of seemingly regeneration-deficient limbs. As Kumar *et al*. state, if we understood how the pattern of the regeneration blastema is specified, we could engineer that pattern into cells of nonregenerating appendages. Growth-promoting molecules could then be supplied exogenously to manifest the pattern without other intervention. How soon this might be possible, particularly in humans, is anyone's guess, but the addition of nAG to the repertoire of necessary factors is an important step forward.

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CHEMISTRY

All at Once

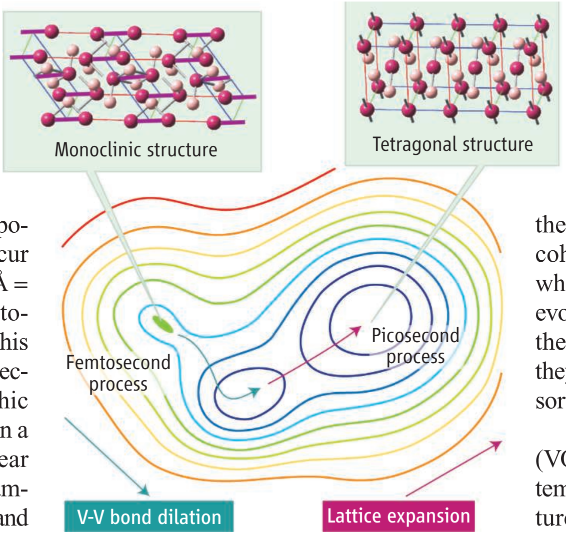
Femtosecond electron crystallography reveals the atomic structural changes that underpin a light-induced insulator-metal transition.

Andrea Cavalleri

Complex solids with strongly correlated electrons exhibit transformations in which more than one microscopic property (such as atomic positions, as well as electronic or magnetic arrangements) changes at once. To sort out the underlying physics, one must be working at the spatial and temporal resolution of the change, which can occur over length scales of a few angstroms (1 Å = 10^{-10} m) and last as little as a few femtoseconds (1 fs = 10^{-15} s). On page 788 of this issue, Baum, Yang, and Zewail use femtosecond electron pulses to take crystallographic snapshots of the evolving lattice structure in a complex solid (*1*). From their data, a clear connection can be made between the dynamics of a single element of lattice symmetry and a change in electronic properties.

In recent years, complex transition-metal oxides have received widespread attention, in part motivated by the quest to understand high-temperature superconductivity in doped cuprates. Along the way, a wealth of new phenomena have been discovered, including unconventional electronic and magnetic phase transitions, colossal negative magnetoresistance, and novel effects at interfaces. This richness arises from the peculiar physics of partially filled 3d orbitals, which dominate the electronic and magnetic properties of transition metal compounds.

Because of their enormous mutual repulsion, and because they are trapped by atomic distortions, the 3d electrons tend to localize on the transition-metal site, making the system insulating. Yet the same electrons also tend to hybridize with 2p orbitals from their oxygen neighbors and spread over many lattice sites to minimize their kinetic energy. When this happens, a metal is formed, and magnetic arrangements tend to change as well. Nowhere is this competition more striking than in the abrupt electronic and magnetic transitions that occur when the density of conducting electrons is changed by chemical doping. Similarly, because of the importance of next-neighbor orbital overlap, small distortions in lattice structure can cause large changes in electronic and magnetic properties.



Coherent transformation. Two-dimensional depiction of the light-induced crystallographic rearrangement in VO_2 studied by Baum and co-workers. At first, the bond between pairs of vanadium atoms dilates rapidly along one axis (**left**). Only on longer (picosecond) timescales does the system relax along the orthogonal direction, transforming a compressed tetragonal structure to a stable product phase (**right**).

With these considerations in mind, it is easy to see how excitation with light (*2*)—which rearranges the filling of different orbitals—can transform the structural, electronic, and magnetic properties of a complex solid (*3*). Because these rearrangements are cooperative, the whole solid may change when just one photon is absorbed for every 1000 unit cells. However, as we try to understand these bewildering phenomena, a new simplicity emerges on the ultrafast time scale (*4*). The reason is that the rapid photoexcitation event can impose coherence (*5*). A coherent change is one where all the unit cells that form the lattice evolve in lockstep with each other, affecting the macroscopic response of the system as they evolve synchronously and allowing us to sort them in the time domain.

The ultrafast physics of vanadium dioxide (VO_2) is a prototypical example. This room-temperature insulator has a monoclinic structure. Pairing and tilting of vanadium pairs along one axis (see the figure, top left) is at the heart of the insulating behavior. Part of the glue that keeps the paired atoms close to one another comes from the localization of two electrons on the vanadium sites, and from the gain in exchange energy when spins point in opposite directions. Photoexcitation removes a fraction of these electrons and slightly weakens a fraction of the bonds—enough to unleash a collective relaxation of the structural distortion, a delocalization of the charge, and a loss of magnetic order. Previous ultrafast optical and x-ray studies showed a rapid, nonequilibrium transition to the metallic phase, accompanied by an equally rapid rearrangement of the atomic structure (*6*). Yet, in these studies, only a single spot in the diffraction pattern was measured, giving insufficient information to elucidate the changes in atomic structure.

In the work published in this issue, Baum *et al.* were able to detect ultrafast changes in vanadium dioxide in a number of diffraction spots at the same time. The most important information comes in their ability to identify

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that the fastest atomic motions during this change occur along one particular axis of the crystal, and are related to pairs of vanadium atoms moving apart from one another (see the figure, left). Only at later times do the other crystallographic planes expand (see the figure, right). The transformation pathway between stable monoclinic and tetragonal phases is then shown to pass through an unstable, tetragonal unit cell, which is compressed along one of the axes. The authors thus establish a direct connection between the femtosecond dilation of the V-V bond and the equally fast changes in conductivity that can be measured with other techniques (*7*).

It is impressive that Baum *et al.* achieve this femtosecond time resolution in the reflection mode of diffraction, because the inherent velocity mismatch between electrons and photons can, in principle, smear out the time response and hinder the observation of the femtosecond movements of the atoms. To this end, the authors ingeniously tilted the front of the optical pump pulse, thus matching the speeds with which the surface of the sample is excited optically and swept by the diffraction probe. Reflection geometry opens the way to femtosecond electron diffraction in most bulk solids, whereas previous experiments performed in transmission were limited to very thin films (*8*, *9*).

In thinking of new advances in the studies of ultrafast structural dynamics, a few key considerations come to mind. Electron pulses can be incorporated in a microscopy apparatus, as shown previously by Zewail and co-workers (*10*). This microscopy advance is important for the study of strongly correlated transition-metal oxides discussed here, which are known to exhibit important phase separation phenomena that are quite difficult to investigate (*11*).

The next frontier will be a time resolution of 10 fs or below, which will allow the movements of the lightest atoms that compose many important organic compounds and liquids to be resolved. Femtosecond electron diffraction is evolving hand in hand with x-ray techniques (*12*), which have developed in the recent past with both tabletop and accelerator-based techniques, offering similar time resolutions but also important spectroscopic capabilities (*13*). The capability of interrogating matter with ultrafast electron and x-ray pulses is opening new horizons that could only be dreamed of as recently as a decade ago.

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CHEMISTRY

No Protection Required

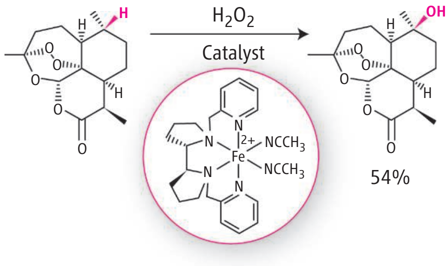
An iron catalyst converts C–H bonds to C–OH groups with predictable selectivity even in very large molecules.

Robert H. Crabtree

Organic synthesis has traditionally relied heavily on activating groups and protecting groups to steer synthetic reactions to the desired products. Activating groups such as halides enhance the reactivity of reactants, whereas protecting groups such as amides or esters block reactivity at undesired sites. On page 783 of this issue, Chen and White (*1*) show that such activating and protection groups are not always required even in reactions involving complex molecules.

With the rise of green chemistry (*2*), more attention is being paid to eliminating activating and protecting groups, wherever possible, for two reasons. First, they generate waste. Second, both activating and protecting groups require extra synthesis steps to be introduced into reactants; protecting groups also need extra steps to be removed after reaction. Catalysis can give reactivity and selectivity without the need for activating or protecting groups. The ideal catalyst reacts with an unactivated reactant with a selectivity that can be tuned by choice of catalyst. In practice, however, we are still far from the goal, particularly when the substrate is a complex organic molecule with multiple functional groups.

Perhaps the greatest challenge is finding catalysts that selectively attack C–H bonds, which are ubiquitous in organic compounds but are often very unreactive. A number of catalysts are known for this "C–H activation" reaction (*3*), but they act only on simple molecules such as hydrocarbons. In more complex organic molecules, such as those commonly encountered in pharmaceuticals, numerous oxygen or nitrogen-containing functional groups are distributed over a core held together by carbon-carbon bonds. In such a polyfunctional molecule, unselective attack at any of a number of C–H bonds can result in a cocktail of final products.



Selective conversion. The antimalarial compound artemisinin (**left**) is extracted from a shrub used in herbal form in Chinese traditional medicine. Although artemisinin has numerous C–H bonds and a delicate peroxide functional group, it gives a single product (**right**) when the Chen-White catalyst is used in conjunction with hydrogen peroxide. This implies that the catalyst has high selectivity even for a complex molecule, but predictability for other cases will require more detailed study.

Chen and White now report a striking counterexample that shows how C–H bonds can be activated selectively even in complex polyfunctional molecules (see the figure for an example). The authors used an iron catalyst to convert specific C–H bonds in a wide variety of molecules to C–OH groups; the benign and inexpensive hydrogen peroxide serves as the ultimate source of the oxygen atom.

Depending on the specific case, the authors ascribe the remarkably high selectivity to a combination of a number of causes. These include the reactive C–H bond being either inherently more reactive than any other, or

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