The yeast genome is, of course, far simpler than the human genome, and we expect many of the problems evident in yeast to be greatly magnified in human. First, we expect the human genome to contain a vast number of potential ORFs given the small size of exons (average size ~140 base pairs) and the complexity of mRNA splicing (*16, 19*). It is doubtful that we will be able to find true genes among these ORFs solely by analyzing their raw nucleotide sequences. In fact, initial estimates of the number of genes in the human genome ranged from 20,000 to >100,000 (*17, 23–25*).

One solution for annotating genes in sequenced genomes may be to return to the original definition of a gene—a sequence encoding a functional product—and use functional genomics to identify them. Moreover, if we add conservation information obtained from cross-genome comparisons, we can streamline the process. Ultimately, we believe that identification of genes based solely on the human genome sequence, while possible in principle, will not be practical in the foreseeable future. Only through large-scale systematic functional genomics experiments and through careful sequence comparisons against related organisms will we be able to convincingly arrive at a definitive annotation of the human genome.

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PLANETARY SCIENCE

A Liquid Core for Mars?

Veronique Dehant

Mars is a planet very similar to Earth. Early in their evolution, both planets must have been sufficiently hot to be molten. Earth still has a liquid core, but the smaller size of Mars would favor faster cooling. Extrapolation from Earth suggests that Mars today should therefore not have a liquid core. However, small differences in elemental composition between the two planets prevent our simply extrapolating from knowledge of Earth's properties (*1*). On page 299 of this issue, Yoder *et al*. (*2*) present evidence that the iron core of Mars is liquid, with important implications for martian geology.

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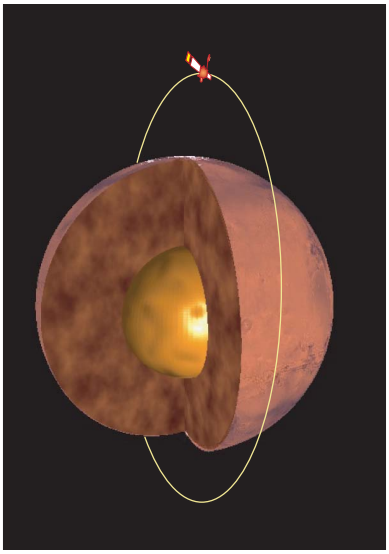
There are a few constraints on Mars' deep interior based on analysis of martian meteorites (*3*, *4*), observation of the absence of a global magnetic field (*5*), and knowledge of the planet's mass and moments of inertia (*6*). Moments of inertia quantify the global mass repartition within Mars. They provide evidence for the existence of a denser martian core and can be used to constrain the core dimension (*7*). However, the uncertainty of the core's density and dimension remains large because they depend on the temperature profile and light element abundance, and these properties are still unknown.

The author is at the Observatoire Royal de Belgique, Bruxelles, B-1180 Belgium. E-mail: veronique.dehant@oma.be

Scientists interested in modeling the martian interior are therefore looking for other kinds of complementary data. As for Earth, the Sun's gravitational attraction induces global phenomena on Mars—namely, tides and precession-nutation (the motion of the rotation axis in space). Tides are deformations induced by the gravitational pull of the Sun. They are related to surface displacements, surface gravity changes (such as those that would be measured by a gravimeter on the martian surface), and mass repartitioning inside the planet. These changes are periodic, with periods related to Mars's orbit around the Sun (and, to a minor extent, to the orbits of the two martian moons, Phobos and Deimos, around Mars).



The physical state of the martian core observed by MGS orbit tracking.

To study these phenomena, long-term observations—for example, of the annual or semiannual periods—are needed. Surface gravity data, surface displacements, and nutations cannot yet be observed because their measurement requires a network of geophysical stations on the martian surface (*8*). But some information can be obtained from a Mars orbiter such as Mars Global Surveyor (MGS), which is (in addition to the classical steady-state self-gravity of the planet) subject to gravitational forces resulting from the mass redistributions induced by the tides. Hence, information on the planet's response to the tidal force may be deduced from the precise reconstruction of the MGS orbit. Because this response depends on the internal structure of Mars, it is possible to infer properties of the core.

The mass repartitioning induced by the tides is usually described by a set of dimensionless numbers called "Love numbers," which express the nonrigidity of the planet. The value of the *k*-Love number (the Love number relevant for the perturbation of the orbit) will be much larger if the core is liquid than if it is solid (liquid versus solid core values change by ~50%) (*9*). Observational constraints on this *k*-Love number would allow the physical state of the core to be determined.

The long time series of Mars Global Surveyor DSN (Deep Space Network) tracking data provides such constraints. Smith *et al*. (*10*) have used these data to deduce the *k*-Love number directly from the position of the spacecraft orbiting Mars. However, the main term of the gravitational potential was unfortunately not very accurate.

Yoder *et al*. now use another indirect observation of the gravitational effect in-

duced by the tides that has been shown to be more effective in determining the state of the core. This component is also proportional to the *k*-Love number. The precision reached by Yoder *et al.*, based on 3 years of DSN data, is higher thanks to the use of long-term changes in the inclination of the MGS orbit. The resulting value for the *k*-Love number is large enough to rule out a completely solid core, indicating that at least part of the core is liquid.

This exciting result has important consequences for our knowledge about Mars's interior and evolution, both of which largely depend on the chemical composition of the planet. The large core radius and high percentage of light elements in the core proposed by Yoder *et al.* (*2*) are at the limit of the present possibilities for modeling the interior of Mars, when considering sulfur inside the core. Alternative possibilities for the light element in the core, such as hydrogen instead of sulfur, must therefore be considered. This will certainly drive new modeling studies of the martian interior. On the other hand, it is very important to know that the martian core is liquid, because geophysical studies of Mars very much depend on the physical state of the core.

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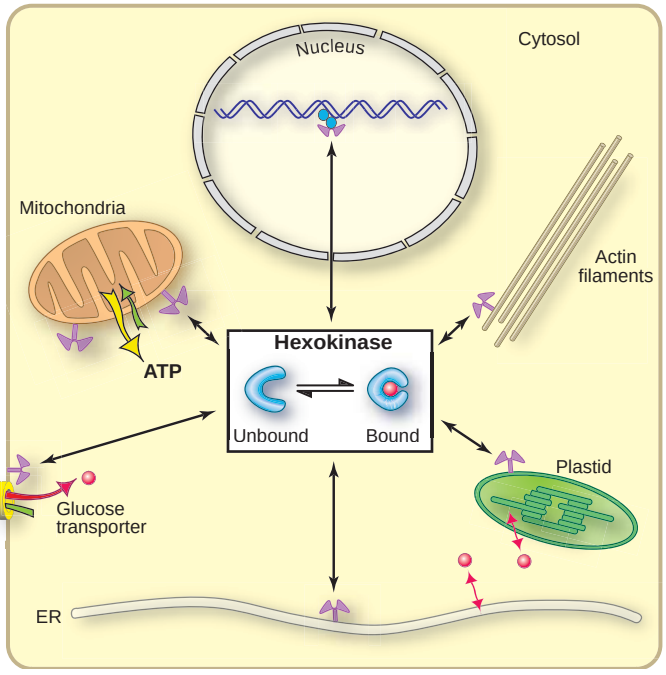
PLANT SCIENCE

Hexokinase, Jack-of-All-Trades

Wolf B. Frommer, Waltraud X. Schulze, Sylvie Lalonde

The classic view in biochemistry is that metabolic pathways are regulated through allosteric regulation of the first enzyme in the pathway. Allosteric regulation is the induction by another molecule of a conformational change in an enzyme that alters the enzyme's activity. Downstream enzymes in metabolic pathways that are not subject to allosteric regulation traditionally have been branded as "boring." But such "boring" enzymes are often crucial checkpoints in metabolic pathways, their activity being regulated through transcriptional or posttranslational mechanisms (*1*). This type of regulation requires the presence of proteins that can sense changes in metabolite levels. On page 332 of this issue, Moore *et al.* (*2*) provide compelling evidence in the model plant *Arabidopsis* that the not-so-boring enzyme, hexokinase, falls into this category and, furthermore, is itself a metabolite sensor. Hexokinase not only catalyzes the ATP-dependent phosphorylation of glucose but also senses glucose levels and the phosphorylation status of glucose, transmitting this information to the nucleus through a signal transduction pathway. By analyzing an *Arabidopsis* mutant that lacks hexokinase activity, the authors were able to separate the catalytic and glucose-sensing properties of this enzyme.

Most higher organisms make multiple isoforms of hexokinase (*3*). For example, unicellular yeast produce hexokinases PI and PII, and glucokinase. Mammalian genomes encode two classes of hexokinase: the first comprises a low-affinity glucokinase; the second contains three high-affinity hexokinases I, II, and III that form dimers (*3*). *Arabidopsis* has six hexokinase genes. Amino acid residues for binding both glucose and ATP have been pinpointed in the crystal structure of hexokinase (*4*). The isoforms of this hexokinase interact not only with each other to form dimers, but also with other proteins and with cellular membranes (see the figure). In addition to their cytosolic localization, hexokinase isoforms are found associated with membranes of the endoplasmic reticulum and plasma membrane (*5*). Some hexokinase isoforms are also found bound to two different binding sites on mitochondria, where they may be coupled to ATP production (*6*). In plants, hexokinases are associated with the chloroplast outer envelope, where they might help in glucose export by phosphorylating glucose before it enters the cytosol (*7*). The development of nanosensors that detect metabolites may help to evaluate the importance of the subcellular distribution patterns of hexokinase (*8*). Mammalian glucokinase is associated with the actin cytoskeleton but, depending on physiological conditions, it can move to the nucleus and alter gene expression (*9*, *10*). The marked differences in the subcellular localization of hexokinase reflect its many activities and suggest that this enzyme behaves as a jack-of-all-trades.



Sticking to membranes. Hexokinases associate with various cellular membranes, and this association affects their activity. These enzymes are not only involved in glucose sensing and metabolism but also in signal transduction. This duality is achieved by switching between a bound and unbound form that interacts with different proteins, such as regulatory DNA-protein complexes in the nucleus. Receptors for hexokinases (purple) must be present to enable differential targeting of these enzymes to different subcellular locations. Hexokinases associate with membranes of subcellular compartments, such as the endoplasmic reticulum (ER) and mitochondria.

Hexokinases are at the gateway to glucose metabolism. Metabolism of glucose leads to increased ATP levels, activation of K^+ channels, and a change in

W. B. Frommer and S. Lalonde are in the Department of Plant Physiology, Zentrum für Molekularbiologie der Pflanzen, Universitat Tübingen, D-72076 Tübingen, Germany. E-mail: frommer@zmbp.uni-tübingen.de W. X. Schulze is at the Protein Interaction Laboratory, Department of Biochemistry and Molecular Biology, University of Southern Denmark, 5230 Odense, Denmark.