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COMPUTATIONAL BIOLOGY



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COVER

A series of spheres with two-dimensional patterns generated by computer simulation shows that Turing's reaction-diffusion model may be the basis for skin patterning in animals. A modulation of one parameter value in a reaction-diffusion-based model causes the pattern to change gradually from spots to labyrinths, with the range encompassing the diversity of patterns seen on animal skin. See page 171 and http://scim.ag/comp_bio.

Image: Seita Miyazawa, Osaka University

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Mercury's outer solid shell is denser than expected, suggesting a deep reservoir of high-density material, possibly iron-sulfide.

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Mercury's topography indicates sustained geophysical activity for most of the planet's geological history.

>> Perspective p. 162

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- A Memory Retrieval-Extinction Procedure to Prevent Drug Craving and Relapse *Y.-X. Xue* et al.
 A behavioral intervention that decreases drug seeking in rat models of relapse can decrease drug craving in heroin addicts.

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EDITORS'CHOICE

EDITED BY KRISTEN MUELLER AND JAKE YESTON

Thorn in TB's Side?

Multidrug-resistant tuberculosis (TB) is increasing in prevalence worldwide and is a particular problem for the poor, the malnourished, and the immunocompromised. Despite the global and uncontrolled epidemic of tuberculosis, relatively few pathogenic mechanisms are understood for the causative cobacterial pathogenic systems are the ESX-1 protein secretion system and the waxy cell wall that protects the bacteria within the host. Joshi *et al.* describe EccA1, an ATPase protein whose gene is located at the periphery The EccA1 protein was found to interact with key enzymes required for the synthesis of mycolic acids, the lipids central to the waxy cell envelope. ing with EccA1 ATPase function caused mycobacterial cells to become more Chem. Biol. 19, 372 (2012).

PHYSICS **Heat in Hiding?**

Control over the propagation of electromagnetic radiation has been revolutionized by the discovery and development of transformation optics. Theoretical and experimental work has shown that the coordinate system of Maxwell's equations that governs how light propagates through a material can be manipulated at will by the careful design of metamaterial structures-giving rise to invisibility cloaks and perfect lenses. Guenneau et al. now show that such transformation principles could also be applicable to heat, whereby the coordinate system of the diffusion equation can be manipulated to control the flow of heat through a particular region. Numerical simulations support the design of fairly simple structures that may function as thermal cloaks or thermal concentrators. If realized, such structures could find use in thermal management systems for microelectronic circuits or stealth applications where hot objects can be hidden from view. - ISO

Opt. Express 20, 8207 (2012).

BIOPHYSICS

A Protein's Magnetic Personality

Cryptochromes, identified in plants as bluelight photoreceptors, may have yet another function to add to their résumé. The proteins are known to help regulate circadian rhythm and development and are found in plants,

link cryptochromes to bacterial DNA photolyases. Maeda et al. have now analyzed how redox signaling through the cofactor flavin adenine dinucleotide (FAD) can make these proteins function as magnetoreceptors. Studying a cryptochrome from Arabidopsis and a DNA photolyase from Escherichia coli, the authors spectroscopically measured microsecond radical-pair kinetics. In response to light, electron transfer from tryptophan residues generates a FAD radical anion. Imposition of a 28-mT magnetic field promoted back electron transfer (presumably by influencing spin state interconversion rates), with a consequent drop in conversion of the initial radical pair to a longer-lived intermediate via tryptophan deprotonation. Effects were apparent in magnetic fields as low as 1 mT. Although this is somewhat stronger than Earth's magnetic field, these particular Arabidopsis and E. coli proteins are not normally known for perceiving magnetic fields. The authors speculate about how cryptochrome proteins would need to be tethered and immobilized to function more efficiently as magnetic compasses in birds. — P]H

insects, and animals. Sequence similarities also

Proc. Natl. Acad. Sci. U.S.A. 109, 4774 (2012).

EDUCATION

Getting the Question Right

An inquiry-based science curriculum requires teachers to generate scientific guestions for their students. Are students studying to be teachers (preservice teachers) learning this skill?

> Graves and Rutherford examined the ability of elementary preservice teachers to generate a testable question from earth science data available online. One group was given ISTOCKPHOTO.CO instruction on what constitutes a testable guestion, and the other was referred to a conclusion rubric in a AND PREVENTION; (BOTTOM) laboratory manual. Generated questions were categorized as testable or nontestable, and testable questions were analyzed using

a rubric designed to evaluate the preservice b identify variables, state meters, and identify relation-riables. The majority of preser-b both groups wrote questions b but still needed modification, be instruction given to the t improve the quality of their ver, it highlights the need to be teachers with more oppor-ence the nature of science by esearch. — MM J. Coll. Sci. Teach. **41**, 46 (2012). teacher's ability to identify variables, state investigative parameters, and identify relationships between variables. The majority of preservice teachers from both groups wrote questions that were testable but still needed modification, suggesting that the instruction given to the test group did not improve the quality of their questions. Moreover, it highlights the need to provide preservice teachers with more opportunities to experience the nature of science by participating in research. - MM

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IMMUNOLOGY

Sorting Out Toll in Flies

Seminal studies of the Toll pathway in Drosophila led to the discovery of Toll-like receptors (TLRs) in mammals and paved the way toward our current understanding of innate immune signaling. In mammals, pairs of adapter proteins couple to TLRs to activate downstream signaling. In particular, a "sorting" adapter (either TIRAP or TRAM) helps to localize TLRs to a region of the cell that promotes signaling. Once sorted, a "signaling" adapter (either MyD88 or TRIF) then binds and initiates downstream signaling that culminates in changes in gene expression. Surprisingly, however, homologs for the sorting adapters have not been found in flies, and the MyD88 homolog in flies (dMyD88) does not appear to act as a signaling adapter. Marek and Kagan investigated the innate signaling mechanisms in Drosophila and

found that dMyD88 instead functions as a sorting adapter and recruits Tube, which functions as a signaling adapter. Similar to mammalian cells, the sorting ability of dMyD88 was dependent on a C-terminal phosphoinositidebinding domain. Flies that expressed dMyD88 lacking this domain exhibited impaired immune defense, and other insect species expressed phosphoinositide-binding dMyD88 homologs, demonstrating the important role of this signaling module in immune defense. — KLM Immunity 36, 10.1016/

j.immuni.2012.01.019 (2012).

PLANT SCIENCES

Splicing Shifts

Alternative splicing, which affects about 40% of intron-containing genes in *Arabidopsis*, is a mechanism whereby mRNA transcripts are adjusted in ways that affect the function or stability of the mRNA or the structure of the translated protein. The circadian clock is also an important regulator of many genes in the plant genome. James *et al.* have now analyzed the intersection of these two complex phenomena, and discovered even more complexity. Although the period of the *Arabidopsis* circadian clock is rather stable over a range of temperatures, the clock does respond to temperature: Low

temperatures can cause a stall, and temperature cycles can entrain the clock. The authors analyzed the handful of core clock genes and found extensive alternative splicing among these transcripts. The splicing events changed in response to temperature, often in surprising ways. For example, transcripts encoding proteins thought to have redundant functions showed divergent splicing patterns in response to temperature shifts. Thus, models of circadian clock function should incorporate the added complexity of alternative mRNA splice variants that are modulated by temperature shifts and acclimations. — PJH

Plant Cell 24, 10.1105/tpc.111.093948 (2012).

ECOLOGY

Climate Model Comparisons

Predicting the effects of climate change on the future distributions of species is an inherently uncertain exercise. There are

uncertainties in climate models themselves and also in the models of species' response to climate change. To address this problem, Cheaib et al. compared the predictions of eight different species' response models for five dominant tree species in the flora of France, representative of the range of forest communities from Mediterranean in the south to

more temperate in the north.

For the two evergreen species considered, there was generally good agreement between models. Holm oak, the dominant Mediterranean species, substantially increases its range under all model scenarios; the range of Scots pine, a species of cooler and mountainous regions, was predicted to contract under most models. However, models agreed relatively poorly in their predictions of range shifts of three temperate broad-leaved deciduous species. A principal source of uncertainty is the current limits to understanding the effects of increasing CO₂ concentrations on the physiology of these species. Such comparisons not only help foresters and conservation managers judge the probability of success (or otherwise) of management alternatives, but also help to focus future research on the areas of greatest uncertainty — AMS

Ecol. Lett. **15**, 10.1111/ j.1461-0248.2012.01764.x (2012).

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LIND

CHRISTIAN R.

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