is, shifts from one key to another) are relatively easy to effect, have similar tonal hierarchies and shared harmonies.

Geometric models, or maps, of these key relations that conform to descriptions in music theory have been generated by computational methods. One such key map in the shape of a torus or ring (*5*), and similar to that used by Janata *et al.* in their experiments, was obtained by training a self-organizing neural network model with experimentally quantified tonal hierarchies (see the bottom figure). This key map provides a visual display of an abstract mental model of key relationships. Results of experiments investigating how the sense of key develops and continuously changes can be projected onto the key map (*6*).

The strength of the Janata *et al.* work is that it brings together various techniques in an original combination. Their study probes the neural correlates of tonality perception in an effort to identify brain regions that respond to musically modulating sequences. In so doing, this study raises a variety of questions. Is the topography of the key map reflected directly in the cortical activation pattern? Alternatively, do the Janata *et al.* findings reflect more general processes of remembering and comparing tones? How are the activation patterns (in particular those of the ventromedial frontal area) observed by Janata and co-workers related to affective responses to music? One might expect sensory-related regions of the superior temporal cortex to be implicated in computing the relationships between tones that result in tonality mapping. However, it is still not known how the perceptual responses of the superior temporal cortex interact with the responses distributed across the activated brain regions reported by Janata and colleagues. Implicit learning of key musical structures may take place over a lifetime of listening to music, so it is possible that tonal maps become widely distributed over the brain. Regardless of the answers to these questions, cognitive neuroscience has benefited from the application of sophisticated cognitive models to explore the correlation between music processing and neuroanatomical regions of the brain.

References and Notes

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PERSPECTIVES: MATERIALS SCIENCE

Nanocubes and Nanoboxes

Catherine J. Murphy

The visions of nanotechnology—smaller, faster, cheaper, smarter information-storage devices, energy sources, and medical devices in which the size of individual device elements approaches that of individual molecules—crucially depend on the ability to make and manipulate objects on the 1- to 100-nm scale.

The engineer's "top down" approach to making nanometer-scale objects is to carve them out lithographically from a substrate; the chemist's "bottom up" approach is to assemble them from molecular-scale precursors. On page 2176 of this issue, Sun and Xia (*1*) use the latter approach to show that simple chemical reactions in solution can produce silver nanocubes of controllable size in high yield. A simple, quantitative oxidation-reduction reaction of the silver nanocubes with gold salts results in hollow gold nanoboxes. The cubic faces of these nanomaterials are crystallographically well defined (*1*), an important feature for connecting these nanometer-scale elements into future devices.

Many applications envisioned for nanotechnology require nanometer-scale elements that are conducting or semiconducting. Inorganic materials such as metals and semiconductors have fundamental length scales in the 1- to 100-nm range (*2*, *3*). In metals, the mean free path of an electron at room temperature is ~10 to 100 nm (*2*). Hence, in a metallic particle with a diameter of ~100 nm or less, substantial deviations from bulk metallic properties are expected, and new size-dependent properties may emerge. For example, gold ceases to be a noble, unreactive metal: Gold nanoparticles 2 to 3 nm in diameter can catalyze chemical reactions (*4*).

The melting temperature of gold decreases drastically with size for spheres smaller than 20 nm (*5*). At diameters from ~10 to 100 nm, the spheres appear red, not gold, when well dispersed, as in stained glass (see the first figure). Nonspherical gold and silver nanoparticles absorb and scatter light of different wavelengths, depending on nanoparticle size and shape (*6*, *7*). Silver and gold nanoparticles have been used as sensors to detect analytes through surface-enhanced Raman scattering and other optical effects peculiar to the ~10- to 100-nm size range (*8*–*10*).

Red gold. Stained-glass window in Milan Cathedral, Italy, made by Niccolo da Varallo between 1480 and 1486, showing the birth of St. Eligius, patron saint of goldsmiths. The red colors are due to colloidal gold.

CREDIT: FOTOTECA VEN. FABBRICA DEL DUOMO

Synthetic chemical methods for making metallic nanoparticles of controlled size and shape are continually being improved. Metals such as silver, gold, cobalt, and platinum have been made into nanospheres, nanorods, nanowires, nanocubes, and nanoprisms through chemical reactions of precursors at room or slightly elevated temperatures (*6*, *7*, *11*–*13*), typically in the presence of a "directing" agent. Unfortunately, multiple shapes and sizes of nanoparticles are frequently produced in these reactions (see the second figure). Purification by centrifugation and size-selective precipitation (or tight control over reaction time) is then required to isolate pure products (*6*, *7*, *11*–*13*).

Control of size and shape was originally attributed solely to the presence of the "directing" agent, which functions as a hard or soft template (such as porous alumina membranes or micelles). It is now widely believed that preferential absorption of molecules and ions in solution to different crystal faces directs the growth of nanoparticles into various shapes by controlling the growth rates along different crystal axes (*11*, *14*, *15*). This view is shared by Sun and Xia (*1*).

In their study, the reaction to make silver nanocubes from silver nitrate takes place at ~150°C in a high–boiling point solvent (ethylene glycol), which also func-

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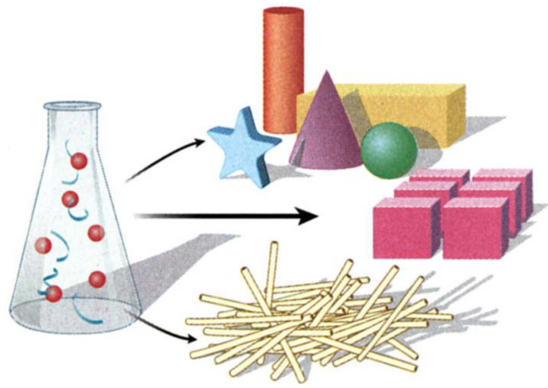
tions as the reductant, in the presence of a polymer directing agent [poly(vinyl pyrrolidone), PVP] (*1*). Highly crystalline silver nanocubes with well-defined {100} faces are made in high yield if all parameters are optimal. If the reaction temperature is too high or too low, irregularly shaped nanoparticles are produced. If the silver nitrate initial concentration is too low, nanowires are the major product. If the polymer concentration is too high, crystallographically defective nanoparticles are produced. Without polymer, crystallographically defective nanoparticles exposing the more stable {111} surface are produced.



Multiple products. Precursors **(left)** can react to form a variety of nanoparticle shapes **(right)**, depending on the reaction conditions.

This sensitivity to conditions implies that the silver nanocube reaction is under kinetic rather than thermodynamic control. Consequently, the timing of the reaction controls the product's dimensions. Shorter reaction times at optimal "cube" conditions reduce the nanocube edge lengths to ~70 nm; longer reaction times lead to nanocubes with edges of up to ~175 nm, in a well-controlled manner. The production of smaller nanocubes (down to edges of 50 nm) is not as well controlled under these conditions.

When the silver nanocubes are treated with a gold salt, an oxidation-reduction reaction ensues. The adsorbed gold salt is reduced to gold metal, with concomitant oxidation of the silver to silver ions. In this reaction, the silver nanocubes serve as a sacrificial hard template to make hollow crystalline gold nanoboxes, whose dimensions are controlled by the size of the silver template. The square facets of the gold nanoboxes mirror the crystallographic facets of the original silver nanocubes.

A major challenge for nanotechnology is the rational assembly of individual nanoscale elements into working devices. To develop a reasonable linkage strategy, detailed knowledge of the positions and identities of the surface atoms of the nanoscale object is required. Sun and Xia (*1*) provide a clear picture of which crystal faces are available for future assembly for their nanocubes and nanoboxes. However, it is still a major challenge to predict what capping agent or combination of capping agents in solution will generate a specific desired shape and size of nanocrystal. Also, the microscopic images of Sun and Xia cannot show where the capping agent is physically located on their cubes.

Future experiments using these cubes for optical sensing, catalysis, or nanoelectronics will require a more thorough understanding of what ions or molecules may be adsorbed to the surface. Here is an opportunity for colleagues from many disciplines—colloid chemists, physicists, geologists, biomineralization experts, surface scientists, and materials scientists—all of which share common interests and complementary views of inorganic crystal growth modified by organic molecules.

Potential device applications of inorganic nanomaterials need not be limited to single metals. Metal alloys with size-dependent magnetic properties have been fabricated into supported nanoparticles for information storage that could lead to recording densities an order of magnitude larger than are currently available (*16*). Still, the basics of making materials on the nanoscale is a work in progress. Sun and Xia are helping to pioneer methods to do so.

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PERSPECTIVES: DEVELOPMENT

Fishing Out a New Heart

Ian C. Scott and Didier Y. R. Stainier

A Promethean goal of modern biomedicine is to repair damaged organs. Stem cells, which have the potential to form a wide variety of different cell types, are widely regarded as being essential to this endeavor. However, the results of recent studies call into question the plasticity of adult stem cells, and there are ethical quandaries associated with deriving pluripotent embryonic stem cells from human embryos. An alternative approach is to stimulate the damaged organ to regenerate or heal itself. Poss *et al.* (*1*) adopt this strategy on page 2188 of this issue with their demonstration that the heart of the adult zebrafish *Danio rerio* is capable of regeneration. As the zebrafish has become one of the preferred genetic models of vertebrate development, this finding should open up exciting new avenues for studying cardiac regeneration.

Mammals, including humans, exhibit only a few examples of regeneration, most notably the ability of liver hepatocytes to regenerate damaged liver tissue. In contrast, broader regenerative capacities have been described in animals such as the salamander, newt, hydra, and flatworm—indeed, flatworms are able to generate an entirely new animal from a small piece of tissue. More recently, regeneration of fins, spinal cord, and retina has been documented in the zebrafish (*2*, *3*). Poss and colleagues set out to establish whether the adult zebrafish heart also has the capacity for regeneration. They performed a simple surgery in which the apex of the ventricle, representing roughly 20% of its volume, was removed. Mouse hearts subjected to similar damage induced by freezing do not regenerate, but instead form scar tissue (*4*). In contrast, the authors found that although initial fibrin deposits did form at the wound site in zebrafish hearts, further scarring and collagen deposition, characteristic of damaged mammalian hearts, did not occur. Instead, cardiomyocytes, the specialized muscle cells of the heart, infiltrated the injured area and sealed off the wound. Remarkably, 60 days after surgery, the zebrafish hearts appeared roughly normal both histologically and based on ex-

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