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 common 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 manifestation 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 gelated 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.

References

1. W. K. Burton, N. Cabrera, F. C. Frank, *Philos. Trans. R. Soc. London* **243**, 299 (1951).
2. S. Mann *et al.*, *Science* **261**, 1286 (1993).
3. L. Addadi, S. Weiner, *Proc. Natl. Acad. Sci. U.S.A.* **82**, 4110 (1985).
4. A. L. Rohl, *Curr. Opin. Solid State Mater. Sci.* **7**, 21 (2003).
5. K. J. Davis, P. M. Dove, L. E. Wasylenki, J. J. De Yoreo, *Am. Mineral.* **89**, 714 (2004).
6. U. Becker, B. Gasharova, *Phys. Chem. Miner.* **28**, 545 (2001).
7. L. A. Touryan, M. J. Lochhead, B. J. Marquardt, V. Vogel, *Nature Mater.* **3**, 239 (2004).
8. T. N. Thomas, T. A. Land, J. J. De Yoreo, W. H. Casey, *Langmuir* **20**, 7643 (2004).
9. S. R. Qiu *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **101**, 1811 (2004).
10. S. Guo, M. D. Ward, J. A. Wesson, *Langmuir* **18**, 4284 (2002).
11. C. A. Orme *et al.*, *Nature* **411**, 775 (2001).
12. D. A. Walters *et al.*, *Biophys. J.* **72**, 1425 (1997).
13. J. B. Thompson *et al.*, *Biophys. J.* **79**, 3307 (2000).
14. G. Fu, S. Valiyaveettil, B. Wopenka, D. E. Morse, in preparation.
15. H. Elderfield, G. Ganssen, *Nature* **405**, 442 (2000).
16. Y. J. Han, J. Aizenberg, *J. Am. Chem. Soc.* **125**, 4032 (2003).
17. E. Beniash, J. Aizenberg, L. Addadi, S. Weiner, *Proc. R. Soc. London Ser. B* **264**, 461 (1997).
18. S. Raz, S. Weiner, L. Addadi, *Adv. Mater.* **12**, 38 (2000).
19. L. B. Gower, D. J. Odom, *J. Cryst. Growth* **210**, 719 (2000).
20. E. D. Williams, N. C. Bartelt, *Science* **251**, 393 (1991).
21. Y. Shirane, S. Kagawa, *J. Urol.* **150**, 1980 (1993).

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-

ed mass (*4*), and the two types ("hot" and "cold") of Kuiper belt objects other than the Plutinos (*5*) could not be explained solely by the migration model. They seemed to suggest that some other mechanism sculpted the Kuiper belt.

A series of more sophisticated models (*6–8*) of the migration process now provide confirmation of the original idea, showing that all the main properties of the Kuiper belt can be explained by planet migration alone. But for this to be possible, the planetesimal disk through which the migration took place must not extend beyond about 30 AU.

The assumption of an outer bound for the original planetesimal disk may appear to be arbitrary, but it is not. The Kuiper belt, which is the last remnant of the disk, ends at about 50 AU, where the period of the objects is exactly double that of Neptune (1:2 resonance) (*9*). The planetesimal disk was thus truncated. But where was its original outer edge? None of the mechanisms proposed to explain the truncation of the planetesimal disk attributes any role to the planets (*10*). It is therefore intriguing that the Kuiper belt ends at the location of a resonance with Neptune. This observation suggests that the outer edge of the planetesimal disk was originally well inside 50 AU, and that Neptune's migration pushed the Kuiper belt beyond the disk's original boundary (see the figure).

There are two reasons to believe that the primordial location of the outer edge of the disk was close to 30 AU. First, it explains why Neptune's migration stopped there. In our model (*7*), the planet tends to reach the outer edge of the disk and stop there. A significantly more extended disk would have driven Neptune beyond its current position (*7*). Second, it explains the current small mass of the Kuiper belt. If the region of space now inhabited by the belt was originally empty, the current mass of the belt reflects the fraction of the disk planetesimals that were pushed there during Neptune's migration. This fraction was presumably small, because most planetesimals were ultimately ejected from the Solar System.

To date, two mechanisms have been identified to push a small fraction (about 0.1%) of the disk's planetesimals beyond the original disk edge and implant them on sta-

ble Kuiper belt orbits. The first explains the "hot" Kuiper belt objects and a part of the plutino population, while the second explains the "cold" Kuiper belt objects.
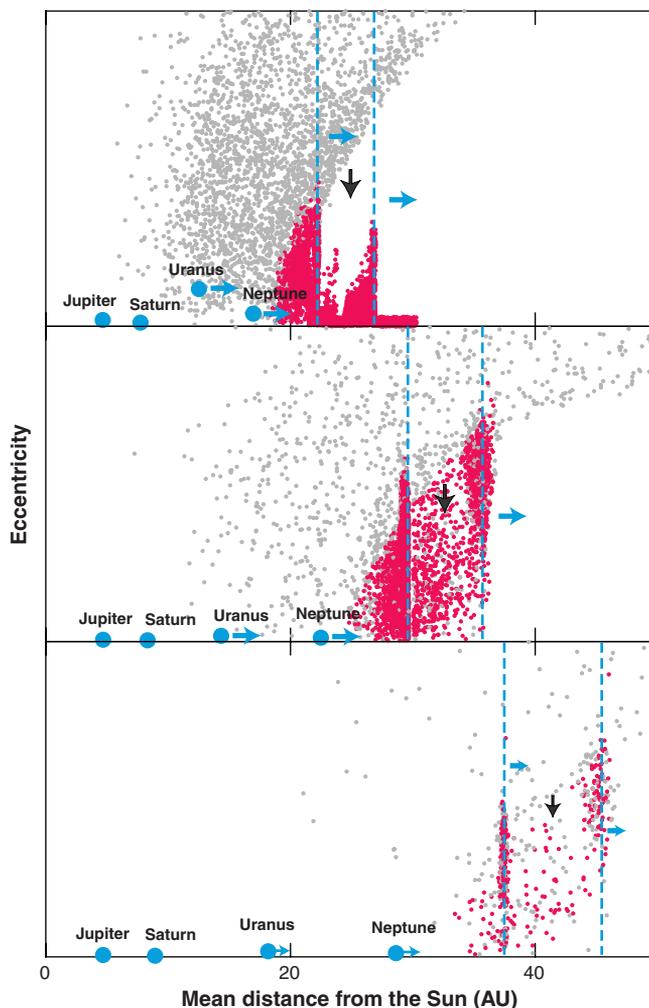
According to the first mechanism, Neptune scattered the planetesimals with which it had close encounters as it moved through the disk. Some planetesimals suffered multiple encounters and were transported outward on elliptic, inclined orbits (gray dots in the figure). A small fraction of these objects still exists today, forming

The orbital evolution of the outer Solar System. The three panels show sketches of the beginning, middle, and end of planetary migration, based on model results in (*7–9*). The vertical axis denotes the eccentricity (a measure of the ellipticity of the orbits). The vertical dashed lines show the locations of the 2:3 (left) and 1:2 (right) resonances with Neptune. The blue arrows indicate the direction of migration of Uranus, Neptune, and the resonances. The disk planetesimals are colored, depending on whether they have had close encounters with Neptune (gray) or not (red). Gray objects should have a wide range of orbital inclinations, whereas red objects should preserve their original small inclination. Most gray objects form the "scattered disk," but a few decrease their orbital ellipticity and mix with the red objects (black arrow). The planetesimal disk is originally truncated at about 30 AU (**top panel**). As Neptune moves outward, some objects are transported beyond this boundary. At the end (**bottom panel**), a small fraction of surviving objects are left in the Kuiper belt, which is approximately bounded by the 2:3 and 1:2 resonances with Neptune.

what is usually called the "scattered disk." Occasionally, some scattered disk objects entered a resonance with Neptune. Resonances can modify the ellipticity of the orbits. If the ellipticity is decreased, the sequence of encounters stops and the body becomes "decoupled" from Neptune, like a Kuiper belt object. Due to Neptune's migration, some of the decoupled bodies escaped from the resonances and became permanently trapped in the Kuiper belt (*8*). These bodies preserved the large inclinations acquired during the Neptune-encountering phase and now form the "hot" Kuiper belt objects. A few scattered objects also reached stable Plutino orbits (*8*). When the latter are put together with the Plutinos generated by Malhotra's mechanism, one obtains a very good match with the observed orbital distribution of the Plutinos, thus removing the problems discussed in (*3*).

According to the second mechanism, while Neptune was migrating through the disk, its 1:2 and 2:3 resonances swept through the disk, capturing a fraction of the disk planetesimals [as in Malhotra's theory (*2*)]. When the 1:2 resonance passed beyond the edge of the disk, it continued to carry its load of objects. Because Neptune's migration was presumably not a perfectly smooth process, the resonance gradually dropped objects during its outward motion, all along its way up to its final position at about 50 AU (*6*) (see the figure). This process explains the current location of the outer edge of the Kuiper belt. Because the 1:2 resonance does not enhance the orbital inclinations by much, the bodies transported by the resonance preserved their initial small inclination, forming the "cold" Kuiper belt objects.

Most properties of the Kuiper belt can thus be explained by invoking planet migration in a truncated planetesimal disk. Does this mean that the true evolution of the outer Solar System has finally been uncovered? Probably not. One only has to look at the Moon to realize that something important is missing in all of the scientists' scenarios. The dark spots on the Moon are huge impact basins that formed some 700 million years after the

Moon itself, during a cataclysm usually called the "late heavy bombardment" (*11*). What caused this bombardment, which occurred throughout the Solar System?

Previous studies (*12*) argued that a massive planetesimal disk in the outer Solar System could have caused the late heavy bombardment. In my opinion, there are not many realistic alternatives to this explanation. However, according to our current understanding, after the migration of the giant planets was over, the Solar System looked essentially like the current one, with no massive planetesimal populations left. It is thus tempting to conjecture that the late heavy bombardment was triggered by a late start of planet migration. But why did migration start late, rather than soon after planetary formation? The answer is not known, yet.

References and Notes

1. J. Fernandez, W. Ip, *Planet. Space Sci.* **44**, 431 (1984).
2. R. Malhotra, *Astron. J.* **110**, 420 (1995).
3. R. S. Gomes, *Astron. J.* **120**, 2695 (2000).
4. The current mass of the Kuiper belt is only 0.01 to 0.1 Earth masses, but a few tens of Earth masses had to exist in the region where the Kuiper belt bodies formed in order for the growth time scale to be short enough. Therefore, the current Kuiper belt apparently contains only 0.1 to 1.0% of its primordial mass.
5. The inclination distribution of the nonresonant Kuiper belt objects is bimodal (*13*). A first component, called "cold population," has inclinations smaller than about 4°. A second component, called "hot population," has a much broader inclination distribution, extending up to 30° to 40°. The hot and cold populations seem to have different physical properties (*14, 15*).
6. H. F. Levison, A. Morbidelli, *Nature* **426**, 419 (2003).
7. R. S. Gomes, A. Morbidelli, H. F. Levison, *Icarus* **170**, 492 (2004).
8. R. S. Gomes, *Icarus* **161**, 404 (2003).
9. C. Trujillo, M. Brown, *Astrophys. J.* **554**, 95 (2001).
10. Four plausible explanations have been proposed: (i) The outer part of the disk was destroyed by the passage of a star (*16*). (ii) It was photo-evaporated, owing to the presence of massive stars in the neighborhood of the Sun (*17*). (iii) The gas disk was extended, but planetesi-
mals beyond some threshold distance could not grow because of the enhanced turbulence in the outer disk (*18*). (iv) Distant dust particles and/or planetesimals migrated to a smaller heliocentric distance during their growth as a consequence of gas drag (*19, 20*).
11. W. K. Hartmann, G. Ryder, L. Dones, D. Grinspoon, in *Origin of the Earth and Moon*, R. Canup, K. Righter, Eds. (Univ. of Arizona Press, Tucson, AZ, 2000), pp. 493–512.
12. H. F. Levison, L. Dones, C. Chapman, A. Stern, M. Duncan, K. Zahnle, *Icarus* **151**, 286 (2001).
13. M. Brown, *Astron. J.* **121**, 2804 (2001).
14. H. F. Levison, S. A. Stern, *Astron. J.* **121**, 1730 (2001).
15. C. A. Trujillo, M. E. Brown, *Astrophys. J.* **566**, 125 (2002).
16. S. J. Ida, J. Larwood, A. Burkert, *Astrophys. J.* **528**, 351 (2000).
17. F. C. Adams, D. Hollenbach, D. Laughlin, U. Gurti, *Astrophys. J.* **611**, 360 (2004).
18. J. M. Stone, C. F. Gammie, S. A. Balbus, J. F. Hawley, in *Protostars and Planets IV*, V. Mannings, A. P. Boss, S. S. Russell, Eds. (Univ. of Arizona Press, Tucson, AZ, 1998), pp. 589–612.
19. A. N. Youdin, F. H. Shu, *Astrophys. J.* **580**, 494 (2002).
20. S. Weidenschilling, in *Comets II*, M. Festou, H. U. Keller, H. Weaver, Eds. (Univ. of Arizona Press, Tucson, AZ, in press).

STRUCTURAL BIOLOGY

Voltage Sensor Meets Lipid Membrane

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Electrical impulses propagate rapidly along the membranes of living cells. The molecular components that make this possible are proteins known as voltage-dependent ion channels. These channels open in response to changes in the voltage across the cell membrane, and it is precisely this voltage-dependent property that allows them to propagate electrical impulses. Thirty years ago, Armstrong and Bezanilla demonstrated that when voltage-dependent ion channels experience a change in the membrane voltage, tiny electrical charges known as gating charges move relative to the membrane electric field (*1*). This fundamental observation suggested that a transmembrane voltage change exerts an electric force on the gating charges, causing the pore within the channel protein to open.

Now we know that voltage-dependent potassium ion (K^+) channels contain an ion-selective pore domain with a gate, and a voltage sensor domain (segments S1 to S4) attached to the pore (see the figure). The gating charges correspond to positively charged arginine residues located on the otherwise hydrophobic S4 segment. Thus, voltage-sensing results from a repositioning of the

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arginine residues within the membrane electric field that is associated with structural rearrangements of the voltage sensor, and these structural rearrangements are linked to the opening of the pore's gate (*2, 3*).

The voltage sensor's structure and the process by which the gating charges are repositioned have been subjects of intense controversy. On the basis of electrophysiological studies, a number of structural models of the voltage-dependent K^+ channel have been proposed. These models share the feature of an S4 helix that is isolated from the lipid membrane by a protein wall consisting of helices S1, S2, and S3 on the channel's lipid-facing perimeter (*4–8*). They posit that a voltage change across the membrane causes a translation or rotation of the S4 helix, which would move the S4 helix and its positively-charged arginine residues within an aqueous "gating pore." Recently, x-ray crystal structures (*9*), biotin-avidin accessibility studies (*10*), and electron microscopy (*11*) of KvAP, a prokaryotic voltage-dependent K^+ channel, have suggested a different model. In this model (the paddle model) the voltage sensor is a highly mobile domain, and it is "inside-out" in the sense that helices S1, S2, and S3 do not isolate S4 from the membrane; instead, S4 itself is located at the protein-lipid interface. Specifically, S4 engages part of S3 to form a helix-turn-helix "paddle" that could somehow move at the

protein-lipid interface. It is the location of S4 that is at the center of the controversy. Is S4 at the protein-lipid interface or is it shielded from the lipid membrane by S1, S2, and S3? The paddle model is based on a collection of data—a full-length crystal structure with obvious distortions of its voltage sensor (*12*), a crystal structure of the isolated voltage sensor (*13*), and accessibility data (*10*)—and thus is conceptual, not atomic, and in many respects still needs to be defined.

A recent report in *Science* by Perozo and his co-workers (*14*) presents new data on the structure of the KvAP voltage sensor. These authors studied the spin-label side-chain accessibility and mobility of KvAP K^+ channels in lipid membranes using electron paramagnetic resonance (EPR) spectroscopy. This is a particularly informative technique for analyzing membrane proteins because it uses accessibility parameters determined from the spectral effects of lipid-soluble (O_2) and water-soluble (NiEDDA) relaxing agents to distinguish between lipid-accessible and water-accessible surfaces (*15*). A spin-label side chain at a specific position on a protein can thus be classified into one of three categories: buried beneath the protein surface, on the surface exposed to aqueous solution, or on the surface exposed to lipid. Furthermore, a side-chain mobility value provides additional information; surface positions tend to have a higher mobility value than those buried inside the protein.

All voltage-dependent ion channels undergo conformational changes. Which conformation did Perozo and his colleagues analyze? The KvAP voltage sensor is held in a closed conformation when the voltage is negative (for example, –100 mV) on the inner membrane surface relative to the out-