Cellular transit system gets meter reading

Using laser-beam "tweezers" that function like Star Trek tractor beams, scientists have measured the forces generated by tiny biological engines inside living cells. The study — in which researchers put the brakes on cell components that normally zip around within cells — provides the first direct measurements of the mechanical energy exerted by this basic machinery of life.

The investigators focused on a miniature monorail system found in many cells. The "rails" consist of protein strands called microtubules. Along this network run specialized cell components called organelles — including mitochondria, the mobile mini-reactors that generate and deliver energy to the farthest reaches of intracellular space. Mitochondria and other organelles move along the microtubules by latching onto one or more "motor proteins" such as kinesin or dynein. These locomotive proteins pull themselves and their cargo along the microtubule railways.

Until now, researchers had only rough estimates of the forces generated by locomotive proteins. The new work, led by physicist Arthur Ashkin of AT&T Bell Laboratories in Holmdel, N.J., and cell biologist Manfred Schliwa of the University of California, Berkeley, replaces those estimates with direct measurements made within living cells.

The team applied a gradient-force optical trap, or "optical tweezers," to mitochondria cruising along microtubules within an amoeba. The tweezers use beams of photons to push around tiny objects or hold them in place (SN: 3/10/90, p.148). First, the researchers applied enough force to bring individual mitochondria to a screeching halt. Then they noted how much they had to tone down the laser before the organelles started moving again, figuring that the minimum amount of force needed to keep the organelles stationary must equal the force of the motor system itself. That comes to about 2.6×10^{-7} dynes per motor, they report in the Nov. 22 NATURE.

"On an absolute scale, it's not a lot of force," Ashkin says. "But on the scale of these beasts, it's quite impressive." He calculates that from a mitochondrion's point of view, that's about 1,000 times the force of gravity. Seen another way, it's enough force to propel an average-size bacterium through water at about 1 millimeter per second. With most mitochondria pulled along by two or three motor molecules at once, the forces create a powerful transport system that can maintain constant mitochondrial velocities over the wide range of viscosities encountered within cells, Ashkin says.

Steven M. Block, a motor-molecule specialist at the Rowland Institute for Science in Cambridge, Mass., comments that the work foreshadows a future when scientists will understand the mechanical details of biological motility on a molecular level. "How chemical energy in cells gets transduced into mechanical displacement remains completely obscure," Block says. "Optical tweezers provide an exciting new tool that may at last make that understanding possible."

For now, the research remains very basic. Block points out, however, that molecular motors play critical roles in such diverse processes as cell division and muscle contraction, and that motor defects may underlie a variety of diseases or cellular abnormalities. — *R. Weiss*

Smoking silences critical pain messages

Cigarette smoking, already known as a heart-disease villain, may also blunt the perception of pain, preventing smokers from noticing potential warning signs of an impending injury. This new finding might help explain previous indications that smokers with coronary artery disease, compared with nonsmokers with similarly clogged arteries, appear less likely to experience chest pain during episodes of ischemia — a reduction in blood flow to the heart that can lead to a sudden heart attack.

Scientists can't explain the smoking-related masking of pain, but animal studies hint that nicotine may block transmission of pain impulses.

Paula F. Miller and David S. Sheps at the University of North Carolina School of Medicine in Chapel Hill focused on 20 healthy men aged 19 to 44 who smoked an average of 23 cigarettes daily, and five nonsmoking men in the same age range. The researchers instructed volunteers not to smoke for 12 hours prior to the study's start. Then they applied a heat probe to each volunteer's forearm, letting the probe heat up gradually, and recorded the individual's pain threshold — the temperature at which he first felt pain. Smokers and nonsmokers showed similar pain thresholds on this initial test.

Having gathered their baseline data, the investigators next instructed smoking volunteers to smoke three cigarettes of their usual brand, with a 10-minute wait after the first cigarette and a 30-minute wait after the second. Repeats of the heat probe test revealed that the smokers had become less sensitive to pain from the heat. On average, this group's "ouch" threshold rose from 44.9°C (112.8°F) before smoking to 45.5°C (113.9°F) after two or three cigarettes — a small but statistically significant difference, says Miller, who described the results in Dallas last week at the American Heart Association's 63rd Scientific Sessions. The maximum pain the 20 men could tolerate increased after smoking, Miller notes, whereas nonsmokers showed no change in pain threshold or tolerance.

While these findings suggest that healthy male smokers tolerate pain better than their nonsmoking counterparts, Sheps says further research must demonstrate this effect among male and female smokers with coronary artery disease. As for the pain-subduing mechanism underlying "silent" ischemia, he speculates that nicotine blunts pain messages by binding with nerve cells.

If studies confirm that suspicion, the implications may extend beyond silent ischemia. Nicotine's proposed pain-masking effect, says Sheps, may help explain why smokers have such a tough time kicking the habit. — *K.A. Fackelmann*

Boreal lake offers preview of warming

While scientists remain uncertain whether the expected global warming has begun, a lake in the boreal forest of Ontario offers a disturbing glimpse of ecological changes that may lurk around the century's corner.

The portentous findings emerge from a unique, long-term project in which researchers have been monitoring conditions within many small lakes in northwestern Ontario over the past 20 years. Because the region has warmed considerably during that time, the project provides an in-depth look at the kinds of changes that could accompany a global greenhouse warming, assert David W. Schindler of the University of Alberta in Edmonton and his colleagues at the Canadian Department of Fisheries and Oceans in Winnipeg, Manitoba. They discuss their observations of one particular lake, known simply as #239, in the Nov. 16 SCIENCE.

"This is going to be an absolutely vital data set for looking at the effects of global warming on aquatic ecosystems in lakes. I don't know of any other region where they have that kind of long-term record," says Eville Gorham, an ecologist and lake expert at the University of Minnesota in Minneapolis.

The Canadian team found that the average air and lake temperatures in this part of Ontario have risen a significant 2°C since 1970. Snowfall and rainfall have dwindled slightly and evaporation has increased dramatically, causing a general drying of the watershed. In the driest years, large fires have swept through the region. The scientists also note that winter ice on Lake 239 now melts several weeks earlier in the springtime than it did at the beginning of the project.

In shallow northern lakes, the temperature increase already recorded could kill off species of fish and invertebrates that cannot tolerate warm water, the researchers say. These cold-loving species, called glacial relicts, have inhabited the lakes since the retreat of the glacial sheets at the end of the most recent ice age, some 10,000 years ago.

Deeper boreal lakes, such as #239, have long provided a haven for such glacial leftovers because these lakes are stratified with a region of cold water beneath a warmer surface layer. But complex ecological changes in the last 20 years have deepened Lake 239's temperature boundary by several meters, squeezing the habitat of the cold-requiring animals and threatening their survival, Schindler says.

Because of evaporation and precipitation changes, the amount of runoff pouring into Lake 239 declined sharply over the study period, slowing the rate of water replacement. "Whereas that lake flushed itself completely every four to six years at the beginning of our experiment, it's now taking 20 years," Schindler says.

That effect, along with an increase in forest fires, can concentrate chemicals in lakes and deepen the temperature boundary in stratified waters — two shifts that would stress the ecosystem, say the Canadian researchers.

Some scientists, noting that lakes in warmer regions to the south generally harbor more wildlife than boreal lakes, have suggested that global warming will increase the biological productivity of these northern lakes. Schindler challenges that assumption, calling it too simplistic. If certain species go extinct, he and his colleagues say, "it is by no means certain that fisheries of comparable value or ecosystems of comparable diversity would be reestablished quickly."

Major research programs on climate change have largely failed to study the effects on freshwater habitats, they add. "But when you look at what resources are probably going to limit human activity or ecosystems, the first one we're going to come up against is fresh water," Schindler warns. — *R. Monastersky*

Mealtime aspirin may boost alcohol high

People who attempt to avoid hangovers by popping aspirin before drinking may be in for an unexpected side effect. New research suggests that aspirin, when taken on a full stomach, can get you drunker.

Physicians recruited five healthy men and gave them alcohol-spiked orange juice — the equivalent of 1.25 to 2 glasses of wine, depending on body weight — one hour after a full breakfast. On another morning, the men took 1 gram (two extra-strength tablets) of aspirin along with the same meal and then drank the same amount of alcohol.

The aspirin increased the men's peak blood alcohol level by an average of 34 percent compared with the peak level without aspirin, report Risto Roine, Charles S. Lieber and their colleagues at the Bronx Veterans Affairs Medical Center and the Mount Sinai School of Medicine in New York City. Moreover, the researchers observed that blood alcohol levels rose more rapidly and remained elevated longer after the aspirin dose.

They note that the aspirin-boosted alcohol levels fell below U.S. legal limits for "driving while intoxicated," since the study involved relatively small alcohol doses. However, they write in the Nov. 14 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, "This increase . . . can be of clinical significance for individuals driving cars or operating other machinery that requires a high degree of mental and motor coordination."

During *in vitro* studies of gastric mucosa from rats and humans, the team uncovered a likely mechanism for the enhanced alcohol levels. Aspirin, they found, halved the activity of gastric alcohol dehydrogenase — an enzyme that helps oxidize alcohol, preventing its absorption into the bloodstream. With enzyme activity subdued, more alcohol reaches the circulation, they assert.

With or without a predose of aspirin, alcohol consumed on an empty stomach also circumvents enzyme activity, passing into the bloodstream so rapidly that the enzyme hardly has a chance to blunt intoxication. Roine adds that taking aspirin *after* drinking probably does not increase blood alcohol levels, since the enzyme has already completed its oxidization task by that time.

Although the breakfast study focused on men, it may have particular significance for women, says Lieber. Earlier this year, the same researchers detected naturally lower activity levels of the gastric enzyme in women compared with men (SN: 1/20/90, p.39). The team began an all-women version of its breakfast study this week and expects early results by January. "We hypothesize that when we give aspirin to women, they may have virtually no gastric [alcohol dehydrogenase] activity," Lieber says.

Roine notes that people who take aspirin with the gastric ulcer drugs cimetidine or ranitidine may face a double whammy from alcohol, since previous studies have shown that these drugs also reduce gastric alcohol dehydrogenase activity. He adds that his group plans clinical tests to verify *in vitro* results indicating that smaller aspirin doses, such as those prescribed to lower heart attack risk, also lower activity of the alcohol-degrading enzyme. — *R. Cowen*

Quick moves claim computer-chess title

After losing decisively last fall to world chess champion Gary Kasparov, chess computer Deep Thought returned to the digital world last week and successfully defended its title as the North American computer-chess champion. But it wasn't easy. Deep Thought lost one game to Hitech — only its third loss to a machine — and had to share the title with Mephisto, a strong contender from Germany, which also lost just one game.

This year's championship, sponsored by the Association for Computing Machinery and held at the Supercomputing '90 meeting in New York City, featured 10 chess machines and computer programs. Belle, world champion in 1980, came out of retirement to participate in the tournament but managed to win only one game.

"That shows how much computer-chess programs have changed and improved," says David Levy of Intelligent Software Ltd. in London, England.

Mephisto ranks as the top commercially available computer-chess player. Last April, a Mephisto computer became the first machine to defeat a former holder of the human chess title when it beat Anatoly Karpov. Even though Karpov was simultaneously playing 23 other opponents, the computer's success remains significant, Levy says.

Last year, Mephisto beat Deep Thought in the final round of the computer-chess championship. This time, Deep Thought won the rematch. "Mephisto played a horrible move in the opening and never recovered," Levy says. "It was a typical computer move, which computers make very often in certain positions, and most people haven't yet worked out how to get it out of their programs."

Deep Thought has remained fundamentally unchanged over the last two years and has a number of weaknesses, says Feng-hsiung Hsu, one of its creators. Now working at the IBM Thomas J. Watson Research Center in Yorktown Heights, N.Y., Hsu and his colleagues are developing a more sophisticated version that can also respond to patterns.

To defeat Deep Thought, Hans Berliner of Carnegie Mellon University in Pittsburgh developed a strategy for giving Hitech a significant advantage at the beginning of the game. That proved enough to overcome Deep Thought's greater speed, which normally provides a clear advantage at the end of a game.

Zerker, a promising newcomer developed at the University of California, Berkeley, can search roughly three times faster than Deep Thought, evaluating up to 7 million moves in 1 second. But damage to the machine during shipment from California forced its withdrawal. — *I. Peterson*