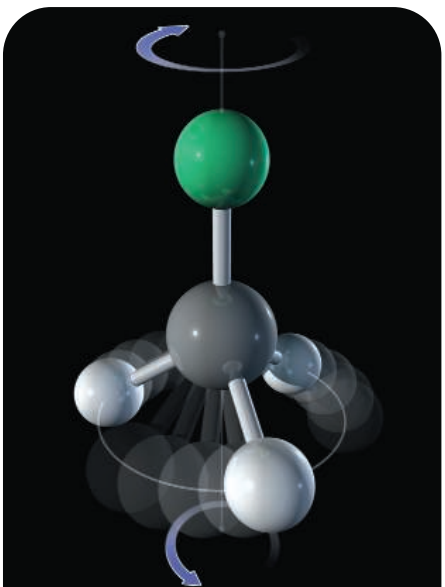


CHEMISTRY

Spinning in Place

Unlike macroscopic objects, molecules vibrate and rotate in discrete increments. To uncover the underlying quantum-mechanical restrictions governing such behavior, spectroscopists induce specific patterns of motion through light absorption. Thus, the molecules under study must be free to move about, but unless they are to some degree restricted, the flurry of different movements can be hard to disentangle. A promising compromise is the use of *para* hydrogen (p-H_2) matrices. When p-H_2 (H_2 with oppositely oriented nuclear spins) is cooled to low temperature, it forms an unusual medium, termed a quantum solid, in which the nuclei delocalize in space. Consequently, guest molecules embedded in a matrix of this solid retain a certain amount of flexibility. Lee *et al.* show through infrared absorption spectroscopy that CH_3F molecules can rotate about the C-F axis in such a matrix, but are restricted from tumbling in orthogonal directions. The study bolsters the utility of p-H_2 matrices for precise spectral characterization of small molecules. — JSY

J. Chem. Phys. **129**, 104502 (2008).

*Helen Pickersgill is a locum editor in *Science*'s editorial department.

MICROBIOLOGY

Adapting to Drug Resistance

Developing a new therapy for drug-resistant infections is an expensive and arduous process that may give relief for less time that it takes to develop the agent. Hence, delaying the onset of resistance by administering drugs in combination is a currently favored strategy, but two groups show this may not be quite so simple to implement wisely. By experimentation and modeling, Hegreness *et al.* made the counterintuitive discovery that synergistically acting drug pairs, such as doxycycline and erythromycin, may actually accelerate the evolution of resistance. In fact, antagonistic drug pairs are more effective at forestalling resistance emergence because as one drug becomes ineffective, its suppressive effect on the other diminishes and unmasks the potency of the second drug. Of course, the precise outcome depends on the drug ratios, doses, pharmacokinetics, and modes of action.

Developing policies for the implementation of drug combinations requires population modeling. Boni *et al.* compared the consequences of the standard wait-and-switch global deployment of drugs for malaria control with the simultaneous deployment of multiple drugs. Their model shows that if three different drugs are offered for use at the same time within a malarious population, the clinical burden is reduced, the emergence of resistance is delayed by two- to fourfold, and the number of failed treatments is almost halved. — CA

Proc. Natl. Acad. Sci. U.S.A. **105**, 13977, 14216 (2008).

DEVELOPMENT

Signal Stability

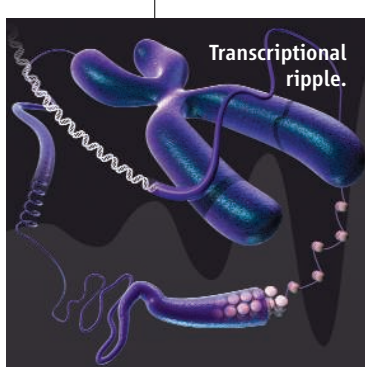
Chordin and BMP signaling develop opposing trends across the *Xenopus* embryo, defining between them the axis from dorsal to ventral and destinations in between. The interactions between these and other factors involve complex regulatory interactions, including both negative and positive feedback loops. Although predictions from some combinations of the known regulatory loops might suggest that axis establishment is rather tenuous, instead, observations of real embryos indicate that dorsal-ventral axis establishment in *Xenopus* is robust to perturbation. Inomata *et al.* identify the protein ONT1 as a stabilizing factor in the signaling networks defining the dorsal-ventral axis. The protein is expressed first in late blastula stages and is generally found in the more dorsal regions as the embryo develops; diminished ONT1 function results in dorsalization of the embryo. ONT1 binds to chordin and also to a protease known to degrade chordin, and seems to function as a scaffold enticing chordin to its demise. The biphasic outcome of this interaction ensures that enough, but not too much, chordin survives to define the developing dorsal axis. — PJH

Cell **134**, 854 (2008).

CELL BIOLOGY

Transcription Without Borders

In bacteria, genes encoding functionally related proteins are often grouped into coordinately regulated modules, one notable instance being the lactose operon. In mammals, the regulation of gene expression is thought to be controlled on an individual basis, such that specific proteins or RNAs bind to the regulatory elements of a single gene and activate or repress its transcription directly.



Using growth factors to induce transcription of immediate early genes (IEGs) in mammalian cells, Ebisuya *et al.* find that a gene that is being transcribed can incidentally activate the transcription of neighboring genes, enabling the coordinated expression of clusters of genes. Activation occurred via a ripple, which traveled both upstream and downstream from the IEG, and also passed through intergenic (non–protein coding) chromatin, resulting in the transcription of noncoding RNAs. Although protein-coding genes account for only 1.5% of the human genome, more than 70% of the DNA is

CREDITS (TOP TO BOTTOM): CHRIS BICKEL/*SCIENCE*

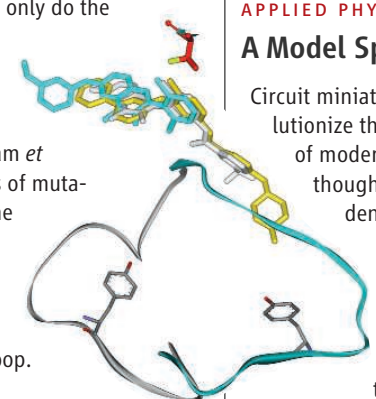
transcribed. These results provide a potential explanation for this pervasive transcription, which may serve to propagate transcriptional activation into neighboring genes. — HP*

Nat. Cell Biol. **10**, 1106 (2008).

BIOCHEMISTRY

Breaking the Back of BCR-ABL

One of the advances in the war on cancer has been the development of small molecules that target protein tyrosine kinases; one such drug, imatinib, is used to inhibit the BCR-ABL kinase in the treatment of chronic myelogenous leukemia. Nevertheless, elation has been tempered by the realization that resistance to imatinib can arise via mutation of a gatekeeper amino acid (threonine 315) to the bulkier and more hydrophobic isoleucine, which hinders access of the drug to its binding site. Similar resistance-mediating mutations have been observed for other drug–tyrosine kinase pairs in solid tumors. Not only do the mutations block drug binding, but they also tilt the kinase structure toward constitutively active conformations. Azam *et al.* have analyzed a series of mutations in a series of tyrosine kinases and find that the critical threonine sits atop a spine of hydrophobic residues linked to the activation loop. Replacing the threonine with isoleucine stabilizes and stiffens the spine and also enhances the coordination of ATP, thereby stimulating kinase activity. They used this insight to refine the inhibitor PD166326 into a candidate drug called compound 14, which packs neatly against the disrupted spine and inhibits the BCR-ABL variant T315I at 0.6 μM versus the lack of effect of PD166326 at 10 μM. — GJC



Interaction of PD166326 (blue), imatinib (yellow), and compound 14 (gray) with the activation loop (blue, gray) and the gatekeeper threonine (red).

CREDIT: AZAM *ET AL.*, *NAT. STRUCT. MOL. BIOL.* **15**, 10.1038/NSMB.1486 (2008)

Nat. Struct. Mol. Biol. **15**, 10.1038/nsmb.1486 (2008).

EVOLUTION

Neutral Plantings

The transcriptome of an organism encompasses all of its gene transcripts at a specific time and changes with the individual's environment and developmental stage. These changes either could be guided by adaptive selection or, like the neutral theory of gene evolution, may result from random events not under selection. Taking advantage of the genomic database of the plant *Arabidopsis*, Broadley *et al.* examined more than 18,000 gene transcripts in leaves of 14 taxa from the cabbage family. They found differences in the expression of a gene among taxa, suggesting that there was plasticity in expression in the most recent common ancestor or that the founder effect of a small population may have resulted in differential changes in gene expression among descendant taxa, but that the changes observed do not reflect functional adaptation. These findings show that appropriate null models are required when comparing transcriptomes in both time and space, and that modeling of transcriptome networks should take evolutionary effects into account. — LMZ

New Phytol. **180**, 10.1111/j.1469-8137.2008.02640.x (2008).

APPLIED PHYSICS

A Model Spin Amplifier

Circuit miniaturization has continued to revolutionize the speed and diverse capabilities of modern electronic systems. At present, though, the increase in device-packing density onto microelectronics chips and the associated problem of managing heat dissipation is becoming an issue in limiting performance. Using the spin of the electrons in place of traditional charge flow is therefore being explored as a possible route to circumvent that performance roadblock. The transistor is the present building block of microelectronics. However, the equivalent spin amplifier, or spin transistor, would require a room-temperature magnetic semiconductor. Because all the true magnetic semiconductors to date have been limited to cryogenic temperatures, the prospect of developing a practical spin transistor seems some way off. Breaking the process down into three stages—spin detection, signal amplification, and spin filtering of that amplified signal—Acremann *et al.* suggest an alternative method that may provide a spin amplifier using a sequence of electrical and magnetic field pulses to manipulate the magnetization of a patterned ferromagnetic layer. Such an engineered spin amplifier using presently available materials may bring forward the development of spintronics, and with it the additional functionality of having sensing, memory storage, and logical operation in a single device. — ISO

Appl. Phys. Lett. **93**, 102513 (2008).

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EVOLUTION: Neutral Plantings

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