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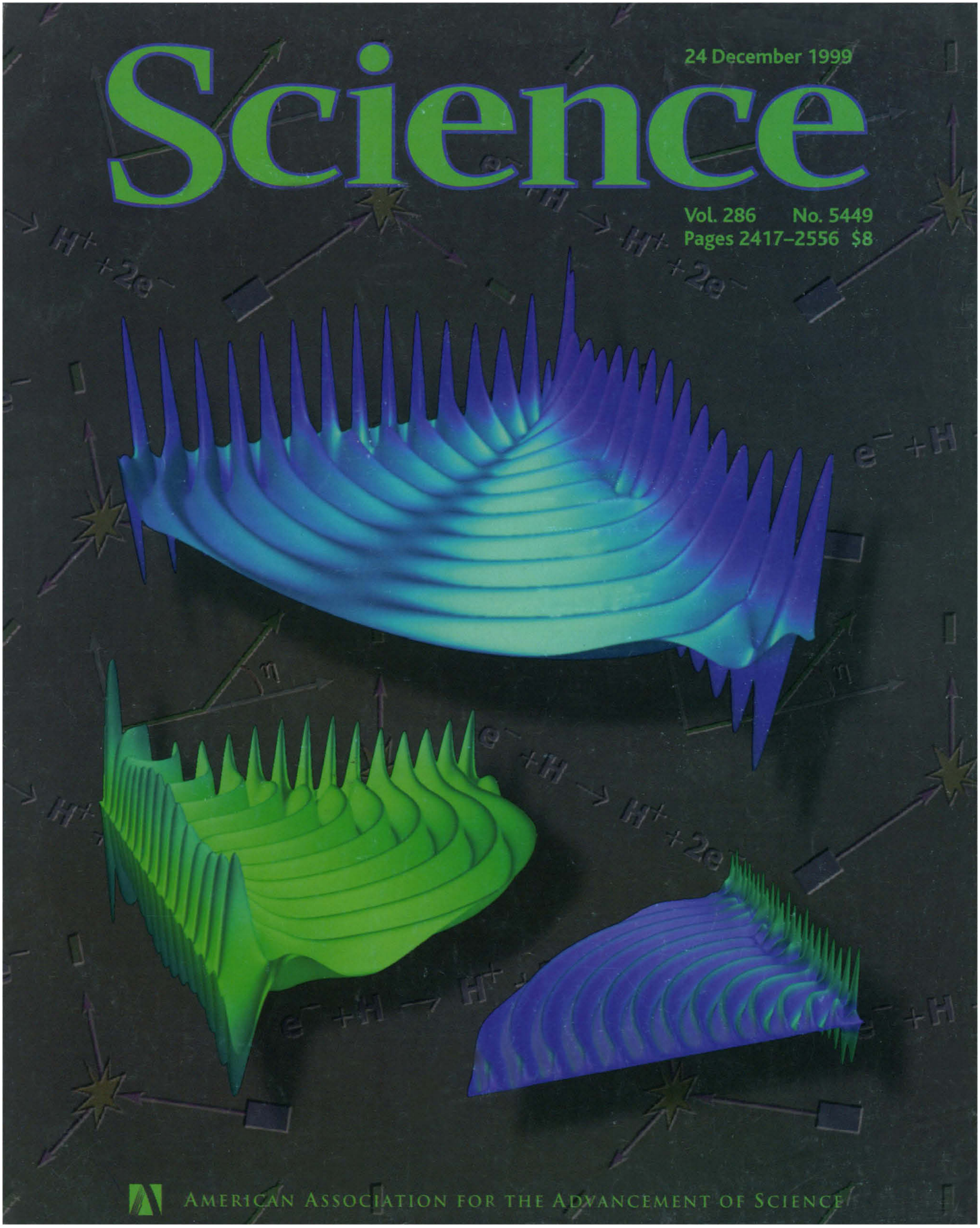

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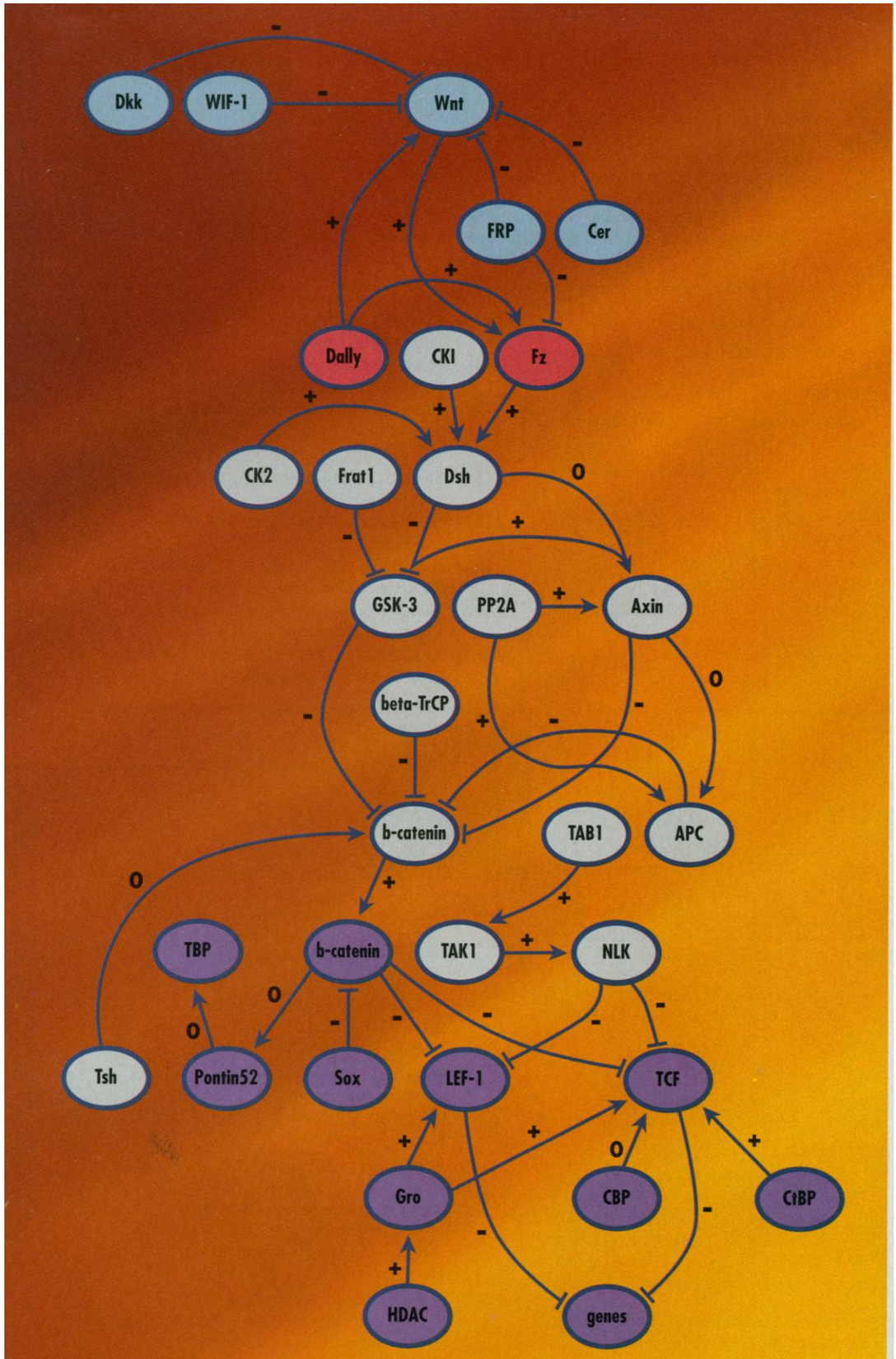

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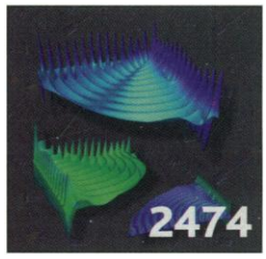

COVER An electron colliding with a hydrogen atom to yield two electrons and a proton is the simplest example of electron-impact ionization. Mathematically formulated in the 1950s, this three-body problem in quantum mechanics has required supercomputers for its solution. Shown are wave functions for the breakup of a system of three charged particles. Understanding collisional ionization is essential for problems such as low-temperature plasma formation. [Image: Mark Baertschy and Terry Ligocki]

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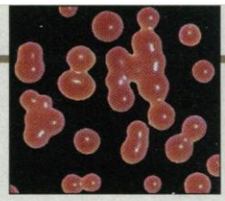

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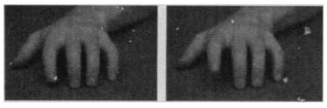

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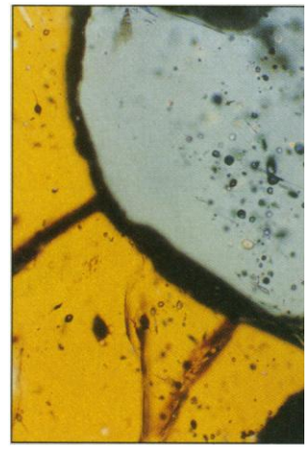

2488
A gassed mantle

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BREAKING UP IS EASIER TO DO

Low-energy electron impact can ionize atoms and molecules. However, even for the simplest case, the ionization of a hydrogen atom, a complete solution to the problem has been lacking, and actual solutions to date have relied on final states in which one electron and the proton are treated as highly excited hydrogen atoms. Rescigno *et al.* (p. 2474; see the cover and the Perspective by Whelan) have transformed the Schrödinger equation with a scaling function so that numerical solutions to high accuracy can be calculated for the breakup of the system into three charge particles. Such an approach could also be used in more complex electron-impact systems.

RICH MUD, POOR MUD

Layers of organic-rich sediments, called sapropels, have been formed in the Mediterranean Sea at irregular intervals seven times during the last 200,000 years. These layers must have formed under dramatically different conditions than those that occur in the well-ventilated, nutrient-depleted environment that exists there today. Sachs and Repeta (p. 2485) measured nitrogen isotopic ratios in molecules derived from chlorophyll in eastern Mediterranean sapropels in order to infer what these conditions were. Their findings also demonstrate that some fundamental assumptions typically made about the preservation of nitrogen isotopic ratios in sediments are likely incorrect.

MAGNIFIED GALAXY GAS

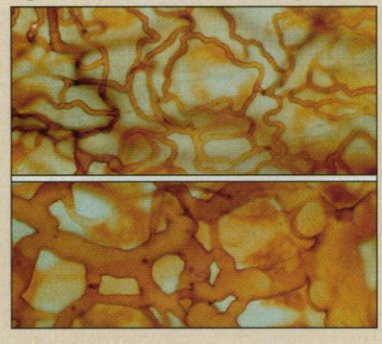
Quasars are quasistellar radio sources that are believed to be powered by supermassive black holes residing within extremely distant galaxies. Planesas *et al.* (p. 2493) used the additional magnification of the gas around a galaxy pair in the quasar 0957+561 created by a gravitational lens to determine the spatial distribution and kinematics of the molecular gas. The main galaxy has an extensive molecular gas cloud that actually limits their ability to see the companion galaxy. The determination of the gas distribution around distant galaxies is useful in refining the value of Hubble's constant.

MANTLE ORIGINS

Biogenic processing of nitrates enriches Earth's crust in the heavier nitrogen isotope, ^{15}N. Earth's upper mantle is enriched in lighter nitrogen, which is thought to be a signature of the planetesimals that accreted to form Earth. Dauphas and Marty (p. 2488) measured the nitrogen and argon isotopic composition of rocks from the Kola Peninsula, Russia, which are considered to be remnants of a 370-million-year old plume and representative of the lower mantle. The rocks had a nitrogen isotopic signature lighter than that of the crust but heavier than that of the upper mantle. These measurements, combined with noble gas isotopic data, suggest that nitrogen in the upper mantle is not primordial. Instead, Earth's early, more reduced atmosphere did not allow the formation of abundant nitrate, and this lighter nitrogen crust was subducted and mixed into the upper mantle and left a lower mantle enriched in heavy nitrogen.

MOLECULAR PLUMBERS' UNITS

Angiopoietin-1 (Ang1) and vascular endothelial growth factor (VEGF) each stimulate growth of blood vessels. Thurston *et al.* (p. 2511) compared the phenotypes of transgenic mice overexpressing one or both of these growth factors in the skin. The vessels induced by VEGF were leaky, whereas those induced by Ang1 were resistant to plasma leakage, even when the mice were exposed to an inflammatory agent. Mice overexpressing both factors had the greatest



number of blood vessels, and these were also resistant to leakage. These results suggest that Ang1 may be useful for reducing microvascular leakage in diseases such as diabetic retinopathy, and that a combination of Ang1 and VEGF may be the optimal therapy in other disease settings, such as limb ischemia, that would benefit from new blood vessel growth.

FEELING LESS PAIN

Morphine is widely used clinically for the treatment of severe pain. Bohn *et al.* (p. 2495) show that this analgesic effect of morphine is enhanced in mice that lack the protein β-arrestin 2. Morphine produces its effects by binding to the μ opioid receptor, a heterotrimeric guanine nucleotide binding protein (G protein)–coupled receptor. However, the receptor has a desensitization mechanism through which it becomes phosphorylated and then interacts with the signaling inhibitor β-arrestin 2. There are actually four related arrestins, but animals lacking just β-arrestin 2 showed increased and prolonged pain-relieving effects of morphine. Thus, β-arrestin 2 appears to show specificity for the μ opioid receptor and to be required for its normal physiological response.

CENTROMERE SURPRISES

Centromeres are the components of chromosomes responsible for their equal partitioning to daughter cells during mitosis and meiosis. Copenhaver *et al.* (p. 2468) exploited the advantages of a particular mutant in the plant *Arabidopsis* as well as complete sequence information for chromosomes II and IV to define DNA sequences responsible for centromere function. The centromeres consisted of a central, repetitive core, surrounded by moderately repetitive DNA that had a very low rate of recombination. Flanking the moderately repeated DNA were stretches of DNA with normal recombination rates and high proportions of mobile elements. Surprisingly, the centromere contained not only repetitive DNA but also sequences that expressed genes. Some of the repetitive elements previously thought to be "centromeric repeats" were more abundant in the DNA flanking the centromere than within the genetically defined centromere, suggesting that the repeats cannot be sufficient for function.

STABILIZING INFLUENCE

Many human tumors contain mutant forms of the tumor suppressor protein p53, and much research effort has been directed toward the development of compounds that restore p53 function. In a screen of a chemical library, Foster *et al.* (p. 2507; see the news story by Pennisi) identified small molecules that restore p53 activity by stabilizing the active conformation of its DNA binding domain. The compounds activated p53 target genes in cultured cells and inhibited tumor growth

in mice. These results establish the feasibility of rescuing p53 function with a pharmacological agent.

FAULTY CHECKPOINTS IN CANCER

The *hCHK2* gene encodes the human homolog of a yeast kinase required for activation of the G_2 checkpoint, a pathway that prevents cells containing damaged DNA from entering mitosis. Bell *et al.* (p. 2528; see the news story by Hagmann) identified germ line mutations in *hCHK2* in a rare subset of families with Li-Fraumeni syndrome, a cancer predisposition syndrome typically associated with germ line mutations in the gene encoding the tumor suppressor p53. This unanticipated link between p53 and the well-defined G_2 checkpoint in yeast highlights the importance of cell cycle checkpoints in tumorigenesis and may lead to the development of more selective anticancer drugs.

SEX, AGING, AND DEATH

Reproductive activity is known to decrease lifespan in animals and plants. In an experimental study with fruit flies, Sgrò and Partridge (p. 2521; see the Perspective by Reznick and Ghalambor) show that these "costs of reproduction" consist of a wave of mortality that is delayed until the onset of aging, and that these delays underlie the evolution of aging. The results support the idea that aging evolves through pleiotropic genes that have beneficial effects at young ages and detrimental effects later in life, rather than by an accumulation of deleterious mutations.

LIFE WITH FATHER

Solely maternal inheritance of mitochondrial DNA (mtDNA) is one of the major dogmas of human evolutionary genetics and has been a key element in the dating of certain events such as the spread of humans into Asia and Europe. Awadalla *et al.* (p. 2524; see the news story by Strauss) now provide convincing evidence that mtDNA is also inherited paternally. Results from their statistical analyses of mtDNA data from humans and chimpanzees are consistent with the occurrence of recombination. Inferences about the pattern and tempo of human evolution may now have to be reconsidered.

DRIVEN TO DISTRACTION

Does the brain process words when we are looking at them even if we are not paying attention? Rees *et al.* (p. 2504) resolve this age-old issue by functionally imaging brain activity while asking human subjects to focus on either words or pictures that had been superimposed. By ratcheting up the difficulty of the picture task, they find that words and non-words (consonant strings) produce exactly the same brain activations. Words were not recognized when all of the attentional resources were diverted to a different task.

HOLDING ONTO ZINC

Amyotrophic lateral sclerosis (ALS), also called Lou Gehrig disease, is an incurable neurodegenerative condition. Its cause in most cases is not known, but 2% of ALS patients carry mutations in Cu,Zn superoxide dismutase (SOD), an enzyme that scavenges the superoxide free radical. Estévez *et al.* (p. 2498) now report that mutant SOD, which is unable to bind zinc (but still binds copper), induces cultured motor neurons to undergo apoptosis. If the wild-type SOD was forced to give up its zinc, it also caused motor neurons to die. When both wild-type and mutant SOD were replete with zinc, then both SODs protected motor neurons from apoptosis upon removal of nurturing growth factors. The authors propose that loss of zinc from SOD induces motor neuron apoptosis through an oxidative mechanism that produces nitric oxide.

TECHNICAL COMMENT SUMMARIES

Population Cycles and Parasitism

The full text of this comment can be seen at www.sciencemag.org/cgi/content/full/286/5449/2425a

Hudson *et al.* (Reports, 18 Dec. 1998, p. 2256) presented experiments showing that interactions between red grouse and a parasite were responsible for periodic crashes in the grouse population and thus implicated wildlife diseases in explaining population fluctuations.

Lambin *et al.* question whether the control experiment used by Hudson *et al.* in which a population was treated to inhibit the parasite was sufficient and unbiased and argue that the inferred "change in fluctuation pattern is equivocal."

Hudson *et al.* respond that their approach does not confound the interpretation of the experiments and clarify that the "decrease in vicariance only occurred when grouse densities were relatively high...."

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Caribe Hilton Hotel and Convention Center, San Juan, Puerto Rico

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The Organizing Committee and the Armed Forces Institute of Pathology invite you to participate in the ***6th International Symposium on Metal Ions in Biology and Medicine***, to be held on May 7-10, 2000, in San Juan, Puerto Rico-USA. The objective of the 6th ISMIBM is to foster exchange of opinions between professionals and specialists working on analysis, research and applications of metal ions, trace elements and minerals in biological, biochemical, medical sciences, toxicology, nutrition, and environmental health. The scientific program, composed of plenary and concurrent sessions, and poster presentations is designed to promote intensive and productive dialogue among experts in these fields. A special program including short courses on toxicology, analytical methods, pathology, remediation strategies, and environmental medicine has also been organized and will take place on the day preceding the beginning of the plenary and concurrent sessions.

Original contributions (oral and/or poster presentations) are invited on the following themes:

Metals and Environmental Health	Metals and Homeostasis
Molecular Toxicology of Metals	Metals and Hormone Actions
Carcinogenicity of Metals	Metals and Enzyme Activity
Speciation of Metals and Other Elements	Metals and Chelation Therapy
Metals in Clinical Applications	Health Effects of Arsenic
Epidemiology and Occupational Health	Metals and Aging

Risk Assessment of Trace Element Status and Health
Metals and Disease: Environmental and Toxicologic Pathology
Effects of Low and High Nutritional Trace Element Status
Advanced Methods for the Analysis of Trace Elements and Metal Ions

The important deadlines for the 6th ISMIBM are:

- Submission of Full Manuscript: March 3, 2000
- Early Registration: January 14, 2000
- Hotel Reservations: April 10, 2000

The 6th ISMIBM will take place in San Juan, Puerto Rico, on the grounds of the Caribe Hilton Hotel and Convention Center. The language of the Symposium is English.

For additional information and to receive a complete copy of the Second Announcement and Final Call for Papers with Registration Form, please contact the Symposium Service Office at:

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Website (for On-line Registration to the 6th ISMIBM): http://www.afip.org/edu