Highlights of Research in This Issue

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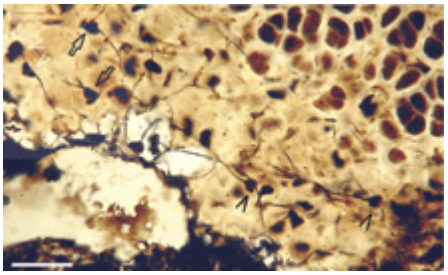
Lichen in the Mists of Time



Fungi form a major branch of the tree of life and also provide important symbiotic relations with other organisms, commonly phototropic bacteria. These relations in part form "lichens"--essentially fungi that practice agriculture using bacteria. Fungi in turn release nitrogen for

plants in human agriculture. **Yuan *et al.*** (p. 1017) now describe a lichen-like association between fungi and cyanobacteria or algae from the Doushantou Formation, China, dating to about 600 million years ago. The lichen (and fungi) occur in a shallow marine setting, which suggests that such symbioses were established well before the rise of terrestrial plants.

CREDIT: YUAN *ET AL.*

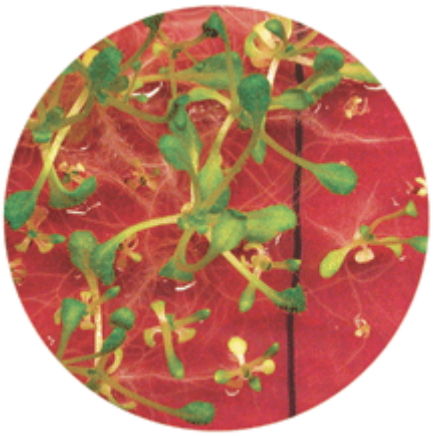
Flipping Across the Membrane

ATP binding cassette transporters pump hydrophobic compounds across the cell membrane and include the efflux pumps implicated in bacterial antibiotic resistance and cancer drug resistance in humans. Hydrolysis of adenosine triphosphate provides the energy for structural changes that mediate substrate transport, but the mechanism remains unclear. Two studies provide insight into the transport cycle of MsbA, a bacterial transporter that transports lipid A and lipopolysaccharide across the bacterial inner membrane (see the Perspective by **Davidson and Chen**). **Dong *et al.*** (p. 1023) used electron paramagnetic resonance to map conformational changes during the ATP cycle of MsbA, and **Reyes and Chang** (p. 1028) determined the x-ray structure of MsbA in a transition state complex with magnesium, adenosine diphosphate, vanadate, and lipopolysaccharide. Both studies are consistent with a mechanism in which ATP hydrolysis drives flipping of amphipathic substrates.

Qubit Version of Fourier Transforms

Interest in quantum computing exploded after Shor developed an algorithm for factoring large numbers in 1994. A key component of that algorithm requires the ability to carry out a quantum Fourier transform on a set of quantum "qubits" that are the analog of binary digits in classical computations. **Chiaverini *et al.*** (p. 997) report their experimental demonstration of a semiclassical quantum Fourier transform using trapped beryllium ions as qubits. The results show the possibility of performing a version of the Fourier transform that requires only single-qubit operations conditioned on the measurements of other qubits in a system that can be scaled up to a large number of qubits.

Coordinating Plant Defenses



Pathogen invasion at one site in a plant triggers defensive reactions throughout the rest of the plant. This systemic acquired resistance is mediated by salicylic acid and the regulatory protein NPR1, and involves the activation of a suite of pathogenesis-related genes. **Wang *et al.*** (p. 1036) found that another group of genes is activated and encodes the cellular secretory machinery. The same regulatory triggers set in motion production of anti-pathogen proteins, as well as enhance the means to deliver them to where they can do the most damage.

CREDIT: WANG *ET AL.*

Marine Nitrogen Pools

Nitrogen is an essential and sometimes limiting nutrient in marine ecosystems whose role in controlling productivity is well-understood. It exists in the surface ocean mostly as dissolved organic nitrogen (DON), but despite decades of research, only a small fraction of the DON in surface ocean waters has been chemically characterized. **Aluwihare *et al.*** (p. 1007) used solid-state ^{15}N nuclear magnetic resonance to characterize two distinct pools of high-molecular-weight (HMW) DON, which comprise about 30% of the total. One pool, which makes up approximately half of the DON near the surface, is more readily hydrolyzed, whereas the deep ocean contains mostly forms that are resistant to chemical hydrolysis and biological degradation. The authors describe how these pools produce the vertical profile of HMWDON that is observed and discuss the chemical transformations that might transfer nitrogen to the deep ocean.

How Hydrogen Hung Around

Hydrogen is lost permanently from our atmosphere as it leaks slowly into space. The atmo- sphere of early Earth was much richer in hydrogen than it is now, and until recently, it was generally thought that its escape rate was so rapid that prebiotic organic compounds must have formed in a relatively oxidized environment. **Tian *et al.*** (p. 1014, published online 7 April 2005; see the Perspective by **Chyba**) report calculations that show that the escape of hydrogen from early Earth occurred 100 times more slowly than previously thought. The hydrogen mixing ratio of the early atmosphere was more than 30%, two orders of magnitude greater than formerly predicted. An atmosphere so rich in hydrogen would have facilitated greatly the formation of prebiotic organic compounds.

Out of Africa Revisited

The route of human colonization of Asia after dispersing out of Africa 60,000 years ago has remained unresolved. DNA sequence

analysis of existing populations can provide phylogenies that can be mapped onto geographic distribution (see the Perspective by **Forster and Matsumura**). **Macaulay *et al.*** (p. 1034) tested alternative models for the settlement of Eurasia by modern humans using complete mitochondrial (mt) DNA genomes (which provide the highest possible resolution of the maternal genealogical tree) by studying the "missing link" of Southeast Asian aboriginal populations. Only one model--a single, rapid dispersal along the coat from East Africa to India and thence to Southeast Asia and Australasia--can explain the phylogenetic patterns observed. Moreover, all subsequent peopling of Europe and Asia can be explained by this initial dispersal event. **Thangaraj *et al.*** (p. 996) identified M31 and M32 mtDNA types among indigenous Andaman islanders which show that these populations became genetically isolated about 50,000 to 70,000 years ago, apparently after their initial migration from Africa.

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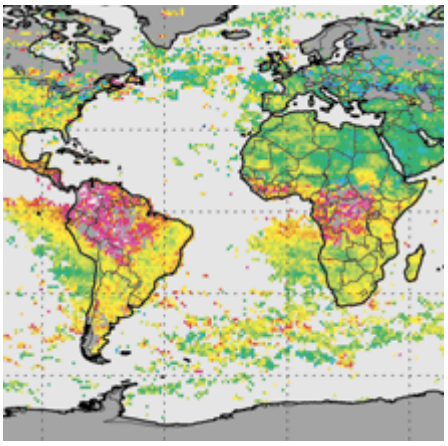
pH Makes the Switch

Adenylyl cyclases (AC) synthesize the second-messenger cyclic AMP (cAMP). **Tews *et al.*** (p. 1020) have characterized an AC from *Mycobacterium tuberculosis* that produces cAMP in a pH-dependent manner. The enzyme consists of two complementary monomers, and high-resolution structures show that interaction between the catalytic and regulatory domains prevents formation of the active site in the inhibited (high pH) state. Two molecular switch regions mediate structural rearrangement of the catalytic domains so that they are positioned to form the active site at their interface. Mutagenesis results support the idea that a pH-dependent structural transition regulates activity.

Leprosy Migrations

Leprosy is a puzzling disease caused by a slowly developing infection with *Mycobacterium leprae*. **Monot *et al.*** (p. 1040; see the news story by **Grimm**) examined the distribution of rare single nucleotide polymorphisms of several isolates of the leprosy bacillus collected from around the world. The pathogen has a very stable genome, and it appears that a single clone has spread north and east from East Africa or the Middle East with successive waves of human migration, reaching West Africa and the Americas from Eurasia within the past few hundred years.

Tropical Degassing



Methane is the second most important trace greenhouse gas, accounting for 20% of their collective absorption of solar radiation, but its sources and sinks are not well understood. **Frankenberg *et al.*** (p. 1010, published online 17 March 2005) present results from SCIAMACHY, an instrument onboard the ENVISAT satellite, which reveal the global distribution of tropo spheric methane. Methane concentrations are unexpectedly high over terrestrial tropical regions, indicating that it is produced in amounts much greater than previously had been assumed. This discovery could help reconcile the disagreement between various estimates of the global methane budget.

CREDIT: FRANKENBERG *ET AL.*

Round-the-Clock Metabolism

The behavior of most organisms is organized around a 24-hour cycle. One of the key molecular regulators of this circadian rhythmicity is a transcription factor called CLOCK. Mice carrying a mutation in the *Clock* gene show profound disturbances in circadian behavior. **Turek *et al.*** (p. 1043, published online 21 April 2005) now show that these *Clock* mutant mice also overeat, become overweight, and develop features of metabolic syndrome, including elevated serum levels of glucose and lipids. The metabolic disturbances were accompanied by alterations in the expression of neuropeptides implicated in appetite control and energy balance.

The Maturing Repertoire of Canary Songs

A canary's song is made up of units of sound organized with syntax and phrasing. **Gardner *et al.*** (p. 1046) have now distinguished some of the forces that shape the adult bird's song. When young canaries were isolated from other birds' songs, they showed remarkable ability to mimic synthetic songs that were far from the normal canary song. However, as these birds matured, their songs became more typical of normal adult canaries, despite having never heard such songs. Thus, with maturity in the canary comes a loss of vocal flexibility, and increasing dominance of an innate program of song structure.

Cold Ocean Stratification

Why has atmospheric CO_2 varied in such a regular manner, and between such narrow bounds, during glacial-interglacial cycles? Biological explanations invoke greater marine productivity to explain lower glacial atmospheric CO_2 concentrations. Physical mechanisms include the suggestion that ocean stratification, which can limit the transfer of CO_2 from the deep ocean where it is concentrated, is important. **Jaccard *et al.*** (p. 1003) report results of measurements from

the Subarctic North Pacific that reveal enhanced stratification there during the cold, glacial intervals of the past 450,000 years, as well as lower productivity. The close correspondence of this record of stratification to similar records in the southern polar regions, and to the temperature and CO_2 records of Vostok, Antarctica, suggests that there must be a mechanism by which cold temperatures cause stratification in both hemispheres, and that this process is important for controlling the concentration of CO_2 in the atmosphere.

Location and Molecular Manipulation

The tip of a scanning tunneling microscope (STM) can be located over molecules with high precision, and this capability has been exploited in controlling the dynamics of single molecules, such as by activation of different vibrational modes. **Lastapis *et al.*** (p. 1000) have now used voltage pulses from an STM tip at low temperatures (5 kelvin) to control a reversible conformational switching of biphenyl on a silicon surface through resonant electronic excitation. How the molecule switches depends not only on the voltage applied, but also on where the STM tip is over the molecules when it delivers the voltage pulse. In some cases, conformational switching occurs by delivering the pulse to the ring that stays in place, rather than to the one that will move.

Chaperones of the World Unite

In microorganisms such as yeast, specialized molecular chaperones interact directly with nascent polypeptides exiting the ribosome tunnel and physically link translation and protein folding. **Hundley *et al.*** (p. 1032, published online 31 March 2005) now report that ribosome-associated molecular chaperones appear to have been maintained throughout eukaryotic evolution and are also used in multicellular organisms. A ribosome-associated J protein is highly conserved in evolution, with orthologs found in yeast, flies, worms, and mammals. In yeast cells, the human Zuo homolog, Mpp11, can substitute for Zuo, and functions together with a yeast Hsp70 homolog to promote cotranslational protein folding.

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