

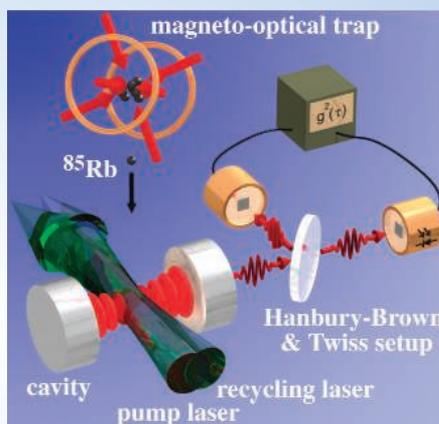
edited by Gilbert Chin

PHYSICS

When Photons Bunch

Being bosons, photons like to group together, with the behavior of photon bunching described as an attribute of classical light. At the other extreme, photons emitted by a single emitter are expected to antibunch, trickling out of the emitter one at a time. Although bunching and antibunching are well established behaviors of classical and nonclassical light, respectively, the transition between the two has not been observed. It is expected that as the number of emitters is increased, a smooth transition should occur. Using a high-quality cavity into which they can place a variable number of atoms, Hennrich *et al.* show that they can probe the transition systematically as the number of emitters (atoms in the cavity) is gradually increased. They observe that the antibunching behavior disappears when the average number of atoms in the cavity is one, and they are able to explain the experimental data well if the emitters are assumed to form an independent ensemble. — ISO

Phys. Rev. Lett. **94**, 053604 (2005).



Setup to probe antibunching to bunching behavior.

through a carbonate (OCO_2) linkage. Activation of the allyl group by an asymmetric palladium catalyst liberates the CO_2 spacer and allows the enol and allyl carbons to join without a deprotonation step. This reaction provides access to a broad range of tertiary and quaternary carbon centers in good yield and enantioselectivity, while minimizing side reactions. — JSY

J. Am. Chem. Soc. **10.1021/ja043472c** (2005).

GEOCHEMISTRY

Elemental Traces

Microbes modify soil. What is obvious to most of us is that they process organic matter derived from higher plants and animals. What is less apparent is that they produce organic ligands and acids that bind to elements such as iron and other metals, and this affects their solubility and mobility. Thus, a soil containing microbes has a different inorganic chemistry than one lacking microbes.

The mobility of elements can be used as a measure of leaching and integrated rainfall and also as an indication of microbial activity. Neaman *et al.* have used elemental mobilities to help ascertain whether microorganisms had managed to invade Earth's land surface in the Archean. For consistency, the authors examined several ancient soils produced on one rock type—basaltic lava flows—and simulated the effects of microorganisms on such a soil in the laboratory. The presence of organic ligands greatly increased the mobility of Fe and P, changing the soil profile. These effects were evident in soils dating to 2.7 billion years ago, implying that at least some microorganisms were a significant presence on Earth's surface then, not just in the oceans. — BH

Geology **33**, 117 (2005).

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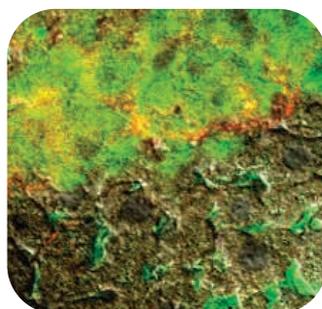
BIOMEDICINE

Stanching the Flow

Hemophilia B is an X-linked genetic disorder caused by decreased levels of factor IX, which functions as part of the blood-clotting cascade. Deficiencies in blood clotting result in uncontrolled bleeding in response to even the slightest trauma. Another problem is bleeding into joints, where subsequent inflammation contributes to deterioration of the joint. Injecting factor IX serves as treatment to stop bleeding, and restoring a fraction of the normal amount can make a difference; however, factor IX does not survive for long in the bloodstream.

Fair *et al.* have shown in mice how embryonic stem cells can be used as a therapy for factor IX deficiency, an approach that would avoid the need for repeated injections and could supply a steady stream of factor IX. In these experiments, the mice carried a mutation in their factor IX gene, and the embryonic stem cells were

derived from mice with a normal factor IX gene. In vitro culture conditions were defined to direct the embryonic stem cells to differentiate into cells with features of endodermal precursors. These putative endodermal precursors were then injected into the livers of factor IX-deficient mice. Mice treated in this way showed factor IX expression and improved long-term survival. Engraftment of the differentiated embryonic stem cells did not require injury or hepatectomy. The results provide a promising step



Liver slice showing colocalization of factor IX (red) and embryonic stem cells (green).

toward a cell-based therapy for factor IX deficiency. — PJH

Proc. Natl. Acad. Sci. U.S.A. **102**, 2958 (2005).

CHEMISTRY

Beyond the Basics

The formation of carbon-carbon bonds via enolate addition to electrophiles is a cornerstone of modern organic synthesis. These types of reactions are generally started by treating a ketone with a base, which deprotonates the carbon atom adjacent to the carbonyl group, leaving a negatively charged O-C-C framework that is the target of the electrophile. However, the product is also a ketone and hence is susceptible to repeated attack by the base, leading to losses in stereo-selectivity and undesirable side reactions.

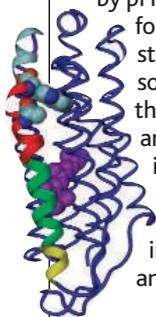
Trost and Xu have found a way around this problem by eliminating the base. They stabilized precursors in the enol form by tethering the electrophile (an allyl group in this case) to the enol oxygen

BIOPHYSICS

Deconstructing Membrane Proteins

Progress in understanding how a protein finds its three-dimensional structure in seconds has been hard-won, and some of the successes have come from studying the intermediate stages (or lack thereof) of protein structures when they are stressed by pH, denaturants, or mechanical

force. The historic nomenclature of structures (primary, secondary, and so forth) largely reflects the current thinking that helices form early and relatively independently, that interactions between helices help steer the folding trajectory (by clamping posts and beams) into domains, and that fitting amino acid side chains into pockets



A view of helix E and the Ala-Trp interaction.

(like tenons and mortises) locks everything into place. Most unfolding studies have avoided the complications of membranes; structure determination of intact membrane proteins is not easy, and the study of pH- or denaturant-treated membrane proteins is truly daunting.

Cisneros *et al.* have applied mechanical force to extract halorhodopsin from its native membrane and compared the force-distance profiles with those of its cousin bacteriorhodopsin. The adhesive interhelical contacts are both weak and spatially diffuse, so that it is the sum total of them and not just a few residues that

lend strength to the functional structure. The unfolding profiles also show, within one of the transmembrane helices in halorhodopsin, a hinge (defined by an alanine-tryptophan pairing) that demarcates two separably movable segments of the helix. — GJC

Structure 13, 235 (2005).

BIOMEDICINE

Pockets of Resistance

Although only 5% of those exposed to mycobacteria go on to develop acute tuberculosis, many suffer latent infections that have escaped antibiotic treatment and may recrudescence with stress or aging. Ha *et al.* tested a combined vaccine-chemotherapy regime for its ability to prevent reactivation of disease in mice infected with *Mycobacterium tuberculosis*. Although protective antigens have not yet been defined precisely for tuberculosis, these authors made a DNA vaccine in a pGX10 vector containing two genes they had tested previously: Ag85A epitopes (recognized by CD4⁺ T cells) are expressed on the surface of macrophages during early infection and PstS-3 epitopes (recognized by both CD4⁺ and CD8⁺ T cells) during late phase. Four weeks after infection, they administered the vaccine to mice along with the drugs isoniazid and pyrazinamide. Subsequent treatment with dexamethasone reactivated the disease in the control groups of mice but not in the vaccinated and antibiotic-dosed mice, suggesting that combining the boosting of the immune response with drugs had eliminated the mycobacteria. — CA

Gene Ther. 10.1038/sj.gt.3302465 (2005).

HIGHLIGHTED IN SCIENCE'S SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT



PIs as Ligands?

Phosphatidylinositol (PI) lipids are implicated in a broad range of processes, from the organization of signaling pathways to vesicle trafficking and control of the actin cytoskeleton. Krylova *et al.* suggest that these lipids may also serve as activating ligands for a class of orphan (so called because no regulatory ligand was known) nuclear receptors. The authors solved crystal structures of three nuclear receptor 5A family members: mouse mSF-1 and the human proteins hSF-1 and hLRH-1. Residual electron density in the ligand-binding pockets revealed that the crystallized proteins (expressed in and purified from bacteria) contained lipids. Testing with eukaryotic lipids revealed preferential binding to phosphatidylinositol 3,5-bisphosphate [PI(3,5)P₂] and phosphatidylinositol 3,4,5-trisphosphate [PI(3,4,5)P₃]. Although biological regulation by such lipids remains to be explored, mutant proteins designed to disrupt lipid binding showed decreased transcriptional activity. The mouse receptor appears to have lost ligand-binding activity, and phylogenetic analysis favors the scenario in which the ancestral nuclear receptor did bind lipids and this capacity was later lost in the rodent lineage. — LBR

Cell 120, 343 (2005).

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A

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Science

PIs as Ligands?

Science **307** (5713), 1173.
DOI: 10.1126/science.307.5713.1173c

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