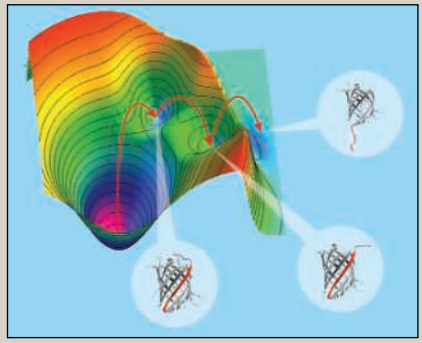
EDITORS' CHOICE

edited by Gilbert Chin

BIOPHYSICS

Unraveling Another Sleeve

Green fluorescent protein (GFP), along with its natural and synthetic relatives, has become a workhorse of the cell biologist because it emits a bright signal that reveals the locations of molecules or changes in calcium or proton concentration. Dietz and Rief have brought another emerging technology to bear, that of atomic force microscopy (AFM), to explore the potential for using GFP as a sensor of force. To begin with, they have spliced GFP into well-characterized protein constructs in order to grab onto its N- and C-termini. Applying force produces a rather complex relation of force to extension, but an analysis based on theory and simulation provides a three-stage description (with two metastable intermediates) of GFP unfolding. First, the N-terminal α helix detaches from the intact β-stranded barrel core and unwinds; second, a β strand is peeled off of the barrel (like prying loose a stave); and this then results in unfolding of the rest of the molecule. — GJC



Unfolding landscape of GFP (α helix, blue; β strand, red).

Proc. Natl. Acad. Sci. U.S.A. **101**, 16192 (2004).

GEOPHYSICS

Trading Places

The southernmost segment of the San Andreas fault extends from the Salton Sea, bends around the San Bernardino and San Gabriel mountains, and intersects with the San Jacinto fault at its northern edge. Bennett *et al.* have found that the faults have been taking turns at sliding along to accommodate plate boundary motions. The San Andreas fault had an average displacement rate of 35 mm/year around 1.5 million years ago (Ma), then decreased to 9 mm/year at about 90 thousand years ago (ka), whereas the San Jacinto fault had almost no displacement at 1.5 Ma and then increased to 26 mm/year at 90 ka.

Map of the San Andreas (green) and San Jacinto (purple) faults.

The big switch occurred at about the time that the bend in the San Andreas fault formed and suggests that the bend created a barrier to slip that was taken up by the San Jacinto fault. Today, the rates have switched back again, so that the San Andreas displacement rate is 27 mm/year whereas the San Jacinto rate is 8 mm/year. These rates do not correlate with seismic activity; the San Jacinto fault has had multiple moderate-to-large–magnitude historic events whereas the southern San Andreas segment has had no large-magnitude events. This could mean that the southernmost San Andreas only ruptures in large-magnitude earthquakes regardless of its average displacement rate. — LR

Geology **32**, 961 (2004).

CHEMISTRY

Two Are Better Than One

The key properties of quantum dots, namely their emission color and efficiency, and their stability and solubility, are controlled by the basic chemistry, particle size, presence of defects, and choice of capping ligand (the shell in a core-shell particle). For the visible regime, CdSe has shown the most promise because it can be tuned to emit from red to blue. However, the standard capping materials CdS and ZnSe can become excited by ultraviolet light, leading to photo-oxidation, and there also are toxicity concerns with both of these materials. ZnS is a better choice for biological applications, but it has a large lattice mismatch relative to CdSe, and this leads to defects that degrade the photoluminescent properties.

Talapin *et al.* have resolved this dilemma by capping the CdSe nanocrystals with two shells. The particles are made with a middle layer of either CdS or ZnSe, which leads to much smaller lattice mismatches at the CdSe/CdS and CdS/ZnS interfaces, and are almost defect-free. The luminescent properties were much less sensitive to the thickness of the capping layers, whereas a single capping material would need to be only two monolayers thick. Surprisingly, the process of putting on two capping layers produces particles with a narrower size distribution. The authors believe that the large lattice mismatch between CdSe and ZnS affects the growth kinetics of the ZnS, and thus this problem too is solved by using sequential capping layers. —MSL

J. Phys. Chem. B. 10.1021/jp046481g (2004).

MICROBIOLOGY

Tackling Trypanosomes

Trypanosoma brucei — the protozoan parasite responsible for causing African sleeping sickness in humans and nagana in cattle — expresses on its surface a variable coat protein linked to the membrane via a glycosylphosphatidylinositol (GPI) anchor. Smith *et al.* demonstrate that the biochemical pathway leading to GPI-linked proteins can be targeted specifically in the parasite. Analogs of intermediates in the GPI pathway were engineered to be able to cross the cell membrane and inhibited GPI synthesis in trypanosomes, while leaving human GPI unaffected. These analogs possessed trypanocidal activity whereas related nonmetabolizable analogs had no such activity. Although these analogs will need to be refined to remain cell-permeable and to survive long enough in serum for bioavailability, they should offer the potential to develop valuable candidate drugs. Currently, there are more than 30,000 cases of African sleeping sickness annually, and the therapies available are often toxic and troublesome to administer. — SMH

EMBO J. 10.1038/sj.emboj.7600456 (2004).

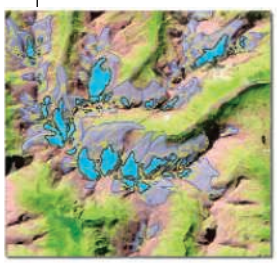
CONTINUED ON PAGE 1441

EARTH SCIENCE

Wasting Away

The mountainous regions of the world are estimated to harbor approximately 160,000 glaciers. They are recognized as being sensitive indicators of global warming, and, if they were to melt, the sea level would rise significantly. Because of their remote location or large size, it has been difficult to accurately measure many of these glaciers and hence hard to say how fast they may be receding.

Using digitized glacier outlines inferred from satellite data from 1985 to 1999, Paul *et al.* circumvent these difficulties and calculate the change in area of about 930 glaciers in the Swiss Glacier Inventory 2000. They find that these glaciers have lost about 18% of their cumulative area during that period, which means that they disappeared at a rate seven times higher than the averaged rate from 1850 to 1973. The variety in the patterns of glacier disintegration observed indicates that massive downwasting (thinning) has been the major mechanism of loss, rather than a dynamic response to climate warming. Even faster rates of loss in the future are forecast, due in part to a delayed response of glaciers to the extraordinarily warm years during the 1990s and the early 2000s. — HJS



The extent of glaciers in the Rheinwald region (1850, blue line; 1973, yellow; 1999, black).

CREDIT: PAUL *ET AL.*, *GEOPHYS. RES. LETT.* **31**, L21402 (2004)

Geophys. Res. Lett. **31**, L21402 (2004).

BIOTECHNOLOGY

Targeting Morphine

Gene silencing via RNA interference has rapidly become a widely used technique. Introducing RNA constructs complementary to endogenous messenger RNAs (mRNAs) leads to degradation of the mRNA transcripts and a decrease in the corresponding proteins. Allen *et al.* have applied this approach to the opium poppy *Papaver somniferum* with satisfying yet unpredicted results.

The enzyme codeinone reductase (COR) converts codeinone to codeine, which is demethylated to morphine. A hairpin RNA designed to target all seven members of the *Cor* gene family yielded transgenic plants displaying varying degrees of diminished morphine production, from 25 to 100%, along with the compensatory accumulation of the morphine precursor reticuline; this result was unexpected because reticuline lies eight steps upstream from morphine. The authors suggest that substrate compartmentalization or multienzyme complexes may explain this distant feedback inhibition. — GJC

Nature Biotechnol. 10.1038/nbt1033 (2004).

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Coordinating Persistent Infection

In patients with cystic fibrosis, chronic infection with the pathogen *Pseudomonas aeruginosa* is the primary cause of death. During the course of long-lasting infections, bacteria respond to their environment, first expressing a set of genes for infection and initial colonization and later expressing components that favor the formation of biofilms that allow aggregation and protection from host defenses. Goodman *et al.* screened for two-component system proteins (histidine kinase sensors or phosphate receiver response regulators) that might participate in control of the early or late gene expression programs. They isolated a gene named *retS* (for *regulator of exopolysaccharide and type III secretion*). Transcriptional profiling showed that expression of *retS* enhanced expression of genes encoding virulence factors and decreased expression of genes that enhance synthesis of exopolysaccharides: cell surface components that support the formation of biofilms. The RetS protein has an unusual structure: It contains two dissimilar response regulator receiver domains and lacks a histidine phosphotransfer domain. The authors propose that one or both of the receiver domains may respond to phosphorylation by proteins other than RetS itself, thus allowing RetS to coordinate multiple inputs in the phenotypic response. — LBR

Dev. Cell **7**, 745 (2004).

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Wasting Away

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