mental design. For example, efforts to improve the precision of optical traps now allow the transcription of DNA to be followed at almost base-pair resolution (*19*). Processes as complicated as DNA packaging by viruses and DNA uptake by bacteria have been studied under near physiological conditions (*20*, *21*). Case *et al*. have now added another wonderful example to this list, not to mention the equally impressive accomplishments attributable to other single-molecule force spectroscopy techniques (*22–24*). In the field of manipulation and force measurements of single molecules, it appears that, so far, one is limited only by one's imagination.

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MATERIALS SCIENCE

Microstructures in 4D

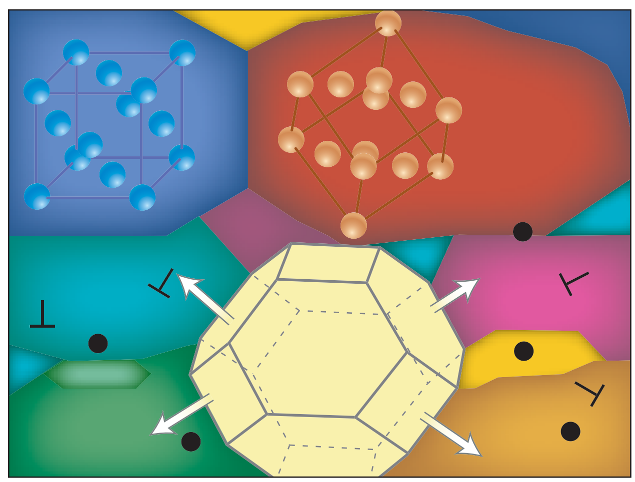
S. Erik Offerman

The ability to watch the three-dimensional growth of a single crystal that is deeply embedded in a bulk sample, as Schmidt *et al*. report on page 229 of this issue, is a breakthrough in materials characterization (*1*). Their work demonstrates the opportunities created for materials research by further development of the three-dimensional x-ray diffraction (3DXRD) microscope at the European Synchrotron Radiation Facility in Grenoble. The 3DXRD microscope, which Schmidt *et al*. developed into a truly 4DXRD microscope by adding the dimension of time, is likely to play a major role in revealing the underlying mechanisms of evolving microstructures of partially or fully crystalline materials such as metals, ceramics, and polymers.

Controlling microstructure is important, because it largely determines the properties of a wide variety of materials. For example, the yield strength of metals is inversely proportional to the average grain size (*2*), the conductivity of superconductors is strongly reduced through grain boundaries (*3*), and magnetic domain walls can be pinned by grain boundaries and precipitates (impurities). Moreover, the degree of crystallinity and the size and arrangement of crystallites in a semicrystalline polymer have a profound effect on its physical and mechanical properties (*4*). Ideally, the formation of the microstructure should be monitored under conditions like those of real processing and in the bulk of the material. This puts high demands on the measurement technique. Schmidt *et al*. have made an exciting step forward by imaging simultaneously the spatial and time-dependent microstructure of bulk material down to the micrometer range, which was not possible until now with any other experimental technique or ab initio calculation.

Traditionally, metallurgists use light microscopy to reveal the microstructure from cross sections of the material. However, the 2D image that is obtained in this way is an oversimplification of the complex 3D microstructure. The combined use of computer-aided reconstruction techniques and light microscopy allows the creation of 3D images of limited parts of the microstructure via repeatedly grinding off a thin layer of material and taking an image (*5*). Despite the effort, light microscopy techniques are limited to ex situ measurements. The advent of electron microscopy techniques drastically improved the resolution of the image to the nanometer level. In addition, in situ electron microscopy measurements have been performed to capture the evolution of the microstructure at high temperatures (*6*). Nevertheless, free-surface effects that are always present in 2D imaging techniques during in situ measurements complicate the analysis and the ability to draw unambiguous conclusions. Neutron and synchrotron radiation facilities, which enable high penetration even in high electron density materials, have opened the possibility for nondestructive imaging of the 3D microstructure. Yet the time dimension was still lacking in 3D imaging with micrometer spatial resolution.

Using the exceptionally high brilliance of third-generation synchrotron sources, Schmidt *et al*. developed a technique to study microstructures in 4D with a spatial resolution of micrometers and a time resolution of minutes. The strength of the technique that Schmidt *et al*. developed is that many relevant aspects of the evolving microstructure can be measured simultaneously for the bulk of the material. This circumvents the need for additional measurements under different conditions and of a different part of the material. This is important because microstructures are very inhomogeneous, as illustrated in the figure.



Microstructural mapping. Schematic drawing of a deformed metal, showing the complexity and inhomogeneities of the microstructure: dislocations (T-shaped symbol), precipitates (small solid spheres), subgrain and grain boundaries, and a recrystallizing grain in 3D (arrows show direction of growth of grain surfaces). Large color differences indicate large differences in crystallographic orientation (top).

Generally, the microstructure of a polycrystalline material is composed of multi-

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ple grains or crystals with different crystallographic orientations that are separated by grain boundaries. As a result of plastic deformation, the original grains are subdivided into smaller grains separated by dislocation (line defect) networks. Moreover, commercial alloys always contain impurities that can form precipitates, which are small particles with a different composition and crystal structure than the matrix.

Schmidt *et al*. have determined the absolute crystallographic orientation, position, volume, and shape of a recrystallizing grain in deformed aluminum. Their work shows that the shape of a recrystallizing grain in aluminum is more or less spherical as it starts to grow, in accordance with general belief, but as it grows the grain progresses in different directions with different speeds and in a jerky fashion. The mobility of the grain boundary, which is an important parameter in models, is unambiguously determined and shown to be anisotropic. The authors show that the jerky movement of the grain boundary reflects the inhomogeneous distribution of dislocations in the deformed aluminum matrix. Knowledge about the density, distribution, and arrangement of the dislocation in the deformed matrix and their influence on the growth of an individual grain, as measured by Schmidt *et al*., is of utmost importance in understanding recrystallization phenomena.

The authors measured the recrystallization process in exceptional detail, which is of great value for theoreticians because theory and experiment can now be compared at the elementary level of a single grain. Characterizing microstructures in 4D opens great opportunities in other fields of materials science. For example, it should now be possible to study the underlying mechanisms of solidification, solid-state phase transformations, and precipitation of a wide range of materials. As a result, the 3DXRD technique will contribute to the development of materials with superior properties and optimal production routes.

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GENOMICS

The Chimpanzee Genome—A Bittersweet Celebration

Maynard V. Olson and Ajit Varki

These are exciting times for those interested in human origins. After almost a century of knowledge gleaned from the excavation of hominid bones in East Africa, the draft sequence of the chimpanzee genome is now providing a flood of molecular data that may shed new light on human origins. The challenge of integrating these molecular data with the fossil record and with behavioral studies of great apes was on full display during a recent symposium at the University of California, San Diego (*1*).

Most speakers discussed one of three principal sources of data: a Japanese-led analysis of chimp chromosome 22 (*2*); a private-sector initiative at Celera Genomics to sequence most of the exons of the chimp genome (*3*); and the National Human Genome Research Institute (NHGRI)–funded project to produce a rough-draft sequence of the whole chimp genome (*4*). Although the recent release of the draft sequence by the Washington University and MIT/Broad Institute sequencing centers (*4*) was the primary impetus for this symposium, many other aspects of our closest evolutionary relative also were explored.

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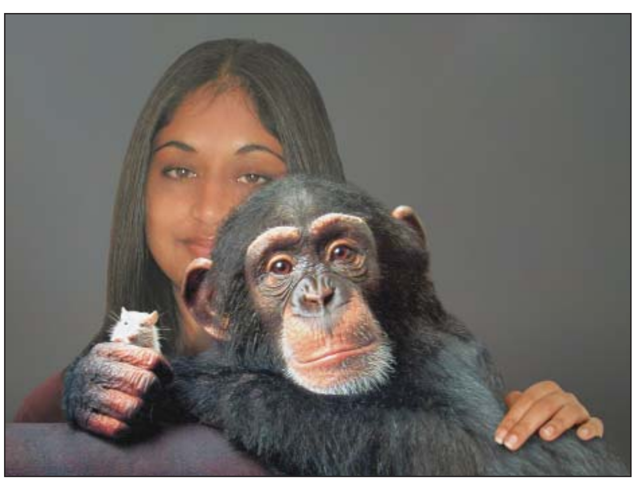
Yoshiyuki Sakaki (RIKEN Genomics Sciences Center) represented the Japanese-led effort. Although this project analyzed only ~1% of the chimpanzee genome, it provides the first look at long-range comparisons with the human genome based on complete high-quality sequence. The long-range organization of chimpanzee chromosome 22 is nearly identical to that of its human homolog, chromosome 21. The level of single–base pair substitutions between the two species is only 1.44%. However, there are tens of thousands of insertion-deletion variants, including one 200-kbp human-specific duplication. Many sequence variations between the chimp and human lineages are attributable to differing activities of large numbers of retrotransposons.



Andy Clark (Cornell University), representing Celera's exon sequencing effort, discussed chimp-human comparisons of inferred protein sequences. Interestingly, proteins involved in amino acid catabolism showed a big positive selection signal in the human lineage, whereas those involved in neural development did not. This finding reminds us that diet and pathogens are dominant selective forces for all species. Other genes undergoing rapid positive selection in the human lineage include those encoding proteins that are involved in hearing, such as α-tectorin, a structural inner-ear protein. Evan Eichler (Case Western Reserve University), who based his analysis on the rough-draft whole-genome sequence, emphasized the same point. He reported major deletions in the chimpanzee genome, totaling at least 8 Mbp, which include a number of genes associated with immunity and inflammation. Eichler also discussed the presence in the chimpanzee of many copies of a retroviral provirus that is absent from the human genome. Its presence in chimpanzees, bonobos, gorillas, and Old World monkeys—but not humans, orangutans, and gibbons—suggests multiple, independent instances of horizontal transmission. This serves as another