Editors' Choice: Highlights of the recent literature

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NEUROSCIENCE: Untangling the Web

Pyramidal cells in layer V of the neocortex form a major excitatory projection system in the brain. Their activity is modulated by a network of excitatory and inhibitory inputs from local intracolumnar neurons and from neurons in other columns.

Schubert *et al.* have analyzed the origin, strength, and spatial distribution of synaptic inputs onto layer V pyramidal cells in the rat somatosensory cortex. Morphologically and functionally, two major classes of pyramidal cells, intrinsically bursting (IB) and regular spiking (RS), were differentiated. Both received excitatory input from all cortical layers. Inputs from layers V and VI were more homogenous, whereas those from layers IV and II/III showed a patchy distribution. Excitatory inputs from layer VI were stronger for IB than for RS cells, and IB cells received only weak inhibitory inputs, mainly of local origin. In contrast, inhibitory inputs onto RS cells were much stronger and originated predominantly from layers II/III and V of the same column and from layer V of the adjacent columns. Thus, the IB cells may be important for integration of excitatory inputs across several cortical columns, and the RS cells may be better suited for information processing within a cortical column. -- **PRS**

J. Neurosci. **21**, 3580 (2001).

CHEMISTRY: Platonic Solids in All Shapes and Sizes

Synthetic strategies for the self-assembly of discrete high-molecular-weight molecules have yielded regular structures based on Platonic solids, as well as related, less regular structures. A key concept in the assembly of such molecules and of larger porous frameworks is the secondary building unit--for example, a molecular square could be used to assemble larger structures.

Moulton *et al.* have used such secondary building units to synthesize unusual structures that have both open (concave) and closed (convex) faces. To assemble these molecules successfully requires control over the angle at which the vertices of the square building units bind to each other. These neutral molecular units are chemically robust and likely can be made chemically diverse because many metals, including those that are magnetic or catalytically active, can fit into the square shape. Furthermore, internal and external sites are available for modification, and the internal cavity can host guest molecules. These molecules may have many uses, from the assembly of larger nanostructures to molecular recognition. -- **JU**

Chem. Commun. **2001**, 863 (2001).

BIOTECHNOLOGY: Out with the Old, In with the New

Maltose binding protein (MBP), a periplasmic binding protein from *Escherichia coli*, has a ligand binding site located at the interface of two domains. Maltose binding initiates a conformational change from an open to a closed state, and earlier work has demonstrated coupling of this change to a fluorescent readout.

Marvin and Hellinga have used rational design to convert MBP into a zinc sensor. Computational analysis predicted twenty potential tetrahedral coordination sites within the interdomain interface. Four of these modified MBPs were engineered: two by altering maltose binding residues (A sites) and two that left the maltose binding site intact (B sites). All four proteins bound zinc, but only the A sites coupled zinc binding to formation of the closed state. A hybrid with both an A and a B site exhibited increased zinc affinity. The affinity also could be improved by refining the coordination sphere or by making mutations designed to favor the closed state. Finally, a substantial enhancement in affinity was achieved by eliminating polar residues that would have formed hydrogen bonds with maltose and that would be vestigial in the zinc sensor. -- **VV**

Proc. Natl. Acad. Sci. U.S.A. **98**, 4955 (2001).

ASTROPHYSICS: Bursting Bubbles

Imagine a planetary nebula as a piece of bubble gum at the end of its life-span: you can blow a few more good bubbles, but after the last burst, it becomes a flavorless wad. A planetary nebula is a dying star that blows large bubbles first of nebular and then of stellar material before the central star collapses into a white dwarf.

The Cat's Eye Nebula (NGC 6543) is a complex dying star. A composite image shows outer shells of slowly expanding, low-temperature nebular material blown away from the star (red and green shells) with inner shells of faster and hotter stellar material from a later bubble. Chu *et al*. have now added another set of inner shell structures (purple and pink shells) on the basis of observations from the Chandra X-ray Observatory. These shells are fast-moving but cool, and they don't fit well with dynamic models of either nebular or stellar material; however, spectra of the shells indicate that the material is stellar in flavor. The cool gas may be a mixture of stellar and nebular material, or the x-ray emission may be sampling gas only at the interface of the edge of the bubble, where the material is denser and perhaps cooler. -- **LR**

Astrophys. J., in press.

PHARMACOLOGY: Evading Search and Destroy

Anticancer agents such as taxol often encounter two barriers to their effectiveness: metabolism by the cytochrome P450 family of enzymes (CYPs) and clearance from cells by the P-glycoprotein efflux pump (MDR1). Synold *et al.* demonstrate that taxol elicits both mechanisms in human hepatocytes and intestinal epithelial cells by activating the steroid and xenobiotic nuclear receptor (SXR), which detects a broad spectrum of drugs. Taxol reversed SXR interaction with nuclear corepressors, thereby allowing the expression of genes such as *CYPs* and *MDR1*. The inability of the taxol analog docetaxel to displace SXR corepressors may explain why it is a relatively effective antineoplastic agent, and the development of more "SXR-transparent" compounds such as docetaxel could improve the retention and duration of anticancer drugs. -- **LDC**

Nature Med. **7**, 584 (2001).

GEOLOGY: A Sleeping Giant

One of Earth's largest recent volcanic eruptions occurred at Toba, Indonesia, about 74,000 years ago. This eruption released an estimated 2800 cubic kilometers of magma and formed a large caldera extending 30 by 100 kilometers; the eruption is thought to have had dramatic effects on Earth's climate.

What might Earth's largest volcano be doing today? Masturyono *et al*. have conducted a geophysical survey across Toba to image its internal structure, and they identify areas where magma is present down to mantle depths. These data reveal that the caldera contains two separate shallow magma bodies, which can be traced upward to small volcanoes that erupted sometime after the main Toba eruption. The larger of the magma bodies, which makes up about one half of the caldera, narrows at depth but can be traced downward to the mantle. It seems likely that melts in the mantle are providing the heat for crustal melting that forms large explosive reservoirs. -- **BH**

Geochem. Geophys. Geosys. **2**, 2000GC000096 (2001).

CHEMISTRY: The Proper Mix in Electron Transfer

Electronic excitations of a molecule can change its normal modes of vibration, as was pointed out by Duschinsky in the late 1930s. The excited state of the molecule can have a different symmetry than the ground state, and thus the computation of the overlap integrals of vibrational states, or Franck-Condon factors, in principle requires a multidimensional calculation to account properly for the resulting mixing of different vibrational levels. In a pair of papers, Sando and co-workers examine how Duschinsky mixing affects transition states for electron transfer reactions, for which many studies have used metal complexes of high symmetry. They find that the effects can be large; for example, the parabolas that describe the "inverted region" of electron transfer are flattened out in some cases. Although individual totally symmetric modes are affected more strongly, the larger number of nontotally symmetric modes add together to a sizeable contribution. -- **PDS**

J. Phys. Chem. A, in press.

MOLECULAR BIOLOGY: At the Core of Splicing

In eukaryotes, the family of Sm proteins is known to participate in RNA processing events, such as splicing of pre-messenger RNAs. It is thought that seven distinct members of the family assemble into a doughnutlike shape and that this provides the binding surface for the uridine-rich region shared among the spliceosomal U RNAs. Related proteins have been identified in *Archaea*, and now two groups describe the crystal structures of these homoheptameric rings.

Törö *et al*. provide the structure of one of the two Sm proteins from *Archaeoglobus fulgidus*; the diameter of the doughnut is 65 angstroms, and the thickness is 30 angstroms. They also have been able to resolve three connected uridines in a complex of AF-Sm1 with a U_5 oligoribonucleotide. The uridines are sandwiched between residues previously suggested to comprise the RNA binding site, and it appears that other bases would not fit nearly as snugly.

Mura *et al.* present the structure of the Sm representative from *Pyrobaculum aerophilum*. Their doughnut is of similar size, 65 by 38 angstroms, with a similar surface asymmetry of charge. On the other hand, their model of the complex with single-stranded RNA resembles a ring-on-a-string, in which the preference for the pyrimidine U over purine bases is explained by the narrowness of the central hole. -- **GJC**

EMBO J. **20**, 2293 (2001); *Proc. Natl. Acad. Sci. U.S.A*. **98**, 5532 (2001).