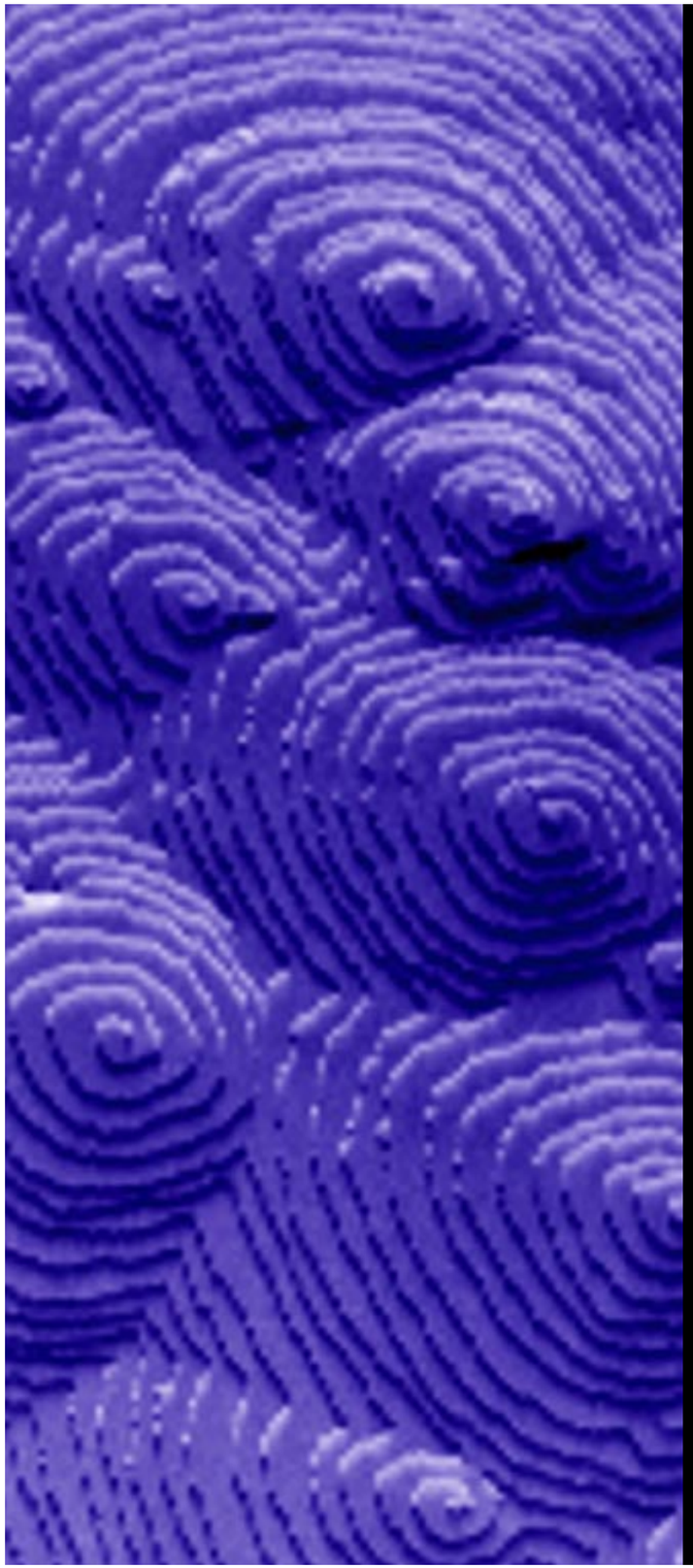


The Secrets of Crystal Growth

Using the powerful atomic-force microscope, Laboratory researchers are discovering the complex growth mechanisms and three-dimensional structures of solution-based crystals. The results portend a new generation of products, ranging from life-saving pharmaceuticals to new manmade materials.

THE crystallized forms of a world of materials—from viruses to semiconductors—hold the secrets to their shapes and functions. With the advent of the powerful atomic-force microscope (AFM), Lawrence Livermore researchers have begun elucidating the growth mechanisms and three-dimensional structures of widely different solution-based crystals on the nanometer (billionth-of-a-meter) scale.

The detailed images reveal, in unprecedented clarity, the complex world of crystal growth, including mechanisms never before seen or even postulated. The results portend a new generation of products, ranging from life-saving pharmaceuticals to new optical materials.

Leading the Lawrence Livermore effort to unravel the mysteries of crystal growth are physicist James De Yoreo and his crystal development team in the Laboratory's Chemistry and Materials Science and Laser Programs Directorates. De Yoreo and his colleagues received an R&D 100 Award in 1994 for developing a process that produces very high quality KDP (potassium dihydrogen phosphate) crystals for inertial confinement fusion lasers.[1] Using this process, which is dramatically faster than traditional methods, they announced in May 1996 that their process had, in only 27 days, produced a KDP crystal measuring 44 centimeters across. Under standard growing conditions, such an accomplishment would have taken up to 15 months.

In 1994, De Yoreo and his colleague Terry Land began using one of the seven AFMs on the Livermore site to explore the growth mechanisms of crystals in a way never before possible. "The AFM has given us the opportunity to study at the nanometer level the physics of crystal growth and how it is affected by impurities, defects, and solution conditions," according to De Yoreo. (See the box, p. 14, for a description of the three-dimensional, atomic-level resolving power of the AFM and the box, p. 15, for a discussion of how crystals grow.)

Research with the AFM is a vital element of LLNL's longstanding crystal growth and characterization effort, born out of the Laser Programs' requirement for large, ultrapure crystals grown from tiny seeds. This work is also part of a much larger Laboratory program to characterize materials on the atomic level, recognized by several R&D 100 Awards to LLNL researchers in the area of nanotechnology. This research offers significant potential payoffs to virtually every major program at Livermore.

Avenues of Research

Much of the crystal development team's AFM work has centered on the need to better understand KDP crystal growth because of its direct impact on the National Ignition Facility (NIF), a planned laser facility essential for the Department of Energy's Stockpile Stewardship and Management Program. High-power lasers like the Laboratory's Nova laser use KDP crystals for optical switching and frequency conversion of the initial infrared light to ultraviolet light. Some 600 plates of KDP approximately 40 centimeters in diameter and 1 centimeter thick will be employed in the forthcoming NIF.[2]

How the AFM Works

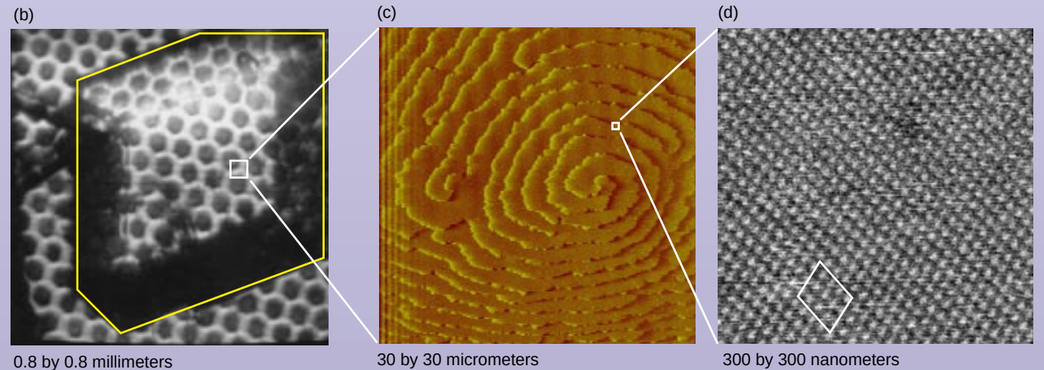
Lawrence Livermore researchers probing the dynamics of crystal growth use an atomic-force microscope (AFM), a recent descendant of the scanning tunneling microscope (STM). Developed in 1981, the STM has become so important to materials scientists that its inventors were awarded the Nobel Prize in Physics in 1986. In 1987, a Lawrence Livermore–Lawrence Berkeley team used the STM to create the first images ever produced of native DNA.*

Many researchers have turned to the AFM, an instrument ideally suited to imaging nonconductive samples such as crystals in solution. The AFM is similar to the STM in that both instruments use an extremely sharp tip to sense the atomic shape of a sample as well as a computer to record the path of the tip and slowly build up a three-dimensional image. The only difference between the two is that the STM electron tunneling tip is replaced by a mechanical tip, and the detection of the STM's minute tunneling current is replaced by the detection of the minute deflection of the AFM's cantilever.

In practice, the AFM tip is positioned at the end of an extremely thin cantilever beam and "touches" the sample with a force of only one ten-millionth of a gram, too weak to budge even one atom. As the tip is repelled or attracted to the sample surface, the cantilever beam deflects. A laser shining on the very end of the cantilever captures the magnitude of the deflection. The sample is oscillating left to right and front to back, and a plot of the laser deflection versus sample position provides the resolution of the peaks and depressions that constitute the topography of the surface. Images take only 20 to 30 seconds to complete.

Just as with a light microscope, researchers can vary the level of magnification of an STM or AFM image. The greater the movement of the sample, the larger the area being imaged. The broad magnifying range is shown below. Here a crystal of the plant protein canavalin is seen in its entirety, then further enlarged to a 30- by 30-micrometer close-up of a growth mound, and then enlarged still further to reveal its three-dimensional molecular lattice.

The AFM can be adapted to sense a range of forces including attractive or repulsive, interatomic, electrostatic, and magnetic forces. This ability allows the AFM to be used on insulating surfaces and in liquids, feats the STM cannot do. Thus, the instrument is ideal for following the dynamics of solution-based crystal growth.



(a) The atomic-force microscope reveals, in ever-increasing magnification (b through d), the complexity of solution-based crystals. In (b) a canavalin protein crystal (within the yellow box) is shown on top of a hexagonal grid. (c) shows growth sources on the crystal's face. Each step is one molecule in height. In (d) the rhombohedral structure of the underlying lattice, outlined by the solid box, defines the macroscopic rhombohedral form seen in (a).

* "Scanning Tunneling Microscopy: Opening a New Era of Materials Engineering," *Science & Technology Review*, UCRL-52000-95-8 (August 1995), pp. 4–11.

The crystal team's research has also focused on the growth of solution-based crystals of biological macromolecules such as proteins and viruses. Slow growth rates, large diameters, and great complexity in composition, structure, and surface make biological macromolecular crystals ideal systems to study with the AFM. The team reasoned that the images might reveal entirely new growth mechanisms not seen in inorganic crystals.

An enhanced understanding of crystal growth of biological macromolecules is likely to advance rational drug design, the technique of using powerful computers to literally design, in three dimensions, molecules that will precisely bind to key sites on proteins and enzymes to trigger or block a biochemical action. Designing new drugs in this fashion is dependent upon using x-ray diffraction to reveal the three-dimensional structure of complex macromolecules. In this technique an x-ray beam is scattered by a crystal of the material of interest, a diffraction pattern is recorded, and the data are transformed into a three-dimensional structure by computer.

However, this technique has been limited by problems encountered in obtaining high-quality crystals large enough to yield precise structural information. In fact, crystallization has become the rate-limiting step in most structure analyses because little is known of the growth mechanisms of the crystals and the orientation and bonding of the molecules in the crystalline lattice. Even less is understood about the role of defects either as a promoter or a limiting factor in crystal growth. Using the AFM to study crystal growth is sure to improve the quality of x-ray diffractions and, hence, help hasten the arrival of new pharmaceuticals.

Biomineralization Revolution

In a similar light, the knowledge gained by the research team will advance the understanding of biomineralization, a process used by a wide variety of organisms from bacteria to humans to synthesize inorganic complexes such as bones, shells, teeth, and even magnetic material. These inorganic complexes are true "nanostructured" composite materials and their physical properties are often superior to manmade materials.

"Biomineralization research represents a revolution in materials processing," De Yoreo says. Understanding the process, however, again requires the ability to investigate crystal growth at nanometer scale.

Most researchers have studied the growth of crystal surfaces by molecular beam epitaxy or chemical vapor deposition, two processes used in the electronics industry. However, these processes are not representative of the liquid environments in which most crystals are grown. Such environments are characterized by varying levels of supersaturation (the driving force of crystal growth studies), where, because

How Crystals Grow—A Short Primer

Watching crystals grow with an atomic-force microscope reveals a frantic world of molecules continually bonding and dissolving, attaching occasionally to the surface of a large crystal seed in one of many ways, and then perhaps joining together as part of a growing structure of spiraling mounds, spreading layers, and small islands.

In the simplest form of crystal growth, molecules land on the surface of a growing seed and become weakly adsorbed. They may join together to form small, two-dimensional islands and spread outward in a layer (called a "step") one molecule thick, with other islands forming and growing on top. In this dynamic growth process, molecules continually adsorb and dissolve from islands.

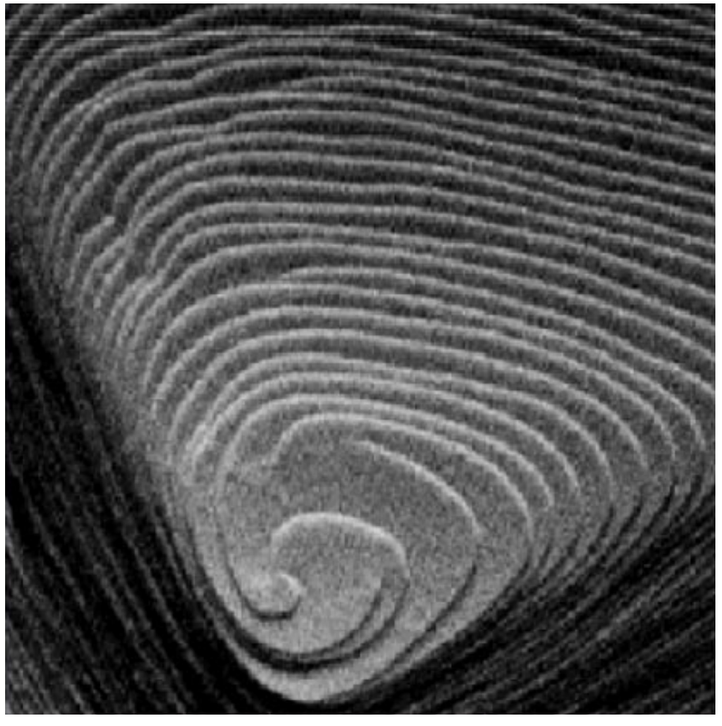
As the step edges advance, single molecules may diffuse from islands in the vicinity of the outer edge of a step or from solution and be "captured" by that edge. In this way the edge acts as a "sink" to diffusing molecules. It should be remembered, however, that molecules have complex shapes that prevent them from bonding in every orientation. For example, a molecule may have to diffuse to the edge of a step many times until it has the correct orientation for incorporation.

Continuous spiraling steps are formed by screw dislocations, actual breaks in the crystal's structure often caused by impurities or from the applied stress of two blocks of crystals that meet up and do not match. Such "screw" dislocations create spiraling, multilayered mounds called vicinal hillocks.

Two other growth phenomena are easily seen with the AFM. The first, three-dimensional growth, consists of small clusters of molecules falling out of solution onto the surface of a growing crystal face, meshing perfectly with the underlying structure. The second consists of the incorporation of sizable "microcrystals" that fall onto the growing crystal surface and create misaligned lattices.

In the dynamic world of crystal growth, all of the growth features described above may occur simultaneously. Which growth processes predominate are determined by the size and shape of the molecule, the physical properties of the material, supersaturation levels, pH, the kind and quantities of impurities present in solution, and defects that may form in the crystal's structure.

Figure 1. At low supersaturation levels, many crystals grow on dislocations (formed by stress inside the crystal lattice) that produce spiraling mounds called vicinal hillocks. Vicinal hillocks on a crystal of KDP (potassium dihydrogen phosphate) are shown here.



8 by 8 micrometers

of increased temperature and pressure, most molecules are dissolved beyond the saturation point and then permitted to precipitate out of solution onto the seed crystal.

Given the dearth of research in high-resolution, solution-based crystal growth, some basic questions need to be answered: What are the dominant growth mechanisms and how do they vary with different supersaturation levels? What are the kinetic factors that control the rate at which crystals grow? And how do impurities and defects affect growth?

To answer those questions, De Yoreo and Land at Livermore and Alex Malkin and Yuri Kuznetsov from the University of California at Riverside have been using AFMs to examine in unprecedented detail the growth of crystals of the plant protein canavalin, the satellite tobacco mosaic virus (STMV), and KDP. Their experiments involve growing the crystals under supersaturated conditions until about 3 to 5 seed crystals in a volume of 3 microliters are produced. The crystals are then transferred to the 50-microliter fluid cell of an AFM. As the crystals grow, supersaturation levels and pH are varied and dozens of images recorded.

Prized Protein Images

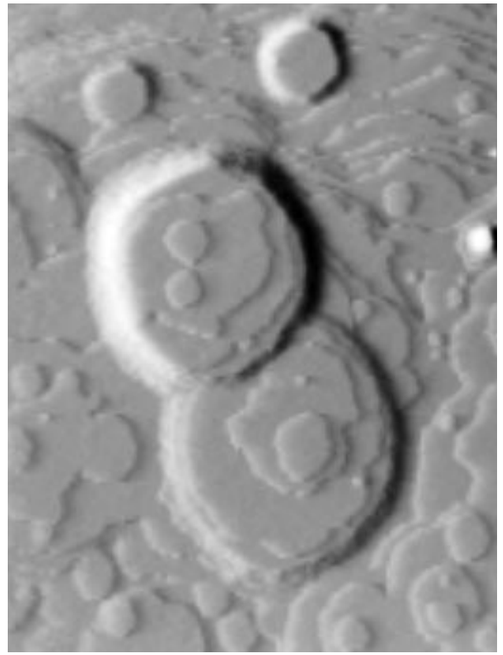
The macromolecule canavalin, the storage protein of the jack bean, was chosen for study because the UC Riverside collaborators know its structure well and can prepare very pure solutions of its crystallizable form. The AFM images (Figure 1 and those on p. 12) show that at low supersaturated levels, the crystals grow by formation of dislocations (formed by stress inside the crystal lattice) and simple diffusion of single canavalin molecules onto the growing spiral layers caused by the dislocations. (See the box on p. 15 for a general discussion of how crystals grow.) The dislocations produce polygonal spiral mounds called vicinal hillocks that appear in several variations: simple hillocks with individual dislocation sources one or two layers high, complex ones with many interacting dislocations, and left- or right-handed hillocks.

As supersaturation increases, two-dimensional growth sets in, seen in the appearance of small islands rising from the surface (Figure 2). At the highest supersaturation levels, another growth source, first discovered at Livermore during STMV studies, is seen: the adsorption of small, three-dimensional

clusters containing 50 to 500 molecules. The most remarkable feature of this so-called three-dimensional growth is that upon adsorption, the molecular clusters reorient so that the cluster lattice merges with the lattice of the larger crystal to which they adsorb, without creating defects or discontinuities. The multilayer islands in Figure 2 are examples of such clusters.

At very high magnification, the images show that the crystal surface supports a dynamic population of small clusters (25 to 50 nanometer in diameter) of 7 to 30 canavalin molecules. While some of the smaller clusters adsorb onto the surface but then dissolve rapidly, others are stable and are incorporated into the advancing steps (or layers) formed by the dislocations.

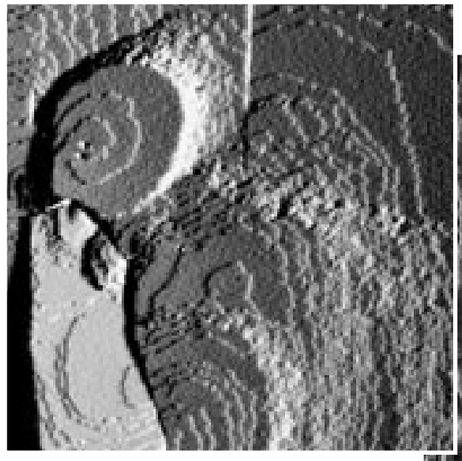
At typical supersaturation levels used in protein crystal growth, a new defect generation mechanism, never before reported, was discovered: the incorporation of sizable "microcrystals" much larger than the clusters (Figure 3). When these microcrystals fall onto the



33 by 58 micrometers

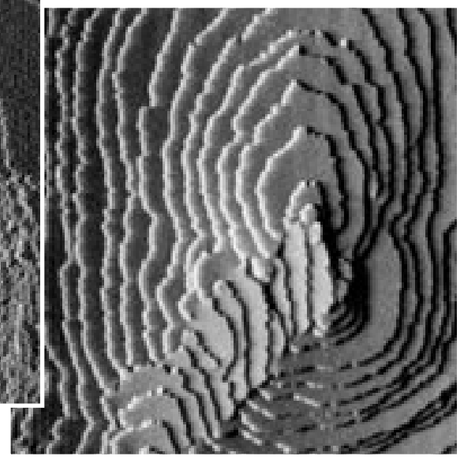
Figure 2. As supersaturation increases, two-dimensional growth of canavalin crystals sets in, seen in the appearance of small islands rising from the surface.

(a)



50 by 50 micrometers

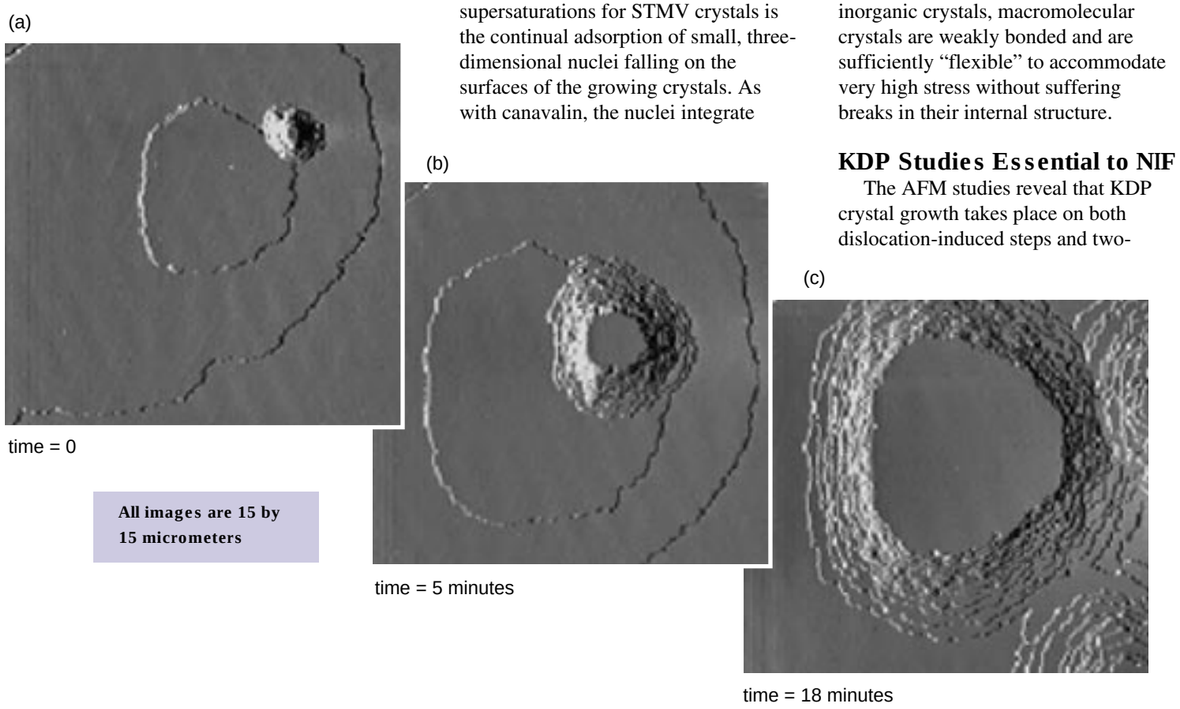
(b)



27 by 27 micrometers

Figure 3. At high supersaturation levels, microcrystals fall onto the growing surface of canavalin crystals and are incorporated into the main crystal, resulting in misaligned and distorted lattices. Shown are (a) crystal being incorporated and (b) defect remaining after incorporation.

Figure 4. (a) Once adsorbed, three-dimensional nuclei grow by (b) lateral spreading and formation of two-dimensional islands on their faces. (c) These islands coalesce in the formation of "stacks" consisting of a few to tens of layers projected above the larger crystal surface.



growing crystal surface, they result in misaligned and distorted lattices. Such defects should significantly impair the ability of crystallographers to resolve molecular structure through x-ray diffraction techniques.

Viruses Prove Good Models

Because of their relatively large size, near-spherical shapes, and simple packing geometries, viruses provide especially good models for investigation of macromolecular crystallization. The research team used an AFM to conduct the first nanometer-scale crystal growth study of STMV. The virus was chosen because past studies have determined its structure and have shown it to be easily crystallized under a wide range of conditions.

The AFM images reveal that the dominant growth mechanism at all supersaturations for STMV crystals is the continual adsorption of small, three-dimensional nuclei falling on the surfaces of the growing crystals. As with canavalin, the nuclei integrate remarkably well with the underlying structure. Livermore crystal researchers believe that this integration suggests that the underlying lattice either "guides" the adsorbing nuclei into preferred orientations as they arrive or that subsequent reorientation by diffusion ultimately produces the correct alignment.

Once adsorbed, the three-dimensional nuclei spread laterally and are accompanied by the formation of two-dimensional islands on their tops. These islands coalesce in the formation of "stacks" consisting of a few to tens of layers projected above the larger crystal surface. Such stacks serve as the growth centers for the entire crystal (Figure 4).

No screw dislocations are observed on STMV crystals during their growth. De Yoreo conjectures that no dislocations occur because, unlike inorganic crystals, macromolecular crystals are weakly bonded and are sufficiently "flexible" to accommodate very high stress without suffering breaks in their internal structure.

KDP Studies Essential to NIF

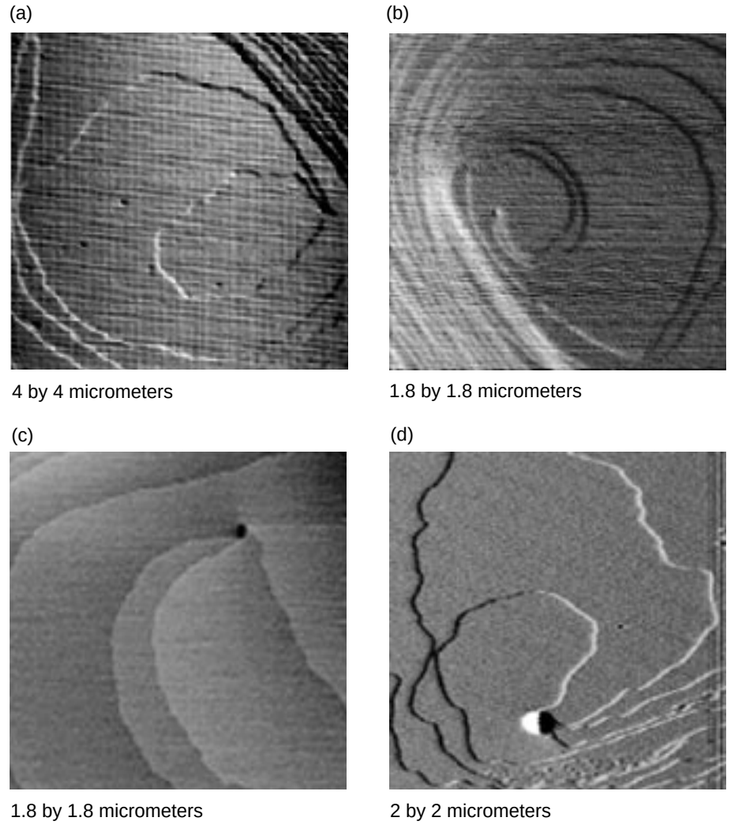
The AFM studies reveal that KDP crystal growth takes place on both dislocation-induced steps and two-dimensional islands. In addition, numerous two-dimensional islands appear on the "terraces" (spaces between layers) formed by dislocations. As with canavalin, the dislocations are caused by stresses in the crystal's "stiff" lattice and produce growth hillocks whose triangular shapes reflect the crystal symmetry (Figure 1). However, because the KDP lattice is much stiffer, the region near the dislocations is highly stressed and unstable. As a result, it exhibits hollow channels full of solution at the dislocation cores (Figure 5). These hollow cores (1 to 50 nanometers in diameter) are a result of stresses near the dislocations. Using the AFM to investigate the details of the dislocation structure has allowed Livermore researchers to show for the first time that core radii are one of the primary determining factors in hillock size and growth rate.

The diffusion and incorporation kinetics of single KDP molecules is 1,000 times faster than seen in canavalin; indeed, typical KDP growth rates—about 100 molecular layers per second—make it impossible to access a wide range of experimental conditions. The crystal research team believes that the disparity in growth rates occurs either because KDP is much smaller and therefore more mobile than canavalin or because KDP molecules have a higher probability of having the proper molecular orientation for direct incorporation into the crystal, as opposed to more geometrically complex biological macromolecules.

First-ever images also show how impurities cause growing layers to exhibit discontinuous motion because they become "pinned." In a dynamic, repeating process, steps encounter impurities, seemingly stop, then grow around the impurities, and once again encounter other impurities. One series of images shows how an adsorbed particle (impurity) is displaced upward as growing steps move through it.

The Laboratory's crystal development team plans additional experiments with various concentrations of known impurities to further understand how they are incorporated in the KDP crystal and how they influence growth. Such experiments are important because despite dramatic gains in growth speed and quality, the number of defects in KDP crystals caused by impurities is still unacceptably high for laser scientists planning the optical systems of NIF. When an intense laser beam strikes a defect in the KDP crystal,

Figure 5. Stresses in the KDP crystal's "stiff" lattice produce growth hillocks with hollow channels full of solution. The size of the channel increases rapidly with the size of the dislocation from (a) one step where no core is observable to (b) two, (c) three, and (d) four steps.



tiny cracks appear in the crystal that grow with each laser shot. Eventually the damage significantly disrupts the laser beam quality by distorting the laser light and reducing its energy.

Future areas of study also include growing several crystallized proteins, among them human insulin, whose use depends on a better understanding of how they grow and dissolve in solution. The crystal development team is also planning to study biomineralization in more detail, in particular the growth characteristics of the essential calcium carbonate mineral that forms the skeletal tissue of most organisms. The study should shed light on how living organisms produce crystalline materials, thereby pointing the way for new, nanostructured materials for industry.

By understanding and then controlling the crystallization process at the molecular level, complex microstructures can be synthesized that will affect many disciplines and technologies, says De Yoreo. "There's a revolution on the horizon in materials and materials processing, but to get there we need to acquire the scientific underpinnings of crystal growth," he says. Thanks to the AFM, that day is rapidly approaching.

Key Words: atomic-force microscope (AFM), protein crystallography, crystals, KDP (potassium dihydrogen phosphate), National Ignition Facility (NIF), scanning tunneling microscope (STM), stockpile stewardship.

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1. "Growing High-Quality KDP Crystals Quickly," *Energy & Technology Review*, UCRL-52000-94-11 (November 1994), pp. 3–5.
2. The December 1994 issue of *Energy & Technology Review*, UCRL-52000-94-12, is dedicated to a complete description of NIF and its planned uses.

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About the Scientists

JAMES DE YOREO joined Lawrence Livermore National Laboratory in 1989 as a physicist in the Chemistry and Materials Science Directorate. He received his B.S. from Colby College and his M.S. and Ph.D. from Cornell University. He is currently the leader of the Laboratory's crystal development team and has done extensive research in crystal growth physics and applications. In 1994, he shared an R&D 100 Award for the development of a rapid growth process for KDP (potassium dihydrogen phosphate) laser crystals with colleagues at the Laboratory and at Moscow State University in Russia. He has written numerous articles on organic and inorganic crystal growth and is co-holder of one existing and one pending U.S. patent related to crystal growth.

TERRY LAND received both her B.S. in chemistry (1988) and her Ph.D. in physical chemistry (1992) from the University of California, Irvine. She joined the Laboratory's Chemistry and Materials Science Directorate in 1992. Her primary area of academic and professional research has been the fundamental growth mechanisms of solution-grown inorganic and macromolecular biological crystals using advanced techniques such as scanning tunneling and atomic-force microscopy. She has co-written over 20 scholarly articles and has been a presenter and invited speaker at meetings and conferences in the U.S. and Europe on the mechanisms and techniques of crystal growth.

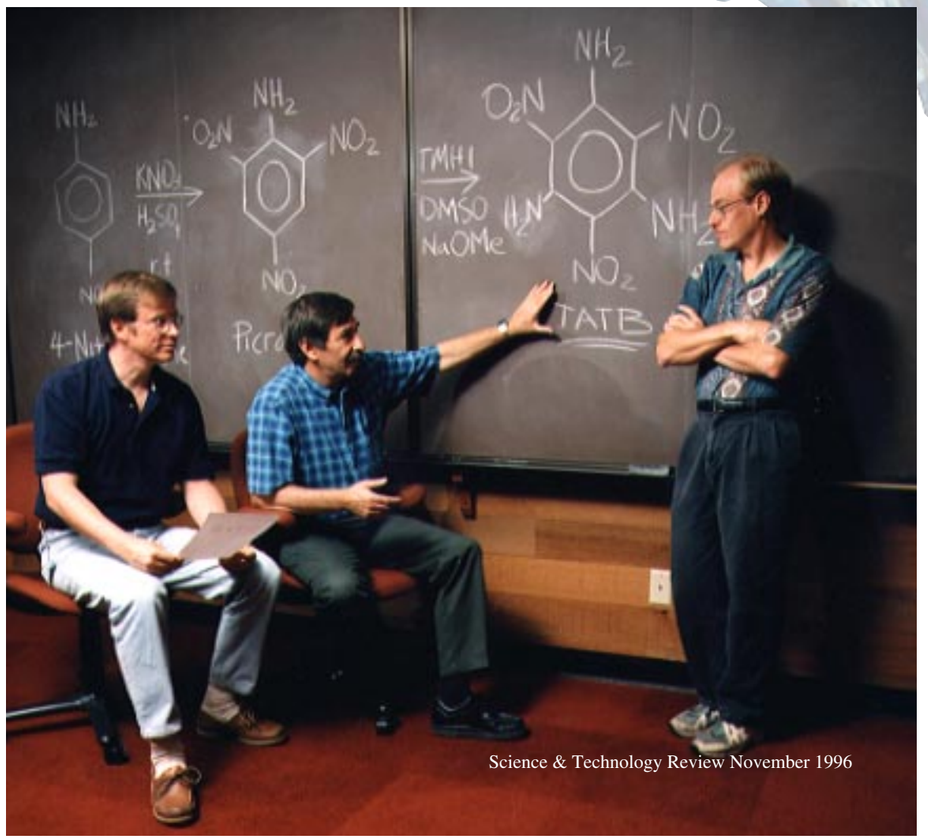
Addressing a Cold War Legacy with a New Way to Produce TATB

ONE of the most important accomplishments made by weapons laboratories' chemists in the past two decades has been the formulation of powerful conventional high explosives that are remarkably insensitive to high temperatures, shock, and impact. These insensitive high explosives (IHEs) significantly improve the safety and survivability of munitions, weapons, and personnel. The Department of Energy's most important IHE for use in modern nuclear warheads is TATB (triamino-trinitrobenzene) because its resistance to heat and physical shock is greater than that of any other known material of comparable energy.

The Department of Energy currently maintains an estimated five-year supply of TATB for its Stockpile Stewardship and Management Program (see the August 1996 *Science & Technology Review*, pp. 6–15), which is designed to ensure the safety, security, and reliability of the U.S. nuclear stockpile. The Department of Defense is also studying the possible use of TATB as an insensitive booster material, because even with its safety characteristics, a given amount of that explosive has more power than an equivalent volume of TNT.

In addition to its military uses, TATB has been proposed for use as a reagent in the manufacturing of components for liquid crystal computer displays. There is also interest in employing the explosive in the civilian sector for deep oil well explorations where heat-insensitive explosives are required.

Despite its broad potential, the high cost of manufacturing TATB has limited its use. Several years ago, TATB produced on an industrial scale in the U.S. was priced at $90 to $250 per kilogram. Today it is available to customers outside DOE for



Rob Schmidt (left), Alex Mitchell, and Phil Pagoria discuss the chemistry of the method for synthesizing TATB (triamino-trinitrobenzene) developed at Livermore. Their method lowers the cost and production time of this insensitive high explosive and increases the environmental friendliness of the manufacturing process. (The reaction scheme on the board appears also in the figure on p. 23.)