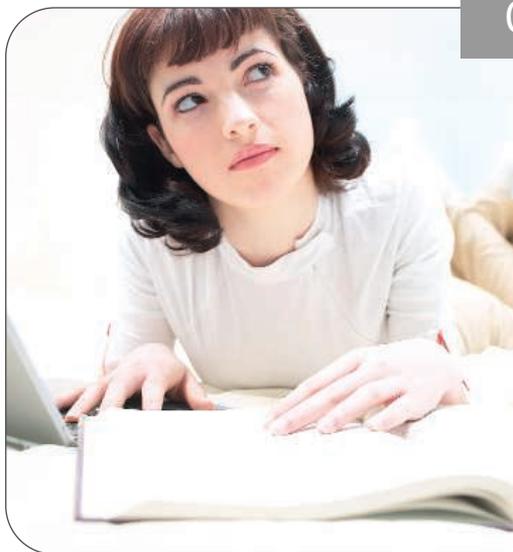


EDUCATION

Questions, Questions



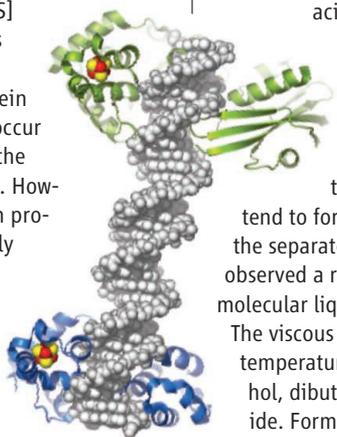
Question-asking is a fundamental element of practicing science; however, the teaching of question-asking skills is often overlooked in science education. Practicing scientists appreciate the value of asking questions, but do students in science classes? Keeling *et al.* asked undergraduate students in a senior-level cell biology class to review background material, detailed protocols, types of data to be recorded, and guidelines for analysis, before their laboratory session. After reflecting on the scientific process behind upcoming experiments, students were asked to write at least three questions about the science to be studied. As might be hoped, students' questioning ability, as assessed by the quality and relevance of questions generated, improved over time. Although repeated practice at writing questions did lead to improvement, "learning by doing" may not be enough, and specifically teaching question-asking skills could usefully be paired with explicit guidance and discussion. — MM

Life Sci. Edu. **8** 131 (2009).

MOLECULAR BIOLOGY

Resolving DNA Repair

Base excision repair (BER) enzymes involved in fixing damaged DNA have low specificity for their targets and occur in low numbers in cells. So how are DNA damage sites located on chromosomes with any efficiency? Boal *et al.* suggest that the key lies in DNA charge transport chemistry, so that repair proteins can signal to each other rapidly over long distances. The ordered stacking that occurs in DNA makes it an excellent medium for electron transport, and the process is very sensitive to the presence of mismatched bases. When a BER enzyme containing an [4Fe4S] cluster binds DNA it becomes oxidized. In the absence of damage, when a second protein binds, electron transfer will occur and the reduced member of the protein pair will diffuse away. However, if there is damage, both proteins remain bound and, fairly rapidly, repair proteins will redistribute to the damaged region. Boal *et al.* used atomic force microscopy to establish that redistribution did take place in complexes of the BER enzyme EndoIII with DNA duplexes containing a sin-



DNA with bound repair proteins.

gle mismatch. As predicted, cooperation was observed between different BER enzymes, the bacterial EndoIII and MutY. These enzymes have human homologs linked to cancer predisposition, although the medical implications of the conservation of these iron-sulfur clusters remain unclear. — BJ

Proc. Natl. Acad. Sci. U.S.A. **106**, 15237 (2009).

CHEMISTRY

A Charge from Sulfur

A zwitterion is essentially a pair of oppositely charged ions connected by a covalent bridge. A common example is the structure of an amino acid dissolved in water near neutral pH—the amino group strips a proton from the carboxylic acid group, leading to a positive ammonium and a negative carboxylate. In general, these highly polarized structures tend to form in solvents that can stabilize the separated charges. Heldebrant *et al.* have observed a rare instance in which a pure molecular liquid adopts zwitterionic character. The viscous yellow substance forms at room temperature on exposure of an amino alcohol, dibutylundecanolamine, to sulfur dioxide. Formally, the sulfur bonds to the terminal oxygen of the alcohol, forming a negatively charged sulfite group, while the proton formerly on that oxygen shifts to the opposite

terminus, forming a positively charged ammonium center. The authors characterized the unusual liquid spectroscopically and discovered that the SO₂ addition is reversible. Raising the temperature under reduced pressure leads to release of the gas and recovery of the amino alcohol precursor. Because the precursor does not react with CO₂, the SO₂ binding and release cycle might be applicable to selective removal and recovery of sulfur from combustion exhaust streams. — JSY

Energy Environ. Sci. **2**, 10.1039/b916550a (2009).

BIOMEDICINE

Great Expectations

Two genetic mutations that in combination cause cell death, whereas each alone does not, are known as synthetically lethal. Fairly recently, the synthetic lethality notion has been applied to the search for anticancer drugs, to identify lethal combinations of drugs with specific tumorigenic mutations. The first targeted anticancer drugs to emerge from this approach were inhibitors of the DNA repair enzyme poly(ADP-ribose) polymerase (PARP). These drugs exploit the synthetically lethal interaction between PARP and the tumor suppressor genes *breast cancer 1 (BRCA1)* or *BRCA2*, which are involved in DNA double-strand break repair by homologous recombination. Mutations in the *BRCA* genes are associated with an increased risk of breast and ovarian cancer, and PARP inhibitors are currently showing great

CREDITS (TOP TO BOTTOM): JUPITERIMAGES; BOAL ET AL., PROC. NATL. ACAD. SCI. U.S.A. **106**, 15237 (2009)

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promise in the clinic. Another tumor suppressor gene, *phosphatase and tensin homolog (PTEN)*, is one of the most frequently mutated genes in human cancers and has been implicated in genome stability. Now, Mendes-Pereira *et al.* have found a role for PTEN in homologous recombination, and they demonstrate the sensitivity of *PTEN* mutant tumor cells to PARP inhibitors. *PTEN*-deficient cells were also highly sensitive to PARP inhibitors. *BRCA* mutations are relatively infrequent and limited mainly to breast and ovarian cancers. This study suggests that PARP inhibitors may also be useful in a far broader range of cancers that involve *PTEN* mutations, such as lung and colorectal tumors and glioblastomas. — HP

EMBO Mol. Med. **1**, 315 (2009).

DEVELOPMENT

Macho Mice

Male-specific behaviors in mice include mating, aggression, and territorial marking. Development of male-specific behaviors in mice, as well as in humans, requires the testicular hormone testosterone. The hormone estrogen, better known for its function in females, is also required. In males, which lack ovaries, estrogen is produced when the enzyme aromatase converts testosterone to estrogen. Estrogen produced by aromatase-expressing cells in the brain then signals through receptors to affect behavior. Wu *et al.* have now analyzed the neurons that express aromatase and their connectivity in mice. Although aromatase-expressing neurons represent only a minority of the neurons in the brain, the locations and patterns of these neurons in the adult mouse brain reflect sexual dimorphism. Sexually dimorphic territorial behaviors are also affected by disruption of estrogen-based signaling. The testosterone surge around the time of birth in mice thus seems to direct masculinization of territorial behaviors through aromatization of testosterone into estrogen in key neurons within the the brain, rather than through androgen receptor signaling. — PJH

Cell **139**, 61, (2009).

APPLIED PHYSICS

What a Whopper

The basic design of a laser sandwiches a gain medium between two mirrors. As the light bounces between the mirrors, the intensity of the electromagnetic field builds up within the cavity and spills out from one of the mirrors.

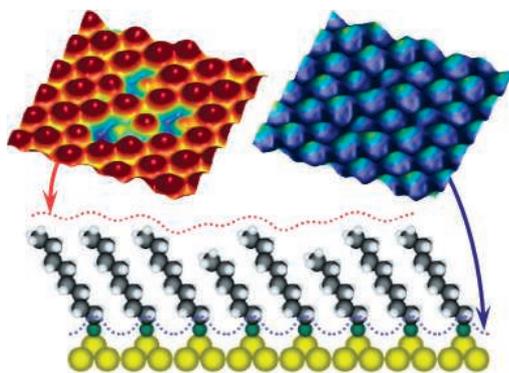
Laser instrument size can vary greatly, from the tiny semiconductor devices in DVD and CD players, to the tabletop-confined systems used in spectroscopy and other laboratory applications. Then there are the football field-sized instruments used to probe high-energy light/matter interactions in attempts to harness the class of fusion energy released by the Sun. Reaching an even greater size scale, Turitsyn *et al.* present a fiber laser with a cavity 270 kilometers long. Such an ultralong laser could be used in secure communications. Because the properties of the waves building up within the medium depend on how the light bounces off the mirrors, a given protocol between a sender and receiver for manipulating the mirrors could provide mode selection for securely relaying messages. — ISO

Phys. Rev. Lett. **103**, 133901 (2009).

CHEMISTRY

Imaging Top and Bottom

Scanning tunneling microscopy of adsorbed molecules on surfaces usually interrogates the topography of the topmost layer of atoms. For small molecules, this information is often sufficient to answer many structural questions, but for long-chain molecules, the bonding of the molecule to the surface can be obscured, espe-



cially at high surface coverages. Han *et al.* imaged both the topmost layer and the bonding interface of alkane thiols containing up to 10 carbon atoms adsorbed on gold. The application of an ac modulation of the tunneling gap allowed the buried methyl groups at the gold/sulfur interface to be imaged in a derivative mode. In the high coverage regime, the coexisting domains of different packing arrangements varied in their gold/sulfur bonding motifs in a manner consistent with previous x-ray diffraction studies. This technique will also be useful in studying other processes where changes in molecular tilt impact function. — PDS

ACS Nano **3**, 10.1021/nn901030x (2009).