steels. Knowledge-based process models take the microstructure evolution into account explicitly. These models are gaining increasing attention as a predictive tool that allows the operational parameters of an industrial process to be linked quantitatively with the properties of the steel product. Current austenite decomposition models with predictive capabilities for industrial conditions are empirical or semi-empirical in nature (*7*) and there is a need to develop fundamental model approaches.

Phase transformations in steels have been investigated more extensively than those in any other material. Any phase transformation involves two stages: nucleation and growth. The austenite decomposition usually follows a sequential pattern. In low-carbon steels, it starts with the formation of ferrite, followed by the formation of other transformation products including pearlite, bainite, and martensite (*7, 8*). However, the mechanisms of the entire transformation process are not fully understood. For example, the role of alloying elements (such as Mn, Mo, Si, Cr, and Al) is poorly understood.

Further understanding of the transformation mechanisms depends critically on the available characterization techniques. Classical phase transformation studies in steels measure changes in specimen dimension to record the volume change associated with the austenite decomposition (*9*). The resulting microstructures are usually observed in an optical microscope. Electron microscopy can be used to increase resolution to the nanometer range. However, the investigated area becomes so small that it limits the statistical relevance of the observations. A number of other techniques can be used to study phase transformations in steel, including neutron and x-ray diffraction, magnetic, and ultrasonic measurements.

Offerman *et al.* have developed an innovative technique to investigate phase transformation in situ with x-ray diffraction at a synchrotron source. By obtaining information on the nucleation and growth of individual ferrite grains in the bulk of the steel specimen, the authors provide new insights into nucleation and growth mechanisms. Extending the limited nucleation data from earlier microscopy studies (*10, 11*), the authors reach new conclusions on the activation energy of ferrite nucleation. Further, the results confirm classical diffusional growth for a majority of grains, but also indicate more complex growth regimes.

Experimental observations with state-of-the-art techniques, such as that presented by Offerman *et al.*, are crucial for the development of fundamental phase transformation models. Better understanding of phase transformation in steels should in turn help to better control these transformations and develop steels with superior properties.

References and Notes

1. S. E. Offerman *et al.*, *Science* **298**, 1003 (2002).
2. R. A. Heimbuch, in *40th Mechanical Working and Steel Processing Conference Proceedings*, Vol. XXXVI [Iron and Steel Society (ISS), Warrendale, PA, 1998], pp. 3–10.
3. J. G. Speer, D. K. Matlock, *JOM* **54** (no. 7), 19 (2002).
4. J. Shaw *et al.*, in *New Steel Sheet and Steel Bar Products and Processing*, SAE-SP 1685, D. W. Anderson *et al.*, Eds. [Society of Automotive Engineers (SAE), Warrendale, PA, 2002), pp. 63–71; see also www.ulsab-avc.org.
5. A. Pichler *et al.*, in *43rd Mechanical Working and Steel Processing Conference Proceedings*, Vol. XXXIX (ISS, Warrendale, PA, 2001), pp. 411–434.
6. U. Brüx *et al.*, *Steel Res.* **73**, 294 (2002).
7. M. Militzer, E. B. Hawbolt, T. R. Meadowcroft, *Metall. Mater. Trans.* **31A**, 1247 (2000).
8. S. J. Jones, H. K. D. H. Bhadeshia, *Acta Mater.* **45**, 2911 (1997).
9. G. T. Eldis, in *Hardenability Concepts with Applications to Steel*, D. V. Doane, J. S. Kirkaldy, Eds. [The Metallurgical Society of American Institute of Mining, Metallurgical and Petroleum Engineers (TMS/AIME), Warrendale, PA, 1978], pp. 126–148.
10. M. Enomoto, H. I. Aaronson, *Metall. Trans. A* **17**, 1385 (1986).
11. M. Enomoto, W. F. Lange III, H. I. Aaronson, *Metall. Trans. A* **17**, 1399 (1986).

12. The author holds the Dofasco Chair in Advanced Steel Processing at the University of British Columbia. This endowed chair is supported by Dofasco Inc., the second largest steel company in Canada.

PERSPECTIVES: MATERIALS SCIENCE

Molecular "Ghosts"

Jonathan W. Steed

The tremendous utility of porous materials such as zeolites (*1*) in catalysis and separation science has led many solid-state chemists to believe that nonporous equals noninteresting. Pores and channels dramatically increase the effective surface area of a solid, facilitate molecular diffusion, and provide sites for attaching catalytically active species in an unsolvated environment. A host of solid-state designers are involved in the tailored synthesis of porous frameworks (*2, 3*).

By comparison, research into the design and synthesis of more conventional close-packed solids is not very fashionable. But this may change with the report by Atwood *et al.* on page 1000 of this issue. The authors show that a very common organic compound, a calixarene, forms an entirely nonporous solid-state structure yet allows rapid bulk diffusion of small molecules without losing its crystallinity (*4*).

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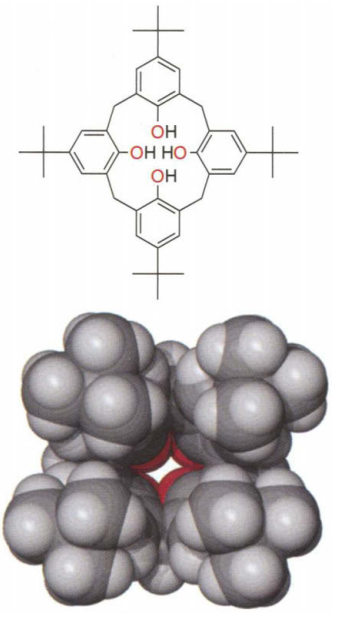
Calixarenes are well-studied molecules, and none more so than *p-tert*-butylcalix[4]arene (see the figure) (*5, 6*). The molecule adopts a bowl shape in both solid and solution phases, reminiscent of a Greek vase called a calyx crater (hence the name). The interior of the bowl can include small-molecule guest species such as toluene. A bewildering variety of calixarene host-guest compounds have been prepared (*5, 6*).

Atwood *et al.* have now crystallized the calixarene without anything inside the molecular cavity, simply by subliming the compound. The pure calixarene is difficult to obtain because of its propensity to include guest species, but is nothing special in itself. The two known x-ray crystal structures (*4, 7*) of the guest-free calixarene show a close-packed solid much like the vast majority of compounds reported in the Cambridge Structural Database, albeit with relatively low densities (*8*).



Well-studied yet full of surprises. (**Top**) *p-tert*-Butylcalix[4]arene. (**Bottom**) Space-filling plot of the calixarene's discrete molecular cavity.

The interesting step taken by Atwood *et al.* was to dip the ordered single crystal used in their x-ray study into liquid vinyl bromide. The solid calixarene is insoluble in vinyl bromide, but when the calixarene is cocrystallized from a solution in a different solvent it typically forms 1:1 host-guest complexes with a variety of guest molecules. Atwood *et al.* observed that this same kind of host-guest compound formed in a single crystal–single crystal phase transition over a period of about 15 min when the solid, guest-free calixarene was immersed without dissolution in the liquid vinyl bromide.

The authors then put their crystal back on the x-ray diffractometer and obtained the x-ray crystal structure of the 1:1 calixarene–vinyl bromide complex. It is worth remarking on their clever choice of vinyl bromide as the guest molecule: In x-ray crystallographic terms, the electron-rich bromine atom of the guest is easy to resolve in the presence of only carbon, hydrogen, and oxygen, and vinyl bromide is therefore easy to locate (*9*).

This simple experiment with well-known materials has tremendous implications for solid-state dynamics. Protein crystallographers have of course been using a similar methodology for years. The method of isomorphous replacement involves soaking protein crystals in solutions containing heavy metal ions. The metals diffuse into the protein crystal and help crystallographers to solve the crystal structure of the original metal-free protein.

But protein crystals are not close-packed solids. They are as porous as inorganic zeolites. Crystals of biomolecules are usually awash with large water-filled channels, which facilitate the diffusion of the metal ions. In contrast, diffusion of a molecule as large as vinyl bromide through a nonporous, close-packed solid without disrupting the regular crystalline structure is difficult to picture. Sulfur dioxide can accomplish a similar feat, but it binds to its platinum-containing host by a strong coordination interaction (*10*). In the study of Atwood *et al.*, the binding only involves van der Waals forces. If nonporous solid-state diffusion can happen with calixarenes, the implication is that it can happen with many other materials. The beauty of the calixarene is that its ability to form complexes with the diffusing guest enables researchers to readily observe the process.

Atwood *et al.* propose a mechanism for this apparent tunneling of the guest involving "a highly synchronized process whereby neighboring host molecules at the advancing phase boundary cooperate with one another, not only to relay the guest through the lattice, but also to maintain continuity of the material such that the crystal does not fracture." This explanation must still be considered speculative, but it seems much more plausible than thinking of the vinyl bromide as a molecular "ghost" that can glide like an ethereal specter through the calixarene walls.

References

1. J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, Eds., *Comprehensive Supramolecular Chemistry, Vol. 7* (Pergamon, Oxford, ed. 1, 1996).
2. M. Eddaoudi *et al.*, *Acc. Chem. Res.* **34**, 319 (2001).
3. N. L. Rosi *et al.*, *Cryst. Eng. Comm.* **4**, 401 (2002).
4. J. L. Atwood, L. J. Barbour, A. Jerga, B. L. Schottel, *Science* **298**, 1000 (2002).
5. C. D. Gutsche, in *Calixarenes*, J. F. Stoddart, Ed., vol. 1 of *Monographs in Supramolecular Chemistry* (Royal Society of Chemistry, Cambridge, 1989).
6. C. D. Gutsche, *Calixarenes Revisited*, J. F. Stoddart, Ed., vol. 6 of *Monographs in Supramolecular Chemistry* (Royal Society of Chemistry, Cambridge, 1997).
7. E. B. Brouwer *et al.*, *Chem. Commun.* **2001**, 565 (2001).
8. F. H. Allen, O. Kennard, *Chem. Design Automat. News* **8**, 31 (1993).
9. W. Clegg, *X-ray Crystallography* (Oxford Univ. Press, Oxford, 1998).
10. M. Albrecht, M. Lutz, A. L. Spek, G. van Koten, *Nature* **406**, 970 (2000).

PERSPECTIVES: IMMUNOLOGY

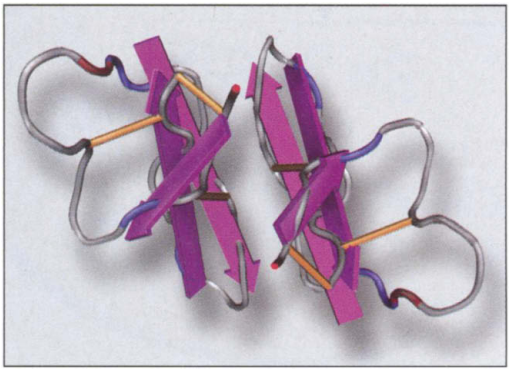
Versatile Defensins

Tomas Ganz

Defensins (see the figure) are a family of antimicrobial peptides abundant in immune cells—white blood cells (specifically neutrophils), intestinal Paneth cells, and barrier epithelial cells—that engage in host defense. There is increasing evidence that in these settings defensins (and other antimicrobial substances) directly contribute to the killing of microbes (*1*). Now, two reports in this issue, by Zhang *et al.* (page 995) and Biragyn *et al.* (page 1025), implicate defensins in a new set of specific activities (*2*, *3*). These investigators show that defensins are important for the anti-HIV activity of human $CD8^+$ T lymphocytes (*2*) and for the induction of cell-mediated antitumor immunity in mice (*3*).

Zhang *et al.* (*2*) propose that defensins are the solution to a puzzle that has challenged AIDS researchers since the early days of the epidemic. $CD8^+$ T lymphocytes from some HIV-infected patients secrete a substance (CD8 antiviral factor or CAF) that interferes with the ability of HIV to infect cells (*4*). This factor is particularly abundant in AIDS patients who are doing well clinically and in those HIV-infected patients (nonprogressors) who do not develop the symptoms of the disease for many years after the initial infection (*5*). Zhang *et al.* now show that $CD8^+$ T cells from long-term nonprogressor HIV patients secrete α-defensins-1, -2, and -3 when stimulated. These α-defensins account for much of the antiviral activity of CAF. The authors used neutralizing antibodies to human α-defensins-1, -2, and -3, and to the β-chemokines MIP-1α, MIP-1β, and RANTES in order to calculate the specific contributions of α-defensins and β-chemokines to CAF activity. These experiments demonstrate that HIV strains using the CXCR4 chemokine receptor for entry into host target cells are predominantly blocked by the α-defensins in CAF. In contrast, HIV strains that use the CCR5 chemokine receptor are only partially inhibited by α-defensins, with most of the remaining CAF activity attributable to β-chemokines. Both purified and synthetic α-defensins inhibited HIV replication in vitro. The authors show that unstimulated human $CD8^+$ T cells contain little defensin, whereas, after stimulation for 2 days with antibodies against their CD3 and CD28 receptors, α-defensin-1, -2, and -3 were readily detected in the cytoplasmic granules of these cells by immunostaining.

The activity of defensins as a component of CAF has important implications. The most optimistic interpretation is that α-defensins and β-chemokines are causally involved in slowing the progression of HIV infection in patients favored by specific environmental or genetic factors. If so, improved understanding of the regulation of defensin production in $CD8^+$ T lymphocytes could potentially extend these benefits to other HIV patients, and eventually a pharmacological substitute for these natural defensins could be developed. Alternatively, defensins may be markers of nonprogression, perhaps by indicating that despite HIV infection of the host, $CD8^+$ T cells



Defensins to the rescue. Human neutrophils secrete the antimicrobial peptides α-defensin-1, -2, and -3 in response to bacterial infection. These peptides form dimeric structures that contain a total of six β-strands (purple arrows). The positively charged side chains of α-defensin-3 are shown in blue, negative charges in red, and disulfide bonds in orange. [Protein structure coordinates from (*12*)]

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