The inescapable conclusion is that a membrane protein containing four or five transmembrane helices, when associated with the translocon, remains in a topologically uncommitted state and can "flip" within the membrane to change its topology. There has been circumstantial evidence suggesting this for a number of membrane proteins for many years (*10*), but Seppälä *et al*. provide the first systematic analysis that suggests the phenomenon. But how can membrane protein flipping, when associated with the translocon, be reconciled with the energy required for tumbling within a membrane? Is it the privileged, protected environment within the translocon that permits such topological gymnastics? This would require a translocon pore size with a diameter of ~50 Å, which is consistent with biochemical data (*11*) but which is too large to be encompassed within a single translocon, thus implying the requirement for oligomers. However, the structure of a eukaryotic translocon (Sec61 complex) bound to a ribosome that is actively translocating a polypeptide chain supports the theory that it functions as a monomer (*12*), although higher oligomeric states could exist transiently during membrane protein biosynthesis. Structures of the ribosome bound to the translocon containing a nascent polypeptide chain may provide some answers, but considerable work on the dynamics of membrane protein synthesis will be required to interpret these snapshots of the process. Engineering topological reporter proteins such as EmrE constitutes an important addition to this field, which should eventually lead to a better understanding of how membrane proteins fold.

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PHYSICS

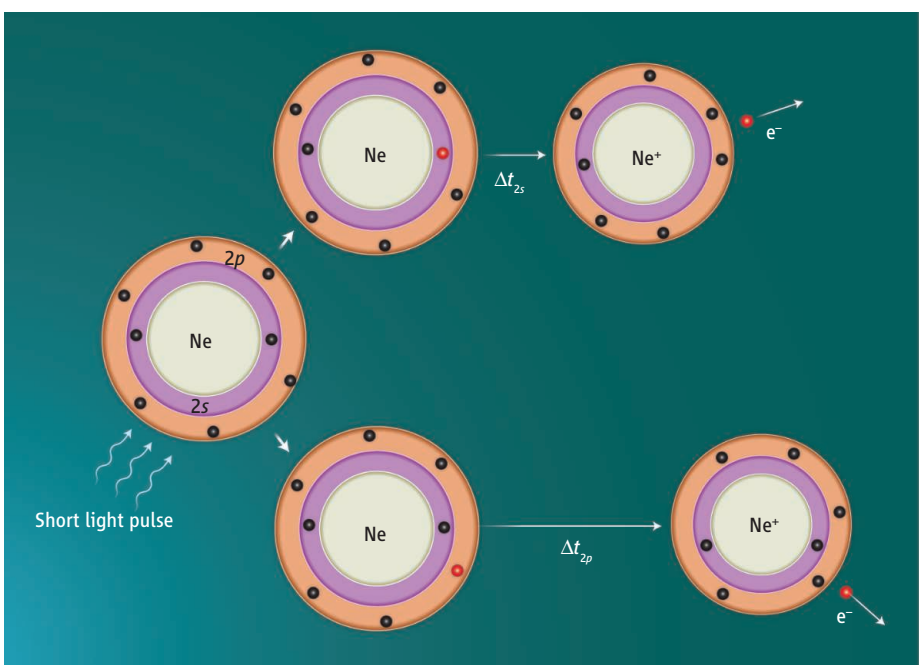
When Does Photoemission Begin?

Ultrafast spectroscopy and multielectron calculations reveal complex electron dynamics occurring just before an atom emits a photoelectron.

H. W. van der Hart

The process of photoemission was one of the effects that led to the formulation of quantum mechanics. If an atom or surface absorbs sufficient energy from incoming light, it can transfer that energy to an electron, which is then emitted. Theories of photoemission mainly focus on energetics—the temporal or dynamic aspects are ignored—but complex electron interactions occur that will create a slight delay between light absorption and electron emission. This time delay has been poorly understood for a fundamental reason: We cannot "see" an atom absorbing a photon. At best, we can follow subsequent emission events and use them to establish a "time zero" when the light was absorbed. A practical challenge has been that the time delay is extremely short, and only recently have direct experiments been feasible with the advent of lasers that emit pulses on the attosecond (as, 10^{-18} s) time scale. On page 1658 of this issue (*1*), Schultze and co-workers present measurements of time delays between different photoemission processes generated by the same ultrashort light pulse. This finding not only allows further studies of the timing of photoemission but also provides a new way to investigate electron interactions in atoms.

The complex dynamics of atomic photoemission has a simple origin—the emission of a negatively charged electron changes the neutral atom into a positive ion. The energy levels of the remaining electrons are different in the positive ion, and as the electrons adjust to their new energy levels, they release energy that is transferred to the outgoing electron. The time needed for this transfer is the origin of the small time delays.



Electron hesitation. Schematic diagram of a photoemission process for Ne. An incoming photon of an ultrashort light pulse is absorbed by either a 2*s* (top row) or a 2*p* (bottom row) electron. After photoabsorption, the electron escapes, while the orbitals of the other electrons adjust to the new surroundings as the atom becomes an ion. This adjustment leads to a time delay Δt in the emission of the electron, which is longer for emission of a 2*p* electron than for emission of a 2*s* electron.

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Schultze *et al*. studied two ionization processes induced by the same ultrashort pulse, emission of a 2*s* electron, and emission of a 2*p* electron from a Ne atom (see the figure). It takes 20 attoseconds longer for a 2*p* electron to be emitted than for a 2*s* electron. The natural orbit time of 2*p* electrons in Ne is about 100 as, so photoemission time delays could affect the interpretation of ultrafast measurements.

The current demonstration of delays in photoemission is an example of the new physics emerging from the capability to generate ultrashort light pulses. Previous experiments have probed responses of a single electron to a light field. For example, ultrafast spectroscopy can be used to relate the kinetic energy of a photoelectron to the vector potential associated with a light field (*2*) and to observe coherent scattering electronic wave packets with the so-called quantum stroboscope (*3*).

The photoemission delays observed by Schultze *et al*. arise from multielectron dynamics, which are substantially more difficult to interpret than single-electron dynamics. The main mechanism for the energy transfer is the repulsive force between the electrons, so photoemission delays are a signature of the collective dynamics of the electron cloud. Schultze *et al*. also performed electronic structure calculations (multiconfiguration Hartree-Fock studies) for Ne and demonstrated a time delay between different photoemission processes. An absolute time delay was established for He by direct solution of the Schrödinger equation.

The neon atom has eight electrons in the outer 2*s* and 2*p* shells. Although two electrons can be described with remarkable precision (*4*), a future challenge for the ultrafast atomic physics community is to investigate how the response of such a large electron cloud can be decomposed into the response of individual electron pairs and look for correlations in electron motion. Recent theoretical studies have demonstrated how two coupled electrons may move in unison on the ultrashort time scale, for example, in doubly excited states in the He atom (*5*) or in an isolated configuration in the C^+ ion (*6*). Further theoretical work is required to extend such a treatment to the response of a full atomic cloud.

The application of attosecond light-pulse technology to measurements of collective electron dynamics in atoms will also require a change in our view of atomic structure. The splitting of energy levels caused by electron-electron interactions is well known. This energy-centered view of atomic structure, found in standard textbooks [e.g., (*7*)] can now be complemented by an alternate view, in which the underlying electron dynamics takes center stage.

The time resolution at which atomic and electronic motion can be observed has increased greatly over the past decades. Femtosecond (10^{-15} s) spectroscopy allowed molecular dynamics to be observed (*8*). Recent advances here have enabled observations of vibrations in even the lightest molecules [H_2, D_2, and D_2^+ (*9*–*11*)] and observation of signatures of multielectron dynamics in CO_2 (*12*). Atoms now form the next frontier. The delay in photoemission in atoms, and the differences in this delay for different electron shells, is a great example of the new physics revealed by crossing this frontier. Attosecond light-pulse technology is now enabling experiments that can be exploited to determine ultrafast collective electron dynamics.

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IMMUNOLOGY

IgA Changes the Rules of Memory

Pathogens and bacteria that normally live in the gut induce different immune responses.

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The human intestinal mucosa is exposed to a complex ecosystem of harmless bacteria (commensals) that are excluded from the sterile environment of the body by an antibody isotype called immunoglobulin A (IgA) (*1*). Characterizing the dynamics of this immune response has been problematic because of constant immune stimulation by such bacteria. On page 1705 of this issue, Hapfelmeier *et al*. (*2*) use a reversible system of gut bacterial colonization in mice to show that responses to commensals lack cardinal features of systemic (extramucosal) IgG responses to pathogenic bacteria.

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Commensal microbes form a diverse community in the gut, estimated to exceed the host's eukaryotic cell number by an order of magnitude (*3*). Commensals break down otherwise indigestible food components, generate essential nutrients, and "educate" the local immune system. Intestinal B cells maintain this mutualistic relationship by producing IgA, an isotype that induces a weak inflammatory response compared to IgG in blood (*1*).

The poor inflammatory activity of IgA permits the intestinal mucosa to impede the entry of bacteria into the body without inducing inflammatory damage of the epithelial barrier (*1*). If invading pathogens breach this barrier, circulating IgG rapidly recruits innate immune cells with phagocytic function (granulocytes, monocytes) through the activation of an inflammatory reaction. With the help of IgG, these innate effector cells clear invading bacteria in a matter of hours.

Systemic IgG responses emerge 5 to 7 days after the immune system encounters a pathogen. IgG provides protection against secondary challenges by generating long-lived memory B cells that circulate like sentinels and produce massive amounts of IgG upon reencountering bacteria (*4*), and plasma cells, which release IgG from the bone marrow into the circulation (*5*). Key features of IgG memory by these cells are the quick increase and higher affinity of secondary responses, and the synergistic effect of repeated exposures. Bacterial products also enhance the half-life of serum IgG by activating memory B cells (*6*). Does intestinal IgA follow the same dynamics as systemic IgG?

To address this question, Hapfelmeier *et al*. directly introduced a mutant strain of the bacteria *Escherichia coli* into the intestine of otherwise germ-free mice. This bacterial