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Charles Day



Physics Today **63** (5), 18–21 (2010);

<https://doi.org/10.1063/1.3431320>



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energies we're seeing not iron but protons behaving in atmospheric collisions more and more like heavy nuclei," says theorist Glennys Farrar (New York University), a member of the Auger team. The center-of-mass collision energy of a 10^{19} -eV proton hitting a nitrogen nucleus in the atmosphere is about 500 TeV, far beyond anything that could be studied at CERN's new Large Hadron Collider.

There's considerable wiggle room in extrapolating the standard model of

hadronic interactions to that terra incognita. But the observation that 10^{18} -eV protons still seem to behave normally in atmospheric collisions makes it questionable that anything short of an abrupt onset of new physics beyond the standard model could account for the requisite doubling of the proton's effective width. In the past, cosmic-ray observations have famously contributed to fundamental particle physics. "It would be wonderful if that's

happening yet again," says Farrar.

Bertram Schwarzschild

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Protein strangles membrane necks by polymerizing into a spiral collar

A biophysical experiment involving fluorescently tagged molecules, an optical trap, and artificial vesicles reveals how a key molecular actor, dynamin, plays its role in neural transmission.

Signals travel along neurons as pulses of electrical polarization, but they're carried between neurons by glutamate, serotonin, and other neurotransmitter molecules. Neurons keep neurotransmitters ready for use inside nanoscale bags called synaptic vesicles, whose skins are made from the same lipids as the neuron's outer membrane.

When it's time to pass on a message, the vesicles fuse with the inside surface of the neuron's membrane and break open. The debouched neurotransmitters diffuse across a gap of a few nanometers to reach the receiving neuron, where, by binding to the surface, they deliver the message. Spent neurotransmitters are broken up by enzymes floating in the gap.

Neurons remake vesicles in a process that's the reverse of the vesicles' destruction. A concave pit forms out of the neuron's membrane. As the pit becomes more spherical, the neck that connects it to the membrane narrows. Vesicle formation ends when the neck is cut to seal the vesicles and trap them inside the neuron. Transporter proteins in the vesicle membrane reload the vesicles with fresh neurotransmitters.

Biologists call the release and reabsorption of vesicles exocytosis and endocytosis. Both processes are rich ground for biophysical study. They involve the topological transformation and continuum mechanics of thin, almost liquid membranes and the participation of several molecular actors, among them a motor protein called dynamin.

Dynamin polymerizes to form a spiral collar around the vesicle's neck during the final stages of endocytosis. But until now, it wasn't clear how the protein is recruited at the right moment or how it begins squeezing the vesicle's

membrane. Aurélien Roux and his coworkers in Patricia Bassereau's group at the Curie Institute in Paris have cleared up both mysteries.¹ Surprisingly, the resolution lies not in a varied cast of biochemical actors, as is often the case in molecular biology, but in the polymerization process itself.

Endocytosis

Figure 1 depicts some of the steps in endocytosis. In the first, molecules of protein called clathrin bind to the inside surface of the neuron's membrane. Clathrin molecules also bind to each other, creating a crystalline cage that deforms the membrane into a spherical pit. Dynamin shows up when the clathrin cage is almost complete and a short neck has formed.

Clathrin is recruited by the advent in the membrane of a lipid called PIP_2 . Like clathrin, dynamin also recognizes PIP_2 , but without an additional means to sense membrane curvature, dynamin would bind promptly—and therefore uselessly—to the pit and not to the more highly curved neck that forms later. Certain proteins that bind to dynamin are sensitive to curvature and could in principle recruit dynamin at the right moment.

Other molecules might help dynamin when it forms a spiral collar. Energy is needed to deform the membrane into the thin tube that dynamin envelops. Conceivably, that energy could come from dynamin's polymerization, or from an unknown molecule that squeezes the membrane in advance of dynamin's adsorption.

Roux didn't set out to find how dynamin senses curvature. At first, he was more interested in dynamin's polymerization. In 1998 Sharon Sweitzer and

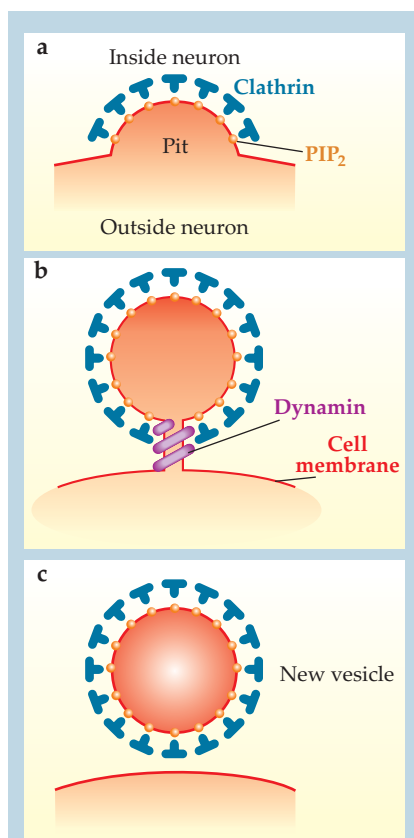


Figure 1. Endocytosis, as the creation of vesicles is known, involves two proteins, clathrin and dynamin, that deform a cell's membrane from inside the cell. **(a)** Clathrin arrives first. It binds to a lipid called PIP_2 and to itself, forming a pit. **(b)** Dynamin arrives when the clathrin-coated pit is almost complete. It polymerizes around the highly curved neck of the partially formed vesicle, squeezing and elongating the neck. **(c)** Dynamin acquires energy from molecules of GTP and twists into a tighter spiral (not shown) to sever the neck and complete endocytosis.

Jenny Hinshaw of the National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Maryland, mixed dynamin and lipids in a test tube and found that the two ingredients form thin membrane tubes wrapped by dynamin spirals.² The spirals have the same inside radius, about 10 nm, as that of the dynamin monomers. Given that dynamin can be coaxed to form spirals of the same radius even without lipids, Roux figured that dynamin's polymerization could provide the energy needed to squeeze and elongate a vesicle's neck. Electron micrographs of dynamin on curved, never flat, membranes were consistent with that proposal.

For verification, Roux sought to measure the force dynamin exerts on membranes when it polymerizes. Cell membranes are thin and delicate. At 300 K, the benchmark temperature of living things, the energy needed to bend or stretch membranes barely exceeds the energy of their thermal fluctuations. They are also transparent. Measuring their mechanical properties is difficult even without added dynamin.

When he joined Bassereau's group in 2007, Roux and coworkers began adapting a method developed by another member of the group, Pierre Nassoy. Nassoy had previously shown how one could measure a membrane's elastic moduli by manipulating cell surrogates called giant unilamellar vesicles. Micron-scale GUVs are much larger than synaptic vesicles, and even some cells (hence "giant"); they have one layer of lipids as opposed to the usual two (hence "unilamellar"); and they carry little more than ambient fluid (hence "vesicle").

Figure 2 shows the basics of Nassoy's method. A micropipette applies suction pressure to hold a GUV in place while a glass bead is chemically attached to the surface. An optical trap pulls the bead away to create a thin tube. The force required to hold the bead in place depends on the stretching modulus, which increases with suction pressure, and on the bending modulus, which doesn't. Adjusting the pressure calibrates a relationship, first derived in 1994 by Evan Evans and Anthony Yeung,³ between the measurable force on the bead and the otherwise unmeasurable radius of the tube.

Figure 2 also shows Roux's modification: the introduction of dynamin (red dots) via a second micropipette. Roux could adjust two control parameters: the concentration of dynamin and, through suction on the GUV, the radius of the tube. By fluorescently tagging dy-

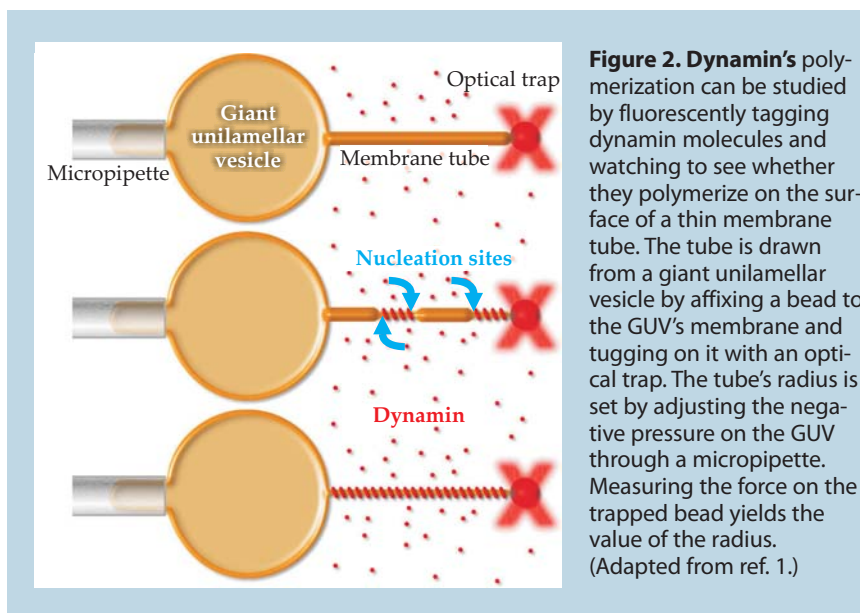


Figure 2. Dynamin's polymerization can be studied by fluorescently tagging dynamin molecules and watching to see whether they polymerize on the surface of a thin membrane tube. The tube is drawn from a giant unilamellar vesicle by affixing a bead to the GUV's membrane and tugging on it with an optical trap. The tube's radius is set by adjusting the negative pressure on the GUV through a micropipette. Measuring the force on the trapped bead yields the value of the radius. (Adapted from ref. 1.)

namin molecules, he could observe the protein sticking to a tube through a microscope. Although the polymer's spiral structure could not be resolved, the accumulation grew in a way consistent with polymerization: by extending at both ends.

At first, Roux found it hard to fix the dynamin concentration. Sometimes the micropipette was too close to the GUV

and the concentration too high; sometimes the micropipette was too far and the concentration too low. To his surprise, dynamin polymerized on a tube even at modest concentration, provided the tube radius was reduced to around 10 nm, dynamin's inside radius. After seeing that polymerization depends on both tube radius and dynamin concentration, Roux controlled the

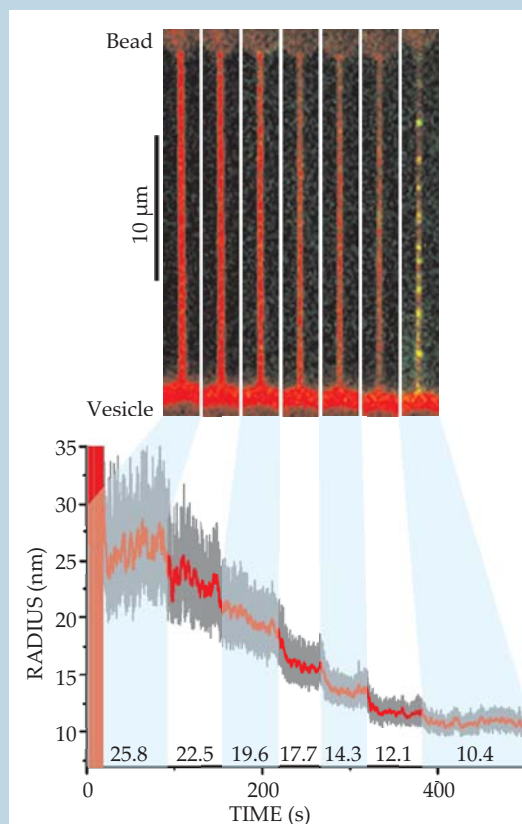


Figure 3. At low concentration dynamin molecules can't polymerize on a tube unless the tube's outside radius matches the molecules' inside radius. To obtain that result, Roux and his colleagues decreased the tube's radius in step-wise fashion giving dissolved dynamin molecules the opportunity to polymerize. As the sequence of micrographs shows, the fluorescently tagged dynamin (green) sticks to the tube only when its radius has reached 10.4 nm. The green dots represent nucleating spiral segments, not individual molecules, which are too small for the microscope to resolve. (Adapted from ref. 1.)

concentration more precisely.

A typical experimental run at low dynamin concentration appears in figure 3. Micrographs are at the top, a plot of the tube radius versus time is at the bottom. Fluorescently tagged PIP₂ (top, red) delineates the GUV and the tube. Fluorescently tagged dynamin (top, green) shows up only when the tube is at its lowest radius, 10.4 nm.

By taking measurements over a range of concentration and radii, Roux and his coworkers could map a phase

diagram of dynamin's polymerization. Below a critical concentration c_v , dynamin never polymerized. At c_v , dynamin polymerized only on tubes whose radius matched dynamin's. As the concentration increased, dynamin polymerized on tubes of a widening range of radii. The lower limit of the range decreased weakly with concentration; dynamin couldn't polymerize on tubes that were too thin. The upper limit increased rapidly with concentration. Evidently, the vigor of dynamin

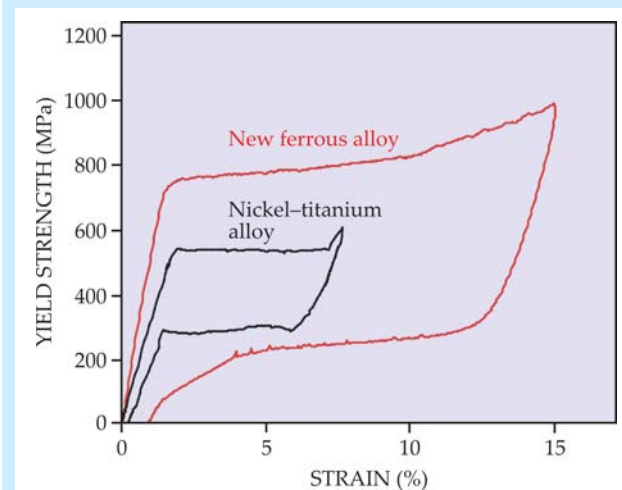
polymerization was enough to deform ever thicker tubes.

A simple mathematical model that balances polymerization energy, which depends on concentration, and the elastic energy, which depends on concentration and tube radius, could reproduce the phase diagram. The molecular picture that emerges from the experiment is of matching geometries. Curved monomers slide around on a curved surface and readily link if the two curvatures match. If they

physics update

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

Stretchy metals recoil. In materials, as the axiom goes, structure follows function: A metal's tightly bonded atomic crystal lattice gives it strength, and a polymer's mesh of macromolecular chains makes it elastic. Medical implants, electronic components, and other similar devices call for multifunctional materials



that are both strong and stretchy. One such material is the shape-memory alloy (SMA), a polycrystalline arrangement of assorted metals that, when stressed, undergoes a structural phase transition from high to low symmetry. The transition is reversible, and above a critical temperature SMAs are superelastic—they fully recover after being stretched well beyond the reversible-deformation strain values of pure metals. Now, materials scientists at Tohoku University in Sendai, Japan, have presented evidence for an iron-based SMA that is 35 times as elastic as pure metals. The new alloy, which also features nickel, cobalt, aluminum, tantalum, and boron, has an elastic strain of 13%, as shown in the figure, almost double the value of the more expensive commercial-standard nickel-titanium alloy. Furthermore, the material's yield strength, 800 MPa, is 1.5 times that of the nickel-titanium SMA. The researchers say that microstructured precipitates similar in composition to the bulk matrix and interspersed through it are a key to the improved mechanical strength. The greater elastic strain and strength could be exploited for mechanical damping in building materials. Also, the ferrous SMA's magnetism is phase dependent, which makes it

potentially useful for electromechanical sensing applications. (Y. Tanaka et al., *Science* **327**, 1488, 2010.) —JNAM

An unexpected cosmic current. According to cosmological theory, the expanding universe has no preferred direction. Thus, the cosmos may be likened to a rising loaf of raisin bread, with the raisins playing the roles of galaxies. Viewed from Earth (or anywhere else), the motion of a distant galaxy should be determined by the overall cosmic expansion. Now, following on their earlier work presented in 2008, Alexander Kashlinsky of NASA's Goddard Space Flight Center and colleagues report that superimposed on the cosmic expansion is a universal flow along the line from Earth to the Centaurus and Hydra constellations. The "dark flow," as the authors call it, was revealed in the cosmic microwave background by minuscule temperature fluctuations that arise when x-ray-emitting gas from galaxy clusters scatters off CMB photons. A catalog of more than 1000 x-ray-luminous galaxy clusters told Kashlinsky and company where in the *Wilkinson Microwave Anisotropy Probe's* five-year data set they should look for those fluctuations. The researchers had to average over ensembles of clusters to see evidence for the dark flow, which persisted unabated to the furthest measurable reaches, 2.5 billion light-years away. It's as if—and this is a literal possibility—matter beyond the edge of the visible universe is pulling the entire cosmos toward it. (A. Kashlinsky et al., *Astrophys. J. Lett.* **712**, L81, 2010.) —SKB

Prototype for a new astronomical detector. Much of the light emitted from stars and other astrophysical objects is absorbed by dust and reemitted at far-IR or submillimeter wavelengths—radiation that is notoriously difficult to detect. Last year researchers from the Jet Propulsion Laboratory proposed a new type of detector for that regime, with an eye toward future, more sensitive space missions. The team has now built a prototype microdevice (see figure), called a quantum capacitance detector (QCD), which would be one pixel in an eventual array. The detection chain goes like this: Photons are received at an antenna and fed into a superconducting absorber where they break Cooper pairs and generate quasiparticles. A superconducting island, called a single Cooper-pair box (SCB), is connected to the absorber in such a way that, at most, one quasiparticle at a time can tunnel onto it; that changes the island's capacitance, which is so small that the charging energy of a single electron has a large effect. With a resonant circuit, the physicists monitor the frequency of capacitance changes from which they can determine the density of quasiparticles in the absorber and thus the photon flux at the antenna. The device's performance is already comparable to that of other superconducting detectors. The advantage of the QCD, say the researchers, is the ease with

don't match, the linking can force a match, provided enough monomers are present.

Roux could also measure the polymerization force, which was manifest as a reduction in the force required to hold the bead in place. In general, the polymerization force depends on dynamin concentration and membrane tension. At a concentration of 12 $\mu\text{mol/L}$, the force is 18.1 ± 2.0 pN.

Interestingly, Roux's results imply that dynamin cannot exert enough

force to overcome the higher membrane tensions measured in real neurons. However, certain membrane proteins appear in a nascent pit to reduce the tension and regulate the onset of endocytosis.

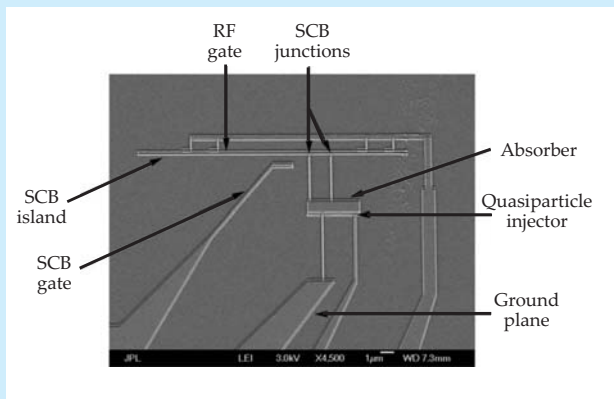
In the final stage of endocytosis, polymerized dynamin obtains energy from molecules of GTP (guanosine triphosphate, a common cellular fuel), twists into a tighter spiral, and garrotes the neck. When Roux was a postdoc in Pietro De Camilli's lab at Yale Univer-

sity, he, De Camilli, and their coworkers had verified the GTP-fueled twisting.⁴ Now, Roux plans to measure the twisting force.

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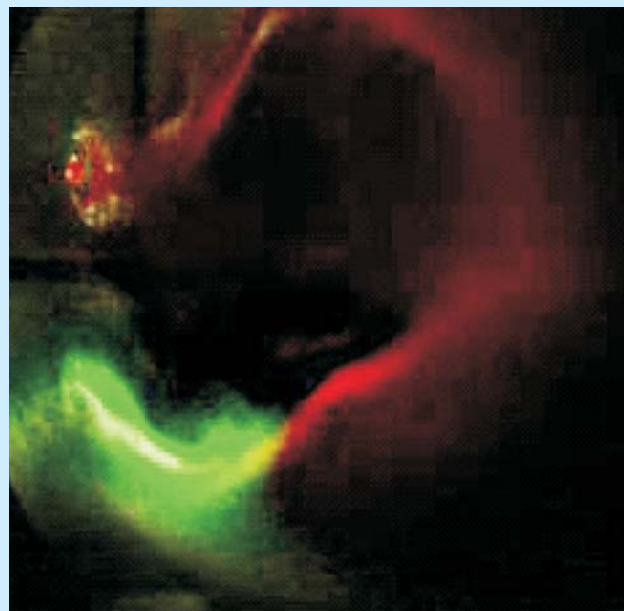
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which it can be read out from an array of detectors. For example, each pixel detector could be fabricated with a different resonance and simultaneous readout could be done with a frequency comb. (J. Bueno et al., *Appl. Phys. Lett.* **96**, 103503, 2010.) —SGB

The intrinsic limits of quantum cascade lasers. One of the hallmarks of lasing is a dramatic narrowing of the light's frequency spread. In 1958 Arthur Schawlow and Charles Townes deduced that the laser linewidth is fundamentally limited by unavoidable spontaneous emission. (Thanks to other sources of noise, a real laser's linewidth is usually considerably broader.) Semiconductor diode lasers required a revision of the intrinsic linewidth formula to account for additional inherent broadening, but quantum cascade lasers (described in *PHYSICS TODAY*, May 2002, page 34) had been thought to obey the original limit. Now Saverio Bartalini and colleagues at Italy's National Institute of Optics–CNR, the European Laboratory for Non-linear Spectroscopy, and the Second University of Naples have confirmed a recent theory predicting that QCLs can in fact beat the Schawlow–Townes limit and yield significantly improved spectral purity. Key to the 2008 theory by Masamichi Yamanishi and coworkers at Hamamatsu Photonics was the recognition that nonradiative transitions in QCLs strongly suppress spontaneous emission. To test the prediction, the Italian researchers tuned their IR QCL to be halfway down a carbon dioxide absorption peak at 4.33 μm (69.3 THz). Thanks to the steep slope of the absorption curve there, frequency fluctuations were converted into detectable intensity variations. That technique enabled the team to measure the noise spectrum over seven decades of frequency and to extract the intrinsic QCL linewidths for various pump currents. The obtained widths, in the range of 500 Hz, agreed well with the new theory and were three orders of magnitude smaller than predicted by the venerable Schawlow–Townes formula. (S. Bartalini et al., *Phys. Rev. Lett.* **104**, 083904, 2010.) —RJF

Astrophysical jets and solar loops in the lab. At the center of many an active galaxy lies an exceedingly powerful engine that, among other things, shoots out collimated jets of fast-moving plasma. Such jets can extend well beyond the galaxy's luminous boundary, ending in vast lobes that light up the intergalactic medium in the radio band. Closer to home, the Sun's atmosphere has many a plasma-filled magnetic loop, the dynamics of which are somewhat mysterious. In February, at the joint meeting of the American Physical Society and the American Association of Physics Teachers, Paul Bellan (Caltech) reported on his group's recent experiments that shed light on both systems. The experimenters used the large currents and magnetic fields of spheromak technology to create plasma jets in a very large vacuum chamber, which ensured that the plasma configurations were unaffected by walls. With a preexisting magnetic field "frozen in," the physicists puffed some gas through an electrode, switched on a current, and watched as a plasma jet formed, self-



collimated, underwent a kink instability, and then detached when the electric current was strong enough. In a different magnetic-field geometry, the figure shows counterpropagating collimated plasma jets—red hydrogen from the cathode and green nitrogen from the anode—colliding head-on within an arched magnetic loop, much like those seen in the Sun's corona. Bellan also developed a physical model for the self-collimation and a dusty-plasma dynamo mechanism suitable for generating actual astrophysical jets. (P. M. Bellan et al., invited APS/AAPT talk H3.2, 2010. Preprint available from the author.) —SGB