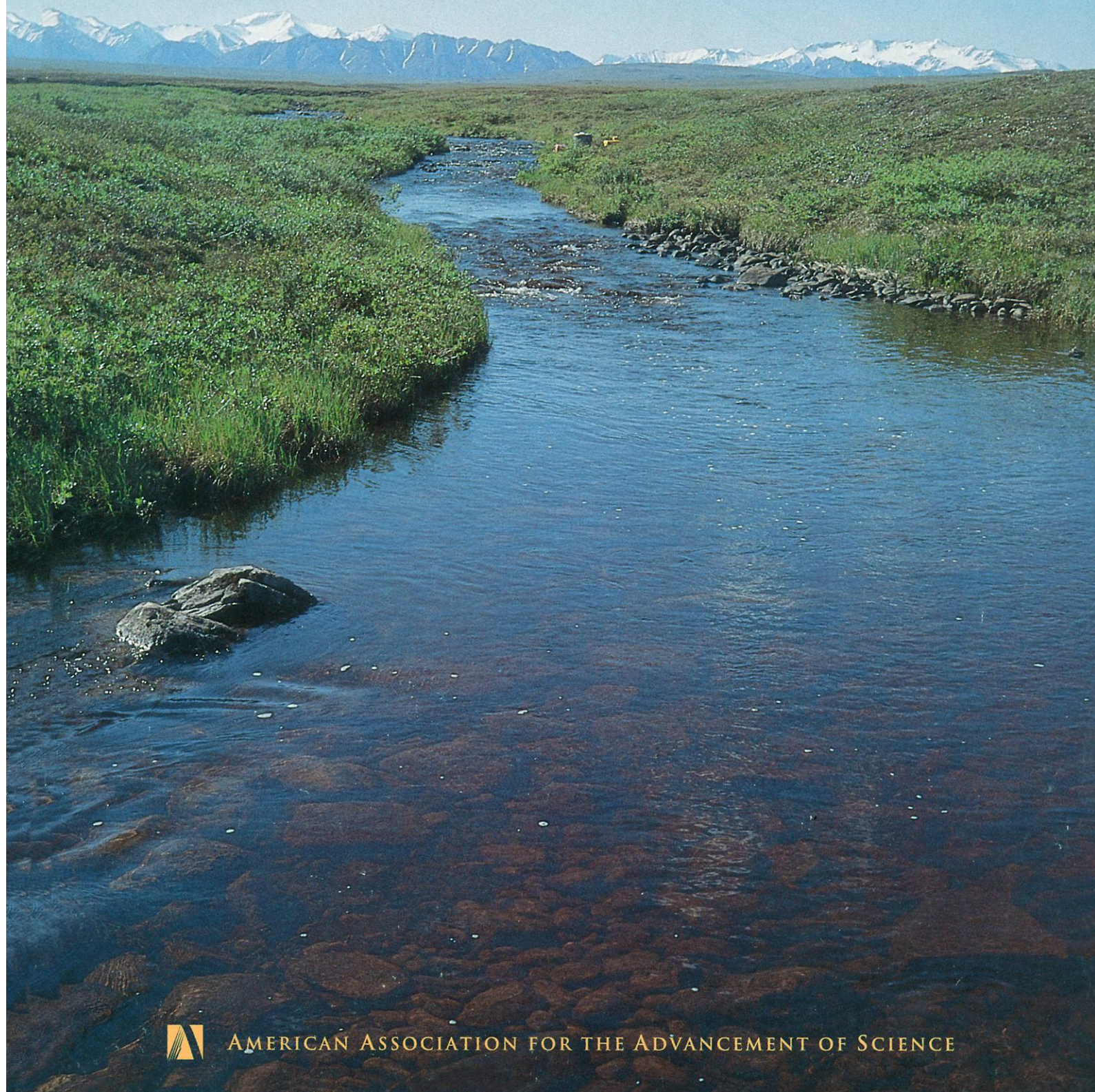


Science

6 April 2001

Vol. 292 No. 5514
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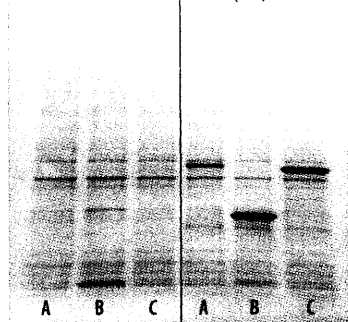
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Science

Volume 292 6 April 2001

Number 5514

7
9
13

SCIENCE ONLINE
THIS WEEK IN SCIENCE
EDITORIAL
David Paydarfar and
William J. Schwartz
An Algorithm for Discovery

15 EDITORS' CHOICE
19 NETWATCH
22 CONTACT SCIENCE
117 NEW PRODUCTS

NEWS

NEWS OF THE WEEK

- 24 AIDS RESEARCH: Merck Reemerges With a Bold AIDS Vaccine Effort
- 25 CLINICAL RESEARCH: Fred Hutchinson Center Under Fire
- 27 ASTROPHYSICS: Farthest Supernova Yet Bolsters Dark Energy
- 27 SCIENCESCOPE
- 28 VENICE PRESERVATION: Climate Change Data Prompt New Review
- 28 BUSH APPOINTMENT: Venture Capitalist to Lead Science Panel
- 29 GERMANY: A Big Boost for Postgenome Research
- 30 GERMANY: Old Guard Battles Academic Reforms
- 30 JAPAN: Court Backs Lab's Safety Practices
- 31 REPRODUCTIVE SCIENCE: Human Cloning Plans Spark Talk of U.S. Ban

31 STEM CELL POLICY: Canadian Panel Aims for Middle Ground

33 ASTRONOMY: Comet's Course Hints at Mystery Planet

NEWS FOCUS

34 ECOLOGY: Words (and Axes) Fly Over Transgenic Trees

▼36 GREENHOUSE EFFECTS: High CO₂ Levels May Give Fast-Growing Trees an Edge

37 SCIENCE IN BRITAIN: Science Centers Blossom, But How Many Will Survive?

39 LUNAR AND PLANETARY SCIENCE CONFERENCE: Rethinking Water on Mars and the Origin of Life

▼41 LONGEVITY: Growing Old Together

104, 107 44 COMPARATIVE GENOMICS: Gene Expression Differs in Human and Chimp Brains

45 SOLID-STATE PHYSICS: Nanotube 'Peapods' Show Electrifying Promise

47 RANDOM SAMPLES

SCIENCE'S COMPASS

51 LETTERS

Considerations in Creating Online Archives I. Mellman. For Free Access, Follow the Brick Red Buttons N. R. Cozzarelli. What's in a PhyloCode Name? W. J. Kress and P. DePriest. Searching for the Heart of Human Nature P. Vjecsner. *Response* A. Maunon. Corrections and Clarifications

ESSAY

55 James Watt and the Lunatics of Birmingham A. Hart-Davis

BOOKS ET AL.

57 PSYCHOLOGY: *The Work of the Imagination* P. L. Harris, reviewed by A. Gopnik

57 COMPUTING: *Quantum Computation and Quantum Information* M. A. Nielsen and I. L. Chuang, reviewed by G. Mahler

PERSPECTIVES

▼59 MICROBIOLOGY: Bacterial Population Genetics and Disease M. Lipsitch

▼60 OPTICAL MATERIALS: Bending Light the Wrong Way M. C. K. Wiltshire

61 ATMOSPHERIC SCIENCE: Solving the PSC Mystery M. A. Tolbert and O. B. Toon

▼63 ECOLOGY: Keystone Species—Hunting the Snark? W. Bond

▼64 MOLECULAR BIOLOGY: The Histone Modification Circus S. L. Berger

▼65 SUPERCONDUCTIVITY: How Could We Miss It? A. M. Campbell

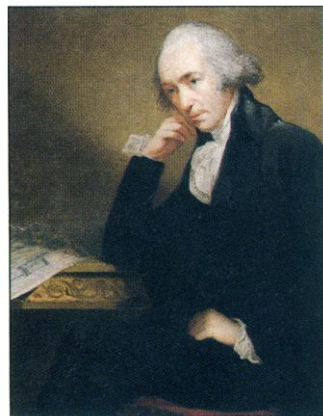
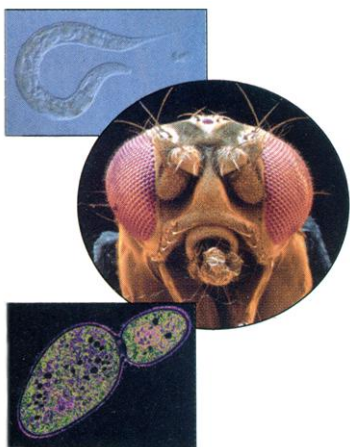


63

A rat and a mouse trade places

41

Similar routes to old age



55

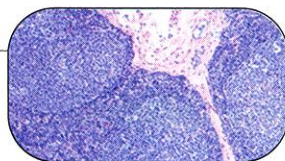
A science club, 18th-century style

RESEARCH ARTICLE

- 69 **Control of a Mucosal Challenge and Prevention of AIDS by a Multiprotein DNA/MVA Vaccine** R. R. Amara, F. Villinger, J. D. Altman, S. L. Lydy, S. P. O'Neil, S. I. Staprans, D. C. Montefiori, Y. Xu, J. G. Herndon, L. S. Wyatt, M. A. Candido, N. L. Kozyr, P. L. Earl, J. M. Smith, H.-L. Ma, B. D. Grimm, M. L. Hulsey, J. Miller, H. M. McClure, J. M. McNicholl, B. Moss, H. L. Robinson

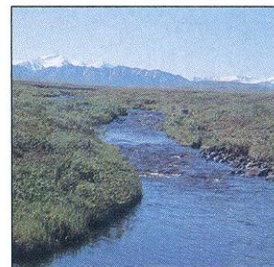
REPORTS

- ▼75
65 **Pressure Dependence of the Superconducting Transition Temperature of Magnesium Diboride** M. Monteverde, M. Núñez-Regueiro, N. Rogado, K. A. Regan, M. A. Hayward, T. He, S. M. Loureiro, R. J. Cava
- ▼77
60 **Experimental Verification of a Negative Index of Refraction** R. A. Shelby, D. R. Smith, S. Schultz
- 79 **Three-Dimensionally Ordered Array of Air Bubbles in a Polymer Film** M. Srinivasarao, D. Collings, A. Philips, S. Patel
- 83 **Carbon Dioxide Degassing by Advective Flow from Usu Volcano, Japan** P. A. Hernández, K. Notsu, J. M. Salazar, T. Mori, G. Natale, H. Okada, G. Virgili, Y. Shimoike, M. Sato, N. M. Pérez
- 86 **Control of Nitrogen Export from Watersheds by Headwater Streams** B. J. Peterson, W. M. Wollheim, P. J. Mulholland, J. R. Webster, J. L. Meyer, J. L. Tank, E. Martí, W. B. Bowden, H. M. Valett, A. E. Hershey, W. H. McDowell, W. K. Dodds, S. K. Hamilton, S. Gregory, D. D. Morral
- 90 **Tropical Origins for Recent North Atlantic Climate Change** M. P. Hoerling, J. W. Hurrell, T. Xu
- 93 **Amphibians as Indicators of Early Tertiary "Out-of-India" Dispersal of Vertebrates** F. Bossuyt and M. C. Milinkovitch
- ▼95
36 **Rising CO₂ Levels and the Fecundity of Forest Trees** S. L. LaDeau and J. S. Clark
- 98 **Ecological Degradation in Protected Areas: The Case of Wolong Nature Reserve for Giant Pandas** J. Liu, M. Linderman, Z. Ouyang, L. An, J. Yang, H. Zhang
- ▼101
63 **Delayed Compensation for Missing Keystone Species by Colonization** S. K. M. Ernest and J. H. Brown
- ▼104
41
107 **Extension of Life-Span by Loss of CHICO, a *Drosophila* Insulin Receptor Substrate Protein** D. J. Clancy, D. Gems, L. G. Harshman, S. Oldham, H. Stocker, E. Hafen, S. J. Leivers, L. Partridge
- ▼107
41
104 **A Mutant *Drosophila* Insulin Receptor Homolog That Extends Life-Span and Impairs Neuroendocrine Function** M. Tatar, A. Kopelman, D. Epstein, M.-P. Tu, C.-M. Yin, R. S. Garofalo
- ▼110
64 **Role of Histone H3 Lysine 9 Methylation in Epigenetic Control of Heterochromatin Assembly** J. Nakayama, J. C. Rice, B. D. Strahl, C. D. Allis, S. I. S. Grewal
- ▼114
59 **A Link Between Virulence and Ecological Abundance in Natural Populations of *Staphylococcus aureus*** N. P. J. Day, C. E. Moore, M. C. Enright, A. R. Berendt, J. M. Smith, M. F. Murphy, S. J. Peacock, B. G. Spratt, E. J. Feil



69

A two-hit vaccine against HIV



COVER 86

A small tundra stream (~5 meters wide) flows between the Brooks Range and Toolik Lake at the Arctic Long-Term Ecological Research site in northern Alaska. Throughout North America, headwater streams such as this actively retain inorganic nitrogen from their watersheds. This retention limits the downstream transport of nitrogen and thereby helps control the eutrophication of downstream lakes and estuaries. [Photo: B. J. Peterson]



98

Panda habitat in decline?

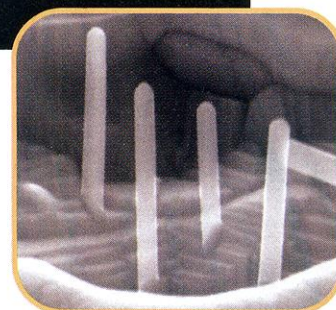
77

Assembled left-handed array giving a negative refractive index



Single-walled carbon nanotubes 7

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SCIENCE EXPRESS www.scienceexpress.org

Single Crystals of Single-Walled Carbon Nanotubes Formed by Self-Assembly R. R. Schlittler *et al.*

Micrometer-scale crystals of single-walled carbon nanotubes are synthesized through thermolysis of nano-patterned precursors.

Regulation of Longevity and Stress Resistance by Sch9 in Yeast P. Fabrizio, F. Pozza,

▼ S. D. Pletcher, C. M. Gendron, V. D. Longo

41 As with other organisms, the life-span of nonreplicating yeast is controlled by homologs of
104 the insulin signaling pathway.
107

HIF α Targeted for VHL-Mediated Destruction by Proline Hydroxylation: Implications for O₂ Sensing M. Ivan *et al.*

Targeting of HIF- α to the von Hippel-Lindau Ubiquitylation Complex by O₂-Regulated Prolyl Hydroxylation P. Jaakkola *et al.*

PERSPECTIVE: **How Do Cells Sense Oxygen?** H. Zhu and H. F. Bunn

Hypoxia-inducible factor is a substrate for proline hydroxylation, and this protein modification appears to play a key role in cellular oxygen sensing.

TECHNICAL COMMENTS

HIV-1 RNA Editing, Hypermethylation, and Error-Prone Reverse Transcription

Examining human immunodeficiency virus-type 1 (HIV-1) transcripts in virus-producing cells, Bourara *et al.* (Reports, 1 Sept. 2000, p. 1564) observed cytosine-to-uracil (C-to-U) and guanine-to-adenine (G-to-A) changes that they attributed to post-transcriptional RNA editing. In a comment, Berkhout *et al.*, focusing in particular on the G-to-A event observed by Bourara *et al.* at site 181, argue that "known editing mechanisms ... cannot easily explain" some of the observed changes and propose "an alternative mechanistic model" based on error-prone HIV-1 reverse transcription to account for those changes. Araya and Litvak, in their response, suggest that the Berkhout *et al.* model is implausible because it requires multiple events with a low cumulative probability. They further argue that the fact that changes were observed only in "transcripts generated by transcription-competent provirus," and not in the proviral sequence itself, strongly favors post-transcriptional RNA editing as the cause.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/292/5514/7a

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Protocol: Terminal Transferase-Dependent PCR (TDP-PCR) for in Vivo UV

Photofootprinting of Vertebrate Cells H.-H. Chen, J. Kontaraki, C. Bonifer, A. D. Riggs

Methods for detecting changes in chromatin structure.

science's next wave

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Global: Careers in Marine Science

Neutraceuticals, personal essays, and a synopsis of the research funding picture populate our April special feature issue on the interdisciplinary world of marine science.

US: Solutions for Pregnant Postdocs E. Klotz

Issues such as lack of maternity leave and an ill-defined professional status can make balancing career and family a particular struggle for postdocs. Here's how some institutions and individuals have responded.

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AD SUPPLEMENT / 20 APRIL ISSUE

UPCOMING FEATURE

Careers & Events in Drug Discovery:

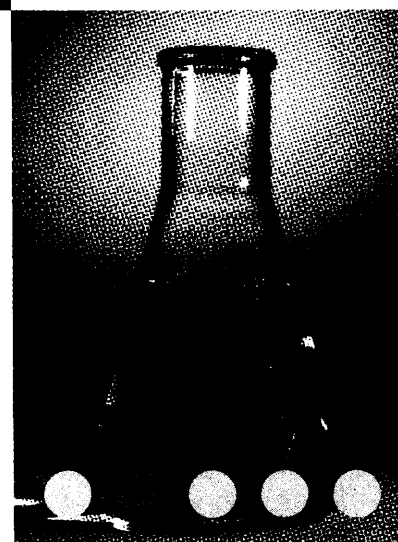
This ad supplement will examine the types of career opportunities in drug discovery and will outline the skills needed for these jobs. Look for it in the 20 April issue.

AD SUPPLEMENT / 13 APRIL ISSUE

LAB TECHNOLOGY TRENDS

Technologies in Proteomics:

This ad supplement will review advances in the technologies used in proteomics, with a special focus on their use in drug discovery. Look for it in the 13 April issue.



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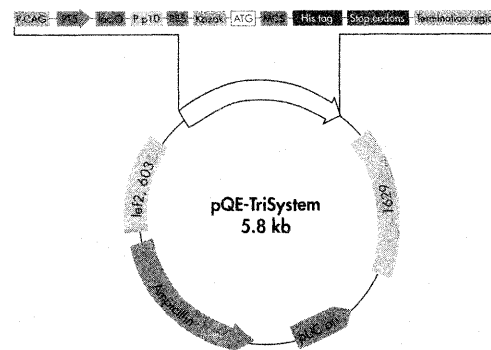
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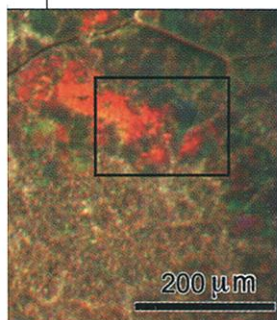
edited by Phil Szuromi

Superconductors Under Pressure

Magnesium diboride (MgB_2) exhibits superconductivity at 40 K, a temperature higher than that thought possible for metals to remain in the superconducting state. This finding has sparked efforts aimed at unraveling the mechanism for this unexpectedly high transition temperature T_c . Monteverde *et al.* (p. 75; see the Perspective by Campbell) report on the pressure and temperature dependence of the electrical resistance of MgB_2 . They see a parabolic decrease in T_c with pressure and thermally activated behavior at low temperatures that suggest similarities to the high- T_c cuprates. ✕

Breath Figures Caught in Polymers

Nanoporous polymers can be made from diblock copolymers, which can join chains of otherwise immiscible polymers that are then forced to phase-separate at the nanoscale. They can also be physically templated with hard colloidal particles. Srinivasarao *et al.* (p. 79) show that an even simpler process can be used. They passed moist air across a thin film of polystyrene dissolved in a volatile solvent. The condensed water formed arrays, or "breath figures," that evaporated to create opalescent films containing three-dimensional ordered arrays of holes. The hole size could be tuned by changing the airflow over the surface. This effect may also contribute to nanoporosity in more complex patterning schemes that also rely on evaporative drying in air.



Monitoring Magma Under a Volcano

The gas emissions from Usu volcano, an active strata cone in southwestern Hokkaido, Japan, have been monitored for several years to look for clues into the flow of magma beneath the surface. Hernández *et al.* (p. 83) measured a large increase in CO_2 flux about 6 months before the March 2000 eruption of Usu and then a decrease in flux about 3 months after the eruption. By combining these data with isotopic measurements and seismic observations, the authors conclude that the gas migration through the magmatic system was controlled by advective processes rather than by slower diffusive processes.

Bending Light the "Wrong" Way

The "bending" of a pencil in a water glass reflects the different speeds of light in air and water, and this difference can be expressed in terms of refractive indices. For most materials, the components of the refractive index affecting the electrical permittivity and mag-

Tropical Connection

90

The extratropical North Atlantic Ocean is a region in which sea surface temperature (SST) and atmospheric pressure patterns are clearly different before and after 1950. These differences have been reflected in trends in Northern Hemisphere land-surface temperatures, weather patterns in Europe and the Middle East, and the corresponding marine and terrestrial ecosystems. Hoerling *et al.* (p. 90) present evidence that North Atlantic climate change since 1950 and the precipitation and heating changes that have accompanied it are linked to increases in SST in the Pacific and Indian Oceans.

netic permeability of the light are both positive. Recent work has suggested that materials can be prepared in which both components are negative. Working in the microwave regime, Shelby *et al.* (p. 77; see the Perspective by Wiltshire) present scattering data as direct experimental verification of such "left-handed" materials.

Progress Toward an AIDS Vaccine

Many AIDS vaccines that have attempted to neutralize the virus with antibodies have been unsuccessful. An alternative approach is to try to produce a vaccine that confers broad cellular immunity instead. Amara *et al.* (p. 69) show that vaccination of rhesus macaques with a DNA vaccine based on multiple HIV proteins, followed by a boost with a recombinant, attenuated vaccinia virus, protected the animals from a pathogenic immunodeficiency virus. The viral challenge was done 7 months after the boost, when the immune response had declined to baseline memory levels and was mucosal in nature, thus mimicking the predominant mode of natural infection. The vaccine did not protect animals from infection but from development of AIDS: Viral RNA was reduced to 1000 copies or less per milliliter of plasma, there was no loss of CD4 cells, and the lymph node architecture was preserved. ✕

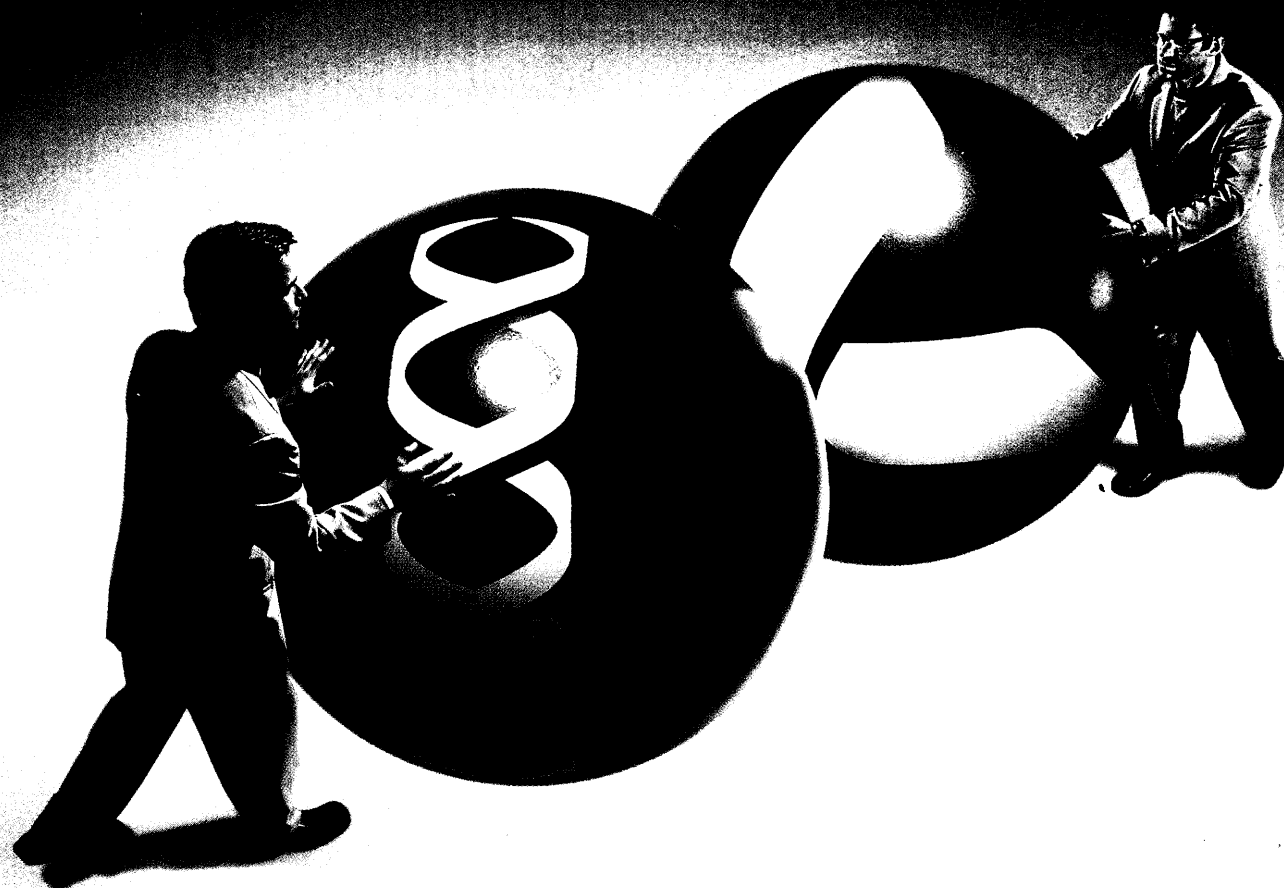
Out of India

After its separation from Madagascar during the Cretaceous, the Indian landmass was an island drifting northeastward across the Indian Ocean until its impact with Asia during the early Tertiary. Zoogeographic evidence has suggested that modern land vertebrates might be derived from ancestral isolated Indian groups that dispersed from India after its merger with Asia. Bossuyt and Milinkovitch (p. 93) performed a molecular analysis of ranid frog phylogeny that supports this hypothesis. Several frog lineages currently endemic to southern India diverged before the collision event, and at least three other lineages, including those in Africa, Europe, and the Americas, dispersed out of India.

Panda Park Perils

The Wolong Nature Reserve in southwestern China was set aside for the protection of the giant panda a quarter of a century ago, and its 200,000 hectares host up to one-tenth of surviving wild pandas. Liu *et al.* (p. 98) used satellite imagery to document the changes in vegetation cover before and after establishment and compared the resulting patterns with those in the surrounded unprotected areas. They see a disturbing trend of increased human activity that has degraded and fragmented the pandas' habitat in the reserve since protected status was given.

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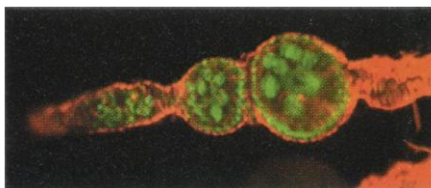
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Seeds of Change

Much can be learned about environmental impacts by looking at changes in plant seedlings. A small number of "keystone" species can be critical to the functioning of their native ecosystems. The kangaroo rat of the Chihuahuan desert in the United States is a case in point. Ernest and Brown (p. 101; see the Perspective by Bond) used a 20-year data set recording the response of granivorous desert rodents to the experimental removal of kangaroo rats. They document a major and persistent decrease of energy flowing through the rodent community. Smaller rodents could not take up the slack, and previously rare large-seeded plants began to replace smaller seeded plants. Only when a new rodent species colonized the plots, after 18 years, did energy use approach that on control plots. Changes in plant growth parameters in response to atmospheric CO₂ concentration have been intensely studied in recent years to look for the potential effects of anthropogenic global change. In a 3-year experiment in a loblolly pine forest, LaDeau and Clark (p. 95; see the news story by Tangle) found a large, rapid, and sustained increase in seed production in response to increased CO₂, as well as early onset of reproductive maturity. The composition of forests could undergo large changes as a result of differential responses of species to rising CO₂.

Fruit Flies at a Ripe Old Age

Life-span is partly controlled by the genetic makeup of an organism. In the nematode *Caenorhabditis elegans*, mutations in the *daf* pathway, which normally regulates an inactive hibernation-like life phase, can prolong life-span dramatically. The *daf* pathway is homologous to the insulin pathway of higher organisms, a tantalizing link to the ability of



caloric restriction to increase rodent life-span. By mutating the genes in the insulin-like pathway of fruit flies, Tatar *et al.* (p. 107) and Clancy *et al.* (p. 104) generalize the participation of this pathway in life-span control. Mutation of the *InR* gene (homologous to the mammalian insulin receptor and the *daf-2* gene) increased by 85%, and mutation of *chico*, an insulin receptor substrate, prolonged fly life-span by 52%. The insulin-like signaling pathway and its control of organismal metabolic activity is thus likely to be a general regulator of the rate of aging in a broad range of species (see the news story by Strauss and Fabrizio *et al.* in the 5 April *Science Express*).

Cracking the Chromatin Code

Covalent modifications on the amino-terminal tails of the histone proteins are thought to be involved in the specification of higher order chromatin structures that are intimately involved in processes such as gene transcription, DNA replication, and repair. For example, heterochromatin plays an important role in silencing gene expression. The protein Ctr4 has been suggested to be involved in heterochromatin formation and can methylate the lysine-9 residue of the histone H3 tail. Nakayama *et al.* (p. 110; see the Perspective by Berger) now show that Ctr4-directed methylation of histone H3 corresponds with heterochromatin assembly in vivo, which is consistent with the role of Ctr4 in epigenetic silencing. H3 methylation results in localization of Swi6, a homolog of the *Drosophila* heterochromatin protein 1. Furthermore, Ctr3, a histone H3-specific deacetylase, is also required for H3 methylation, Swi6 localization, and heterochromatin formation, supporting the hypothesis that a histone modification "code" exists for the establishment of chromatin structures. ✕

Clones in the Community

Staphylococcus aureus is a common pathogen of humans and a major public health concern, yet most of the people who carry this bacterium display no disease symptoms. Day *et al.* (p. 114; see the Perspective by Lipsitch) have discovered that specific ancestral genotypes of *S. aureus* that circulate among humans within a defined geographical area are disproportionately common causes of severe disease. Even when there is no disease outbreak, the abundance of hypervirulent clones suggests that factors that promote the spread of a clone of *S. aureus* also promote its virulence. The loss of virulence in less abundant isolates appears to be the outcome of recombination sometime in their ancestry.

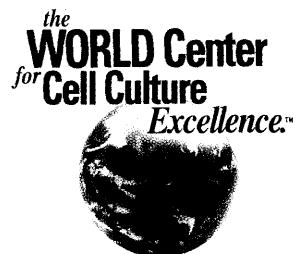
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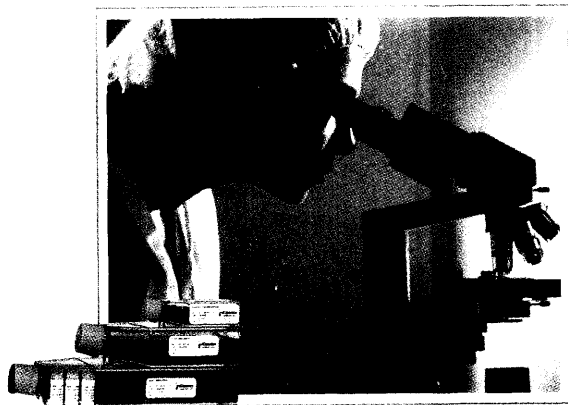
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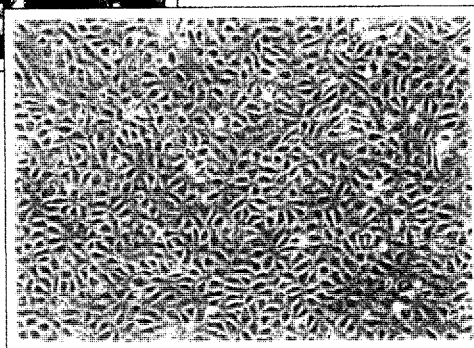
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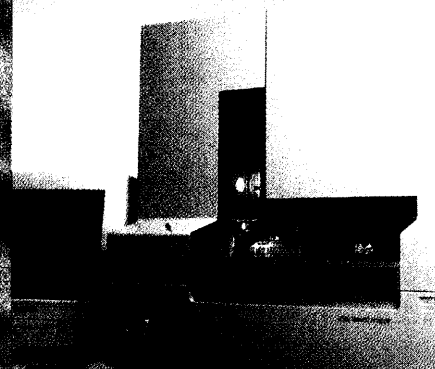
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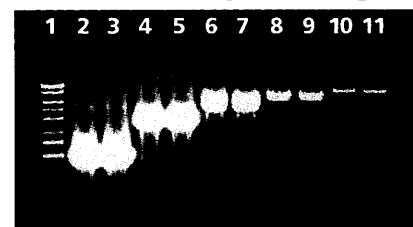
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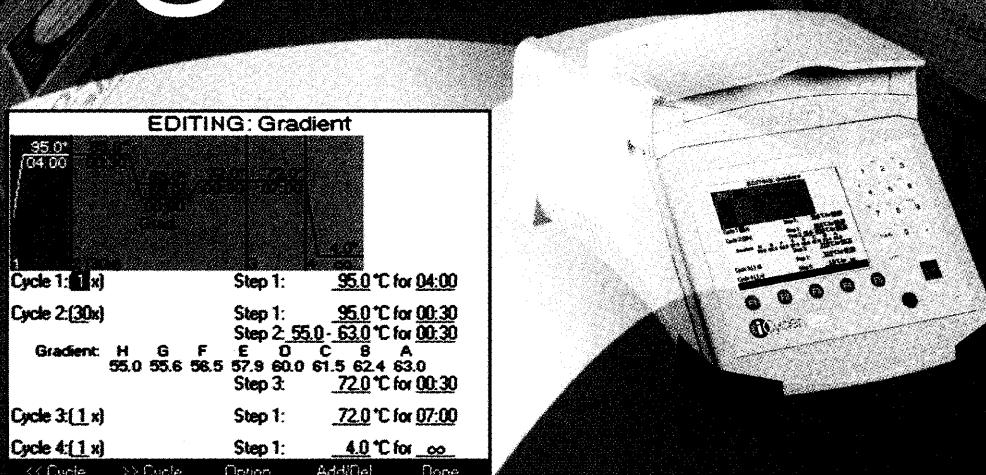
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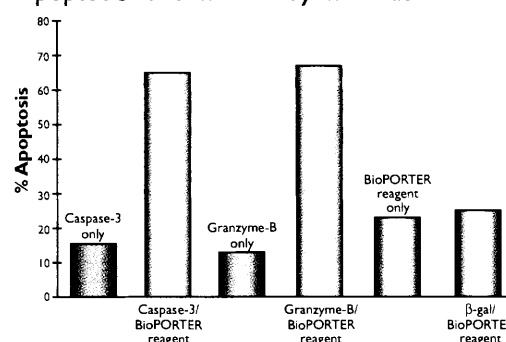
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Apoptotic Protein Delivery in Ki-ras 267B1 Cells



Granzyme B (450 ng), Caspase-3 (3.3 ng) or β-galactosidase (2 μg) were added to Ki-Ras 267 cells (prostate cancer) with or without BioPORTER reagent. 24 hours after protein delivery, cells were directly analyzed for apoptosis by flow cytometry using an Annexin V-FITC assay kit.

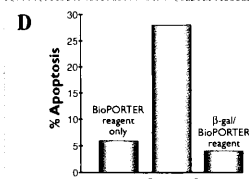
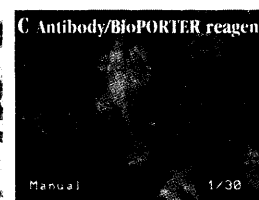


Fig. B/C FITC-Antibody or β-gal Delivery Into Mouse Fibroblasts
FITC-labeled antibody (2 μg) or β-gal (0.5 μg) were delivered with 2.5 μl of BioPORTER reagent into NIH/3T3 cells grown on coverslips in serum free conditions. Cells were examined 4 hours after protein delivery.

Fig. D Functional Granzyme-B Delivery Into Jurkat Cells
Granzyme-B (450 ng) or β-gal (1 μg) were delivered into cells growing in serum-free medium. 24 hours after protein delivery, cells were directly analyzed for apoptosis by flow cytometry using Annexin V-FITC.

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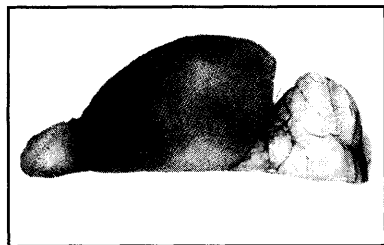
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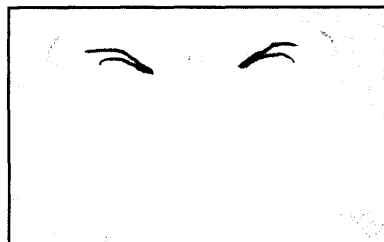
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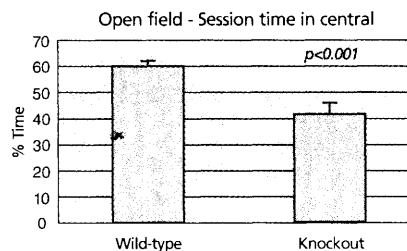
Gene: Orphan G protein-coupled receptor



The lacZ reporter gene present in the knockout construct allows for the analysis of gene expression. In mutant mice, lacZ expression is detectable in the cortex region of the brain, as shown in this whole-mount image.



Within the brain, lacZ is highly expressed throughout the cortex, hippocampus and amygdala. In normal animals, the hippocampus is essential for spatial processing and some types of exploratory behavior, while the amygdala is important for fear and anxiety behaviors.



The homozygous mutants spent less time in the central region in the open field test, indicating a higher level of anxiety compared to their wild-type siblings.

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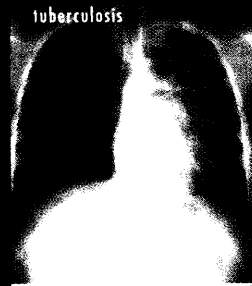
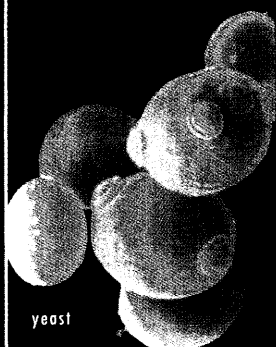
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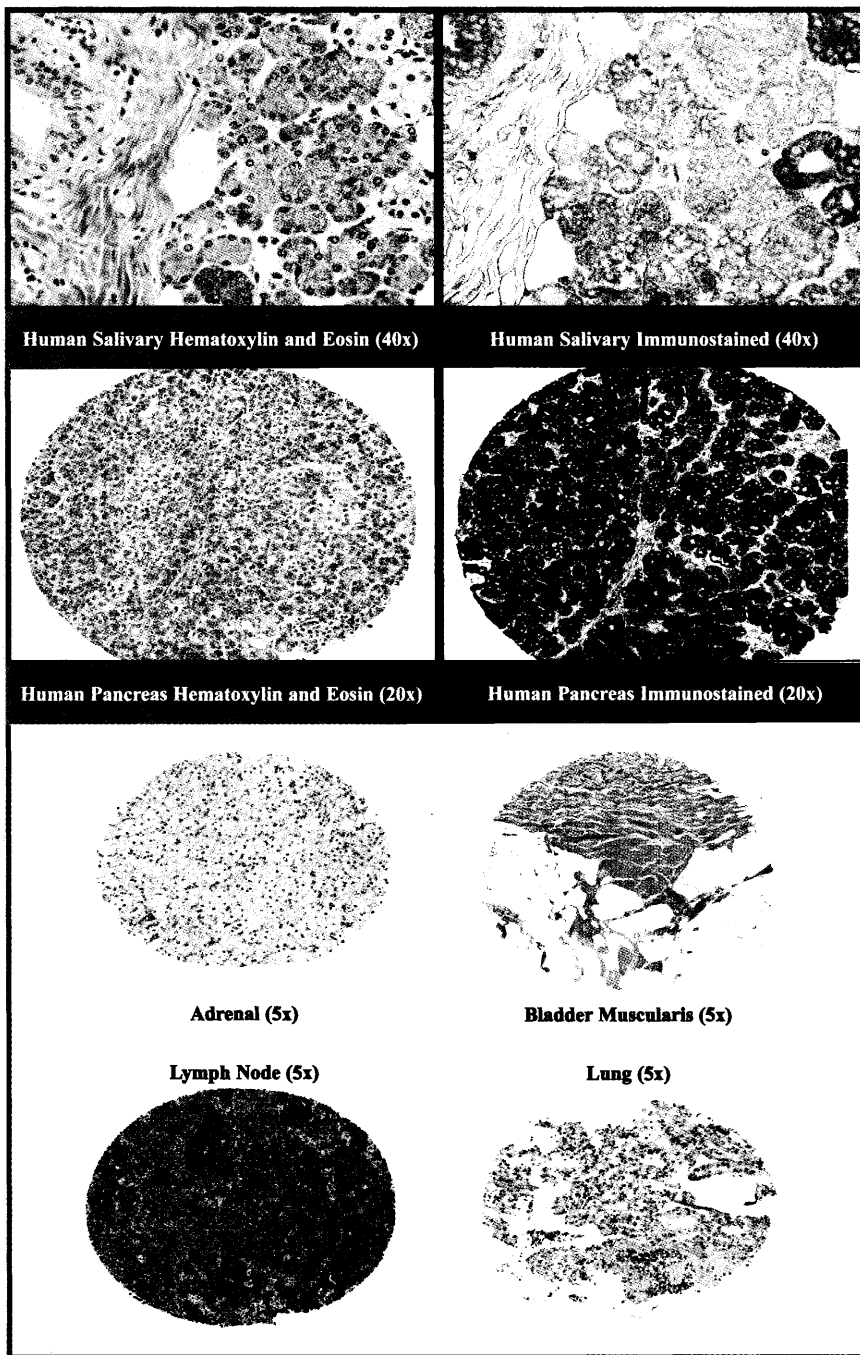
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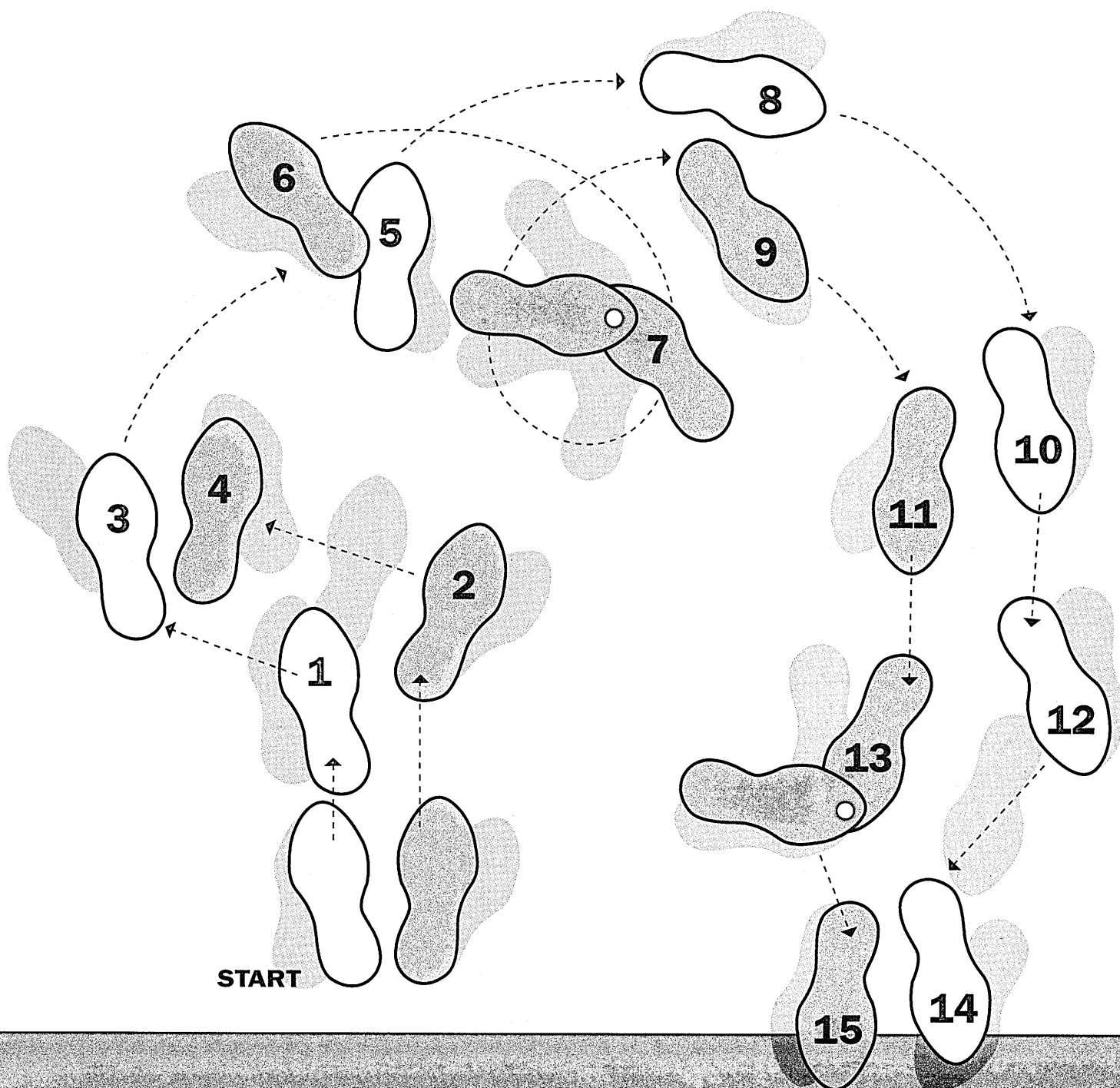
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