controlled by different means, such as laser pulses, terahertz radiation or rapid, transient magnetic fields. Thus, adapted, time-resolved holography might provide a new way to generate images on both microscopic and mesoscopic scales, overcoming the formidable challenges for those who seek to understand the dynamic physics of complex solids. Equally important, time-resolved imaging will offer a new way of looking at problems in biology and soft matter, in which many different scales in space and time are in play. ■

Andrea Cavalleri is in the Department of Physics, Clarendon Laboratory, University of Oxford, Parks Road, Oxford OX1 3PU, UK.
e-mail: a.cavalleri1@physics.ox.ac.uk

1. Chapman, H. N. *et al. Nature* **448,** 676–679 (2007).
2. Ackerman, W. *et al. Nature Phot.* **1,** 336–342 (2007).
3. Rischel, C. *et al. Nature* **390,** 490–492 (1997).
4. Siwick, B. J., Dwyer, J. R., Jordan, R. E. & Dwayne Miller, R. J. *Science* **302,** 1382–1385 (2003).
5. Schoenlein, R. W. *et al. Science* **287,** 2237–2240 (2000).
6. Cavalleri, A. *et al. Phys. Rev. Lett.* **87,** 237401 (2001).
7. Lindenberg, A. M. *et al. Science* **308,** 392–395 (2005).
8. Gedik, N., Yang, D.-S., Logvenov, G., Bozovic, I. & Zewail, A. H. *Science* **316,** 425–429 (2007).
9. Sayre, D. *Acta Cryst.* **5,** 843 (1952).
10. Fienup, J. R. *Appl. Opt.* **21,** 2758–2769 (1982).
11. Miao, J. W., Charalambous, P., Kirz, J. & Sayre, D. *Nature* **400,** 342–344 (1999).
12. Gabor, D. *Nature* **161,** 777–778 (1948).
13. Neutze, R., Wouts, R., van der Spoel, D., Weckert, E. & Hajdu, J. *Nature* **406,** 752–757 (2000).
14. Chapman, H. N. *et al. Nature Phys.* **2,** 839–843 (2006).
15. Eisebitt, S. *et al. Nature* **432,** 885–888 (2004).
16. Pfeifer, M. A., Williams, G. J., Vartanyants, I. A., Harder, R. & Robinson, I. K. *Nature* **442,** 63–66 (2006).
17. Abbamonte, P. *et al. Nature* **431,** 1078–1081 (2004).

SYSTEMS NEUROSCIENCE

Timing is everything

Phillip Larimer and Ben W. Strowbridge

Interactions among neurons in brain circuits underlie sensory perception and information storage. Work in locusts shows how the timing of different neuronal signals is synchronized to ensure effective communication.

Most biological systems can adapt to different conditions and environments. The nervous system has elaborated on this ability and developed mechanisms that use prior experience to predict future events. Many of these mechanisms could potentially support behavioural prediction. However, little is known about which specific mechanisms are used during common tasks, such as learning how to hit a baseball or remembering to avoid poison ivy. In a seminal study, Cassenaer and Laurent[1] (page 709 of this issue) demonstrate a specific predictive mechanism that operates during olfactory learning in locusts.

In both mammals and insects, olfactory stimuli trigger diffuse, but reproducible, patterns of neural activity in many interconnected brain regions[2]. At the initial processing stage, odorants in the environment evoke all-or-none electrical discharges, which are recorded in neurons as spikes (action potentials). As the cells involved in the odorant-to-spiking conversion have only broad selectivity[3], the activity of any one neuron is a poor predictor of odorant identity. Instead, odorant identity seems to be encoded by populations of neurons whose activity becomes transiently synchronized in response to sensory stimulation. Individual neurons often respond to several odorants and probably participate in many transient 'cell assemblies'[2]. The insect brain affords excellent accessibility for electrical recordings from several neurons, making it useful for determining how odorant-evoked activity patterns develop.

Network oscillations also have an important role in the processing of olfactory information by linking together the neurons that collectively represent a specific odorant. The presence or absence of a single spike on a specific oscillation cycle defines cell assemblies that are activated by an odorant. In honeybees[4] the disruption of network oscillations impairs olfactory discrimination, highlighting the oscillations' relevance to information processing.

Olfactory information is processed sequentially by different brain regions that are linked by network oscillations. In insects, simple olfactory stimuli activate large subsets of projection neurons in the antennal lobe — a region analogous to the olfactory bulb in mammals. The neural representation of sensory information becomes significantly sparser in the second[5]- and third[1]-order stages of olfactory processing (Fig. 1a). Sparse coding is advantageous because it facilitates the recall of memories from partial cues and allows for denser, more reliable storage of biological information[6].

As several stages of the insect olfactory system represent sensory information as sparse cell assemblies that are tightly linked by network oscillations[2], small perturbations in the timing of single spikes in constituent neurons can potentially disrupt sensory coding. Thus, the olfactory system has the difficult task of maintaining the temporal precision required to generate odorant-linked cell assemblies. Propagation of information through neuronal circuits typically results in a loss of temporal precision due to randomness associated with the mechanisms by which neurons communicate. The decrease in timing precision (increased jitter) is especially large when target cells are activated by relatively few, but