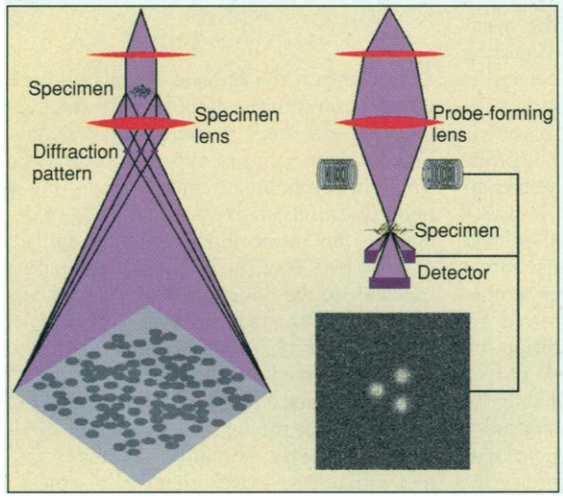
The Imaging of Individual Atoms

David A. Jefferson

Knowledge of the relative positions of atoms is crucial in many areas of physical and biological science. Indeed, many scientists create atomic images without realizing it. An undergraduate student, for example, wrestling with the infrared spectrum of a symmetric top molecule such as CH_3Br is actually constructing an image of the atoms. This is essentially atomic imaging, although by very indirect means. More desirable are direct imaging techniques, which avoid some of the pitfalls of modeling and computation. On page 413 of this issue, Nellist and Pennycook present a state-of-the-art example of direct imaging: atoms on supported catalysts at high resolution (*1*).

When it became technically feasible, direct imaging replaced indirect methods. A classic case of indirect imaging that illustrates the limitations is the determination of atomic structure by diffraction. Diffraction methods are based on elastic scattering of x-rays or neutrons, although electron diffraction (*2*) continues to make a significant contribution. The starting point is elastic scattering at the specimen, altering the phase of the incident radiation. This gives rise to diffracted beams whose magnitudes are recorded. These are recombined with deduced phase information, a computational process (*3*) now almost wholly automated, to form an image of the structure. Although computational, this process of Fourier transformation is exactly the same as the formation of an image by a lens (*4*). The difference is that no lens is available for either x-rays or neutrons and operator input is necessary for the phases. Resolution is simply a function of the range of diffracted beams included, and although only the overall conformation is needed in many large biological molecules, the wavelength of x-rays and neutrons is such that atoms, and even the detail within atoms (*5*), is nevertheless visible.

Whether structural features obtained in this way correspond to images of individual atoms is open to question. This doubt arises because the structure map is the sum of repeated units in a periodic crystal. The need for structural repetition is a serious drawback of conventional diffraction because systems such as biological membranes, adsorbed molecules, and small clusters are aperiodic. Repeated averaging may be reduced if the magnitude of the scattering events is increased, and in electron diffraction, where the interaction is far stronger than with x-rays, microcrystalline specimens containing fewer unit cells may be used. The stronger interaction also brings unwanted effects such as multiple scattering (*6*), but its effects may be calculated. However, the fundamental drawback of diffraction—namely, the need to record the data and then deduce the phase information before transformation into the image—still remains. In an aperiodic specimen, the number of phases to be deduced becomes infinite and formation of the image by computation becomes impracticable.



Making atomic detail visible. Conventional HRTEM (left) is like optical microscopy, except that electrons are used and the lenses are electromagnets. Only electrons that lose no energy contribute to this image. In the STEM (right), a fine probe of electrons is scanned across the specimen, and all scattered electrons are used to form the image.

Electrons enable high-resolution direct imaging. Being charged particles, they can be focused by an inhomogeneous magnetic field with cylindrical symmetry, and consequently, it is possible to build a magnetic analog of a normal glass lens. Fourier transformation of diffracted beams into an image then becomes possible without the need to deduce phases, and periodic specimens are unnecessary. This magnetic focusing is the basis of all conventional high-resolution transmission electron microscopy (HRTEM). Imaging of atomic detail in crystals started over a quarter of a century ago: Pioneering studies of nonstoichiometric oxides (*7*) with cation-cation distances of 0.4 nm were followed by determination of finer detail, limited only by the quality of the electromagnetic lenses used. As shown by Scherzer (*8*), these lenses introduce additional phases into diffracted beams before recombination that, coupled with slight fluctuations in electron energy and lens field strength, plus the finite size of the electron source, have the effect of replacing a point in the idealized image by a spread function. In mathematical terminology, the real image consists of an ideal image convoluted with the Fourier transformation of the aberration function. Reduction of lens aberrations has been a major task in HRTEM in the intervening years, and now the attainable resolution is approaching 0.1 nm. As this resolution is less than atomic dimensions, the imaging of individual atoms by HRTEM should be possible.

A more subtle problem associated with HRTEM imaging of single atoms in a nonperiodic array is obtaining a sufficiently high signal-to-noise ratio. The proportion of electrons undergoing elastic scattering depends both on their energy and on specimen composition and thickness. Estimates vary, but for most specimens used in HRTEM studies, it is not particularly high, and the remainder of the electrons either passes through the specimen without interacting or undergoes energy transfer with atoms in the specimen. There are innumerable ways in which this can happen, but in general, all of these inelastic events are incoherent, and these electrons can no longer contribute to the elastic image but instead form a quasi-continuous background upon which the latter is superimposed. For crystalline materials, this low rate of interaction is not a problem, as the structure is viewed in projection and rows of atoms parallel to the electron beam are imaged. For nonperiodic specimens, however, the contrast from each atom must be considered in isolation, and then, except in very special cases, the atomic contrast is lost against the general background. Even when atom clusters are quite large, such as icosahedral particles of metals, the lack of long-range periodicity can make image interpretation extremely difficult (*9*), and individual atoms may only be imaged at the edges of the cluster.

Because of this difficulty, attempts were made to use all of the scattered electrons, rather than just those undergoing elastic scattering, in the scanning transmission

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electron microscope (STEM) (*10*). The scattering cross section of an atom for both elastic and inelastic processes varies with atomic number; consequently, a record of the total scattering is just as good a method of forming images as is interference of elastically scattered waves. The problem lies in how to monitor total scattering as a function of position within the specimen. In the STEM, this is achieved by scanning a fine probe of electrons across the specimen. Formation of this electron probe uses the technology developed over the years for HRTEM operation, in that if electromagnetic lenses can produce a highly magnified image of a specimen with a very small spread function, they may also be used to produce a highly de-magnified image of the electron source. If this image is then focused at the specimen, it can be scanned while the total scattering is monitored by a annular detector placed beneath the specimen, with the unscattered electrons passing straight through. This mode of imaging is equally suited to all types of specimens, periodic or not. The gain in contrast is considerable, and the method is limited only by probe size and specimen thickness because the diameter of the probe increases as it passes through the specimen. With STEM, isolated atoms, dimers, and trimers of moderately heavy atoms on a support of lower atomic number can be resolved, as reported by Nellist and Pennycook (*1*). In addition, by correlating directions in the atomic images with images of the support recorded with the unscattered electrons, the exact crystallographic relation between monodispersed species and the supporting medium can be established, information that is crucial to understanding the reactivity of such species, as in heterogeneous supported catalysts.

Although frequently used for the study of surface-supported species, STEM resembles HRTEM in that it is a technique for bulk structural examination. For example, atom clusters can be observed even when they are accommodated within a second phase, as is frequently found when one metal is dispersed within another. If investigation is limited to atoms adsorbed on surfaces, although STEM and even HRTEM (*11*) techniques have been used, the ultimate atomic images have been produced by means of the scanning tunneling microscope (STM). In this method, all resemblance to optical imaging methods has been lost, as the probe used is a mechanical one, but the tunneling current that is recorded as the probe is scanned involves such short-range effects that "contrast" from all but the atom under study can be minimal. If an atomic image is defined merely as a pictorial representation of the atom arrangement, STM images must surely represent the most spectacular achievement of imaging science.

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Signaling Across Membranes: A One and a Two and a ...

Jeff Stock

Receptors on the surfaces of cells transmit information into the cytoplasm to effect appropriate responses to extracellular signals. One kind of receptor—type I—consists of a single hydrophobic, membrane-spanning α helix that links an extracellular sensory domain to an intracellular signaling domain (*1*). But how does the binding of a signaling molecule to the domain of the receptor outside the cell change the catalysis performed by the part of the receptor inside? According to current models, transmembrane signaling is accomplished either by dimerization of the receptors once the signalling molecule binds or by altering the orientation of one monomer with respect to the other within a preexisting dimer. In this issue of *Science*, two genetic studies of the bacterial chemotaxis receptor for aspartate, Tar, seriously question a fundamental assumption made by all of the models (*2*), namely, that a dimer is necessary at all. In fact, the Tar receptor functions quite well with a monomeric intracellular domain.

The sensing and signaling domains of type I receptors are each an independent soluble cassette that can be synthesized and studied alone. Although type I receptors all seem to use a common mechanism for transmembrane signaling, their structures are startlingly different. The x-ray crystallographic structure of the sensory domain of the human growth hormone receptor, hGHR (*3*), is not at all like that of the bacterial receptor Tar (*4*): Whereas the sensing portion of hGHR is composed of two seven-stranded β sandwich domains, the sensory domain of Tar is a bundle of four parallel α helices. The only common feature is that both ligands, hGH and aspartate, bind within single asymmetric binding sites at the interface between sensory-domain monomers. This commonality provides a structural basis for the dimer-interaction mechanisms that have been proposed to explain type I receptor function.

Type I receptors have also been termed catalytic receptors because their signaling domains either are signal-transduction enzymes or are proteins that form complexes with such enzymes. Virtually any signal-transduction enzyme can function as a type I receptor signaling cassette. The signaling domains of type I receptors such as the insulin receptor or hGHR either are protein tyrosine kinases or form complexes with protein tyrosine kinases (*5*), and the signaling domains of bacterial receptors such as Tar either are themselves protein histidine kinases or form complexes with protein histidine kinases (*6*). Other type I receptors

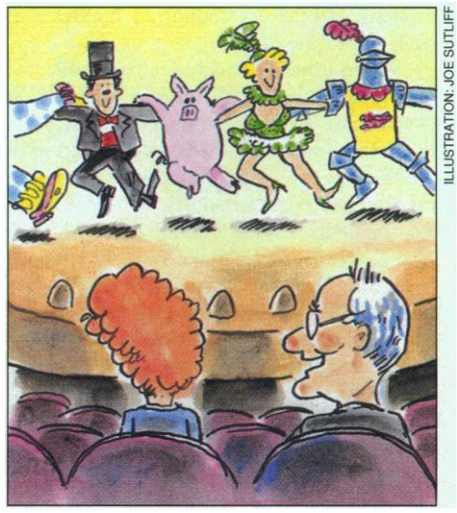

ILLUSTRATION: JOE SUTLIFF

"And she's a marvelous soprano!"

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