10 July 1998

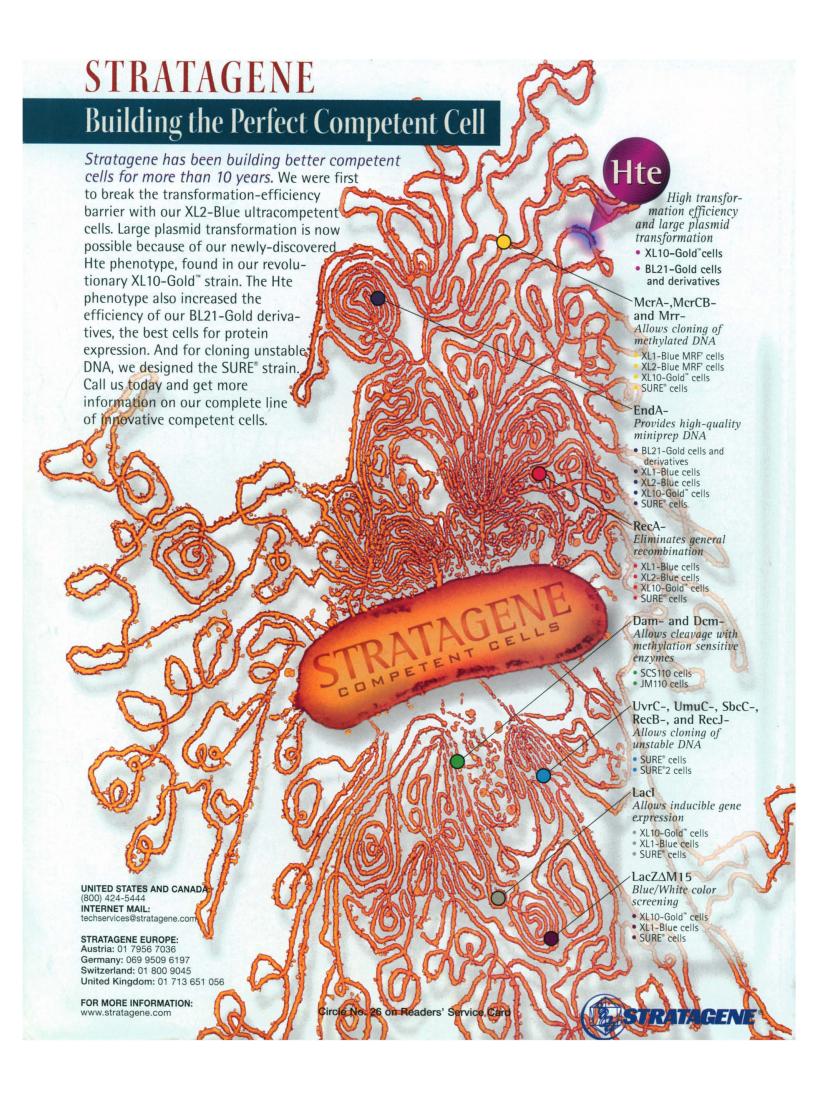
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COVER Photomosaic of a 6-meter-tall submarine hydrothermal deposit. Composed mostly of sulfide minerals, many thousands like it form along the mid-ocean ridge system. Hot, nutrient-rich fluids blend with cold seawater, supporting symbiotic fauna on the surface of the edifice and diverse microbial activity within and beneath it. See Delaney et al. and the special section beginning on p. 189. [Mosaic: D. Yoergerk, M. Elend]





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Building small proteins with B sheets

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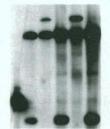
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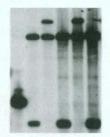
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Southern blot: Cosmid DNA digested with Not I and EcoR I, probed with a I.1 kb probe labelled with AlkPhos Direct (left) and digoxigenin (right).

(Courtesy of Janet Bartels-Carr, Yale University, USA.)

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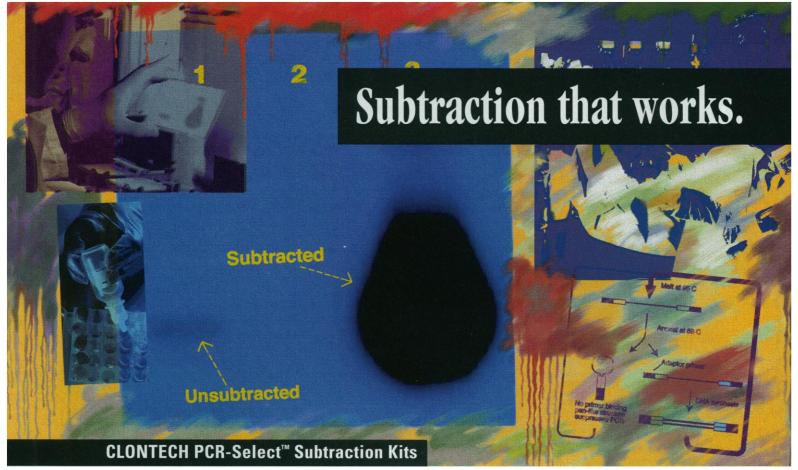
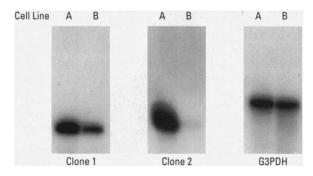


Illustration inspired by the art of Robert Rauschenberg (1925).



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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

OCEANIC NITROGEN

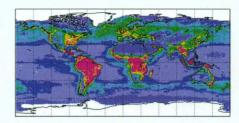
Most reduced nitrogen in the oceans is in the form of dissolved organic nitrogen (DON), a mixture of compounds that has been difficult to characterize. Contamination with living organisms, caused by limitations in filtration methods, has complicated analyses, and thus the sources and cycling mechanisms of this important component of seawater have remained largely unknown. McCarthy et al. (p. 231) present data from a range of locations comprising deep water, as well as surface waters, in different oceanic basins and show that the enantiomeric ratios of certain amino acids show similar, distinctive patterns in all of these locations. The observations point toward peptidoglycans, a component of bacterial cell walls, as one of the major sources of DON.

PACIFIC CLIMATE

The climate of the Pacific Ocean appeared to change in the mid-1970s and to have increased the frequency and intensity of El Niño events, which impacted many marine communities in the North Pacific. Guilderson and Schrag (p. 240) examined some of the possible causes and effects of this change using a coral carbon-14 record of upwelling from the Galápagos Islands and suggest that the change coincided with a deepening of the thermocline in the eastern Pacific (less upwelling). In an article, McGowan et al. (p. 210) consider the effects of this climate shift on marine ecosystems throughout the North Pacific.

ASSESSING OCEAN PRODUCTIVITY

One way of assessing our understanding of the processes that affect ocean productivity is to evaluate whether sources and sinks of key components are in balance (see the article by Falkowski et al., p. 200). Overall, ocean ecosystems are thought to act as a sink for CO2, that is, gross production and consumption of CO2 exceed respiration rates. One concern is that large parts of the ocean are "unproductive," and CO2 should be released from these ecosystems. Duarte and Agustí (p. 234) compared community respiration and production rates for these unproductive ecosystems. They quantified the carbon budget by using oxygen evolution as a proxy for carbon fluxes. They conclude that most of the ocean ecosystems do release CO2 but that one-fifth of the ocean is highly productive, which leads to an overall near balance for CO2 exchange. The net primary productivity of the biosphere as a whole (both oceanic and terrestrial components) affects the fluxes of carbon through the biosphere (see the Perspective by Tans, p.183). Similarities and differences exist between oceans and land, such as for the time scales of turnover and the relative importance of the primary limitations (light, water, and nutrients).



Existing models tend to stress the differences, and few attempts have been made to integrate the two components. Field *et al.* (p. 237) used parallel satellite data sets to devise models that can describe both components and then estimated primary production for both oceanic and terrestrial ecosystems. Such whole-biosphere models are essential for understanding the global carbon cycle and its dynamics.

PUTTING OUT EARLY FIRES

The reported presence of charred bones, ash, charcoal, and colored soil at Zhoukoudian, China, dated to as old as 500,000 years ago, has been widely assumed to be the first solid evidence for the controlled use of fire by early hominids. Weiner et al. (p. 251; see the news story by Wuethrich, p. 165, and a related book review by Goubsblom, p. 180) have now reanalyzed the soils and bones. They could not detect ash, charcoal, or fire-related alteration in the soils. Although the bones were indeed burned, they were not burned at the site. Thus, the site does not provide conclusive evidence for the controlled use of fire.

SOLUTION ROUTE TO DIAMONDS

Diamonds are usually synthesized through high-pressure or chemical vapor deposition routes. Li et al. (p. 246) report a chemical route that modifies the Wurtz synthesis for coupling alkyl halides by sodium reduction to form alkanes and salts. They instead used carbon tetrachloride as the reactant with the expectation that a similar process would couple the

carbon atoms into a tetrahedral network. The reaction proceeds at 700°C and is catalyzed by a nickel-cobalt catalyst. Although the yield of diamond is low (2 percent), the catalytic nature of the reaction suggests that further improvements may be possible.

ALL-β-SHEET PROTEIN DESIGN

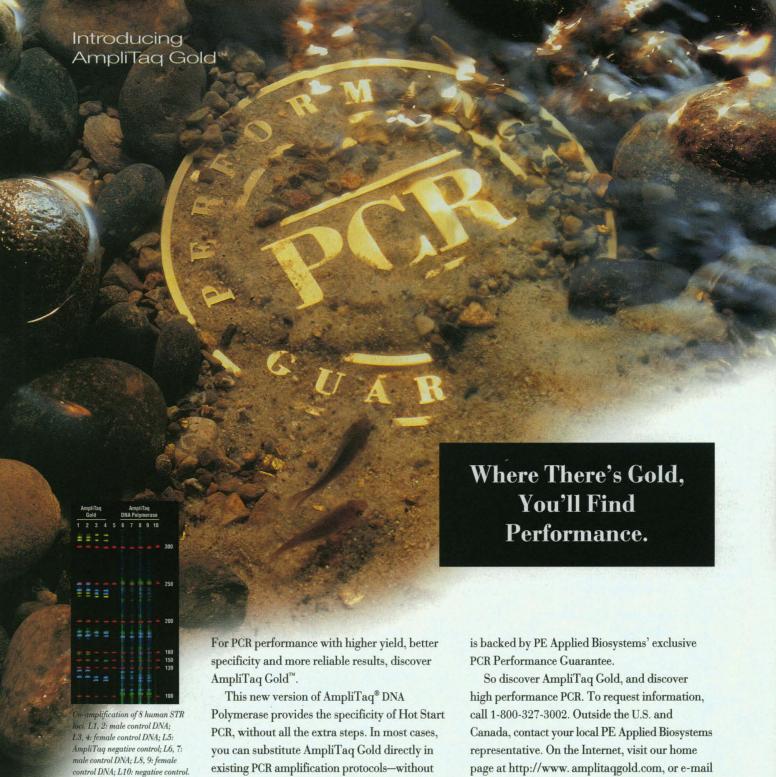
Of the two key secondary structure elements of proteins, β sheets and α helices, the former are much less tractable in terms of the rules that govern their formation and stabilization. Studies of small peptides and proteins have provided much insight into α helices, but small β sheets tend not to be stable in aqueous solution without aggregation unless they are stabilized, for example, by disulfide bridges. Kortemme et al. (p. 253) used a hierarchical design approach combining modeling and experiment to design a 20 residue protein in which the central 16 residues form a threestrand antiparallel β sheet; the small protein shows a cooperative two-state folding-unfolding transition, a property which is central to natural proteins.

SMALL G-CSF MIMIC

Transmembrane receptors are potential targets for therapeutic drugs, but realization of this potential would require the development of small nonpeptide compounds that mimic activation of such receptors that are normally bound by relatively large protein ligands. Tian et al. (p. 257) provide evidence that such molecules can be found. The small molecule called SB 247464 was isolated in a screen for compounds that could mimic transcrip-

tional activation characteristic of the cytokine granulocyte—colony-stimulating factor (G-CSF). SB 247464 appears to bind to the extracellular domain of the G-CSF receptor but at a site distinct from that where G-CSF itself binds. SB 247464 produced effects like those of G-CSF when applied to cells in culture or injected into mice. The compound has considerable specificity: it did not activate other related receptors and activated the mouse G-CSF receptor but not the equivalent human receptor.

CONTINUED ON PAGE 143



Amplification of HIV-1 Control DNA. L2: 0 copies, AmpliTaq DNA Polymerase, No Hot Start; L3: 10 copies, AmpliTaq DNA Polymerase, No Hot Start; L4: 10 copies, AmpliTaq DNA Polymerase, manual Hot Start; L5: 10 copies, AmpliTag Gold.

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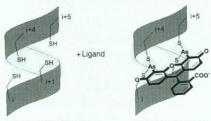
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MALDI AND GENOME ANALYSIS

New technologies for the analysis of large nucleic acids would greatly facilitate the analysis of genomes from humans and model systems. Although matrix-assisted laser desorption/ionization (MALDI) has been considered as a possible alternative to gel electrophoresis, there has not been evidence that it could be applied to fragments of DNA on the order of 2000 nucleotides in length. Berkenkamp *et al.* (p. 260) show that when a suitable liquid matrix is used, the mass of DNA (2200 nucleotides in length) or RNA could be determined to an accuracy of 1 percent.

TAGGING AND DYING PROTEINS

Methods that allow visualization of specific proteins in living cells have numerous applications in cell biology. Griffin et al. (p. 269) report a method in which a protein of interest can be labeled with a six—amino acid peptide that binds with high affinity to a small, membrane-permeant fluorescent ligand. They found that a reversible covalent binding reaction occurs between trivalent arsenic compounds and closely



-helical CCXXCC domain

Fluorescent complex

spaced pairs of cysteine residues in proteins. They designed a peptide to provide optimal interaction of four cysteines with appropriately spaced trivalent arsenics in an organic molecule. In the presence of a small vicinal dithiol compound to reduce binding to endogenous cellular dithiols, detection of the labeled protein with high specificity was possible. The method is expected to have wide utility for protein labeling in live cells and for affinity tagging to allow rapid protein purification.

ASSEMBLING RNA POLYMERASE

In *Escherichia coli*, the enzyme responsible for converting the sequence information from DNA into RNA, RNA polymerase, consists of four subunits, two identical α subunits and two related subunits known as β and β . The latter two subunits catalyze the template-dependent polymerization of ribonucleotides, whereas the pair of α subunits initiate assembly of the complex and interact with other proteins that dictate which genes are transcribed and which remain inactive. Zhang and Darst (p. 262) present a high-resolution structure of the α subunit amino-terminal domain and combine their structural picture with sequence comparisons to identify the likely homologs of these subunits in eukaryotic organisms.

IMMUNE SUPPRESSION BY NON-INFECTIOUS HIV

The Vpr protein encoded by the human immunodeficiency virus (HIV) is packaged into viral particles (virions) and is needed for infection of nondividing cells such as macrophages. Although it was previously known to induce cell-cycle arrest in the G_2 phase, Poon et al. (p. 266) have now found that Vpr can do so when it is associated with virions containing noninfectious HIV. Most of the virus particles in an infected individual are noninfectious, and it thus appears that these particles may contribute to immune dysfunction even after treatment with antiretroviral agents.

TECHNICAL COMMENT SUMMARIES

Materials with Negative Compressibilities

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/281/5374/143a

R. H. Baughman *et al.* described (Reports, 6 Mar., p. 1522) "rare crystal phases that expand in one or more dimensions" when compressed and showed them to have "negative Poisson's ratios."

J. A. Kornblatt comments that the "biological literature is just beginning to recognize that this phenomenon might be occurring when proteins and other biologically important species are subjected to pressure." E. B. Sirota and H. E. King Jr. comment that "this phenomenon ... is also exhibited by a rather wide class of common compounds containing alkyl chains."

In response, Baughman *et al.* discuss their "static-lattice" model, as well as the temperature dependence of various crystals. "The importance of this property observation for the rotary phase," they state, "is in the mechanism resulting in the reported negative linear compressibility and the possibility of generalizing this mechanism to identify materials useful for applications."

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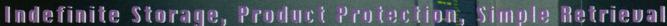
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Fig. 1. Multicolor detection using TSA-Direct.
Courtesy of Kevin Roth, M.D., Washington University School of Medicine, St. Louis, Missouri,

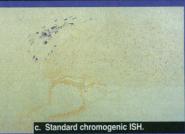
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Figs. 2 a-b. Fluorescent detection of chromosome centromere probes in metaphase spreads. Figs. 2 c-d. In situ chromogenic detection of oxytocin in rat brain tissue sections.

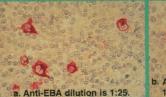
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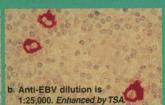
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Fig. 3





Figs, 3 a-b. IHC of EBV antigen in F

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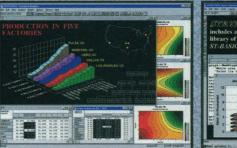
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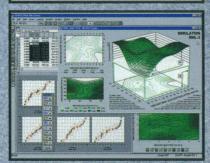


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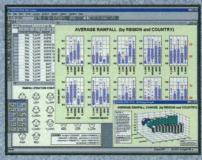
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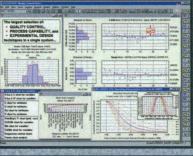


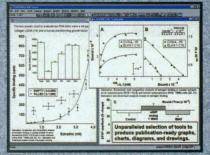


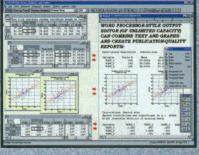






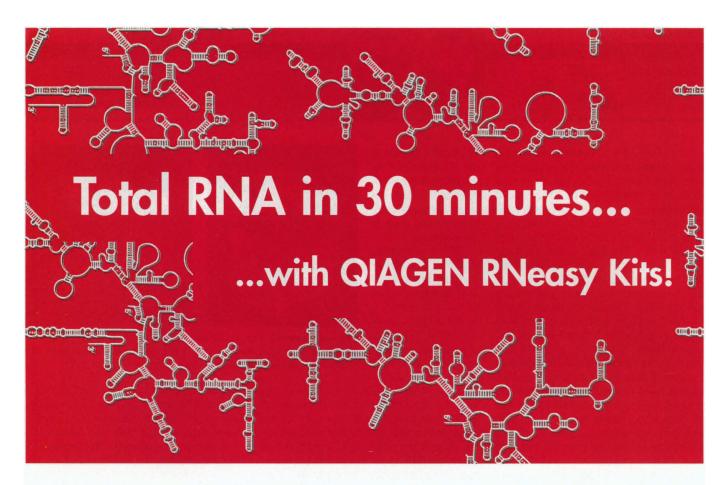








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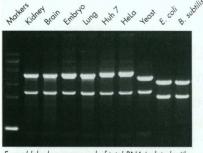
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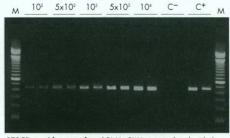


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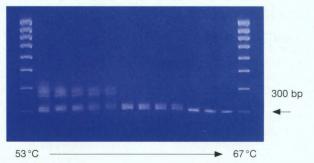
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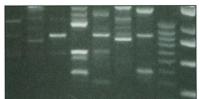
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- Heid, Christian A., et al. 1996. Real Time Quantitative PCR. Genome Research 6: 986-994, from Molecular Endocrinology
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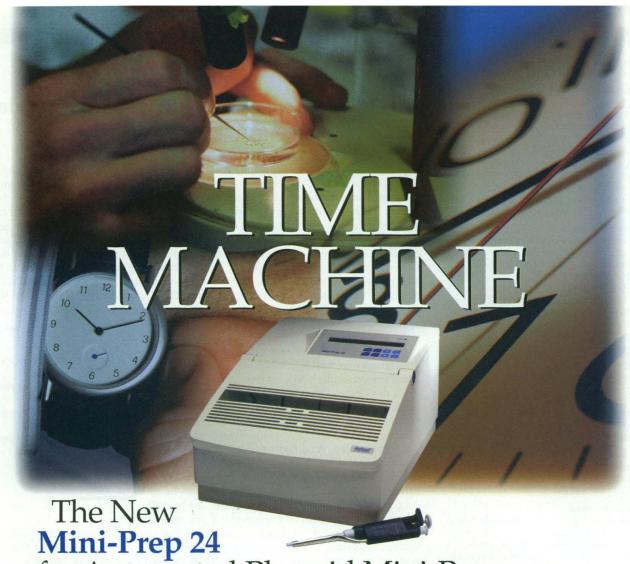
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