Molecular physics

Break-up breakdown

Tim Reddish

Molecules ionize and fragment when subjected to energetic radiation. The behaviour of a simple molecule, deuterium, can now be tracked through this process in greater detail than ever before.

It is said that when physicists want to know what is going on inside a microscopic object, they just blow it up and see what happens. This reductionist approach has certainly proved useful in particle physics and in studying the structure of atoms, molecules and nuclei, using a variety of projectiles. The explosive experiments reported by Weber *et al.*[1] on page 437 of this issue demonstrate that even simple molecular hydrogen is full of surprises. Their study addresses the fundamental question of what exactly happens to an atom or molecule when it absorbs sufficient energy to fragment completely. Put another way, what governs the motions of the free charged particles in a so-called Coulomb explosion?

If a molecule absorbs enough energy, bonds can be broken and ions can form, allowing neutral and charged constituents to react with neighbouring molecules. These processes occur everywhere, from car engines to industrial chemical plants. Molecular ionization and fragmentation also occur naturally in Earth's upper atmosphere, driven by the Sun's energy, and are the mechanisms responsible for radiation damage to our bodies. In general, the more energy that is absorbed — either from light or through a collision with another energetic particle — the greater the number of possible reaction pathways and the greater the 'damage' done to the molecule itself and its nearest neighbours.

The removal of two electrons from helium, the simplest multi-electron atom, leaves behind a completely bare nucleus — an α-particle. Thus, the double-ionization process produces three charged particles: the positively charged nucleus, and two electrons that escape under the influence of the long-range Coulomb force. In the case of molecular hydrogen, once the electrons have been ejected, the 'glue' that held the molecule together has gone and the protons explode apart in opposite directions, because like charges repel. One of the initially surprising results, for both helium and hydrogen, was that if the two escaping electrons have equal energies, they do not leave in opposite directions, as might be expected. Quantum mechanics, as well as the Coulomb force, determines the outcome.

It should be emphasized that, even when it is energetically possible, the double-ionization process in helium and hydrogen is still about 30 times less likely to occur than the ejection of a single electron. This is because the process for the simultaneous emission of two electrons is dominated by interactions between the electrons themselves — they must be treated as a correlated pair and not as independent particles — and this improbability makes the experiments much more difficult. Ultrafast timing techniques are used to ensure that the pairs of electrons detected really do come from the same atom or molecule. Even so, as the two electrons can be emitted in any spatial direction, efficient methods of particle detection are needed that cover as large a solid angle as possible. Completely new instruments have been invented to enable the fragment products to be detected and to measure both their energies and their angles. Some groups have developed doughnut-shaped 'toroidal' analysers to view the process in one plane[2–4], while others have produced an elegant three-dimensional detection system[5–7]. All of these experiments have benefited from technological advances at synchrotron sources, as ideally they require extreme-ultraviolet radiation with 100% linear polarization to initiate the Coulomb explosion.

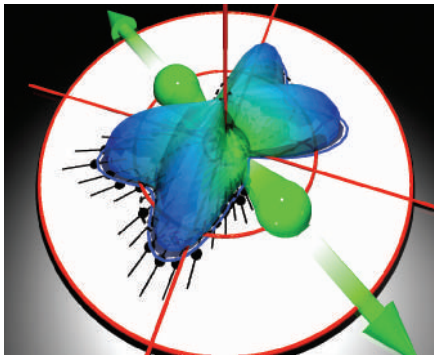

Figure 1 **A three-dimensional 'photograph'[1] of the double ionization of deuterium molecules, initiated by the absorption of photons. The surface represents a model fit to a sample of Weber and colleagues' data[1], showing the angular distribution of one ejected electron in the plane containing the molecular and light polarization axes; the other escaping electron (of the same energy) is emitted directly upwards, out of the plane. The direction of the molecular axis is given by the exploding nuclei (green), whose energies have been selected such that the vibrating nuclei are as close together as possible at the instant of photoabsorption.**

The new study by Weber *et al.*[1] builds on earlier experimental studies, by this group[5,6] and others[2–4,8–10]. Their three-dimensional momentum-imaging approach has reached new heights of sophistication, giving a view in unprecedented detail of the molecular double-ionization process for the hydrogen isotope deuterium. The experimental set-up is surprisingly simple in principle. In the central interaction region, deuterium molecules are ionized by a beam of synchrotron light. A controlled, uniform electric field surrounds the interaction region and accelerates the two positive ions in one direction and the electrons in the opposite direction. After the charged particles have left the electric field, they drift onto position-sensitive detectors. The final ion energies (about 9.5 electronvolts) are governed by the repulsive Coulomb force between the two deuterium nuclei and depend on their initial separation in the neutral molecule. The electrons, however, can have any amount of energy — as long as energy is conserved overall.

A uniform magnetic field is imposed along the symmetry axis of the apparatus to constrain the trajectories of fast electrons and to ensure that they are able to reach the detector. This creates complicated spiral trajectories for the electrons but does not significantly perturb the motion of the much heavier ions. For each charged particle, the position of impact on the detector and the overall 'time of flight' are measured, and from them the initial momentum of all four particles can be deduced directly. Even more excitingly, in the case of hydrogen, the ions leave in opposite directions so quickly (compared with their rotational motion) that even the alignment of the molecular axis can be determined with respect to the polarization direction of the incident light. Thus, this gives a three-dimensional 'photograph' of the Coulomb explosion.

Weber *et al.*[1] have, for a specified direction of one electron, determined the spatial distribution of the other escaping electron as a function of the alignment between the molecular and polarization axes in the double ionization of deuterium (Fig. 1). From their data, it is clear that the degree of alignment of the molecular axis affects the escape directions of the electrons and that those directions do not depend solely on the polarization of the synchrotron light. This is no surprise, but the fact that the effect can now be measured is truly impressive. As if that were not enough, by carefully selecting the energy of the ions, the electron emission patterns can be probed as a function of the initial internuclear separation of the ion cores, just before the double ionization happens. This sensitive three-dimensional molecular camera captures images of the Coulomb explosion at various bond lengths, as the molecular bond stretches and contracts through its own vibrational motion.

In the past, theories have generally had to integrate over molecular orientation and

internuclear separation — smearing out interesting physics — just to be able to compare with experiment. Those days are now apparently over. These remarkable experimental results create a timely theoretical challenge: to describe the observations accurately and predict new areas of interest. The next obvious development is to study a molecule comprising one hydrogen atom and one deuterium atom — still a simple molecule, but with its symmetry broken. In this case, the orientation of the molecular axis, not just its alignment, can be determined — that is, which end is 'up', not just which way it is pointing; chiral effects are also anticipated with circularly, instead of linearly, polarized light. In terms of the 'big picture', these studies will provide remarkable physical insight into multi-electron processes whose effects are even more significant in larger atoms and molecules. ■

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Cancer

An inflammatory link

Fran Balkwill and Lisa M. Coussens

The NF-κB protein is a key player in inflammation. It now seems that it might also activate signalling pathways, in both cancer cells and tumour-associated inflammatory cells, that promote malignancy.

Inflammation is central to our fight against pathogens, but if it is not ordered and timely, the resulting chronic inflammation can contribute to diseases such as arthritis, heart attacks and Alzheimer's disease. A functional link between chronic inflammation and cancer has also long been suspected[1,2]: population-based studies show that susceptibility to cancer increases when tissues are chronically inflamed; and long-term use of non-steroidal anti-inflammatory drugs reduces the risk of several cancers[3]. Moreover, most solid tumours contain many non-malignant cells, including immune cells and blood-vessel cells, that are important in inflammation. But the crucial molecular pathways that permit communication between abnormally growing cancer cells and these inflammatory cells remain unknown. A complex network of pro-inflammatory mediators is probably involved, because deletion of certain key molecules can reduce cancer susceptibility in mice[1,2,4]. Two mouse models of inflammation-associated cancer now implicate the gene-transcription factor NF-κB and the inflammatory mediator known as tumour-necrosis factor-α (TNF-α) in cancer progression[5,6].

Using a mouse model of inflammatory hepatitis that predisposes mice to liver cancers, Pikarsky *et al.*[5], writing on page 461 of this issue, present evidence that the survival of hepatocytes — liver cells — and their progression to malignancy are regulated by NF-κB. (NF-κB is an important transcription factor that controls cell survival by regulating programmed cell death, proliferation and growth arrest.) Moreover, Pikarsky *et al.* find that the activation state of NF-κB, and its localization in the cell, can be controlled by TNF-α produced by neighbouring inflammatory cells (known collectively as stromal cells). Greten *et al.*[6], reporting in *Cell*, come to a similar conclusion by studying a mouse colitis-associated cancer model. Their work does not directly implicate TNF-α, but instead found enhanced production of several pro-inflammatory mediators ('cytokines'), including TNF-α, in the tumour microenvironment during the development of cancer.

An important feature of both studies is that NF-κB activation was selectively ablated in different cell compartments in developing tumour masses, and at different stages of cancer development. These approaches offer new insight into the differential regulation of pre-malignant and malignant states by inflammation and NF-κB in distinct cellular compartments.

In Pikarsky and colleagues' inflammation-associated model of liver cancer[5], TNF-α, produced by stromal cells, activated NF-κB in adjacent hepatocytes that were undergoing 'transformation' into malignant cells. Selective deletion of NF-κB in hepatocytes, or inhibition of TNF-α produced by stromal cells, induced programmed cell death of transformed hepatocytes, and subsequently reduced the incidence of liver tumours. The authors also found that activation of NF-κB was not important in the early stages of tumour development, but was crucial for malignant conversion. Thus, preventing NF-κB activation in hepatocytes after seven months of chronic liver inflammation was sufficient to inhibit the

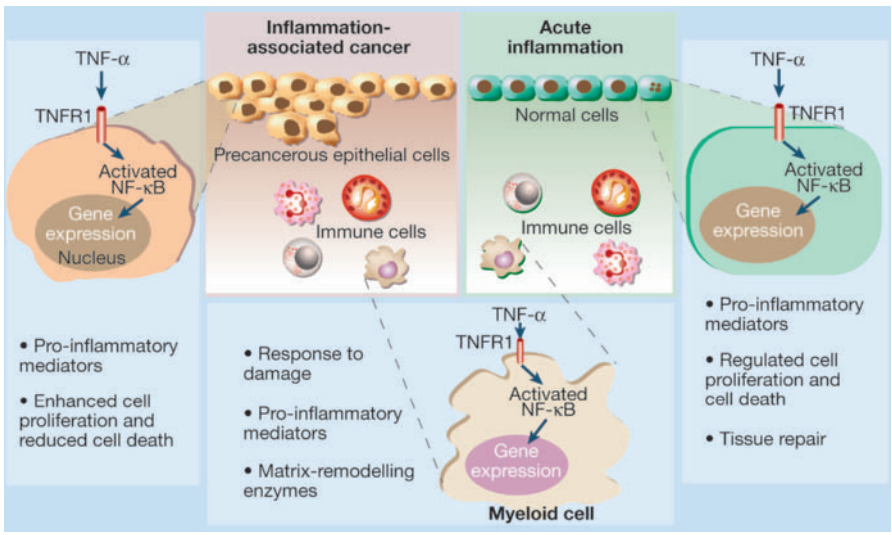

Figure 1 **Opposing effects of the NF-κB protein in normal tissues and in cancer. Tumour-necrosis factor-α (TNF-α) acts through its receptor, TNFR1, to activate the gene-transcription factor NF-κB. During acute inflammation in 'normal' epithelial cells (right), NF-κB activation leads to increased expression of genes that encode pro-inflammatory mediators called cytokines, and activates genes that regulate the balance between cell proliferation and cell death. In inflammatory immune cells (myeloid cells; bottom), NF-κB activation can also regulate cell death, but more importantly regulates short-term expression of pro-inflammatory mediators to repair the tissue damage. Ablation of NF-κB in inflammatory cells impairs the expression of pro-inflammatory cytokines. Precancerous epithelial cells (left) use NF-κB to enhance their survival, and their propensity to become malignant cells, by augmenting their expression of pro-inflammatory and cell-survival genes while inhibiting the death-promoting machinery. If NF-κB activation is disabled in these epithelial cells, while pro-inflammatory gene programmes are maintained, cell death is favoured and tumour progression is reduced.**