APPLIED MATHEMATICS

Open and Shut

During photosynthesis, plants collect carbon dioxide through openings called stomata but also lose water vapor when these pores are open. Thus, the plant must continually optimize the aperture diameter, a process thought to be global (coordinated over large regions of the leaf surface). To better understand the optimization mechanism, researchers inject dye into a plant leaf and then use time-lapse videography to track fluorescence changes as the stomata open and close. However, processing the video sequence is mathematically tricky: Standard methods to identify the synchronized dynamics of fluorescing patches in two spatial dimensions and one time dimension can neglect important changes or overemphasize unimportant detail. Luttman and Bardsley have devised an algorithm based in variational calculus to extract the three-dimensional evolution of stomatal patch dynamics from experimental data. After preprocessing video of a fluorescing cocklebur leaf to remove noise and normalize changes in lighting, they identified the patches by looking for segmentations of the data that yielded the optimal division of light and dark regions. Processing of the spatial and temporal data as a whole proved essential; analyzing each frame independently resulted in meaningless segmentation. — DV

SIAM J. Sci. Comput. **29**, 1550 (2007).

Magnified stoma.

MOLECULAR BIOLOGY

Islands of Silence

In eukaryotes, DNA is packaged into chromatin, which serves as a platform for regulating access to the genome and modulating transcription, repair, and replication. Heterochromatin marks regions where, generally, genes are silenced; it is largely restricted to centromeres, the inactive X chromosome, and telomeres, and is thought to spread unless constrained by molecular barriers. Euchromatin, on the other hand, defines regions where genes are active. Yet silenced genes can be found among active genes. Do they exist as microdomains of heterochromatin, or are they some other form of repressive chromatin?

Regha *et al.* have examined the IgfR2 imprinted region on mouse chromosome 17. Here, the overlapping *Air* and *Igf2r* genes, with promoters a mere 28 kb apart, are reciprocally repressed on maternal and paternal chromosomes. Though silenced by different mechanisms—*Air* by DNA methylation and *Igf2r* via a noncoding RNA—the promoters of both genes bear highly localized marks on the histone components of their chromatin that match those found in classically defined regions of heterochromatin, specifically histone H4 trimethylated on lysine 20 (H4K20me3) and H3K9me3. Furthermore, these marks do not spread through the body of the gene. The results indicate that heterochromatin and euchromatin can be highly interspersed, even to the point where heterochromatin peaks can exist within the transcribed region of a neighboring active gene. In contrast, genes in regions that show tissue-specific repression are marked with broad swaths of H3K27me3, which delineates a second and perhaps long-term repressive chromatin state. — GR

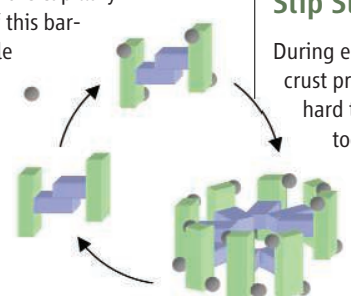
Mol. Cell **27**, 353 (2007).

BIOMEDICINE

A Kick in the Kidneys

The unsurpassed filtration ability of the kidney is underpinned by the exquisite cellular architecture of the podocytes. These cells extend foot-like processes that abut the multilayered barrier of basement membrane and epithelial cells, on the other side of which lies the capillary lumen. The integrity of this barrier (which is permeable to water and small molecules), and in particular the mesh-like connections between the podocyte feet, are essential for preventing the escape of proteins into the urine (proteinuria). Sever *et al*. show that an intracellular GTPase, dynamin, is required for the maintenance of podocyte morphology. Dynamin contains a cleavage site for the intracellular protease cathepsin L, and in proteinuric kidney disease, cleavage leads to the rearrangement of the actin cytoskeleton in the podocytes and collapse of the feet. In a mouse model of proteinuria, introduction of a protease-resistant dynamin or a dynamin that assembled into protease-resistant higher-order structures restored podocyte function and resolved their symptoms. Dynamin has previously been implicated in endocytosis in neuronal and other cells, but a specific role in kidney anatomy was unanticipated. — SMH

J. Clin. Invest. **117**, 2095 (2007).



GTP (spheres) promotes higher-order assembly of dynamin (green/purple).

GEOPHYSICS

Slip Sliding Away

During earthquakes, very high stresses within the crust press the two sides of the fault together so hard that they should be effectively locked together by friction. In the laboratory, rocks are similarly difficult to rip apart. Yet in the landscape setting, faults rupture suddenly and easily. Various explanations for this conundrum have been put forward, including fault lubrication by fluids or weakening by seismic vibrations. Recent experiments suggested that the rocks themselves may become slippery during rupture if they are heated or interact with

CREDITS (TOP TO BOTTOM): BRIAN SULLIVAN/GETTY IMAGES; SEVER *ET AL., J. CLIN. INVEST.* **117**, 2095 (2007)

fluids; silica gel may lubricate quartz rocks and fine powder may ease sliding in carbonate rocks. Hirose and Bystricky have found support for another hypothesis: fault weakening through dehydration of embedded phyllosilicate clays. They carried out high-velocity friction experiments on natural serpentinite (a phyllosilicate) under conditions mimicking an earthquake and measured the heat generated by friction and the resulting rock strength. An observed increase in humidity implied that water was lost from the serpentinite during sliding. Dehydration requires temperatures of about 500°C, which the authors argue might be attained where bumpy asperities rub together. — JB

Geophys. Res. Lett. **34**, L14311 (2007).

CLIMATE SCIENCE

Trop Chaud?

The summer of 2003 was the hottest on record in Europe over the past 500 years; the summer of 2006 was almost as hot, and the heat was even more widespread. Were these extremes part of a trend that can be expected to continue? Della-Marta *et al.* compiled 54 temperature records from western Europe (6 based in Scandanavia, 12 in the Iberian Peninsula, and 36 in the central region) to determine how the daily summer maximum temperatures there have changed since 1880. They found that the length of summer heat waves has doubled and that the frequency of hot days has nearly tripled over that interval. These changes are the result of a combination of a long-term trend toward higher temperatures and a significant increase in the intrinsic variability of western European daily summer maximum temperatures, particularly in the central region. — HJS

J. Geophys. Res. **112**, D15103 (2007).

IMMUNOLOGY

A Regulatory Trio

Immune responses rely on many regulatory strands that may act independently or cooperatively. Madhav *et al.* provide evidence for the intersection of three prominent regulatory mechanisms in mice that develop in response to tumors. Their study builds on the previous identification of an immune-suppressive dendritic cell (DC) subset present in lymph nodes that drain from tumors. Although the potent tryptophan-degrading enzyme indoleamine 2,3-dioxygenase (IDO) produced by these cells already has its own direct immune-suppressive credentials, it emerged that this source of IDO could rouse local regulatory T cells. These cells also possess their own direct suppressive activity, but in this case provided additional feedback on IDO-expressing DCs to induce the expression of the cell-surface protein PD-L1, which curbed the proliferation of T cells in culture. Blocking PD-L1 with antibodies or growing tumors in IDO-deficient mice interfered with the inhibitory activity exerted by regulatory T cells. This study raises the question of whether equivalent suppressive pathways induced by IDO-producing DCs and linked through the activity of regulatory T cells might also develop in response to tumors in humans. — SJS

J. Clin. Invest. **117**, 10.1172/JCI31911 (2007).

BIOCHEMISTRY

Studying Ions in Depth

Detailed understanding of how particular proteins function in human cells can provide the foundation for pathophysiology-based therapies, but it rarely is feasible to study these proteins directly. Instead, bacterial substitutes are usually more tractable, and the application of homology modeling and site-specific mutagenesis of mammalian proteins can yield useful insights. Forrest *et al.* offer a rigorous example of this approach, starting with a previously published structure of a bacterial amino acid transporter, LeuT, which is representative of transporters that couple the movement of small molecules, such as leucine and serotonin, to the transmembrane Na^+ gradient. From an analysis of a structure-based sequence alignment of LeuT with the serotonin transporter (SERT), they find that the carboxylate of a buried glutamate in LeuT, in which leucine transport is Cl-independent, occupies the same location as a chloride ion (coordinated by a serine) in SERT, which exhibits Cl-stimulated serotonin transport. Changing the serine to a glutamate or aspartate had no effect on the basal transport activity of SERT but fully abrogated the stimulation by Cl^-, and further mutagenesis of other Cl-coordinating residues in other amino acid transporters confirmed the predicted effects on activity. Other modulators of leucine transport by LeuT include the tricyclic antidepressants, as shown by Singh *et al.* (see also Zhou *et al.*, *Science* Express, 9 August 2007) — GJC

Proc. Natl. Acad. Sci. U.S.A. **104**, 12761 (2007); *Nature* **448**, 10.1038/nature06038 (2007).

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