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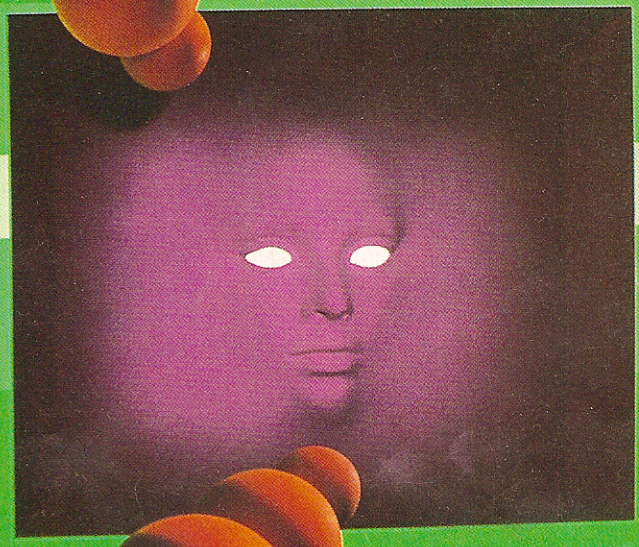

HUMAN HIBERNATION:
CURE FOR AGING AND OBESITY?

KILLER ROBOT

INTELLIGENT CELLS

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SMART CELLS

LIFE

By Kathleen McAuliffe

I experienced metaphysical angst for the first time in a high-school biology class as I peeped down the barrel of a microscope at a paramecium. The creature that confronted me was not the inert blob of cytoplasm I had expected. For all its simplicity, the paramecium demonstrated a dazzling array of behaviors as it agilely maneuvered about clumps of cellular debris, poked its tiny cigar-shaped body into thickets of algae in a feeding orgy, and engaged several partners in vigorous sexual flings. It had animus, spirit, consciousness—that indefinable quality that sets living things irreconcilably apart from lifeless matter.

"Smart little buggers!" I exclaimed within earshot of my teacher, who promptly set about squelching such unscientific thinking by accusing me of anthropomorphizing. Paramecia, she pointed out, could not be intelligent since they have no trace of a nervous system or brain. Indeed, a paramecium is smaller than a single brain cell.

Although I accepted her reprimand, I never quite accepted the theory. So it was with great interest and enthusiasm that I greeted new evidence indicating that living cells may actually possess computer "minds"—ultraminiature protein networks called microtubules.

Researchers using high-powered electron microscopes first spotted them in the early Seventies. Microtubules and related proteins were initially thought to be skeletons or supporting frameworks that give cells their characteristic shape. But theoretical calculations have now led investigators to hypothesize that these protein networks might be ideally suited for information processing. Because of their extremely small size, such computers—if that is what they are—would be many times faster and more efficient than any existing electronic device. As such, they might elevate microbes to the status of sentient beings—albeit simpleminded ones.

Interestingly enough, microtubules are also found inside the cells of higher organisms. And that discovery suggests that their role could extend beyond the psychic lives of microorganisms and all the way up the evolutionary scale to man. In fact, these structures are most abundantly represented in brain cells. There, they have been strongly implicated in such key cognitive processes as long-term memory and sensitization to learning. Some scientists speculate that microtubules, because of certain molecular-architecture characteristics, might be capable of generating images and storing information in a form similar to a hologram, a three-dimensional, lifelike image of an object.

The chief champion of this radical new view of microtubules is Tucson-based anesthesiologist Stuart Hameroff, who divides his time between medical practice and basic research at the University of Arizona's Health Sciences Center. Bearded, with a soft-spoken Western style that belies his New York origins, Hameroff entered his specialty with the goal of understanding how something as ephemeral as thought could have its origins in the physical structure of the brain. "If we can understand how anesthetics shut down neural activity," he observes, "we may better understand consciousness."

Although he now believes that anesthetics inhibit the activity of microtubules and associated proteins, what initially caught his attention about these cellular components was their uncanny resemblance to certain computer elements. An isolated microtubule is a long, hollow protein cylinder, reedlike in appearance. Inside the cell, however, these filamentous structures are tightly woven into a jungle-gym configuration that looks virtually identical to a high-tech bubble memory. During university lectures, Hameroff has even been known to slip a slide of such a device in place of one depicting a microtubule array. Invariably, the class mistakes the man-made invention for its biological likeness.

There is one big difference, though: size. Microtubules are dwarfed by today's electronic parts, which are several orders of magnitude larger. If anything, microtubules more closely resemble the futuristic biochips scientists hope to

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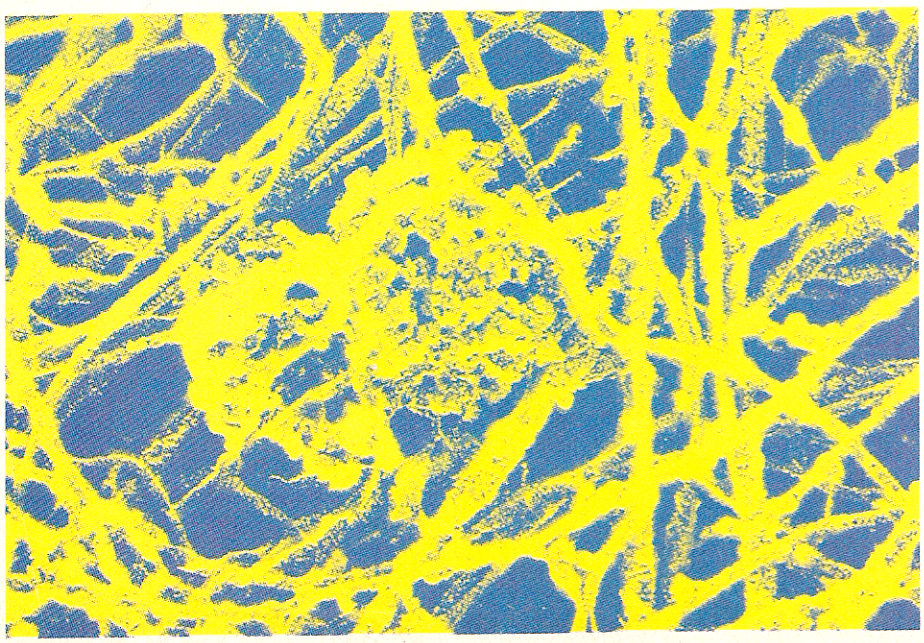

Microtubules, tiny reedlike structures that surround cellular organelles, may serve as cell computers.

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build, with the aid of genetic-engineering technology, out of molecules. For example, Gentronix, in Rockville, Maryland, a company in the vanguard of the burgeoning field of molecular electronics, believes the ultimate computer will take the shape of a three-dimensional protein lattice small enough to fit inside a cell. As Hameroff observes, Gentronix might just as soon be describing microtubules—a coincidence that does not strike him the least bit odd. "It's perfectly logical," he notes, "for technology to evolve toward biology, since natural selection would heavily favor the most efficient information-processing systems."

In bacteria, certainly, microtubules are instrumental in "sensing" external stimuli, processing the incoming signal, and orchestrating an integrated response—activities normally performed in higher organisms by the central nervous system. Microtubules inside the amoeba can somehow detect a nearby food source and orient their filaments toward it. As if woven by a spider, the protein web then grows out in that direction, dragging the main body of the amoeba with it until the particle is fully engulfed. Likewise, the hairlike cilia that paramecia use both to "feel" their environment and direct their propulsion are composed of microtubules. And when it comes time for the bacterium to replicate, its microtubules pull dividing chromosomes to opposite poles in much the same way as iron filings are affected when put on a piece of paper and held over a magnet. This phenomenon has led some scientists to theorize that microtubules may be capable of generating and sensing low-intensity electromagnetic fields.

In complex multicellular organisms, microtubules perform many of the same functions—only their role is considerably expanded. During fetal development, for example, they not only mastermind cell division, but they are thought to play a key role in determining which descendants will be specialized into skin, muscle, bone, and other body tissue. Just as an amoeba uses its protein network to gauge events in the outside world, Hameroff theorizes, a fetal cell may employ the same structure to sense changes in surrounding cells and thus "learn" what tissue it is to become.

It is within brain cells, however, that microtubules demonstrate the most intriguing properties. John Cronly-Dillon, a British professor at the University of Manchester, has uncovered evidence suggesting that these structures are vital in cognitive development, shaping the brain's internal-wiring scheme during the so-called critical period—a limited span in early life when the organism is particularly sensitized to learning. Experimenting with rats, he discovered that the animals' critical period for visual learning coincides with the availability of tubulin—the protein

building blocks of microtubules. Cronly-Dillon reports that on the thirteenth day of life, when rat pups usually open their eyes for the first time, the genes in the visual cortex that control the manufacture of tubulin suddenly step up their production. The excess of this raw material causes a neuron to spin out intricate protein gossamers, bridging the entire length of the cell and inducing it to form numerous connections with neighboring neurons. On day 35, when the critical phase for visual learning comes to a close, the rats' genes drastically reduce the level of tubulin output.

What happens at this stage, according to Cronly-Dillon, is that many nerve connections dissolve without a steady supply of tubulin. The effect would be similar to Ma Bell's suddenly being forced to limit the number of trunk lines leaving Manhattan from, say, 10 million to 10,000. How would the phone company decide which communications links to keep? If Cronly-Dillon is right, it would find much the same solution as the brain would: Maintain only those connections that are used most frequently. What survives, then, is by definition useful. Cronly-Dillon's model might also explain a paradox: Why is it that the more an organism learns, the less adaptable its nervous system becomes? Perhaps the plasticity of youth depends on a high level of tubulin.

Still other studies suggest that brain cells may store memories in their microtubule matrix. In goldfish, for instance, drugs that prohibit neurons from spinning out more protein webs effectively block the establishment of long-term memory, whereas drugs that have stabilizing effects on these structures facilitate learning.

In a related finding, the brains of mice that were reared in stimulating environments were found to have a much greater density of microtubules than the brains of mice raised otherwise identically in boring, impoverished environments.

Of course, none of this proves that microtubules are the physical framework on which consciousness rests. Yet enough clues have surfaced to make scientists like Hameroff wonder whether inherent properties of these proteins could endow them with information-processing capabilities. As his survey of the literature revealed, the tubulin subunits within individual filaments are arranged on a cylindrical grid, like kernels on a hollow ear of corn. To Hameroff, this design immediately suggested the stacked array of on/off switches that computers use to record binary code. To test this hypothesis, he and electronic engineer Richard Watt set about "programming" a computer-graphics-generated model of a microtubule. They found that they could induce it to simulate some of the functions of its real-life counterpart. From their model, they were also able to show that every time a neuron fires, microtubules inside the cell generate a different pattern of on/off states, setting a new cycle of information processing in motion.

Apart from operating at much faster speeds, their hypothetical microtubule seems to process data in much the same manner as today's linear processors. New dynamics apparently come into play, however, when microtubules are considered not as individual computer elements but as the tightly interwoven group they form in nature. Borrowing mathematical equations from a new branch of physics that goes by the arcane name of nonlinear electrodynamics, Hameroff, Watt, and computer scientist Steven Smith have shown how a nerve impulse could cause clusters of microtubules inside the cell to oscillate in unison, much like reeds swaying in the wind. These vibrations would in turn set up traveling wave fronts of energy. Where wave fronts overlap, the scientists have further shown, the pattern of interference could generate hologram-type images in the brain.

Not everyone is convinced by the sensational theories that have sprung up around microtubules. A major criticism is that such notions rest on layer upon layer of circumstantial evidence. "Sure, microtubules might have computing capability," says James McAlear, president of Gentronix and an acknowledged leader in the field of biochip development. "But no one has been able to demonstrate conclusively that they play a key role in the intelligence of higher organisms."

As father of the holographic-brain theory, Stanford neuroscientist Karl Pribram is more favorably disposed to Hameroff's ideas: "The model is highly theoretical," he concedes, "but it's also very elegant in that it could explain within one coherent framework many baffling phenomena in the field of consciousness studies."

When the pros and cons of the theory are tallied up, even critics agree that Hameroff has opened up an avenue of research that warrants further investigation. Microtubules may not turn out to be the double helix of the science of consciousness. But today's scientists are more willing than they were a decade ago to consider the possibility that tiny organisms have awareness. Ironically, this notion puts scientific thinking closer to that of such early naturalists as Charles Darwin, who assumed consciousness was manifested—at least in a rudimentary form—in the lowliest one-celled creatures. Reflecting this popular viewpoint at the turn of the century were books bearing such evocative titles as *The Animal Mind* and *The Psychic Life of Micro-Organisms*, the latter penned by none other than Alfred Binet (as in Stanford-Binet), best remembered as the father of intelligence testing.

Perhaps the tendency to anthropomorphize is not so unscientific after all. I may yet be vindicated if this irresistible temptation is shown to reflect the continuity of consciousness across all living forms, from paramecia to people. ∞

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