Atomic photography

Louis F. DiMauro

No ordinary camera can capture the motion of electrons inside an atom. But the advent of ultrafast laser pulses brings the necessary 'shutter speed' for snapping them as they tumble between energy levels close to the nucleus.

In stop-action photography, a moving body is frozen on film by the speed of the shutter or the flash of a strobe light. In this photograph (Fig. 1) of the great American pastime baseball, the shutter speed was sufficient to freeze the motion of the crowd, and the batter's anxious expression, as the pitcher throws the ball towards him. But there is one detail that the camera failed to capture — the motion of the ball. The ball's speed was so high (around 150 kilometres per hour) that it is blurred in the photograph, masking such details as the stitching on its surface. So there are different timescales for the action on the ball field, some too fast to register easily. The same limitation applies at the atomic scale, but the paper by Drescher *et al.*[1], on page 803 of this issue, is set to change this. The authors have introduced a new type of 'photography' that freezes an atom in motion and heralds a new field of research — attophysics.

Consider a water molecule moving through a solution on a picosecond timescale ($1\,\text{ps} = 10^{-12}$ s). On a faster timescale (down to 10^{-14} s), the atomic nuclei of hydrogen and oxygen inside the water molecule also vibrate and bend relative to each other. Scientists have studied this motion since the late nineteenth century by unravelling the mysteries contained in the spectrum of radiation that can be emitted by such a molecule. But the advent of ultrafast laser pulses has revolutionized time-resolved spectroscopy over the past quarter-century.

Using the technique of 'pump–probe' laser spectroscopy, the experimentalist can initiate (pump) and watch (probe) the motion of molecules in real time with a resolution of a few femtoseconds ($1\,\text{fs} = 10^{-15}$ s). This has not only resulted in a direct measure of how molecules move during a chemical reaction but, perhaps more importantly, it has opened up a new school of thought that views the quantum world in terms of moving 'wave packets' representing the evolution of quantum-mechanical amplitudes and phases. In 1999, Ahmed Zewail received the Nobel prize in chemistry for his seminal contributions to this field of femtochemistry.

Although femtosecond light pulses are still an important scientific tool, they cannot freeze every aspect of atomic motion that is relevant in the structure of matter, just as the photograph fails to capture the details of the baseball. The frontier in ultrafast spectroscopy is the study of the motion of electrons bound inside the atom, in orbits close to the nucleus. This new scale is defined by the time it takes the electron in the innermost orbit of the hydrogen atom to complete one turn around the proton nucleus. The period of this orbit — 24×10^{-18} s, or 24 attoseconds — is at least 100 times shorter than the duration of the shortest laser pulse.

L. F. DIMAURO

Figure 1 **Spot the ball — the limitations of action photography.**

But the period of the laser-pulse cycle at or near visible wavelengths imposes a fundamental limit on the resolution that can be achieved, at approximately a few femtoseconds. Consequently, researchers trying to make light pulses of attosecond duration have looked to other wavelengths, particularly those around the border between the X-ray and ultraviolet (XUV) regimes. One successful approach, using the strong-field phenomenon known as high-harmonic generation, produced the first measurable light pulses in the attosecond regime[2,3].

But forming attosecond light pulses is only one of the scientific challenges to be faced in making attophysics a reality. Equally challenging is the detection and propagation of these fragile pulses. Drescher *et al.*[1], however, have solved all of these problems for the specific case of measuring the decay time

of an inner-shell electron excitation, which until now had been studied only indirectly through the emission spectrum.

The authors used an attosecond XUV pulse to initiate the excitation process in an atom of krypton. This pulse frequency is high enough to ionize the atom, knocking out an inner-shell electron and leaving behind an unstable 'hole'. The decay path from this excited state involves two electrons; one drops from a higher shell to fill the hole, and another — the 'Auger electron' — is shaken out of the atom. The Auger decay process occurs between 10^{-14} and 10^{-16} s after ionization, and by sending in a second, longer (femtosecond) optical pulse, Drescher *et al.* could pick up the emission of the Auger electron. The time of release and the final energy of the Auger electron in the intense optical field are related. So by measuring the Auger electron's energy as a function of the time delay between the XUV and optical pulses, Drescher *et al.* were able to measure the Auger decay time with attosecond resolution.

The emergence of new areas with broad scientific impact is usually the result of creative contributions from a large community of researchers over a long period of time. But there are a few papers that announce the beginning of a new era, and the paper by Drescher *et al.*[1] falls into this category. We are entering a new realm of hyperfast measurement; the age of attophysics has begun. ■

Louis F. DiMauro is at the Brookhaven National Laboratory, Upton, New York 11973, USA.
e-mail: dimauro@bnl.gov

1. Drescher, M. *et al. Nature* **419,** 803–807 (2002).
2. Paul, P. *et al. Science* **292,** 1689–1692 (2001).
3. Hentschel, M. *et al. Nature* **414,** 509–513 (2001).

Cell biology

Survival in three dimensions

Kenneth M. Yamada and Katherine Clark

Whether a cell lives or dies depends on various local cues. New work reveals that those cues include a cell's spatial relationship with its neighbours and polarized interactions with the adjacent extracellular matrix.

Successful cancer treatment requires both the efficient killing of tumour cells and the survival of normal cells. Because cancer chemotherapy involves drug-induced apoptosis (programmed cell death)[1], a crucial question is what actually determines susceptibility to this process or protection from it. As described in *Cancer Cell*, Weaver *et al.*[2] have identified a mechanism that is relevant to both normal and cancer cells, in which — surprisingly — the determinants are the three-dimensional organization of the cells and their interactions with the surrounding extracellular matrix.

Most human cancers arise from epithelial cells, which cover body surfaces and the interior of organs such as the breast, lung and intestine. Epithelial cells are normally anchored to an extracellular matrix called the basement membrane, which gives them polarity. They are organized into three-dimensional structures such as glands. This tissue organization is disrupted when malignant cancer cells invade across basement membranes and into other tissues. Indeed, the ability of tumour cells to thrive in the absence of contact with basement membranes or other such substrates is a well-known characteristic of malignancy[3]. Weaver *et al.*[2] now show that these features also make cancer cells vulnerable to drug-induced apoptosis.

In a three-dimensional cell-culture model system, there is a marked difference in tissue organization between a non-malignant breast epithelial cell line and a malignant cell line derived from it. When grown with components of basement membrane, the non-cancerous cells form small, gland-like structures surrounded by locally secreted basement membrane (Fig. 1a, d). In contrast, the tumour-cell counterpart fails to form glandular structures (Fig. 1b). Weaver *et al.* found that treatment with a variety of drugs or immunological inducers of apoptosis killed the tumour cells, but not the well-organized normal cells.

The authors then tested whether three-dimensional organization was crucial to these outcomes. They disrupted the organization of epithelial tissue by growing the cells on flat tissue-culture substrates, producing a single layer (a monolayer). Alternatively, cell-to-cell adhesion could also be disrupted by inhibiting the function of the adhesion molecule known as E-cadherin.

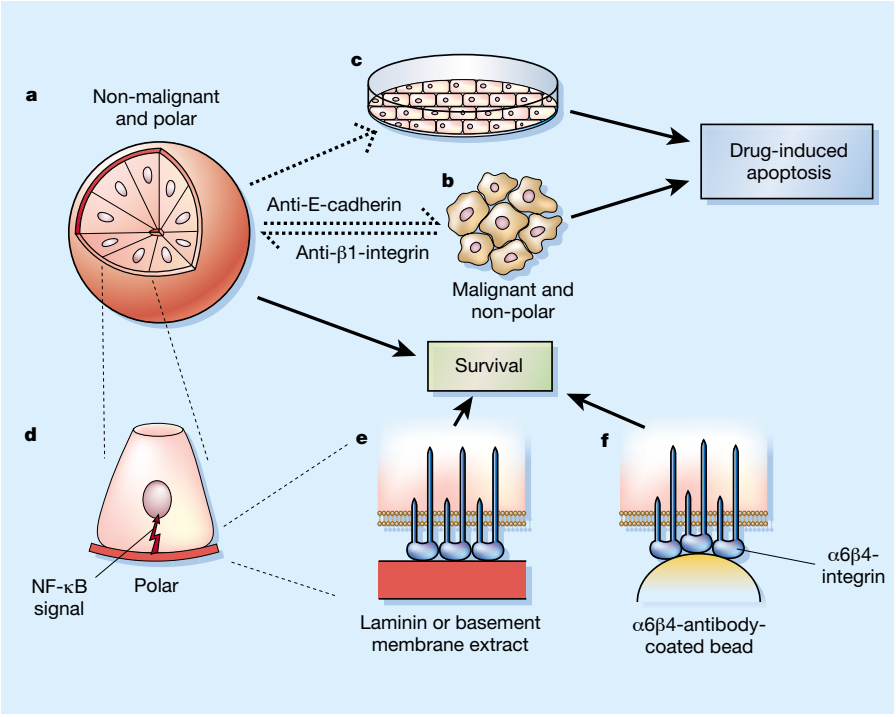

Figure 1 **Three-dimensional cell organization and polarity regulate sensitivity to drug-induced apoptosis — a summary of the results of Weaver *et al.*[2].** a, **Normal, non-malignant breast epithelial cells have polarity and are anchored to a basement membrane (red); they are resistant to drug-induced apoptosis.** b, **Malignant breast cells lack polarity and are susceptible to drug-induced apoptosis.** c, **Converting normal cells to a monolayer by growing them on a flat collagen-coated plastic dish, or disrupting epithelial organization using anti-E-cadherin antibodies, produces cells that are sensitive to apoptosis. Conversely, treatment of breast tumour cells with anti-β1-integrin antibodies induces polarized organization and protects the cells against apoptosis.** d, **Protection is mediated by the NF-κB signalling pathway, which is active in epithelial cells that possess polarity.** e, f, **Key molecules involved in this process are laminin in basement membranes and an adhesion receptor, the α6β4-integrin. Cells are also protected from apoptosis by the addition of laminin or a basement-membrane extract** (e) **or by binding to beads coated with an antibody that mimics laminin by binding to the α6β4-integrin** (f).