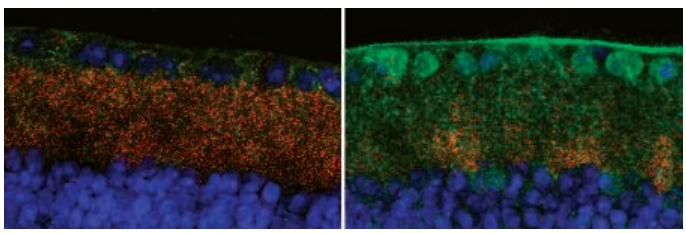
NEUROBIOLOGY

Immune Molecules Prune Synapses In Developing Brain

The complement cascade is part of the body's innate immune defense: a protein work crew whose duties include tagging bacteria and other bad guys for elimination. A new study suggests that complement proteins may have a surprising yet analogous function in the developing brain, tagging unwanted synapses for removal. The work also hints that these proteins may promote synapse loss in early stages of neurodegenerative disease.



Early indicator. C1q (green) can be seen early in glaucoma (*left*), even before synapses (red) and neurons (blue) disappear as the disease progresses (*right*).

"It's a pretty provocative finding," says Greg Lemke, a neurobiologist at the Salk Institute for Biological Studies in San Diego, California. "This is part of a growing body of evidence that many molecules of the immune system have a second set of jobs in the brain," says Lisa Boulanger, a neurobiologist at the University of California, San Diego.

The new study, which appears in the 14 December issue of *Cell*, began as an attempt to determine whether neural support cells called astrocytes have a role in refining synaptic connections between neurons during development, says senior author Ben Barres of Stanford University in Palo Alto, California. Postdoc Beth Stevens and colleagues used gene chips to look for changes in gene expression in neurons from the developing retinas of rats when the neurons were cultured with astrocytes.

To their surprise, astrocytes spurred the neurons to crank out a complement protein called C1q, which elsewhere in the body kicks off a cascade of chemical events that culminates in the destruction of an intruding cell. In experiments with mice, the researchers found that C1q concentrations in the retina and brain peaked a week or so after birth and dropped dramatically as mice matured. The peak coincided with the period when unwanted synapses are pruned. More intriguing, C1q seemed to concentrate ▶

PHYSICS

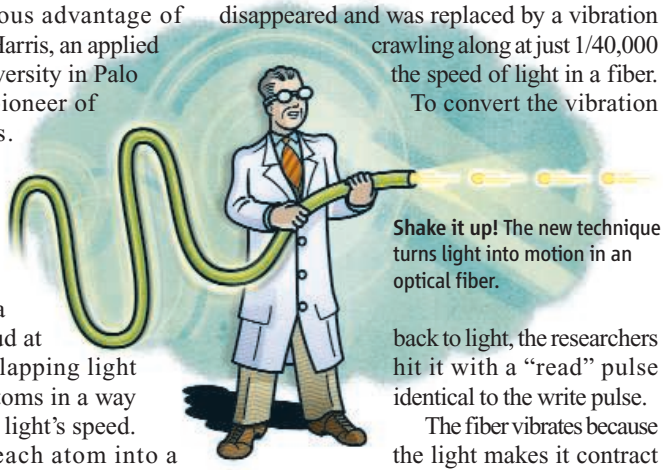
Simple Scheme Stores Light by Converting It Into Vibration and Back

A few years ago, physicists slowed light to a crawl and then stopped it entirely (*Science*, 26 January 2001, p. 566). To do that, they exploited strange quantum-mechanical interactions between light and atoms in a gas, converting a pulse of light into a subtle arrangement of spinning atoms. On page 1748, three physicists report a simpler way to hit the brakes: They convert light in an optical fiber into a slow-moving vibration and then back into light.

"This has the enormous advantage of simplicity," says Stephen Harris, an applied physicist at Stanford University in Palo Alto, California, and a pioneer of the atomic techniques. "Conversely, it can't do some things that the other techniques can."

To store a pulse of laser light in a cloud of atoms, researchers shine a second laser into the cloud at the same time. The overlapping light fields interact with the atoms in a way that greatly decreases the light's speed. The light also nudges each atom into a strange quantum-mechanical condition in which it spins in two different directions at once. The precise spin mixture varies from point to point in the cloud, effectively freezing the light pulse into the atoms when the reference laser is turned off and holding it until the laser comes back on. Others have managed to store light by shunting it into tiny optical "resonators" for a fraction of a nanosecond.

To find another way, Zhaoming Zhu and Daniel Gauthier of Duke University in Durham, North Carolina, and Robert Boyd of the University of Rochester, New York, opted for an optical fiber. They fed a "data" pulse in one end and a short, intense "write" pulse in the other. When the two collided, the data pulse disappeared and was replaced by a vibration crawling along at just 1/40,000 the speed of light in a fiber. To convert the vibration back to light, the researchers hit it with a "read" pulse identical to the write pulse.



Shake it up! The new technique turns light into motion in an optical fiber.

The fiber vibrates because the light makes it contract in the spots where the light is most intense. To make the conversion efficient, the team tuned the frequency of light in the read pulse slightly lower than that in the data pulse. The two had to differ by the frequency of the vibration, which was fixed by the properties of the fiber. The researchers showed they could store a train of three 2-nanosecond pulses and retrieve it as much as 12 nanoseconds later.

The new technique works for any frequency of light that will pass through the fiber, Gauthier says. The atomic and resonator techniques generally work at one frequency.

The conversion doesn't depend on quantum mechanics, notes Lene Hau, a physicist at Harvard University and one of the first to stop light. That should make the effect more robust but rules out truly bizarre embellishments. For example, Hau and colleagues have encoded a light pulse in one cloud of atoms and revived it in another cloud by letting a few atoms drift between the two, as they reported 8 February in *Nature*. Such a feat would be impossible with the fiber technique. Still, Hau says, "it's very important to try different systems."

The atomic systems might someday provide the memory for quantum computers, Harris says. Gauthier sees more immediate uses for the fiber-optic approach. For example, it might be used to measure the correlations between signals in optical networks. But first researchers must increase the storage time and reduce the power in the read and write pulse from a walloping 100 watts. That's enough to shake up anybody. **–ADRIAN CHO**

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at puny, immature-looking synapses in the developing nervous system.

When the researchers examined the brains of mice lacking a functional *C1q* gene, they found that development had gone awry in the lateral geniculate nucleus, a relay station in the brain that receives synaptic inputs directly from retinal neurons. In normal mice, geniculate neurons initially receive inputs from both eyes and then prune them so that they only receive input from one eye or the other. In the mutant mice, geniculate neurons maintained extraneous inputs from both eyes into adulthood.

That's a striking finding, Boulanger says: "When you get rid of these proteins that we thought just functioned in the immune system, it disrupts a very specific event that we think is involved in making the precise, final connections in the developing visual system." Many questions remain, however. Barres suspects that complement proteins mark unwanted synapses for removal by microglia, immune cells in the brain. More work is needed to demonstrate that, Boulanger says, and to figure out why only certain synapses are flagged for removal.

Finally, Barres and colleagues collaborated with Simon John's group at the Jackson Laboratory in Bar Harbor, Maine, to investigate whether C1q might have a role in synapse loss in a mouse model of glaucoma. Compared to normal adult mice, adult glaucoma mice exhibited elevated C1q levels: The protein accumulates at retinal synapses early in the disease, even before synapses disappear and neurons die off.

Synapse loss precedes cell death in Alzheimer's and other neurodegenerative diseases, Barres notes. He speculates that drugs that block the complement cascade may forestall neurodegeneration in a number of disorders. It's an exciting idea, says Monica Vetter, a neurobiologist at the University of Utah in Salt Lake City: "There's good evidence that these complement components are upregulated in other diseases."

–GREG MILLER

ECOLOGY

Parasites From Fish Farms Driving Wild Salmon to Extinction

A new study suggests that fish farming could rapidly wipe out some populations of wild salmon in British Columbia. Although some researchers are calling for dramatic controls on the industry, others say the risk hasn't been established firmly enough. At stake is the $450 million aquaculture business.

One of the top concerns about aquaculture is the spread of disease and parasites to wild species. On page 1772, the first population-level analysis suggests that sea lice from farmed salmon will cause several populations of one species of salmon in British Columbia to plummet by 99% within 8 years. "It's a shocking number," says salmon conservation expert John Reynolds of Simon Fraser University in Burnaby, Canada, who was not involved in the research. But environmental physiologist Scott McKinley of the University of British Columbia in Vancouver worries about rushing to judgment. "You cannot conclude anything from a correlation," he says.

Sea lice are small crustaceans that latch onto salmon and other fish. They feed on tissue and create lesions that make it hard for fish to regulate their body fluids. The saltwater parasites naturally occur on adult salmon in the sea but not on juveniles, which hatch in fresh water and then swim to the sea. In 2001, however, researchers found significant numbers of sea lice on wild juveniles that had passed by fish farms in British Columbia. The situation was alarming because young pink salmon are more vulnerable to damage from lice than adult salmon are.

Graduate student Martin Krkošek of the University of Alberta, Edmonton, started studying the problem in 2003. In previous papers, he and colleagues calculated that juvenile pink salmon are 73 times more likely to be infected with sea lice after they passed by salmon farms than are fish that didn't pass by and that lice can kill between 9% and 95% of juvenile pink salmon, depending on how many fish farms they must swim by. Some researchers are unconvinced, however, and point to other studies that suggest lower mortality from sea lice.



Ouch! Young pink salmon suffer from sea lice, which dig in when salmon swim past fish pens.

CREDIT: M. KRKOŠEK *ET AL.*, *SCIENCE*

In the new work, Krkošek and colleagues investigated the extent to which sea lice are affecting pink salmon populations throughout the Broughton Archipelago near Vancouver Island. They analyzed 35 years of records from the Canadian fisheries agency on the number of salmon in seven rivers that flow into marine channels with fish farms. They also looked at 64 rivers from which migrating salmon do not pass by fish farms. Using a standard model, they calculated that pink salmon not exposed to fish farms showed the same range of population size for all 35 years, varying from year to year.

The pink salmon that swam past salmon farms showed the same pattern, until the lice infestations began in 2001. Then all seven populations shrank year after year. If these populations continue to decline at this rate, they will be 99% gone within four generations. "It's very fast," says Krkošek, who says immediate conservation steps are necessary. "We can't sit around and do more research, because these fish will be gone." Senior author Mark Lewis of the University of Alberta in Edmonton and another co-author were among 18 scientists who in September called for requiring salmon farms to be surrounded by barriers to prevent the spread of parasites or disease.

As with previous papers, the reaction to the new finding is polarized. McKinley and others say that there are too many unknowns to conclude that sea lice from farms harm wild salmon. Many factors influence their abundance, including fluctuations in ocean nutrients. But fisheries biologist Ray Hilborn of the University of Washington, Seattle, says it is too risky to farm fish in open pens near wild relatives: "The bigger concern is that [sea lice] are just one of many pathogens. There could be other things out there that we don't know about."

–ERIK STOKSTAD

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