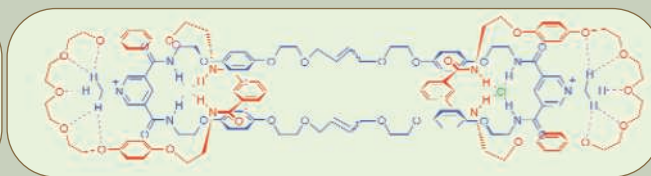
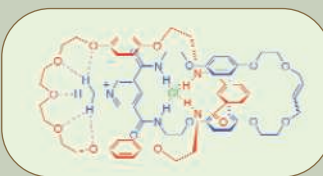
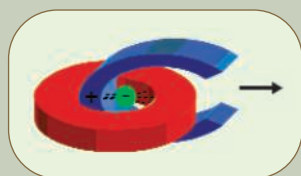


edited by Gilbert Chin



Cyclization strategy and products (chloride, green).

CHEMISTRY

Catenane Closure via Chloride

The assembly of interlocking molecular rings, or catenanes, normally relies on some sort of templating mechanism to hold the components together while chemical reactions complete the cyclization. Sambrook *et al.* report on the use of anions as templating agents. They use a catenane precursor and a macrocyclic ring, each of which bears a cleft region that brings two amide groups into close proximity. Binding of

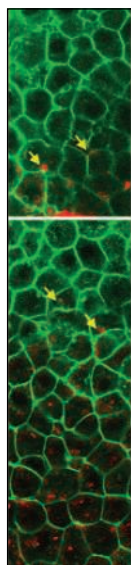
a single chloride ion by these four amides holds the precursor onto the macrocyclic ring; this interaction is also stabilized by π - π stacking interactions between hydroquinone groups on both molecules. Ring-closing metathesis cyclizes the precursor, either as a monomer to form two interlocked rings or as a dimer to form a [3]catenane. The [2]catenane product selectively binds chloride anions over acetate and dihydrogen phosphate. — PDS

J. Am. Chem. Soc. 10.1021/ja045080b (2004).

DEVELOPMENT

Restricting Morphogens

During embryonic development, gradients of morphogens and signaling molecules help to define how development proceeds. Scholpp and Brand examined how the gradient of a member of the fibroblast growth factor family, Fgf8, is generated and maintained in the nascent neuroectoderm of living zebrafish embryos. By looking at fluorescently tagged Fgf8 as it spread from its site of origin through target tissue, the authors obtained evidence for a restrictive clearance mechanism in which the factor is cleared from the immediate environment around target cells by endocytosis and subsequent degradation. When endocytosis was blocked, Fgf8 accumulated extracellularly and activated gene expression in more



Fgf8 (red) spreads 4 cells away after 1 hour (top) and 12 cells distant after 3 hours (bottom).

distant target cells, whereas activating endocytosis had the opposite effect, restricting the effective range of Fgf8.

Belenkaya *et al.* looked at the movement of another growth factor-related morphogen, Drosophila Decapentaplegic (Dpp), during anteroposterior patterning of the wing. In this system, movement of the growth factor was restricted by binding to extracellular proteoglycans rather than by endocytosis,

leading again to a gradient of morphogen response. — SMH

Curr. Biol. 14, 1834 (2004); *Cell* 119, 231 (2004).

IMMUNOLOGY

The Cost of Escape

Cytotoxic CD8 T cells (CTLs) begin their assault on the HIV pathogen soon after infection occurs, and the efficiency with which they achieve early control is a deciding factor in the course infection takes. Conversely, the virus defends itself by mutating the epitopes targeted by the CTLs in an attempt to escape recognition. Jones *et al.*

explored which characteristics of early CTL responses to HIV corresponded with the subsequent ability to control the viral load.

In an individual showing good viral control, the number and breadth of epitopes recognized by CTLs were relatively large, in contrast to the strong focus of CTLs on a handful of immunodominant epitopes in two individuals exhibiting poor viral control. In these two people, new viruses with numerous CTL epitope mutations appeared soon after infection, suggesting that early selective pressure from CTLs had been countered successfully by the virus. On the other hand, the individual with good viral control carried viruses with far fewer mutations, consistent with the relatively slow emergence of new escape mutants in the months after the acute phase of infection. Early control thus appears to be determined by broad recognition of multiple viral epitopes, increasing both the opportunity for viral detection by CTLs and the potential cost of escape mutations to intrinsic viral fitness. — SJS

J. Exp. Med., 200, 1243 (2004).

BIOPHYSICS

Unraveling the Knitted Sleeve

The surroundings in which membrane proteins reside consist of a hydrophobic interior (the fatty acid tails of phospholipids), a polar interfacial zone (the phospholipid head groups), and the aqueous compartments on either side of the bilayer. Rather than analyzing the energetics and dynamics of membrane protein insertion in the midst of such heterogeneity, Ganchev *et al.* have resorted to extracting peptides in a model membrane system. A shorter peptide and a longer one, both of which were previously shown to adopt a single-span α -helical conformation in membranes, and two phospholipids, one gel-like and one fluid, were mixed and probed by atomic force microscopy. Pulling (at a range of speeds) resulted in extraction of the peptide, at forces of about 90 pN applied to the gel-like mixture and only 60 pN for the more fluid membrane. A closer look at the resistance to extraction suggests that it arises primarily from the energy required for

CONTINUED ON PAGE 1263

unwinding the first turn of the helix and dragging these residues from the hydrophobic interior into the interfacial region. — GJC

Biochemistry 10.1021/bi048372y (2004).

MATERIALS SCIENCE

A Brighter Future by Working Together

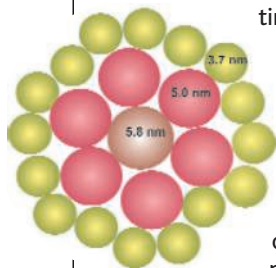
Both metal nanoparticles and semiconducting nanowires have interesting optical and electrical properties, but what happens when they are coupled together?

Lee *et al.* try to answer this question for a collection of CdTe nanowires that are complexed with Au nanoparticles using the biotin-streptavidin ligand-receptor pair to connect the two together.

When these components were mixed in solution, the authors observed a fivefold increase in the peak luminescence intensity and a blue shift of the spectra that

developed gradually with

time. Surprisingly, as the intensity increased, the photoluminescence lifetime decreased, which is in contrast to normally observed trends. The authors interpreted their observations within a model in which the Au nanoparticles form a coaxial shell around the nanowires. They find that the gold particles generate an electro-magnetic



Cross-section (with diameters in nm) showing the nanowire, streptavidin-biotin linker, and nanoparticle.

field that stimulates photon emission from the nanowires, in a process that is reminiscent of surface-enhanced Raman scattering. This effect is not due to individual nanoparticle-nanowire interactions but instead to the collective effect of the aggregated metallic nanoparticles. — MSL

Nano Lett. 10.1021/nl048669h (2004).

GEOLOGY

Residence Time

Agricultural and industrial activity has increased the amount of N added to rivers far above natural levels. This N, added mostly as nitrate, is a major pollutant that contributes to eutrophication and produces anoxia in water bodies of all sizes; it also is a source of the greenhouse gas nitrous oxide (N₂O). The magnitude of the impact of riverine N is hard to judge, however, because of large gaps in our knowledge about its removal during transport through the river system.

Donner *et al.* use an aquatic transport model to investigate in-stream N removal and N₂O emissions in the Mississippi River system and how they may be affected by interannual climate variability. Their results show that the fraction of N removed in the river system can vary by nearly a factor of 2, with a threefold range in the associated N₂O emissions, depending on precipitation. The lowest fraction of N removal and the greatest N₂O emissions occur in the wettest years, when river flow is greatest and the residence time of the water in the rivers is shortest. — HJS

Geophys. Res. Lett. 31, L20509 (2004).

HIGHLIGHTED IN SCIENCE'S SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT



Calcium Signals from the Mitochondria

Xu *et al.* used human cell lines that expressed inducible nitric oxide synthase under the control of regulated promoters to investigate the effects of inhibiting mitochondrial respiration with nitric oxide (NO). NO, acting independently of soluble guanylate kinase activity, stimulated expression of glucose-regulated protein 78 (Grp78), an endoplasmic reticulum (ER)-resident chaperone protein whose expression is enhanced as part of the ER stress response. NO produced an increase in the amount of the soluble transcription factor p50 ATF6, which is generated through a calcium-dependent process involving regulated intramembrane proteolysis. NO-dependent stimulation of p50 ATF6 production and of Grp78 expression was attenuated in cells depleted of intracellular calcium, and both an intracellular calcium chelator and cyclosporin A (which interferes with mitochondrial calcium signaling) reduced NO-dependent ATF6 cleavage and prevented the NO-dependent increase in Grp78. Thus, the authors propose that NO-dependent inhibition of mitochondrial respiration affects calcium signaling between the mitochondria and the ER, thereby stimulating production of p50 ATF6 and the expression of genes involved in the ER stress response. — EMA

Nature Cell Biol. 6, 1129 (2004).