pendences. Telling them apart requires repeating the measurement for many values of the pump–probe delay τ. That limits the size of the area the researchers can image during the time they have access to a painting. They're working on improving their detection sensitivity to make measurements more quickly.

So far, Warren and colleagues haven't revealed anything about *The Crucifixion*, or any other painting, that isn't already known. Their focus has been on validating their method by comparing their images with those obtained by the scalpel method. But potential applications abound. Conservators are reluctant to take their scalpels to pristine regions of historic paintings, so their work has been concentrated on the paint adjacent to existing cracks. Pump–probe microscopy, having no such limitation, offers the freedom to look beneath the surface over a painting's entire area.

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A fruit-fly gene network may be tuned to a critical point

Precise measurements of fluctuations and correlations in gene expression levels reveal some striking behavior.

Every cell in a multicellular organism has the same DNA; cells in different organs acquire their different forms and functions by using different subsets of that DNA. It's largely a mystery how an organism conveys to its constituent cells where they are in the body, and therefore which of their genes should be active, but some pieces of the puzzle are known.

For example, in developing fruit-fly embryos, a network of so-called gap genes is involved in telling cells where they're positioned between the head and the tail. Each of the four main gap genes, first described[1] in 1980, gets its name from the consequences for a fly in which the gene is mutated: giant (Gt), hunchback (Hb), knirps (Kni, German for little person), and Krüppel (Kr, German for cripple). At a brief, specific point in development, when the embryo consists of some 6000 cells, the proteins expressed by the genes form a characteristic spatial distribution that goes on to influence larger networks of genes that govern the fruit-fly body structure. The gap genes are known to be mutually repressive: High levels of the protein encoded by one inhibit the expression of the others. But the quantitative details of those interactions, and how they create the distinctive protein pattern, are unknown. Different interaction strengths with different functional forms create a many-dimensional parameter space of possibilities.

Now Princeton University theorists William Bialek and Dmitry Krotov argue that the gap-gene network may be operating at a critical point: a division in parameter space between regimes of qualitatively different behavior.[2] To reach that conclusion, they used experimental data collected by their colleagues Thomas Gregor and Julien Dubuis.[3]

Effective potentials

A network of two genes, A and B, has a two-dimensional space of outputs, (g_A, g_B), where g is the concentration of the protein expressed by each gene. The output as a function of time depends on the rates of production and degradation of each protein, which in turn depend on a multitude of other factors, including the interaction between the genes. If the genes interact only weakly, the system has a single steady-state output: When, as often happens in real organisms, the system experiences a perturbation that pushes the protein concentrations away from their steady-state values, it responds with an effective "restoring force" back toward the steady state—much like a particle in a damped harmonic potential, as shown in figure 1. (Real gene-network dynamics aren't necessarily captured by an effective potential, but many aspects of the network behavior can be qualitatively understood in those terms.)

When genes A and B are strongly mutually repressive, the system enters a bistable regime with two steady-state outputs: one in which A is expressed and B is suppressed, and one in which A is suppressed and B is expressed. To

switch from one steady-state output to the other, the system must surmount a barrier, characterized by a saddle point on the effective potential surface.

At some intermediate interaction strength, therefore, there must exist a boundary between the monostable and bistable regimes. At that boundary, or critical point, the single potential minimum is on the verge of turning into a saddle point, and the potential surface features a single elongated, flat-bottomed well.

Criticality manifests in several ways. One of them is a strong anticorrelation between fluctuations in g_A and g_B. The system is, more or less, equally likely to be found anywhere at the bottom of the potential well—and less likely to be found outside it—so an increase in g_A is likely to result in a decrease in g_B.

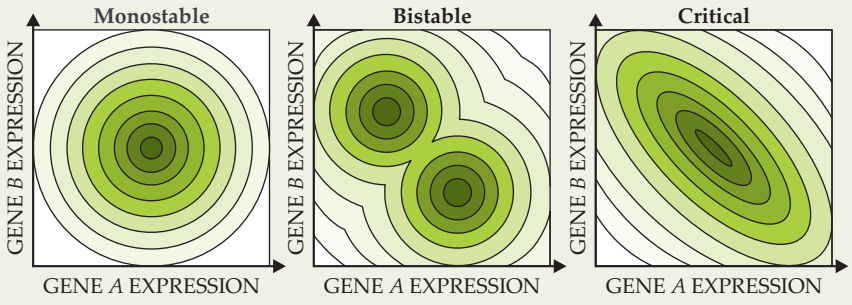


Figure 1. Effective potential-energy surfaces can qualitatively explain many aspects of the dynamics of a two-gene network. Here, darker shading represents lower potential energy. When the two genes interact only weakly, the system is monostable, with a single energy minimum. When the genes are strongly mutually repressive, the system becomes bistable, with two energy minima separated by a saddle point. At the boundary between the monostable and bistable regimes is a critical point, with a single elongated, flat-bottomed energy well.

Precision measurements

Until recently, measuring correlations in gene expression fluctuations was impossible. The standard method for measuring gene expression profiles is immunofluorescence: staining a dead tissue sample with a fluorescent antibody that attaches to the protein of interest. Staining a single sample for more than one protein was a challenge, because the antibodies could interfere with each other chemically and because their fluorescence spectra could overlap. And accurate comparisons of protein levels between different specimens were precluded by various sources of systematic error. In the case of the fruit-fly gap genes, two embryos at even slightly different points in their development would have such different expression levels that they'd be impossible to compare.

Gregor and Dubuis developed the first set of fluorescent antibodies to the four main gap genes that could all be used simultaneously. And they developed a new way of measuring the time of embryonic development to within one to two minutes. As a result, they can now measure protein levels, fluctuations, and correlations to within a few percent.[3]

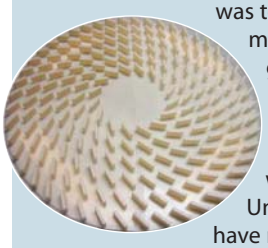
Bialek and his colleagues were initially interested in analyzing those measurements to quantify the information conveyed by the gap genes about each cell's physical position.[4] But gradually they realized that they could also learn something about the structure of the gene network itself.

The gap-gene network has four genes, not two, so the simple two-gene picture is of limited use. But there are several regions in the expression profile—shaded

physics update

These items, with supplementary material, first appeared at http://www.physicstoday.org.

Metamaterials twist sound. In 2006 John Pendry of Imperial College London and his coworkers tackled a problem straight out of *Star Trek*—electromagnetic cloaking, the deflection of waves around an object to render it invisible. Within five months, they had a working device, at least for microwaves (see PHYSICS TODAY, February 2007, page 19). The trick was to design artificial structures known as metamaterials and configure them in a given region of space such that their electric permittivity and magnetic permeability produced the optimal refractive-index profile to deflect the waves. Jian-chun Cheng (Nanjing University in China) and his colleagues have now demonstrated that the same principles can be used to manipulate sound waves. The Nanjing metamaterials, though, produce variations not in electric and magnetic properties of the propagation medium but in mass density. As proof of concept, they built a device that rotates an incident broadband acoustic field by an arbitrary angle, so that the waves inside it appear to propagate from a different direction. The device, shown here, consists of nested rings, each composed of numerous plastic rectangles a centimeter tall, that are sandwiched between two plexiglass plates; the rectangles are oriented at angles that produce the position-dependent mass density needed to rotate the incident field. The researchers' measurements of the acoustic pressure throughout the device's interior closely matched their simulations. They expect that their approach to controlling acoustic waves will find application in medical ultrasound imaging. (X. Jiang et al., *Appl. Phys. Lett.*, in press.) —RMW



To catch a solar neutrino, search at night. A neutrino is created or detected in one of three flavor states named after the electron, muon, and tau particles. But those are not the stationary states of well-defined mass. As a result, an electron neutrino leaving the Sun and headed toward Earth, for example, could change flavor on the way and avoid notice by electron-neutrino detectors. That phenomenon—vacuum neutrino oscillation—has been confirmed in numerous experiments and was a key to understanding one of the great mysteries of 20th-century physics: Why do we observe so many fewer solar electron neutrinos than we expect based on reliable models of neutrino production in the Sun's core? But vacuum neutrino oscillation alone is not enough to solve the solar-neutrino problem. The second important ingredient leading to neutrino metamorphosis arises because electron neutrinos traveling from the Sun's core to its surface interact more strongly with solar matter than do other flavors. The

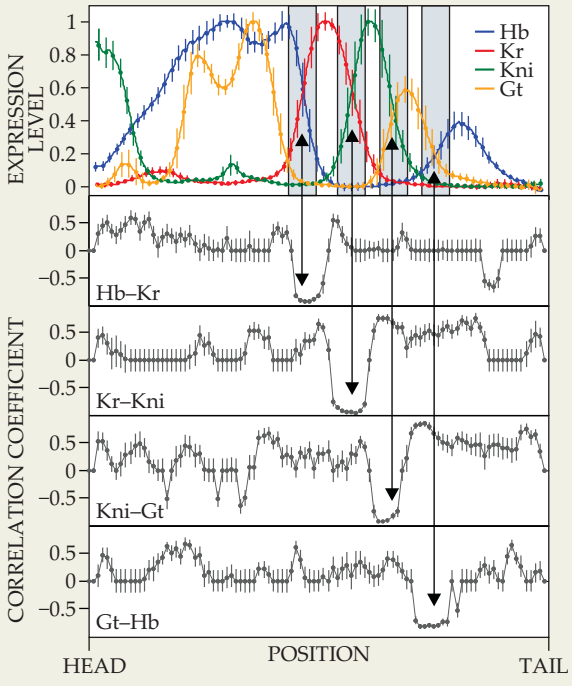


Figure 2. Four main gap genes—giant (Gt), hunchback (Hb), knirps (Kni), and Krüppel (Kr)—create a characteristic expression pattern in developing fruit-fly embryos. In each of the four shaded regions in the top panel, the two active genes exhibit strong anticorrelations, one sign of a network tuned to a critical point. (Adapted from ref. 2.)

in the top panel of figure 2—where just two of the genes have significant expression levels, and the network dynamics are simplified. "Even so," explains Bialek, "one has to make some perhaps arbitrary choices about the kinds of models one wants to consider." He and Krotov looked at several possibilities and found that in each case, the model parameters that best fit the data were close to a critical point. "Although we started with specific models, we realized that we could say things in a much more general language. We'll probably get back to the detailed models at some point."

Strong local anticorrelations are a universal feature of a two-gene network at criticality, and indeed, in each of the shaded regions of figure 2, the correlation coefficient between the two active genes approaches −1. Bialek and Krotov identified several other signatures of a two-gene network tuned to a critical point—including slow dynamics, long-range spatial correlations, and non-Gaussian distributions of fluctuations—and found that the gap-gene network exhibits all of them.

Still, they don't regard their observations as airtight proof that the network is operating at a critical point, because each of the signatures could also arise in other ways. And the implications of criticality (or of a network that mimics one at criticality) are still far from clear. Critical points constitute a small and distinctive region of parameter space, and the odds that a genetic network would find itself near a critical point by chance, from network parameters chosen at random, are small. Then again, life itself occupies a small and distinctive region of parameter space: As Bialek explains, "Most of the ways we can imagine putting molecules in a small box together don't result in the system organizing itself and walking out of the lab." Looking further into the question of how and why evolution would guide a system toward critical behavior could, he argues, lead to new insights into what is so special about life. "We take some stabs at this question," he says, "but we're still very much in the dark."

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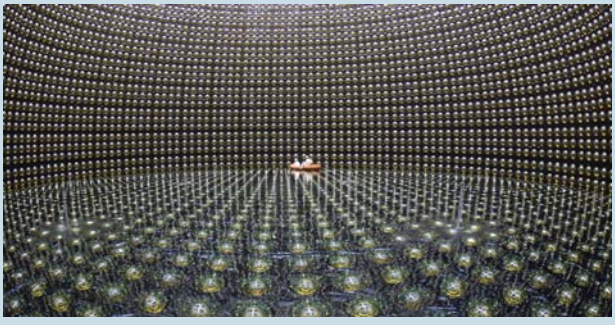

effect of matter on neutrino identity has now been directly observed by the enormous Super-Kamiokande neutrino detector in Japan (see the figure). The Super-K experiment is conceptually simple: Experimenters compare the flux of solar electron neutrinos observed during the day and night. The neutrinos detected after sunset must have passed through Earth to reach the detector, so a day–night flux differential confirms flavor changes induced via matter interactions. The 3% enhancement in electron-neutrino flux observed during the evening hours—a 2.7-sigma effect—is in accord with theoretical expectations based on well-established vacuum-oscillation parameters. (A. Renshaw et al., Super-Kamiokande collaboration, *Phys. Rev. Lett.* **112**, 091805, 2014; figure courtesy of Super-Kamiokande.) —SKB

Mimicking microcapillaries. Thanks to microscopes and high-speed video cameras, it's possible to follow the flow of red blood cells (RBCs) through the 10-μm-diameter capillaries that service mammalian cells. It's also possible to follow RBCs through 10-μm-diameter glass tubes—which is how researchers discovered that under outwardly similar conditions, the flow of RBCs is significantly slower *in vivo* than *in vitro*. The forest of molecules—mainly protein–sugar hybrids—that sprouts from the inner surface of capillaries and known collectively as the endothelial glycocalyx is suspected as the discrepancy's principal source. That attribution is now on firmer experimental ground. Giovanna Tomaiuolo of the University of Naples in Italy and her colleagues have mimicked the effect of the endothelial glycocalyx by using methacrylate polymer chains. When RBCs are sent through polymer-lined microcapillaries, they conceivably encounter two sources of resistance. The first is the restriction of the channel's diameter by the polymer layer. The second source is the increased dissipation that results when RBCs pass by the chains and cause them to jiggle. It turned out that the second source is the more important: For the same surface density of chains, the reduction in RBC flow was independent of layer thickness. Tomaiuolo's results could help elucidate the pathology of diabetes, atherosclerosis, and other vascular diseases that entail alterations to the endothelial glycocalyx. (L. Lanotte et al., *Biomicrofluidics* **8**, 014104, 2014.) —CD