nothing that can convince this government of the usefulness and the need to support the social sciences," says Renaud, a sociologist who was at the University of Montreal when he was recruited in 1997 to rescue a body embroiled in internal bickering (*Science*, 11 April 1997, p. 195). "The question for me is: Am I going to stay in Ottawa?"

–WAYNE KONDRO

Wayne Kondro writes from Ottawa.

CIRCADIAN RHYTHMS

A Time to Rest: Clock Signal Identified

Pet hamsters love to run on their wheels at night, the time when their wild cousins venture out of their burrows to scurry around in search of food. Wheel-running—or its natural equivalent—is just one of many activities and physiological states that follow a daily rhythm, cycling up and down about every 24 hours, under the control of an internal biological clock known as the circadian clock. Researchers have made tremendous progress recently in identifying the molecular gears and levers that run the clock, but they have remained in the dark about an equally important part of the clock: the signals it sends out to control circadian behaviors.

Now, on page 2511, a team of researchers led by Charles Weitz at Harvard Medical School in Boston reports that it has discovered the first known output signal from the mammalian clock, a molecule called transforming growth factor alpha (TGF-α), known for its role in cancer and embryonic development.

Clock researcher Michael Menaker of the University of Virginia in Charlottesville calls the work "a pioneering effort" that opens the way for clock researchers to begin to study the neural circuits by which the clock controls behavior and physiology. Joe Takahashi of Northwestern University in Evanston, Illinois, agrees: "One of our big gaps in understanding is how signals leave the [clock]." This paper, he says, begins to fill that gap.

Weitz's team based its quest for clock signals on work by several research teams showing that the brain's suprachiasmatic nucleus (SCN), home of the mammalian clock, secretes something that controls wheel-running. Weitz postdoc Achim Kramer searched for molecules secreted by SCN neurons, and Weitz scanned the literature for known SCN products. "About 20 secreted peptides have been documented from SCN," Weitz says, "and no one knows what most of them do."

Weitz's team took a selection of newly discovered and previously published SCN products and collaborated with Fred Davis's lab up the street at Northeastern University in Boston to test each candidate molecule's effects on wheel-running in hamsters. They infused each molecule continuously for 3 weeks into the brain near the SCN and monitored the animals' wheel behavior. Of 32 molecules they tested, TGF-α stood out: It completely stopped the animals from running in their wheels. Other experiments done with Tom Scammell across the street at Beth Israel Deaconess Medical Center showed that the hamsters weren't paralyzed or otherwise impaired. They just lost their nocturnal urge to run.

The researchers hypothesized that TGF-α may be produced by the clock during the day to inhibit running. If so, they reasoned, TGF-α production by the SCN should be high during the day and low at night—and that is exactly what they found. What's more, TGF-α would need to act on a nearby brain area called the subparaventricular zone (SPZ), which controls daily running rhythms. And when they looked in the SPZ, they found that its cells contained the epidermal growth factor (EGF) receptor, which is also the receptor for TGF-α.

To run or not to run. Hamsters and other nocturnal rodents run at night when TGF-α levels are low.

To confirm that TGF-α acts through the EGF receptor to block wheel-running, the researchers tested EGF, a molecule that works through the same receptor but is not made by the SCN. They found that it also suppressed wheel-running. What's more, Weitz's team found that mutant mice with impaired EGF receptors don't seem to register TGF-α's signal; they run during the day more than normal mice do.

The mutant mice were oblivious to external signals as well. Normal mice stop running at night if the lights are turned on. This response, called "masking," seems to work like an emergency backup system to assure

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ScienceScope

Orbach to DOE Theoretical physicist Ray Orbach, chancellor of the University of California (UC), Riverside, is slated to become the Department of Energy's next science chief. President George W. Bush on 11 December said he will nominate Orbach, 67, to head DOE's Office of Science, which oversees a $3.2 billion research program. Orbach is a veteran academic and administrator who has led UC Irvine for nearly a decade. His appointment is getting good reviews. But one congressional aide warns that Orbach will have his hands full "promoting science in an agency that seems to be losing interest."

Super Concerned Japanese researchers hope to recreate the events that led to last month's accident that destroyed nearly 6800 of the 11,000-plus photomultiplier tubes (PMTs) at the Super-Kamiokande neutrino detector (*Science*, 23 November, p. 1630). Leading theories involve the effects of water pressure, the energy released by the collapse of the 60-cm-diameter vacuum tubes, and the impact of debris from the first broken tube. "We are going to try to reproduce the disaster," says Yoji Totsuka, a professor at the University of Tokyo's Institute for Cosmic Ray Research and head of the observatory, which in 1998 recorded the first convincing evidence that neutrinos have mass.

The first test will shatter one PMT at the tank's bottom and watch its impact on others nearby. A second experiment will test the ability of prototype plastic cocoons to protect the tubes from shock waves and debris. Totsuka hopes to complete the experiments in time to present the results to an investigative committee early next month.

EPA Seeks Advice The Environmental Protection Agency (EPA) has put on hold plans to use studies in which companies dose people with pesticides while the National Academy of Sciences studies the issue. A 1996 law that requires new safety limits for pesticides on produce prompted industry to expose paid volunteers to chemicals to determine the minimum level at which a toxicant causes effects. The Clinton-era EPA barred using the human data due to ethical concerns, but last month agency officials said they were reviewing some studies (*Science*, 14 December, p. 2285). Now EPA has shelved the studies until the academy weighs in on whether some human research is "unacceptable," and on how the agency should handle studies that don't follow federal ethics guidelines.

that nocturnal rodents aren't scurrying around when predators can see them. The mutant mice were "grossly deficient" in masking, Weitz says.

Masking seems to be controlled by a signal carried directly to the SPZ by a small subset of ganglion cells, neurons found in the retina. Because the EGF mutants ran despite the light, that suggested that the EGF receptor is also responsible for masking and sent the researchers looking for that signal. They found that a small percentage of ganglion cells—about the percentage that are known to connect to the brain area called the hypothalamus, where both the SCN and the SPZ are located—contain EGF. "We don't know that those cells project to the hypothalamus yet," says Weitz, "but the numbers and distribution are very similar to the subset of ganglion cells that do." Weitz cautions that the data are not conclusive, but they suggest that both light and the clock may use the same molecular pathway to send the "don't run" signal. Clifford Saper of Harvard Medical School plans to use a method developed in his lab to see whether the EGF-containing retinal cells connect to the hypothalamus.

Meanwhile, Weitz and colleagues will continue to test molecules secreted from the SCN, looking for others that regulate wheel-running. For example, there must be a positive regulator that triggers the running activity at night. With such a molecule in hand, Weitz says, they can then look at how the positive and negative signals interact in the SPZ, whether they are received by the same or different neurons, and how those neurons interact to tell the motor centers of the brain to run or not to run. –**MARCIA BARINAGA**

LASER TECHNOLOGY

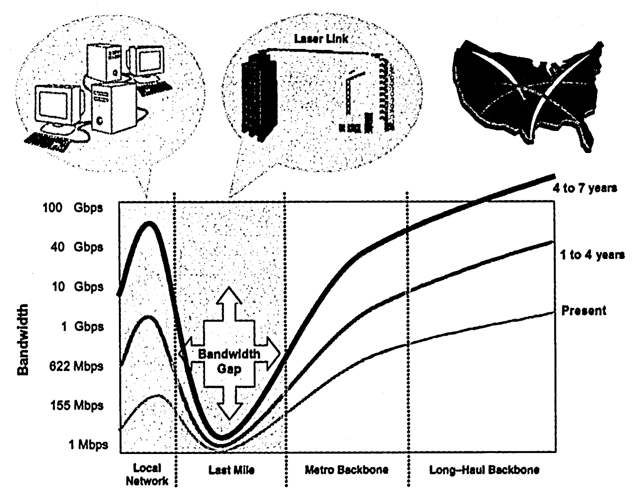
Hot New Beam May Zap Bandwidth Bottleneck

Still waiting to download full-length movies over the Internet or chat on a video phone? Blame the "last mile problem."

Long-distance fiber-optic cables transmit billions of data bits every second, plenty for these applications. But it would require digging up city streets, and more, to connect those cables to your home or office. Companies have recently been pursuing an alternative to laying fiber called free-space optics, in which an infrared (IR) laser beams data to a receiver on your rooftop. But the only cheap semiconductor lasers available aren't really up to the job. They work at a relatively short wavelength of about 1.5 micrometers, and the beams typically travel only a few hundred meters before being absorbed by water vapor in the air.

A report published online this week by *Science* (www.sciencexpress.org) suggests a new way to go the distance. A Swiss research team led by Jérôme Faist and Mattias Beck of the University of Neuchâtel describes making a new semiconductor IR laser with a wavelength of about 9 micrometers. Because water vapor—and even rain, snow, and smog—absorbs only a tiny amount of light at that wavelength, free-space optical systems built with the new laser should work at distances of 2 kilometers.

"We're very excited about it," says Jim Plante, president of Maxima Corp., a San Diego, California, company that is working to develop free-space optics technology. "With this technology we can conquer the weather." The longer wavelength lasers could also open a wealth of new research opportunities in atmospheric chemistry and medical diagnostics.



Filling the gap. A new laser may boost short-range data flow on a par with long-range fibers.

The Swiss group's lasers operate in a section of the spectrum known as mid-IR. Mid-IR lasers that generate light in a chamber filled with CO_2 gas have been around since the 1960s. But these lasers are bulky and expensive and must be cooled with cryogenic liquids. Research teams have begun to make semiconductor chip–based models that are small and potentially cheap, but they also require very low temperatures to keep them from burning out. Even then, the lasers spit out only intermittent pulses, rather than the continuous stream of light that is preferable for most applications.

To solve these problems, Faist, Beck, and their colleagues designed a novel structure for a "quantum cascade laser." QCLs, first developed in 1994 by Faist and Federico Capasso at Lucent Technologies' Bell Laboratories in Murray Hill, New Jersey, are an offshoot of traditional semiconductor lasers. In standard chip-based lasers, different semiconductor alloys emit different wavelengths of light. Gallium arsenide, for example, emits red light, whereas gallium nitride emits blue. In a QCL, however, the wavelength of the light is determined by the thickness of the active materials used. Each device consists of numerous semiconductor layers. When an electric current flows through them, electrons cascade down an electronic waterfall, an energetic staircase with numerous steps; when an electron hits a step, it emits a laser photon.

That's the theory. In reality, however, not all the electrons cascading in mid-IR QCLs are converted to photons. Many are absorbed by the semiconductor lattice, which generates enough heat to burn out the devices quickly. Researchers coped with the heat buildup by cooling the lasers to cryogenic temperatures and generating staccato pulses instead of a continuous beam.

The Swiss researchers, however, decided to make the laser shorter and narrower. "That allows electrons to tunnel more efficiently through the whole structure" and generate less heat, Beck says. Embedding the active region of the device in indium phosphide, an excellent heat conductor, whisked away the remaining heat. The new lasers not only work at room temperature but can produce a continuous beam of light without burning out.

Plante says the approach could revolutionize free-space optical communications. Although companies specializing in the technology have raked in more than a billion dollars in investments, Plante says, the industry has been struggling to put shorter wavelength lasers to work. "The use of mid-IR allows you to get the job done," he says. His company has already begun testing Faist and Beck's new QCLs, the latest versions of which can transmit data hundreds of times faster than a standard ISDN or T1 line.

The novel mid-IR lasers could be equally important for spectroscopy studies designed to detect particular gases in the air, says Frank Tittel, an applied physicist at Rice University in Houston. Potential users include atmospheric scientists measuring pollutants and medical researchers diagnosing disease from compounds in a patient's breath. Cheap and portable mid-IR QCLs, says Tittel, "would be a great jump forward." –**ROBERT F. SERVICE**

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