Seeing synapses: New ways to study nerves

Studying the linkages among the brain's billions of nerve cells is a bit like maneuvering through a dense thicket while trying not to break any branches. Tangled cellular appendages, called axons and dendrites, form a virtually impenetrable network for anyone who wants to observe nerve-to-nerve connections intact.

Nevertheless, two groups of neurobiologists are making headway. By using a nerve-muscle junction as a surrogate, one team has demonstrated how permanent changes in nerve connections can occur, changes that may underlie learning. A second team used special molecules, unleashed by lasers, to trace the circuitry created by these linkages. Both groups reported their findings this week at the annual meeting of the American Association for the Advancement of Science, held in San Francisco.

During development, nerve cells reach out to many other cells. Ultimately, however, they form only a few permanent connections, called synapses, between their axons and the dendrites of particular target cells. Experience can further modify these synapses.

To understand this paring of initial connections and subsequent modifications, Jeff W. Lichtman of Washington University School of Medicine in St. Louis studies neuromuscular junctions — the sites where nerve endings reach into muscle fibers. He and his colleagues observe these junctions intact in anesthetized mice. They label an axon's terminals with one dye and receptor molecules on the target cell with another. Thus they can see hourly, even weekly, changes in a given synapse.

"He's got the only real data [along] a time course and [with] a causal nature," comments Scott E. Fraser of the California Institute of Technology in Pasadena. "That's quite exciting."

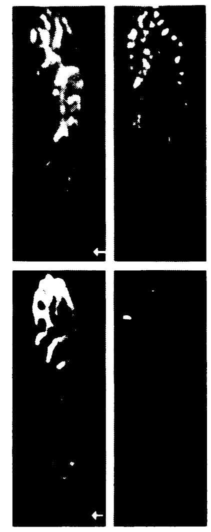
Neurobiologists have traditionally viewed axons as rivals that compete with one another during nervous system development to create a particular synapse. "The axon that wins that competition is more or less married to that postsynaptic cell," explains Lichtman. But as with many courtships, the dynamics of the relationship are not as they first appear. Lichtman's surveillance has revealed that postsynaptic cells play a key role in choosing the axons with which they will tie the knot, so to speak.

Initially, target muscle cells possess lots of receptors, and several axons form synapses with each cell. But then some receptors disappear, and eventually the axons at those spots withdraw. However, the successful axon does not expand onto the spots vacated by other axons, Lichtman says.

To investigate this dynamic further, he and colleague Rita J. Balice-Gordon exposed a tiny section of the target-cell surface to a chemical that blocks receptor activity. Afterward, they allowed each mouse to resume its normal life but reexamined these synapses almost weekly for a month.

After a week, the distribution of the dyes revealed that paring had begun; a week later, the receptors at that spot and their connecting nerve endings had disappeared, Lichtman reports. "A relatively simple manipulation of the activity of the target cell can cause a dramatic change in the synaptic input of that cell, [a change] that is permanent," he concludes.

At Duke University in Durham, N.C., Lawrence Katz takes a different tack. His group bathes slices of mammalian brain in a solution of caged glutamate, a chemical that cannot excite the nerve cells while encased. He and his colleagues then monitor activity in one nerve cell as they scan the slice with a laser.



Nerve terminals (top row) withdraw (right) when receptor targets (bottom row) disappear (right).

Lichtman/Washington Univ.

At each spot, the laser briefly releases glutamate, which activates the nerve cell there. But the monitored nerve cell reacts only if the activated cell connects to it, a technique that enables the researchers to map just that particular nerve cell's connections. Thus the Duke team witnessed how developing nerves first make many connections but later pare those linkages in a specific pattern, Katz reports. *— E. Pennisi*

A refrigerator with the coolest sound

Glassblowers have heard the sounds of cooling for centuries. Take a glowing hot glass bulb, join it to a cool glass tube, and listen for an ethereal hum. As the tube warms, it "sings," emitting a glorious tone.

In theory, that reaction can run in reverse. Sound, injected into a system at just the right power and pitch, can cause cooling.

Tinkering with such "thermoacoustic cooling," Steven L. Garrett and his colleagues at the Naval Postgraduate School in Monterey, Calif., have built a small refrigerator that cools its contents by blasting them with sound waves.

The idea is fairly simple: Loudspeakers at each end of a gas-filled, U-shaped tube emit alternating pulses of sound. The gas heats up as it is compressed and cools as it expands. To remove excess heat, a heat exchanger — acting like a car's radiator — pulls heat away from the tube, cooling the gas down. Using this system, Garrett's group has fashioned a cube-shaped unit that will become the prototype for a household thermoacoustic refrigerator, he reported this week in San Francisco at the annual meeting of the American Association for the Advancement of Science.

Garrett's efforts to cool gases with sound began at Los Alamos (N.M.) National Laboratory in the early 1980s and resulted in the production of a small test unit — the Space ThermoAcoustic Refrigerator (STAR) — that flew in the space shuttle Discovery in January 1992. His latest unit, the ThermoAcoustic Life Sciences Refrigerator (TALSR), employs improvements specially tailored for domestic use. TALSR, which is 40 times more powerful than STAR, is similar in design and cooling capacity to a home refrigerator, cooling to 4°C with 205 watts of energy; the freezer compartment chills to a frigid −22°C.

The little fridge achieves that feat by blasting a sustained, deafening tone at 160 decibels — 10,000 times louder than a rock concert — into a mixture of inert gases. Yet, with virtually no moving parts (only the speaker driver), the sealed, heavily insulated cooler remains quiet on the outside.

"We need a stethoscope to tell if it's running," says Garrett.

With an approaching 1996 ban on the production of ozone-damaging chlorofluorocarbons (CFCs), used in most refrigerators, sound-driven coolers offer some appeal. Using no CFCs, they are simple, safe, and environmentally benign. In theory, they can cool down to liquid-nitrogen temperatures or chill a room by a few degrees. Potential uses include portable air conditioners, storage units for heat-sensitive vaccines, cargo containers for tropical fruit, and cooling systems for computers.

Today, the sound-fridge is neither as cheap nor as efficient as conventional appliances. But Garrett contends that they could be "competitive in terms of cost and energy efficiency," and possibly available to consumers, within 2 to 3 years. So far, TALSR has met its most important laboratory test — successfully chilling its designers' beers.

— R. Lipkin