ordering of the beds. That supports both the geological analysis and the accuracy of the dating, says Bowring. "It used to be that plus or minus 5 million years was great. Now the question is: Can we split hairs at the 200,000- or 300,000-year level?" Bowring intends to find out by dating more ash beds in Namibia.

The new high-precision dating argues against a gap that would keep the Ediacara from contributing to animal evolution in the Cambrian, but Grotzinger and his colleagues concede that their new dating does not rule out most of the proposed scenarios. The Ediacara could have continued to evolve into more familiar animals; they could have perished at or very near the boundary and not contributed anything to later evolution; or they could have been a sister group of the Cambrian animals, as Seilacher is now suggesting, sharing a common ancestor that was not preserved in the fossil record. The MIT-Harvard group's discovery of Ediacaran fossils in some of the youngest strata in southern Namibia, younger than any Ediacarans known elsewhere, is a reminder of how spotty the ancient fossil record can be. More fossil collection is needed to resolve the Ediacarans' role, paleontologists say. Namibia, they add, looks like a good place to start.

–Richard A. Kerr

NEUROBIOLOGY

New Clue to Brain Wiring Mystery

The most complicated wiring task in the world occurs right inside our heads. During brain development, many billions of neurons must make precisely the right connections for our brains to work as they should. Developmental neurobiologists have learned in recent years that both the electrical activity of neurons and the presence of neuron-nurturing proteins called neurotrophic factors appear to be key to the final sculpting of neural connections. But they have not been able to figure out just what characteristics allow neurons to respond to those nurturing proteins.

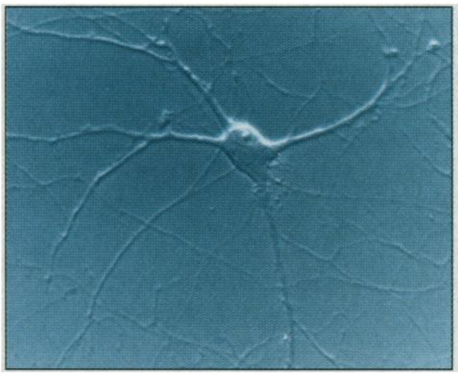
Now, in a paper in the October issue of *Neuron*, Barbara Barres and her colleagues at Stanford University School of Medicine provide a clue. In their studies of the survival of neurons in culture dishes, they discovered that pure preparations of neurons from rats' eyes must be in an activated state to be susceptible to the neurotrophic factors' effects.

The paper provides a "missing link," by connecting neural activity and neurotrophic factors, says Washington University neurobiologist William Snider. "It is a striking result," adds developmental neurobiologist Carla Shatz, of the University of California (UC), Berkeley, whose own work has implicated neurotrophic factors in the activity-dependent wiring of the visual cortex. The revelation that active neurons respond better to neurotrophic factors, she says, "may help interpret a lot of [other] results."

Barres's team was not directly addressing the problem of brain wiring, but rather was trying to determine the best conditions for growing cultures of purified retinal ganglion neurons, which in the developing embryo send their axons from the retina of the eye along the optic nerve to the brain. Central nervous system neurons such as these are notorious for dying when they are maintained in culture for any length of time, and sure enough, the retinal neurons died even though the researchers fed them an elaborate cocktail of trophic factors that they would be expected to encounter en route to the brain.

They tried stimulating the neurons, because other groups had shown that electrically activated nerve cells are more likely to survive in culture. That alone didn't do the trick, but when the researchers combined activation and trophic factors, the neurons at last survived. Apparently, activity raised levels of the intracellular signaling molecule, cyclic AMP, and that somehow enabled the neurons to respond to the trophic factors. Earlier studies had suggested activity may play such a role, but Barres is the first to verify it with pure cultures of neurons.

That finding caught the interest of developmental neurobiologists who study the remodeling that occurs during brain development. Developing neurons in the brain first make somewhat imprecise links with other neurons that must later be rearranged to create the specific wiring patterns needed for the brain to carry out its numerous functions. In the past decade, work from many research teams has shown that neurons whose electrical signals arrive simultaneously at a spot in the brain will add more connections in that area, while neurons that are inactive when others in the area are active tend to lose the connections they've already made. And in the past year, several groups have shown that neurotrophic factors may also play a role in this activity-dependent remodeling (see Article by Hans Thoenen on p. 593).



B. BARRES/*NEURON*

Survivor. Retinal ganglion neurons, such as this one, can live in culture when appropriately stimulated.

Now the Barres team has shown—at least in the culture dish—that it is the electrical activity itself that is the key to the selective effect of the neurotrophic factors. And these findings "fit together as a nice story" with another neuron culture study published last year, says UC San Francisco developmental neurobiologist Michael Stryker. In that study, Harvard University neurobiologist Michael Greenberg and postdoc Anirvan Ghosh showed that cultured neurons from the cerebral cortex of embryonic rats produce more of the neurotrophic factor BDNF when they are electrically active, and that the BDNF in turn enhances the cells' survival in culture (*Science*, 18 March 1994, p. 1618). But, says Ghosh, who's now at Johns Hopkins University, when the researchers simply added BDNF to the cultured neurons without stimulating them, it did little to help the neurons survive. Barres's work suggests that "not only did the cell need the BDNF it was making," says Ghosh, "but it actually needed to be in the [activated] state" to respond to the BDNF.

Together those papers suggest a model, says Stryker, in which a neuron receiving a signal produces more neurotrophic factor, and that factor in turn has a growth-promoting effect on nearby neural connections that are active at the same time.

While intrigued by the Barres paper, many neurobiologists caution that going from studies of neuron survival in a culture dish to predictions about synapse formation in a developing brain is a major conceptual leap that may not be justified by the Barres results alone. But despite his caution, Larry Katz of Duke University says his "gut feeling" is that the hypothesis will turn out to be right. Indeed, preliminary work, which will be presented next month at the annual meeting of the Society for Neuroscience by members of his lab and that of his Duke colleague Don Lo, shows that blocking the activity of neurons in slices of rat cerebral cortex blocks the growth-inducing effects of neurotrophic factors on those neurons. And that is just one of many related findings that are in the works in a number of labs, says Katz.

If these upcoming results continue to support the conceptual leap from the culture dish to the developing brain, researchers will be a bit closer to understanding how nature has solved the toughest wiring problem around.

–Marcia Barinaga