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NEUROSCIENCE, MATHEMATICS

Better math for better brain images

The internal mechanics needed to produce fMRI images—the colorful snapshots of functional brain activity—are largely made up of mathematical algorithms that process a massive stream of data. Ingrid Daubechies et al. explored why some algorithms work better for analyzing fMRI than others. Currently, the most effective results for paradigm-independent separation come from independent component analysis (ICA) algorithms. The authors tested whether these algorithms' emphasis on the independence of the data's components enabled their effectiveness. Comparing 2 commonly used ICA algorithms, the researchers found that InfoMax offered systematically better results than FastICA, but was far less selective for independence. The authors determined that sparsity, or separation in space of the brain patterns, plays a significant role in the effectiveness of the algorithm. To confirm the relative importance of sparsity over independence, the authors tested a third algorithm that had performed well in handling independence, and it performed less well in fMRI experiments. Daubechies et al. show that although InfoMax and FastICA are effective in fMRI studies, more powerful algorithms may need to be designed that emphasize the components' sparsity over independence. — T.H.D.

"Independent component analysis for brain fMRI does not select for independence" by I. Daubechies, E. Roussos, S. Takerkart, M. Benharrosh, C. Golden, K. D'Ardenne, W. Richter, J. D. Cohen, and J. Haxby (see pages 10415–10422)

APPLIED PHYSICAL SCIENCES, BIOPHYSICS AND COMPUTATIONAL BIOLOGY

An ensemble of protein structures

An increasing number of protein structural models in the publicly available Protein Data Bank (PDB) has led to a number of redundant submissions that present a snapshot of an enzyme or transcription factor at a particular conformational state. Prasad Burra et al. studied multiple models of identical proteins in the PDB and derived the proteins' conformational states by clustering models with low root-mean-square deviations. The number of nonredundant pairs used in their analysis was >220,000, and the proteins ranged in size from <100 amino acids to ≈1,500 residues. The authors found that nearly all proteins have regions of high rigidity, where the structure varies little from model to model, and of high mobility, where fluidity and flexibility dominate. The extent of local flexibility typically correlated with the functional class of the protein. Proteins that act like motors or transduce signals, for example, had a higher number of conformational states than enzymes or binding proteins. These results suggest that no single protein model can accurately represent the ensemble of conformations a protein can adopt, which belies the commonly held view that a protein's structure can be determined from its amino acid sequence, according to the authors. — F.A.

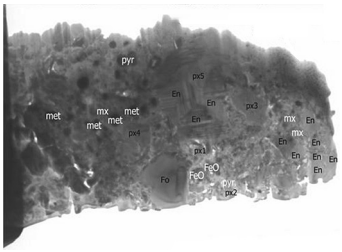
Variability in a protein's conformational state.

"Global distribution of conformational states derived from redundant models in the PDB points to non-uniqueness of the protein structure" by Prasad V. Burra, Ying Zhang, Adam Godzik, and Boguslaw Stec (see pages 10505–10510)

ASTRONOMY

Clues to the solar system

Isheyevo, an iron-rich chondrite that likely formed within the first million years of our solar system, contains a xenolith with pristine mineralogy similar to interplanetary dust particles. Giacomo Briani et al. found that the xenolith PX-18 contains a wide continuum of nitrogen isotopic variation, from very light to some of the heaviest ratios recorded from solar system material. The authors measured isotope ratios of hydrogen, car-



Micrograph of PX-18 in the Isheyevo chondrite.

bon, and nitrogen and report that neither hydrogen nor carbon isotope ratios showed large deviations from terrestrial reference samples. However, PX-18 contains diffuse areas of 15N concentrations twice that found on Earth, and localized anomalies with 15N concentrations >5 times higher. Areas of very low 15N concentrations are also present in PX-18, indicating that parts of the xenolith may be remnants of the early solar system. The authors suggest that PX-18 may have originated in the Kuiper Belt or elsewhere in the outer solar system, and that its mineralogy may include organic material, which could be used to help researchers study the origin of the solar system. — C.A.

"Pristine extraterrestrial material with unprecedented nitrogen isotopic variation" by Giacomo Briani, Matthieu Gounelle, Yves Marrocchi, Smail Mostefaoui, Hugues Leroux, Eric Quirico, and Anders Meibom (see pages 10522–10527)

ENGINEERING

Why concrete creeps

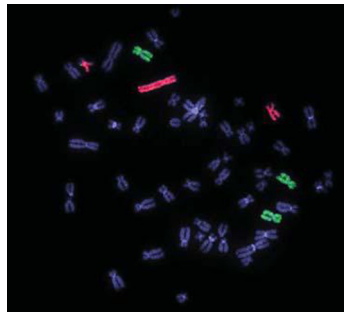
Despite concrete's status as one of the world's most ubiquitous construction materials, the nanoscale origins of its gradual deformation, or "creep," remain unclear. Over time, load-bearing concrete—a mixture of Portland cement, water, sand, and aggregates—frequently suffers from deformities that can lower a structure's durability and lifespan. Matthieu Vandamme and Franz-Josef Ulm found that the calcium–silicate–hydrate (C–S–H) building blocks of concrete exhibit a logarithmic deterioration that depends on the density of C–S–H packing. The authors devised a statistical nanoindentation technique that revealed the mechanical properties of 9 types of concrete. Most creep occurs because of C–S–H nanoparticle sliding that follows the free-volume dynamics theory of granular physics. The authors found that concrete with high and ultra-high densities of C–S–H showed reduced creep over a long-term extrapolation compared to low-density C–S–H concrete. Although higher-density concrete has a greater initial cost, the authors suggest that it might be cost effective over time due to its reduced creep and increased lifespan. — C.A.

"Nanogranular origin of concrete creep" by Matthieu Vandamme and Franz-Josef Ulm (see pages 10552–10557)

BIOCHEMISTRY

Induced chromosomal translocations

Recurrent chromosomal translocations form an important tumorigenic step in hematologic cancers, sarcomas, and prostate cancer. Contemporaneous DNA double-stranded breaks on heterologous chromosomes likely initiate this process, followed by a nonhomologous end-joining pathway to bring the ends together. Erika Brunet et al. induced and recovered translocations in a test cell line, the human embryonic kidney cell line 293, using a quantitative PCR screen for translocation breakpoint junctions. The screen used a 96-well, high-throughput nested PCR, followed by a calculation of translocation frequency. The authors extended this approach to pluripotent human embryonic stem cells and multipotent human mesenchymal cells, the latter being a precursor for many sarcoma types. Although readily recovered, translocation breakpoint junctions were less likely to repair a single chromosome break than nonhomologous end joining or homologous gene targeting. As found in patients with chromosomal translocations, the breakpoint junctions showed small, frequent DNA deletions. These results may allow researchers to target specific tumorigenic translocations to understand the resultant disease, according to the authors. — C.A.



Chromosome 6 (green) in TOS4A cells.

"Chromosomal translocations induced at specified loci in human stem cells" by Erika Brunet, Deniz Simsek, Mark Tomishima, Russell DeKelver, Vivian M. Choi, Philip Gregory, Fyodor Urnov, David M. Weinstock, and Maria Jasin (see pages 10620–10625)

BIOPHYSICS AND COMPUTATIONAL BIOLOGY

Controlling gene expression

Phloretin, a plant-based antimicrobial compound, may be incorporated into a skin lotion capable of providing a transdermal gene therapy treatment. Marc Gitzinger et al. used the phloretin-triggered TtgR operon to engineer a genetic system that allows for adjustable and reversible gene expression in gene therapies. The authors cotransfected Chinese hamster ovary (CHO) cells with 2 chimeric viral constructs: a fusion of the TtgR operator and the human cytomegalovirus immediate early promoter, and a fusion of TtgR to the herpesvirus-derived transactivation domain. The addition of phloretin to the CHO cells reduced expression of the marker protein SEAP in a dose-dependent manner. Further tests revealed similar results in other immortalized mammalian cell lines and in human fibroblasts and keratinocytes. The authors microencapsulated the cotransfected CHO cells and inserted them subcutaneously in mice. Application of a petroleum jelly-based lotion containing different concentrations of phloretin controlled how much SEAP the inserts produced. The rapid degradation of phloretin in the body, combined with its safety, may make it a good candidate for adjusting and reversing gene expression in gene therapies, according to the authors. — C.A.

"Controlling transgene expression in subcutaneous implants using a skin lotion containing the apple metabolite phloretin" by Marc Gitzinger, Christian Kemmer, Marie Daoud El-Baba, Wilfried Weber, and Martin Fussenegger (see pages 10638–10643)

ECOLOGY

Fire mitigation treatments need better planning

Only 11% of National Fire Plan treatments are implemented near where people live and work, researchers have found. The result suggests that federal efforts are likely not effectively mitigating the threat of wildfire to homes and people in the western United States. Tania Schoennagel et al. examined 44,000 fuels treatments (a type of controlled burning or forest thinning effort) applied between 2004 and 2008 and found that most of the treated areas were in forests and wildlands far from humans. The risk from forest fires is increasing due to expansion of humans into new, unprotected wildlands, warmer and drier summers, flammable invasive species, and the inability to prevent fires in at-risk lands not under federal control. Fire mitigation far from houses may have only small benefits, and is most effective near the wildland–urban interface. The authors suggest that better home construction, development planning, and cooperation and cost-sharing between government and private entities are the best ways to limit fire risks. — P.D.

Smoke plume over Boulder, CO, from the 2003 Overland fire. Image courtesy of Kevin League.

"Implementation of National Fire Plan treatments near the wildland–urban interface in the western United States" by Tania Schoennagel, Cara R. Nelson, David M. Theobald, Gunnar C. Carnwath, and Teresa B. Chapman (see pages 10706–10711)

ENVIRONMENTAL SCIENCES

Exiting the poverty trap

Researchers report on a Chinese government program that may help decrease poverty while increasing environmental sustainability. The technique shows that financial incentives could allow people to escape the cycle of environmental degradation and poverty known as the "poverty trap." Shixiong Cao et al. spent ≈$1.4 million (USD) in Chinese government funding to promote sustainable development in China's Fujian province. The authors worked with farmers in Changting County, which has been severely deforested and had erosion and biodiversity problems. The farmers received subsidies that compensated them for preserving trees and promoting ecosystem restoration by using coal instead of wood as fuel, developing methane generation, using organic fertilizer, planting fruit trees, and raising pigs and fish. After 8 years, the environment and socioeconomic conditions have improved more than in comparable towns, resulting in more biodiversity, vegetation, employment, and income. The authors say that when these subsidies end, the farmers should be able to continue using the infrastructure and industry they have developed and not revert to destructive practices. The study shows how effective conservation policies that protect the livelihood of affected populations can potentially reduce poverty and preserve ecosystems, according to the authors. — P.D.

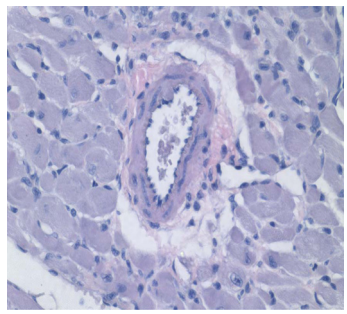
Government-paid farmers performing environmental restoration work.

"Development and testing of a sustainable environmental restoration policy on eradicating the poverty trap in China's Changting County" by Shixiong Cao, Binglin Zhong, Hui Yue, Heshui Zeng, and Jinhua Zeng (see pages 10712–10716)

IMMUNOLOGY

A step toward an alternative to immunosuppression

When organs are transplanted, immunosuppression is necessary to prevent the body from rejecting the foreign tissue, but lowering the body's defenses weakens its ability to fight against pathogens. Costimulation blockade is an emerging alternative to immunosuppression: antibodies or fusion proteins are used to prevent costimulatory interactions between T cell and antigen-presenting cells. However, costimulation blockade has proven ineffective in preventing organ rejection in many transplantation models that are physiologically relevant to humans. Xueli Yuan et al. introduce another option that may restore the power of costimulation blockade. The authors worked with transcription factor T-bet knockout mice, which prevented differentiation into Th1 helper T cells. In cases where Th1 cells are weakened—as happens with immunosuppression—an amplified alloimmune response is driven by the cytokine IL-17. Blocking the interaction of Tim-1 with its ligand inhibited the secretion of IL-17 by T17 cells. T-bet knockout mice rejected transplanted organs faster than wild-type. The authors show that costimulation blockade is ineffective in T-bet knockouts unless blocking of Tim-1 is applied in parallel. A similar approach may help human patients, the authors say. — K.M.



Cardiac allograft in a knockout mouse treated with Tim-1.

"Targeting Tim-1 to overcome resistance to transplantation tolerance mediated by CD8 T17 cells" by Xueli Yuan, M. Javeed Ansari, Francesca D'Addio, Jesus Paez-Cortez, Isabella Schmitt, Michela Donnarumma, Olaf Boenisch, Xiaozhi Zhao, Joyce Popoola, Michael R. Clarkson, Hideo Yagita, Hisaya Akiba, Gordon J. Freeman, John Iacomini, Laurence A. Turka, Laurie H. Glimcher, and Mohamed H. Sayegh (see pages 10734–10739)