

Shaping Crystals with Biomolecules

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The shapes of crystals found in biomineral structures such as the skeletons of marine organisms differ dramatically from those of crystals grown in pure solution. The formation of these complex, often hierarchical structures is difficult to reconcile with the simple mechanistic model of crystal growth by step propagation across crystallographic faces (often referred to as the terrace-ledge-kink model) (1). Two decades ago, researchers developed the stereochemical recognition model (2, 3), which holds that these shapes are stabilized through the binding of peptides and proteins to otherwise unstable faces, presumably because the stereochemi-

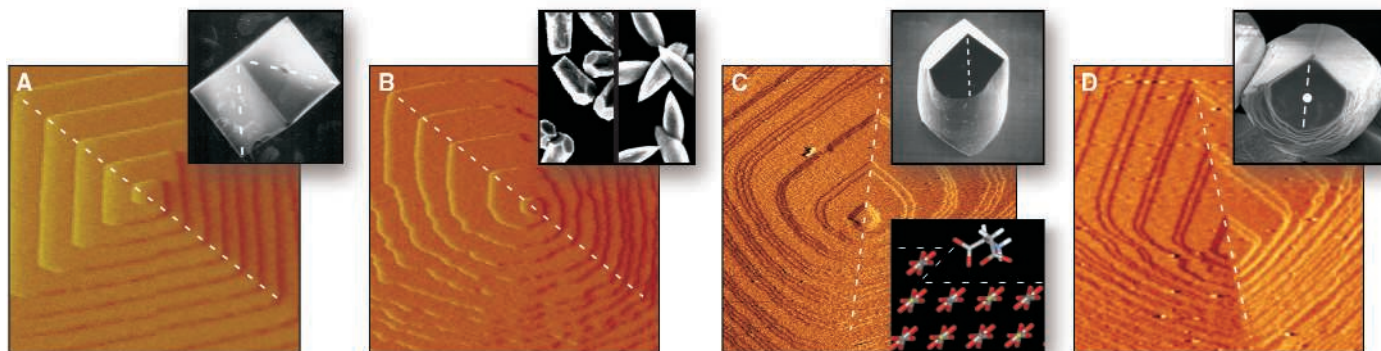
semblance of the carboxylate group of aspartic acid to the carbonate group of calcite and the strong affinity of carboxylates for calcium provided a rational basis for the conjectured stereochemical match. In addition, the presence of proteins in the mineral phases suggested that they actively control crystal growth. In several cases, specific geometric relationships between the modifier and a particular crystal face were proposed that suggested an excellent stereochemical match. Even detailed molecular modeling studies focused on such arrangements (4).

However, the paradigm depended heavily on macroscopic examination of crystal shapes. The subtle links between atomic-

ganic molecules (9, 10), amino acids (11), peptides (10), and proteins (9, 12–14) (see the figures). These studies have led to a new understanding of shape modification.

We first look at the effect of magnesium, a major constituent of seawater that plays a key role in carbonate modification (15). Magnesium preferentially inhibits step motion at the corners of growth hillocks (see the first figure, panels A and B). This effect should flatten the corners of the calcite rhombus, leading to elongation and roughening of the crystal shape (5). Recent nucleation and growth experiments have confirmed this shape evolution (16) (first figure, panel B).

Calcite shape can also be modified by acidic amino acids. When individual enantiomers are added to calcite growth solutions, the glide-plane symmetry of calcite is broken. The resulting crystal shape reflects both the chirality of the amino acid and the step-specificity of the interaction (first figure, panel C) (11). The shape change of the resulting macroscopic crystal mimics that



How crystals change shape I. Studies of calcite show that changes in crystal shape are directly related to modification of step morphology for a wide range of modifiers. Each panel shows an atomic force microscope image of growth hillocks (main image) and a scanning electron microscope image of the crystal shape (inset), with dashed lines to indicate the glide plane sym-

metry. (A) Pure calcite. (B) Calcite plus Mg^{2+} (5); inset shows crystals grown at $Mg^{2+}:Ca^{2+}$ mole ratios of 1.5 (left) and 2.0 (right) [after (16)]. (C) also shows D-aspartic acid binding to a particular step on calcite (11). (D) Calcite plus AP8 protein extracted from abalone nacre [after (14)]. (C) also shows D-aspartic acid binding to a particular step on calcite (18).

cal match to the crystal lattice lowers their surface energies. Recent studies show how the two models can be reconciled.

The stereochemical recognition paradigm found support in a series of investigations of the macroscopic shapes of calcium carbonate crystals. Some of the crystals were grown in the presence of proteins extracted from carbonate biominerals; others were grown with organic additives that mimic those proteins. The extracted proteins were highly acidic, often containing large fractions of aspartic acid residues (3). The re-

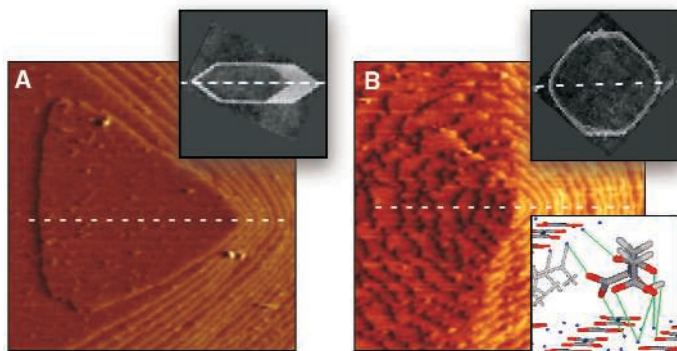
scale dynamics and macroscopic expression were not examined. Moreover, the term “stabilization” suggested a reduction in surface free energy—yet the newly expressed faces were typically rough and nonplanar, indicating that they were not stable in a thermodynamic sense. Finally, even in pure systems, crystal shapes are as much an expression of growth kinetics as they are of equilibrium energetics. And growth kinetics is controlled at kinks on atomic ledges, not on flat faces (1).

Over the past decade, a series of studies has examined the atomic-scale dynamics of crystallization. They explored the growth of crystal surfaces in a variety of systems including carbonates, oxalates, phosphates, and phthalates, with the use of growth modifiers composed of small inorganic molecules (5–8), moderate-sized or-

of the elementary steps (first figure, panel C). Molecular models show that step edges provide the most favorable binding environment and give binding energies that exhibit the same asymmetry seen both at the atomic scale and in the macroscopic crystal (11).

A more complex system is represented by the growth of calcium oxalate monohydrate, a pathological biomineral, in the presence of citrate, a naturally occurring inhibitor and therapeutic agent. Citrate is a nonplanar molecule with three carboxylate groups and a hydroxyl group. Its impact on step morphology or kinetics depends strongly on the type of face (9) (see the second figure). Molecular modeling shows that several factors—including calcium spacing, step riser angle, hydroxyl-to-oxalate distance, and electrostatic interactions—determine the magnitude of the binding energy.

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How crystals change shape II. Similar changes as in the first figure can be seen for calcium oxalate monohydrate crystals. (A) Pure calcium oxalate monohydrate. (B) Calcium oxalate monohydrate plus citrate (9). Insets after (21). (B) also shows minimum energy configurations for citrate binding to a particular step from molecular simulations (9).

The change in macroscopic crystal shape again mimics the change in growth hillock shape (second figure, panel B).

Finally, closer to the *in vivo* situation, we consider how calcite crystal shapes are modified by the introduction of AP8, a protein extracted from abalone nacre (14). Even for this complex modifier, the changes in atomic-scale morphology are step-specific and directly determine the shape of macroscopic crystals (first figure, panel D) to give morphologies that are quite similar to those caused by simple amino acids and polypeptides (11, 12, 14).

Although the mechanisms of growth modification are diverse, the source of shape change in these studies is clear: Crystal shape is controlled by step-specific interactions between growth modifiers and individual step edges on preexisting crystal faces. The com-

mon appearance of new, rough, rounded surfaces, which clearly are not faces, is not a result of stereochemical matching to a particular atomic plane of the crystal. Rather, changes in the elementary step shape generate a similarly modified bulk crystal shape through the self-replicating process of crystal growth.

The emergence of new faces is thus a macroscopic mani-

festation of the kinetics caused by molecular-scale interactions at the step edges. In this way, the terrace-ledge-kink model (1) merges smoothly with the concept of stereochemical recognition proposed two decades ago.

Subsequent to the development of the stereochemical recognition model, a growing body of evidence has shown that the shape of biominerals is often controlled through molding of solid or gelled amorphous precursors (17–19). Nonetheless, many biomineral structures present clear evidence for active control during crystal growth. Furthermore, the concept can be used to aid the design and synthesis of crystalline materials.

Despite this new level of understanding, one mystery remains. How are changes affecting elementary steps on one face translated into the emergence of adjacent faces?

The answer seems to lie at the corners between faces. Here, steps from adjacent faces must converge in regions of high curvature. This convergence provides an opportunity for surface energy terms associated with curvature to become important and for steps to bunch, either for energetic reasons or as a result of kinetic fluctuations (20). The behavior of steps in this regime remains to be explored. Such studies should provide the final piece to the puzzle of shape modification.

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PLANETARY SCIENCE

How Neptune Pushed the Boundaries of Our Solar System

Alessandro Morbidelli

Planetary scientists are finding increasing evidence that the orbital separations between the giant planets increased substantially as a result of interactions between the planets and a disk of “planetesimals” that were left over after planet formation. The evidence comes from the Kuiper belt, a population of small (diameter <1000 km) bodies at the outer edge of today’s Solar System that are the last remnants of this disk.

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Twenty years ago, computer simulations (1) showed that planetary orbits should expand or contract to conserve energy and angular momentum while the planets eject the planetesimals left over from planet formation from their neighborhoods. A decade later, Malhotra (2) proposed that the orbits of Pluto and the “Plutinos”—a subpopulation of the Kuiper belt—were probably caused by Neptune’s migration. She concluded that Neptune, which is now at 30 astronomical units (AU; 1 AU is the mean distance from the Earth to the Sun), has moved outward by at least 7 AU since its formation.

The orbital period of the Plutinos is 1.5 times that of Neptune, a behavior referred to as a 2:3 resonance. As the orbit of Neptune expanded, the orbital period of the planet increased. Hence, the location of the 2:3 resonance with Neptune also moved outward through the planetesimal disk (see the figure). Malhotra (2) showed that when planetesimals were swept by the resonance like house dust by a broom, they were likely to be “trapped” in resonance. Trapped planetesimals then moved outward with the resonance, while the ellipticity of their orbits slowly increased. In contrast, untrapped planetesimals kept their original orbital radius and small orbital ellipticity and inclination. According to this picture, the current Plutinos are the trapped planetesimals.

However, the study was not definitive. The proportions of Plutinos with high and low orbital inclinations could not be reproduced in Malhotra’s migration model (3). Furthermore, important properties of the Kuiper belt, such as its lower-than-expect-