

the unfolding of fibrin(ogen) domains has been measured by single-molecule atomic force microscopy (see the figure, right panel) (11). These results suggest that the α -helical coiled-coils unfold first, acting as a molecular source of clot resilience, which may be the first clearly demonstrated biological function for protein unfolding.

Molecular dynamics simulations can help clarify experimental results (12, 13), but simulations on appropriate time scales for this large and complex molecule may require the use of coarse-grained methods. Knowing which fibrin domains are mechanically stable and which domains unfold might one day help to clarify the associations between molecular and clot properties and suggest novel sites for drug targeting.

Better understanding of the molecular origins of clot elasticity should make it possible to relate mechanical properties of dif-

ferent clots to their structures. Studies of clots made from recombinant or naturally occurring fibrinogen mutants are likely to be useful for these efforts. Clots including platelets are more complex, because the platelets control fibrin polymerization, and the structure of thrombi is also determined by the forces and transport of blood flow. Furthermore, platelets are filled with contractile stresses on fibrin clots, somewhat like other active-gel systems, such as actin filaments with myosin (14) or microtubules with kinesin or dynein (15).

The challenges to determining the microscopic and molecular properties of fibrin are manifold, but overcoming them will lead to an understanding of the clot mechanical properties at the molecular, fiber, and whole-clot levels. These insights may enable us to prevent many life-threatening maladies and develop new treatments.

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PLANETARY SCIENCE

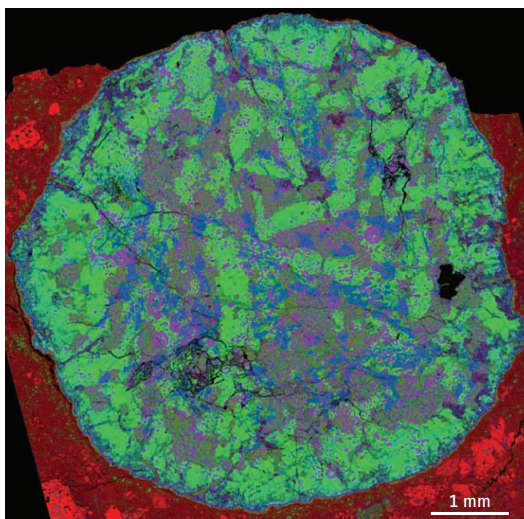
Identifying Ancient Asteroids

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More than 400,000 asteroids have been identified in the solar system to date. These objects are thought to be the surviving remnants of the planetesimals that formed the planets about 4.6 billion years ago. The ages and mineralogical characteristics of these planetesimals can be estimated through high-precision laboratory analyses of the compositional and isotopic properties of meteorites, of which more than 30,000 samples exist. Until now there has been no way to estimate when an asteroid formed, other than assuming that its age was similar to that of most meteorites. On page 514 of this issue, Sunshine et al. (1) present results of a remote spectroscopic study to show that a number of asteroids are enriched in the oldest known objects in the solar system (calcium-aluminum inclusions or CAIs) (see the figure), thereby making them the most ancient asteroids currently known.

CAIs are common components of the most primitive meteorites, carbonaceous chondrites, which have not undergone significant heating and are thought to be representative of the composition of the solar nebula. CAIs are predicted to be the first condensates that formed out of the solar nebula and can

have ages as old as ~4.567 billion years (2). Also commonly found in carbonaceous chondrites are chondrules, cooled molten droplets that formed during the rapid heating and then cooling of solid precursor material. On average, chondrules appear to have formed 2 million to 3 million years after CAIs (3). This age



Ancient asteroids. False-color x-ray elemental map (10) of a calcium-aluminum inclusion (CAI) in the Allende meteorite. The predominantly greenish, circular object is the CAI and spinel minerals are the violet areas in the CAI. Red, areas enriched in Mg; green, areas enriched in Ca; blue areas enriched in Al.

Remote spectroscopy has identified the oldest asteroids in the solar system.

difference between CAIs and chondrules indicates that CAIs were removed from the innermost regions of the protoplanetary disk, where they are assumed to have first formed, soon after they first condensed. Without this early removal, the isotopes of the CAIs would have been reset during the heating and cooling period of chondrule formation and the ages of the CAIs would resemble chondrules. Thus, the identification of a CAI-rich asteroid would date its formation at ~4.567 billion years ago.

In the early 1990s, spinel ($MgAl_2O_4$) was shown to be abundant on the surfaces of some asteroids (387 Aquitania and 980 Anacostia) (4). Near-infrared data (5) indicated that these objects have a very strong absorption feature centered at wavelengths around 2 μm , which is indicative of spinel with at least a small concentration of Fe^{2+} . Pyroxene, a likely suspect as the most common mineral with an absorption band centered near 2.0 μm , could be ruled out because it also has a strong absorption at ~0.9 μm , which was not present in the spectra of these asteroids. CAIs, the only component in meteorites that contain spectrally significant abundances of

spinel, were the most likely source of the absorption, but a spinel-rich surface due to igneous processes could not be ruled out.

In a study that should be the template for future analyses of asteroids because of its combination of telescopic observations, meteoritic characterization, and spectral modeling, Sunshine *et al.* can now precisely link spinel-rich asteroids and CAIs. A visible spectroscopic survey of more than 1000 asteroids (6) identified possible spinel-rich objects in the visible-wavelength region due to their strongly reddish (reflectance increasing with increasing wavelength) spectra below ~ 0.75 μm and their featureless flat spectra from ~ 0.75 to 0.92 μm . Near-infrared measurements using SpeX (7), a medium-resolution infrared spectrograph located at the NASA Infrared Telescope Facility on Mauna Kea, found that these objects had the strong absorption characteristic of spinel. To determine the best compositional analog for these asteroids, CAIs and CAI-free matrix material from the

CV chondrite Allende were separated out and characterized. Spectral modeling of the components was then done to best match the spectra of the asteroids and to narrow down the mineralogical interpretation.

One unanswered question is why these asteroids did not melt, which would have obliterated the spectral signature of the CAIs. If these asteroids contained the typical, initial $^{26}\text{Al}/^{27}\text{Al}$ ratios found in CAIs, their high aluminum contents should have caused melting. Perhaps these objects contained much lower abundances of $^{26}\text{Al}/^{27}\text{Al}$ and therefore constitute evidence for heterogeneous distribution of ^{26}Al in the solar nebula, or perhaps they contained very high abundances of ice (8) that acted as a buffer against full-scale melting and differentiation.

Sample return from an asteroid has been attempted only by the Japanese Hayabusa mission (9) from a near-Earth object (NEO), whereas the objects identified by Sunshine *et al.* reside in the main asteroid belt. If a

spinel-rich NEO can be identified, it surely would be an attractive target for a sample return mission: obtaining for laboratory analysis some of the most primitive material still remaining in the solar system.

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CELL BIOLOGY

A One-Sided Signal

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Lipids are increasingly recognized as essential for cells to transduce signals. Phosphoinositides—the phosphorylated derivatives of the membrane lipid phosphatidylinositol—control diverse cellular processes, including cell proliferation and survival, cytoskeletal organization, and vesicle trafficking. Similarly, the membrane lipid phosphatidylserine is key to initiating processes as important and dissimilar as blood coagulation and the clearance of dead cell remnants (apoptotic bodies). Defects in phosphatidylserine metabolism can lead to serious disorders including Scott's syndrome (a rare hemorrhagic disease) and autoimmune diseases such as systemic lupus erythematosus (1). Yet despite its importance, little is known about how phosphatidylserine functions during signal transduction. On pages 528 and 531 of this issue, Darland-Ransom *et al.* (2) and Mercer and Helenius (3) provide new insights into the biology of phosphatidylserine and reveal an unappreciated role in viral infection.

Unlike other phospholipids, the signals conveyed by phosphatidylserine do not entail

metabolic conversion but are instead encoded by its subcellular localization. Phosphatidylserine is enriched in the plasma membrane. In healthy cells at rest, virtually all the phosphatidylserine is found in the inner leaflet of this lipid bilayer, where it serves as a molecular beacon for proteins that contain a structural motif called the C2-domain. Moreover, because phosphatidylserine is very abundant (≥ 20 mol % of the inner leaflet) and is anionic, it contributes substantially to the negative charge of the cytoplasmic face of the plasma membrane and promotes the recruitment of positively charged, polycationic proteins.

The mechanism that generates the striking asymmetry in the transmembrane distribution of phosphatidylserine has been debated extensively, but recent evidence suggests that a class IV P-type ATPase may be the long-sought enzyme (aminophospholipid translocase) that maintains this unequal distribution in the membrane bilayer (4, 5). However, because the mammalian genome encodes at least 14 potential class IV ATPases, definitive genetic confirmation has been lacking. The likelihood that multiple isoforms of this lipid translocase (ATPase) would display redundant

Changes in the distribution of a lipid within the plasma membrane affect normal cell function and virus infection.

function has made removing or silencing the endogenous encoding genes in mammalian cells a daunting task. To circumvent this complication, Darland-Ransom and colleagues took advantage of the model nematode *Caenorhabditis elegans*, which contains only six homologs of these ATPases, also referred to as transbilayer amphipath transporters. Systematic gene silencing using RNA interference revealed that only the ATPase encoded by the gene *tat-1* is required to maintain phosphatidylserine asymmetry. Furthermore, cells that exposed phosphatidylserine on the outer (exofacial) leaflet of their plasma membrane, due to the elimination of *tat-1*, were subject to phagocytosis (internalization) by other cell types, even though the engulfed cells were not overtly undergoing cell death (apoptosis). Interestingly, the phagocytosis of cells exposing phosphatidylserine at the outer surface of their plasma membrane was not exhaustive and appeared to be random. This raises the possibility that engagement of cell surface receptors for phosphatidylserine, such as PSR-1 in *C. elegans* or Tim-1 and Tim-4 in mammalian cells (6), may not suffice to trigger phagocytosis, and that other signals

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