

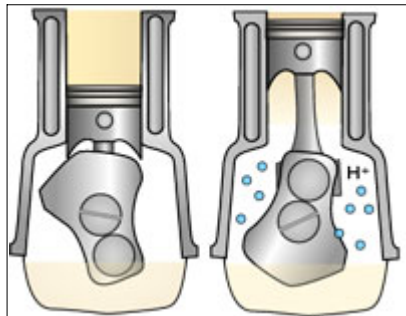


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Alternative Energy for Biomotors

Freeing nanodevices from the constraints of an ATP economy | [By Bennett Daviss](#)

Erica P. Johnson



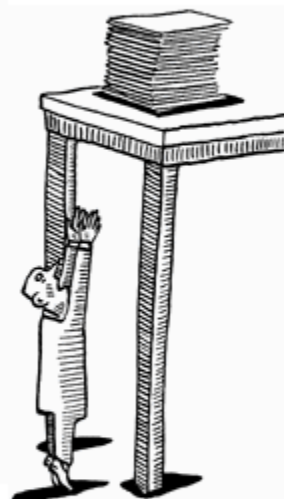
⬆ A biomolecular 'piston' derived from viral peptides should respond to changes in pH.

Engineers expect that tomorrow's nanomachines--biomolecular devices that might patrol cells, repair genes, scour out infections, and haul away debris--will be powered by nature's own motors: the proteins kinesin, myosin, and dynein, which turn adenosine triphosphate (ATP) into fuel and move loads along microtubular tracks of actin and tubulin.

It makes sense to use these off-the-shelf engines as they're 1,000 times smaller than anything humans can yet build. But recent research indicates that by the time bioengineers are ready to begin assembling their intracellular delivery vehicles, they will have a wider range of motors to choose from. Tiny pistons borrowed from HIV and other viruses, G-protein springs, and even nucleic acid-based motors are finding their way to the drawing board. Each uses a different source of energy to accomplish a different task, and may enable future nanodevice designers to choose just the right tool for a specific job.

PICO POWER Because they are already complete and ready to use, proteins that hydrolyze ATP to deliver a lever-like power stroke are likely to lead the biomolecular motorcade. Kinesin and myosin have inspired investigators like Henry Hess, a research assistant professor in molecular bioengineering at the University of Washington in Seattle, to envision "a nanoscale train system, complete with tracks, loading docks, and a control system." In Hess' microscopic train yard, "specialized motor proteins connect to small containers filled with

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proteins and transport them along the skeleton of the cell," he says.

A molecule of myosin hydrolyzing a molecule of ATP yields about three picoNewtons of power; kinesin, delivers about 7 pN. (Dynein, a weakling, can manage only about 1 pN.) Although 1 pN is just a trillionth of the force needed to accelerate one kilogram 1 m/sec/sec, in the nanoworld this is serious power. Like ants able to heft far more than their own weight, a single protein hydrolyzing one ATP molecule produces enough force to shift a bucket of water 0.1 mm in diameter or lift an entire cell, according to Hess' calculations.

PISTONS FOR PUSH Some applications for nanodevices, however, probably won't require such gross hauling capacity, they just may need to give molecules a push. Constantinos Mavroidis, a mechanical engineer and associate professor at Northeastern University, is exploring biological pistons that might do just that. With Martin Yarmush, a professor at Harvard's medical school and a visiting professor of bioengineering at Rutgers University in Piscataway, NJ, Mavroidis and his students are testing a new kind of protein-based motor provided by HIV, influenza, and other viruses.¹

In 2001 Mavroidis was working in robotics and smart materials; Yarmush was researching biomedical engineering. "It was a natural outcome to start talking together about using bimolecular entities as nanoactuators," Mavroidis recalls.

Yarmush observed that a virus senses environmental changes when it enters a cell. As the pH falls from a neutral 7 to 5 or less, a coiled loop of protein lying just beneath the virus's surface becomes erect. Mustering a force of about 0.1 pN, the coil reaches out nearly 10 nm to bond with the cell's endosomal membrane.

The peptide comprises a variety of amino acid residues, which at rest have a negative net charge. As the pH falls, some of the amino acids take on loose hydrogen ions. Now positively charged, the amino acids repel, and are repelled by, their neutrally charged neighbors. Yarmush saw that the peptide portion of the viral protein snapping to attention mimicked the movement of a piston. A decrease in pH prompts it to push an object away, and an increase causes the piston to fall back to its original position. By channeling that motion through a microcylinder or some other small, structured space, the groups hope to capture and direct the proteins' motion and force.

So far, Yarmush and Mavroidis have been able to chart the speed and degree of the protein's expansion and contraction through different pH fluctuations. Next, they plan to tether the peptide's inert end to a substrate and begin to determine ways to direct the thrust. "We also believe that, compared to ATP-fueled motor proteins, viral protein motors require significantly less energy," Mavroidis says. NASA's Institute for Advanced Concepts has given the group a grant to develop what Mavroidis calls "novel, extremely small devices to explore space," and develop "smart nanobio suits." But nondisclosure agreements keep

him from discussing any details.

Hess acknowledges that working without ATP, as these viral motors do, "has advantages in electronic applications because you can change pH by passing a current through an electrode. You could micropattern electrodes onto a substrate and apply voltages in ways that would activate or deactivate viral proteins." The technology also could be useful in operating liquid crystal diodes or making microarray chips. "That kind of thing is obviously much easier to do than connecting proteins to a constant source of ATP," Hess notes.

UNBRIDLED ENER-G An alternative source of motive power resides in the G proteins, which hydrolyze GTP instead of ATP. These evolutionary cousins of myosin and kinesin act primarily as molecular switches, playing a key role in cell signaling. They can produce even more power than conventional motor proteins, although these alternative generators would have quite a different use.

The active regions for the two protein classes are strikingly similar, notes Ioan Kosztin, a physicist at the University of Missouri in Columbia. Kosztin is part of a group that first discovered that H-Ras, the simplest G protein, can exert at least as much force as motor proteins powered by ATP.²

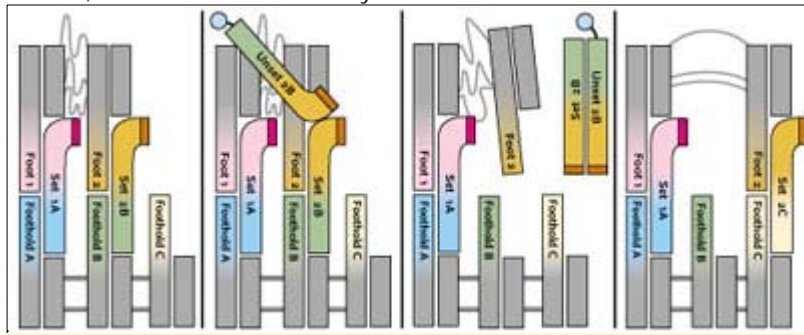
Although well studied as an oncogene, says Kosztin, "no one had looked at force generation in these proteins. Our idea was that because these two classes of proteins are so similar, G proteins must also generate some force." They do, but through a different mechanism. "There's no power stroke here as you see in ATP motor proteins," Kosztin says. Instead, after H-Ras hydrolyzes GTP, areas of the protein's surface fluctuate dramatically as it separates from other proteins that have catalyzed the reaction.

"The motion is like a spring that's held at one end and bouncing around at the other," Kosztin explains. Still, Kosztin and his group calculate that the random motions can yield a force as strong as "tens of picoNewtons." To capture that energy for work, engineers would need to find a way to channel G protein's power, which Kosztin admits is a difficult prospect. "It wouldn't be a very efficient motor, but in cases where you needed a small motor combined with a switch, G proteins would be a possibility." He speculates that because G proteins generate force and act as a switch when interacting with other molecules, they might someday be programmed to bond or "weld" together the components of a nanodevice.

'TIDAL POWER Biomolecular energy can also come from other sources. Chengde Mao, a chemist at Purdue University, has demonstrated a DNA motor prototype that contains the 10-23 DNA enzyme, a molecule that cleaves RNA segments based on complementarity.³ "It works in the same way as natural protein motors by continuously extracting chemical energy from covalent bonds and converting this energy into mechanical motions," says Mao. For now,

the "motor" simply opens and closes, like a switch, exerting a force that he estimates at about 10 pN.

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STRANDS ON THE RUN: In this model for a DNA biped motor, double helices connected by flexible linkers are anchored to DNA footholds on a track when homologous 'set' strands are added. To take a step, 'unset' strands are added, binding the set strand and freeing one leg of the biomotor to move onto the next foothold with the addition of the next set strand. (Redrawn from W.B. Sherman, N.C. Seeman, *Nano Lett*, 4:1203-7, 2004.)

Mao began thinking about mobile DNA while working with Nadrian Seeman at New York University. In April 2004, Seeman and his colleague William Sherman reported fashioning a DNA biped that follows a track and eventually could be made to tote loads.⁴ Two DNA double helices connected by three flexible "linker strands" walk a path of single-stranded DNA when short nucleotide strands are added to displace and move the legs.

"The walker now takes a step when we add a new ingredient to the pot," Seeman says, "But there's no question that this could be automated." Seeman envisions eventually using a team of these walkers to braid polymers into superstrong strands. It's "not something chemists today can do easily if at all," he notes. If the biped is fixed to a superstructure, its moving feet could move a walkway. If the path were circular, like a gerbil's treadmill, the walker could spin it like a gear.

As engineers imagine more and more uses for these biomolecular nanomachines, they'll need an expanding catalog of useful parts, including a variety of engines that can work across a spectrum of specialized needs without being tethered to a single shape, function, or fuel source. "The more ideas there are for making these motors," says the University of Washington's Hess, "the happier I am."

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