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EWS

COVER Biofilms of sulfate-reducing bacteria (blue) growing in dilute groundwater (~1 part per million dissolved zinc) associated with an abandoned lead-zinc deposit produce sphalerite (ZnS) particles that aggregate (light green) and form micrometer-diameter spheres (gold). Such biomineralization may assist in groundwater remediation and may play a role in the genesis of some ore deposits. [Scanning electron microscope image: J. F. Banfield, S. A. Welch, M. Diman, M. Labrenz]



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1779 From blood into brain

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LUNAR CATACLYSM

Dating of impact melts from Apollo and Luna samples of the moon suggest a large number of impact events occurred around 3.9 billion years ago (a lunar cataclysm). All of the lunar samples collected from the moon are from the equatorial nearside so that impact events on the farside or near the poles may not have been sampled in our small collection. Cohen et al. (p. 1754; see the news story by Kerr) have measured ⁴⁰Ar-³⁹Ar ages for impact melts in lunar meteorites, which should provide a more global lunar sampling. They found 6 to 10 impact events between 3.92 and 2.43 billion years old, which provides further support for the lunar cataclysm hypothesis.

NANOSCALE VARIABLE RESISTOR

The successful utilization of carbon nanotubes in nanoelectronics will require a reproducible way in which to make good electrical contacts. Paulson *et al.* (p. 1742) show that the contact resistance of the nanotube-graphite interface changes by more than one order of magnitude when the nanotube is rotated in the plane with an angular periodicity of 60°. The junction resistance is lowest when the orientation of the nanotube matches that of the underlying graphite substrate and highest when it is midway between these preferred directions.

GLACIAL ALTITUDES

One of the many indications that tropical sea surface temperatures (SSTs) were cooler during the last glacial maximum than today is that tropical glaciers extended to about 900 meters below their present positions. So large an "equilibrium line altitude" difference implies that glacial SSTs were colder than those determined by CLIMAP, the pioneering paleoclimate study of the early 1980s. Hostetler and Clark (p. 1747) apply a glacier mass balance model to the output of an atmospheric global climate model in order to calculate what temperature and precipitation fields are needed to account for observed glacier distributions. Their results indicate that tropical SSTs were 2° to 3.5°C cooler than those reconstructed by CLIMAP and highlight some of the potential subtleties about changes in the thermal structure of the troposphere that affect the elevations of glaciers.

COLLECTING ZINC

Zinc, arsenic, and selenium can be important groundwater contaminants; zinc in particular is also found in many major ore deposits, as the mineral sphalerite (ZnS). Labrenz et al. (p. 1744; see the cover and the Perspective by Vasconcelos and McKenzie) now provide evidence that bacteria may be responsible for the precipitation of much sphalerite and that this process may help clean natural waters of these elements. The authors studied a biofilm growing underwater in an abandoned mine and show through microscopic analyses, geochemical modeling, and fluorescent tagging that Desulfobacteriaceae bacteria concentrate zinc to levels 10⁶ above that in the water by producing biogenic sphalerite. Arsenic and selenium are also sequestered in the sphalerite.

FAST IN THE MIDINFRARED

Despite a host of possible applications in biology, chemistry, and environmental monitoring, a convenient source of ultrafast radiation in the midinfrared (wavelengths of 3 to 15 micrometers), or the so-called molecular-fingerprint

CUT, TAGGED, AND SENT OFF

Activation of a set of proteases known as caspases is an important part of the cellular signaling mechanisms that lead to cell death or apoptosis. One caspase target is the protein BID, which, after cleavage, translocates from the cytosol to the mitochondrial mem-

brane. There it interacts with other proteins to influence mitochondrial function and the release of cytochrome c. Zha *et al.* (p. 1761) now provide a surprising mechanism for how cleavage of BID results in mitochondrial targeting. Cleavage of BID exposes an NH_2 -terminal glycine residue, which then undergoes a lipid modification (myristoylation) that enhances its binding to mitochondrial membranes. Furthermore, a mutant that cannot be



myristoylated has reduced apoptotic activity. Previously, myristoylation of mammalian proteins has only been observed as a cotranslational modification. Myristoylation may be acutely regulated and serve as a switch that alters localization of signaling proteins.

THIS WEEK IN SCIENCE edited by PHIL SZUROMI

regime has been lacking. Paiella *et al.* (p. 1739; see the Perspective by Faist) now describe the fabrication and operation of a midinfrared solid-state laser capable of generating picosecond pulses. Their design, which is based on the fast intersubband transitions of a quantum cascade laser, takes advantage of the large photorefractive nonlinearity of the transitions to provide a self-mode-locked mechanism of operation.

TO FIGHT ANOTHER DAY

Natural enemy-victim relations abound in ecology and include predator-prey, hostparasite, and host-pathogen systems. Keeling et al. (p. 1758; see the Perspective by Hastings) propose the equivalence of three important elements of enemy-victim dynamics: Spatial heterogeneity, temporal delays (such as delayed density dependence), and behavioral responses. Behavior, in the sense of limited movement of individuals, is known to create spatial structure in ecological models, and the authors show that the effect of spatial structure on the dynamics of mean population numbers can be described with time delays in the form of delayed density dependence. By bridging the gap between three fundamental modeling approaches, a large area of theoretical ecology can now be viewed in a unified way.

CRUCIAL EDITING FOR RNA

Before translation into protein, certain RNA transcripts are edited by enzymes called ADAR (adenosine deaminase acting on RNA). By replacing adenosines with inosine at specific target sites, these editing enzymes create new stop codons and splice sites within the transcript and thus influence protein function. In an attempt to generate mice deficient in one of this family (ADAR1), Wang et al. (p. 1765; see the Perspective by Keegan et al.) revealed this enzyme to be critical in the early development of the hematopoietic system. Embryonic stem (ES) cells in which one of the alleles was disrupted (ADAR1^{+/-}) had severe defects in erythropoiesis that led to early embryonic death.

WHEN IN THE BRAIN, DO AS THE NEURONS DO

A further example of the remarkable plasticity of stem cells is the subject of two Reports (see the news story by Vogel). Brazelton *et al.* (p. 1775) and Mezey *et al.* (p. 1779), using different approaches, show that cells from the bone mar-CONTINUED ON PAGE 1651

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row, marked either by expression of green fluorescent protein or by genetic markers, can find their way into the brain after transplantation into mice lacking functional bone marrow cells. These displaced cells show certain aspects of phenotype and marker expression that suggest they may have taken on neuronal character.

A CALL TO ARMS

Information is parsed by the brain into different sensory modalities, and distinct attributes must then be recombined intelligibly and proportionately. Graziano et al. (p. 1782; see the news story by Helmuth) have studied how a simple task, accurately locating arm position, is carried out in the brain of the macaque. A visual signal (seeing the arm) and a somatosensory signal (feeling where the arm is) are combined in a 1:4 ratio in neurons in area 5 of the parietal lobe. Furthermore, these same neurons appear to integrate the location information with identity attributes, as revealed by the lack of response to an arm-dimensioned piece of paper but an authentic response to a fake arm prepared by a taxidermist.

THE ABCS OF CHOLESTEROL TRAFFICKING

Sitosterolemia is a rare inherited disorder characterized by excessive intestinal absorption of dietary sterols and impaired clearance of these sterols from the liver into the bile. Individuals with this disease have high plasma levels of cholesterol and develop coronary atherosclerosis at an early age. Berge *et al.* (p. 1771; see the Perspective by Allayee *et al.*) show that sitosterolemia is caused by mutations in two adjacent and oppositely oriented genes on chromosome 2p21, ABCG5 and ABCG8, which each encode proteins with homology to the ATP binding cassette (ABC) transporters. Other members of this family of membrane proteins have been implicated previously in cholesterol transport. These results identify potential targets for therapeutic intervention and raise the possibility that subtle sequence variations in these genes may contribute to interindividual variability in responsiveness to high cholesterol diets. Normally the concentration and distribution of cholesterol is carefully controlled within the cell. In a separate review, Simons and Ilkonen (p. 1721) discuss recent findings on the cell biology of cholesterol and how cholesterol affects the fundamental properties of distinct cellular membranes.

RUMINATING AND ANTICIPATING

The prefrontal cortex is thought to play a crucial role in the coherent, planned behavior across long periods of time exhibited by humans and other primates. However, nearly all of the neurophysiological experiments dealing with the prefrontal cortex analyze the activity of nerve cells at the very moment of the task under investigation. Hasegawa et al. (p. 1786) studied the relation between individual nerve cell activity in the prefrontal cortex and behavior over long periods of time. Neuronal activity in a subpopulation of cells could be related to the tracking of events that occurred up to half a minute ago either in the recent past or planned to happen in the near future.

TECHNICAL COMMENT SUMMARIES

Screening for Cervical Cancer

The full text of these comments can be **seen at** www.sciencemag.org/cgi/content/full/290/5497/1651a

Cain and Howett (Policy Forum, 9 June, p. 1753), assessing approaches to cervical cancer screening, noted that human papillomavirus (HPV) testing carries a higher average cost than traditional cytology (Pap smears)-and that, because it also yields more false positives, it may lead to needless anxiety and overtreatment. Wright and Goldie find a number of statements by Cain and Howett "potentially misleading." In several clinical studies, they point out, HPV testing showed a higher sensitivity, with only "somewhat lower" specificity, than cytology. Cost-effectiveness, they suggest, hinges not on the absolute price differential between the tests but on "the cost-effectiveness of the screening program" incorporating them. And "women who test positive for high-risk types of HPV are not 'false positives'; they are infected with a DNA tumor virus associated with more than 98% of cervical cancers." Cain and Howett respond by citing other studies suggesting that "HPV testing is more likely to be positive in the absence of histologic abnormality" that is Pap smearing. And, they note, many of the objections in the comment "stem from studying groups from among the U.S. population," whereas both disease demographics and issues of cost-effectiveness differ between developed and developing countries. "The best combination of screening options is not yet evident," they conclude, "and the proper role for HPV testing is clearly still in flux."

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Membrane (10 cm x 10 cm)	\$5.00	\$5.00	\$4.00	\$4.00	
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Primary Antibody (10 ml)	\$2.40	\$0.49	\$24.50	\$24.50	
Secondary Antibody (10 ml)	\$0.10	\$0.02	\$1.42	\$1.42	
Substrate (10 ml)	\$2.50	\$26.00	\$5.30	\$20.80	
Film (CL-XPosure [™] Film vs. Hyperfilm [™] Film)	\$0.60	\$0.60	\$1.88	\$1.88	
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Fig. <u>1</u>

The ALZET pump operates as interstitial fluid is attracted into the pump by the osmotic layer at a rate limited by the outer, semi-permeable membrane. As the osmotic layer hydrates, it compresses the flexible reservoir, which expels drug from the delivery portal of the pump.



Fig. 2

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