"Since the tissue itself makes estrogen, there is enough present to make high levels of estrogen metabolism to make genotoxic activity plausible," says Stanten.

Plausible but not certain. Most estrogen metabolite researchers believe that certainty will come in time as the studies continue to roll in. Studies of mice that have been engineered to either over- or underexpress particular metabolite-controlling enzymes could be particularly enlightening, says Eppley Institute biochemist Eleanor Rogan. But even then, sorting out all the signals won't be easy because of the complexity of the system, she says.

But the effort will be worthwhile, because if further evidence does nail down the idea that estrogen metabolites are mutagenic, it may be possible to intervene to reduce the risk of cancer, says Longfellow. If it turns out that women who over- or underexpress crucial enzymes have an increased cancer risk, for example, researchers could try to design drugs to bolster or block the levels of these compounds. "After all, these are things that can be modulated," Longfellow says. But for now the primary challenge remains confirming the role of estrogen metabolites in the first place. "The evidence is building," says Yager. "But the burden of proof still lies in developing more direct evidence."

–**Robert F. Service**

Additional Reading

B. T. Zhu and A. H. Conney, "Functional role of estrogen metabolism in target cells: Review and perspectives," *Carcinogenesis* **19**, 1 (1998).

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J. Fischman *et al.*, "The role of estrogen in mammary carcinogenesis," *Annals of the New York Academy of Sciences* **768**, 91 (1995).

EVOLUTION

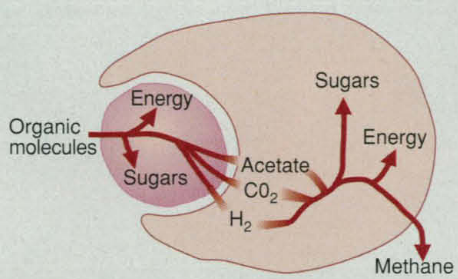
Did the First Complex Cell Eat Hydrogen?

Successful unions can start off in the strangest ways. Take eukaryotic cells, which compose all "higher" organisms and generally contain energy-producing organelles called mitochondria. Mitochondria were once free-living bacteria, and most researchers believe that early in evolution ancestral eukaryotic cells simply ate their future partners. But two researchers are now arguing for a less haphazard start to this ancient partnership. The first eukaryotes, they say, had an appetite for the waste products of the original mitochondria. The union of these organisms was simply a matter of survival.

In last week's *Nature*, William Martin of Braunschweig Technical University in Germany and Miklós Müller of Rockefeller University in New York City draw on genetic data, biochemistry, and the lifestyles of some simple organisms today to argue that the first eukaryote evolved from a methanogen, a microbe that consumes hydrogen and carbon dioxide and produces methane. Its partner—the future mitochondrion—was a bacterium that made hydrogen and carbon dioxide as waste products.

Scientists pondering how the first complex cell came together say the new idea could solve some nagging problems with the prevailing theory. "It's eminently sensible," says evolutionary biologist Russell Doolittle of the University of California, San Diego. But he and others aren't ready to embrace the new scenario. "It's elegantly argued," says Michael Gray of Dalhousie University in Halifax, Nova Scotia, but "there are an awful lot of things the hypothesis doesn't account for."

In the standard picture of eukaryote evolution, the mitochondrion was a lucky accident. First, the ancestral cell—probably an archaebacterium, recent genetic analyses suggest—acquired the ability to engulf and digest complex molecules. It began preying on its microbial companions. At some point, however, this predatory cell didn't fully digest its prey, and an even more successful cell resulted when an intended meal took up permanent residence and became the mitochondrion.



B. FINLEY/INST. OF FRESH WATER ECOLOGY

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So happy together. Exchanges of molecules including hydrogen may have bound microbes together in the first complex cell. In a modern analog, bacteria snuggle close to hydrogen-producing organelles (dark structures, ~2 micrometers long) inside a protist *(left)*.

For years, scientists had thought they had examples of the direct descendants of those primitive eukaryotes: certain protists that lack mitochondria. But recent analysis of the genes in those organisms suggests that they, too, once carried mitochondria but lost them later (*Science*, 12 September 1997, p. 1604). These findings hint that eukaryotes might somehow have acquired their mitochondria before they had evolved the ability to engulf and digest other cells.

How it might have happened came to Martin one evening when he looked at a picture of a protist called *Plagiopyla*. These one-celled eukaryotes have hydrogen-producing organelles called hydrogenosomes, which are thought to be related to mitochondria. And in their cytoplasm, clustered among those organelles, live hydrogen-consuming methanogens.

Looking at those hungry methanogens, Martin recalls, "the cell sort of evolved before my eyes." He discussed the idea with Müller, and "all of a sudden everything fell into place," Martin says. They concluded that what they saw inside the protist—the partnership of the organelles and the methanogens—mirrored the union that had led to the first eukaryotic cell.

Müller and Martin think that the association between the ancestral methanogen and a hydrogen-producing bacterium started casually, in an oxygen-free, hydrogen-rich environment. The microbial pair later found itself far from that original environment, where the methanogen could not survive without its partner. Then, Martin and Müller suggest, a transfer of genes cemented the partnership, allowing the host to enclose its guest completely. The new genes enabled the methanogen to import small molecules, make sugars, and break them down into food for the enclosed cell. These genes probably came from the guest bacterium, which could also use oxygen to produce energy—as mitochondria do today.

The hypothesis is "the most cogent explanation for why a eubacterium and an archaebacterial cell should get together in the first place," says Gray. If it is right, current ideas about the relationship between eukaryotes and archaebacteria might shift. In the current picture, eukaryotes originated near the base of the tree. They branched off from the archaebacteria long before those organisms diverged into the main groups present today, such as the methanogens. Martin and Müller's hypothesis would shift the first eukaryotes well up the tree, tying them more closely to the archaebacteria.

But Gray and others still have reservations about the scenario. "It's possible, but it's not as plausible as the standard idea" that the original host of mitochondria was a bacteria eater, says evolutionary biologist Tom Cavalier-Smith of the University of British Columbia in Vancouver. "It makes more sense if the host came from a bacterium that had experience digesting food and had transporter enzymes already," so that it could import small molecules and feed its guest.

Martin and Müller say that an analysis of the complete sequences of eukaryotic and archaebacterial genomes should show who is right. Their theory predicts that on the whole, the genes that eukaryotes derived from archaebacteria will look most like those of methanogens. It also suggests that direct descendants of the earliest eukaryotes may still lurk in dark, anaerobic environments. The best places to search for a living example of the ancestor of us all, Müller says, "are, of course, foul-smelling, muddy, or inside of a digestive tract."

–Gretchen Vogel

PLANETARY SCIENCE

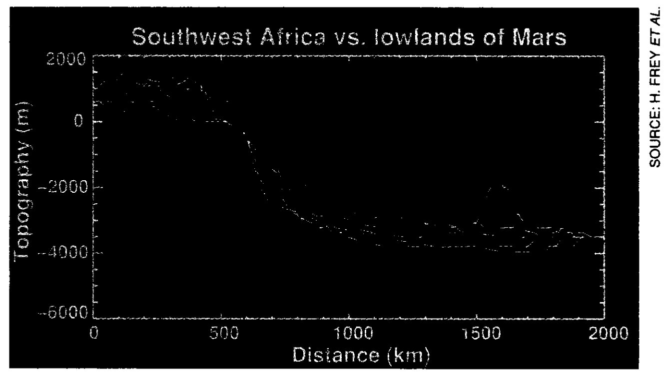
Surveyor Shows the Flat Face of Mars

Every planet harbors a mystery that is key to understanding its fundamental nature. Earth's concerned its division into either low-lying ocean basin or high-standing continent. Once researchers realized that plate tectonics created dense ocean crust that sinks to form deep basins and light continental crust that floats high, the mystery was solved and the essential forces shaping Earth's surface were understood. Now, the first results from the altimeter aboard the Mars Global Surveyor (MGS) spacecraft are helping to solve an equally fundamental puzzle about that planet.

On Mars, the mystery is a great crustal dichotomy: Much of the planet's northern hemisphere is a low-lying plain roughly centered on the north pole, while the rest of that hemisphere and all of the southern hemisphere are ancient highlands. Explanations have ranged from Earth-like plate tectonics to the cosmic catastrophe of a huge impact. The MGS altimeter results, reported on page 1686 of this issue by a team led by geophysicist David Smith of NASA's Goddard Space Flight Center (GSFC) in Greenbelt, Maryland, hint that Earth-like tectonic forces and perhaps even an ancient ocean have shaped Mars's northern lowlands.

The MGS results show that the northern lowlands are remarkably flat across thousands of kilometers and smooth on a scale of hundreds of meters. It's "the flattest surface in the solar system for which we have data," says geophysicist Maria Zuber of the Massachusetts Institute of Technology, a teammate of Smith's. "The only thing that comes close is the heavily sedimented floors of Earth's oceans; it's actually flatter than that." The similarity to Earth's oceans suggests that Mars's great basin formed the same way—by plate tectonics. But altimetry alone can't solve the riddle of martian topography or rule out other origins for its giant basin, she warns.

The tantalizing new data come from the Mars Orbiter Laser Altimeter (MOLA) aboard the MGS. MOLA works much the way a ship's acoustic depth finder traces out the sea floor, but instead of using sound waves, it bounces an 8-nanosecond laser pulse of infrared light off the martian surface at 300-meter intervals.



Matching a martian profile. The flat martian lowlands resemble the topography of the South Atlantic ocean floor off Africa.

By measuring the light's round-trip time, MOLA gauges with 10-meter accuracy the height of the land, averaged over the width of the laser's 150-meter-wide beam. Changes in the shape of the pulse after reflection provide a measure of the smoothness of the surface the beam scanned.

After 18 north-south tracks, "the remarkable thing is that the northern hemisphere is flat over thousands of kilometers," says Zuber. On the scale of the 2000-kilometer-long tracks within the lowlands, the surface is level or slopes up toward the south at about 0.05°, she says. In most places between 50°N and the polar ice cap at 80°N, topography rises and falls by only 50 meters over hundreds of kilometers. This means, Zuber says, that the northern lowlands are flatter than the lava floods of the lunar maria, flatter than the vast volcanic plains of Venus, flatter than deserts on Earth. The smoothest part of the central Sahara, for example, is twice as rough as the martian lowlands. The most comparable topographic profiles Zuber could find are from terrestrial sea floors, for example the one running from the middle of the South Atlantic Ocean onto the edge of South America (see diagram for a similar oceanic profile). On the 100-meter scale, the smoothness of the martian lowlands is also comparable to that beneath terrestrial oceans. "You can see where this is going," says Zuber.

Indeed, this tempting match between Mars's lowlands and Earth's ocean basins fits a 1994 proposal by geophysicist Norman Sleep of Stanford University. He suggested that the lowlands are an "ocean" basin created by a martian version of plate tectonics that long ago ground to a halt. The lowlands would be underlain by dense crust produced by sea-floor spreading, and plate motions would have raised and roughened the boundary between the lowlands and highlands, another feature seen by MOLA.

Others have proposed that whatever the basin's origins, there might once have been water filling it (*Science*, 12 February 1993, p. 910), a notion consistent with the extreme smoothness. Such smoothness is typically produced by some kind of sedimentation, such as the steady rain of tiny particles that smooth out the roughness of ocean crust.

But other explanations of the basin's origins remain. For example, some researchers have suggested that one or several large asteroids or comets blasted Mars billions of years ago, leaving a thinned crust that sank as it cooled, an idea favored by MOLA team member Herbert Frey of the GSFC. No one knows just what kind of topography such a monumental impact would leave, so the altimeter data can't yet support or refute that idea. And Frey also points out that massive lava flows might account for the smoothness of the lowlands, especially with a patina of windblown sediments on top.

Finding out what made northern Mars so flat will take more data. For now, says planetary geologist Michael Carr of the U.S. Geological Survey in Menlo Park, California, "we just don't know" what created the great martian dichotomy. But an Earth-like ocean basin is the hometown favorite.

–Richard A. Kerr