ATTENTION, BIOLOGICAL CLOCKWATCHERS

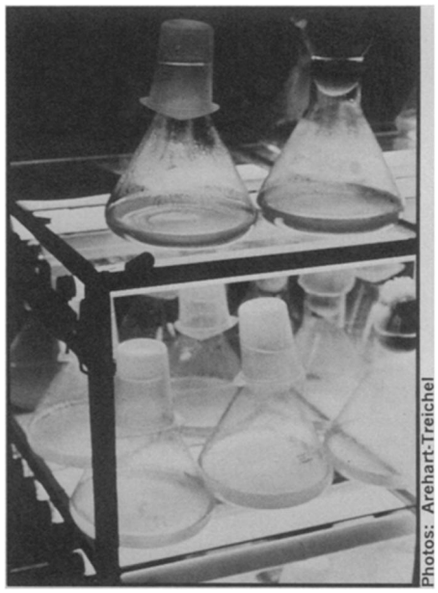
The cell membrane may be the time keeper of your body

by Joan Arehart-Treichel

Many human functions oscillate between minimum and maximum levels. Body temperature, blood pressure, breathing, pulse, blood sugar, amino acids—all rise and fall in circadian (24-hour) cycles. Biological rhythms such as women's menstrual periods occur on a monthly basis. Still others are annual. People secrete thyroid hormone during the summer to combat heat. Children show growth spurts in the spring. Births in the northern hemisphere are most common in March.

Human beings, understandably, hardly have an exclusive on biological rhythms. Dogs and cats can show an uncanny sense of clock hours as they appear for meals or walks. Oysters adjust their sleeping, eating, body temperature and hormone cycles to solar-lunar tides. Dinoflagellates, the algae that cause the dread red tide, give off an eery blue light every night. Annual rhythms in animals and plants make spring a festival of rebirth, autumn a time of dying.

Although external factors such as light, jet travel and social interaction can alter biological rhythms, they cannot do away with them. For this reason a number of biologists are convinced that while external factors can reset "the biological clock"—throw it out of phase—the clock is internal (SN: 9/11/71, p. 179). But where? Not a few investigators pinned their hopes on the major molecules of the cell—DNA RNA or protein. When they used chemicals to inhibit the synthesis of these molecules, the chemicals suppressed or enhanced cells' biological rhythms, such as algae's movement toward light. But once the chemicals were removed, the rhythms reappeared exactly as they had before. In other words, while the chemicals temporarily removed the hands of the clock or threw a cloth over the face of the clock, they did not succeed in extinguishing the clock itself. So many biologists came to conclude that the biological clock does not lie in the cell's genetic apparatus.



Photos: Arehart-Treichel

Dinoflagellates give off eerie light.

J. Woodland Hastings of Harvard University was one of the biologists who hoped that DNA, RNA or protein would turn out to be the biological clock and has since been disillusioned. So now he, with biophysicist David Njus and biologist Frank M. Sulzman, have come up with a new theory for the biological clock. It is the cell membrane. "We think," says Njus, "that it may be the way to go rather than DNA."

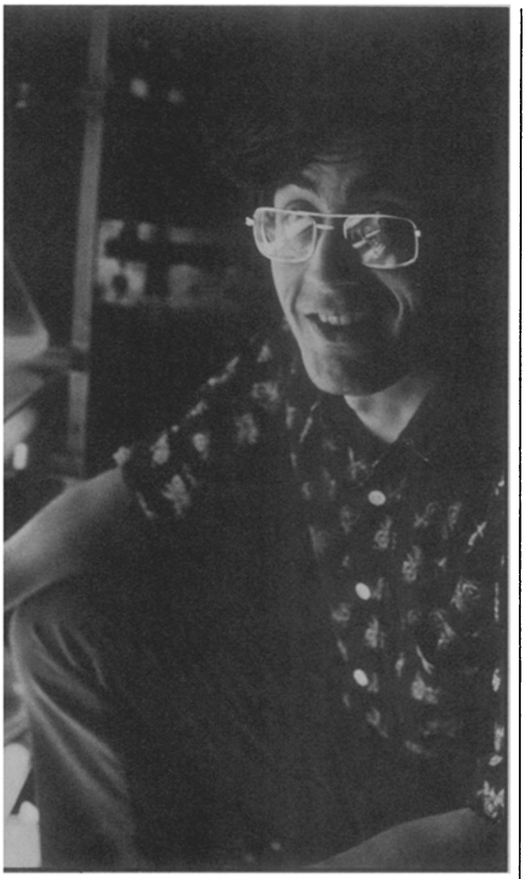
Their model of the clock consists of ions passing back and forth through the cell membrane as a feedback system. Hence the membrane is able to generate self-sustained 24-hour oscillations independently of DNA, RNA or proteins. This is a pleasing aspect of the model since nucleic acids and proteins don't look promising as the biological clock.

Evidence from the laboratories of both the Harvard group and other scientists supports a membrane clock model. For instance, ions passing through the membrane of nerve cells are known to exert feedback control over more ions trying to get through the membrane. Valinomycin, a carrier of the potassium ion through the cell membrane, causes a shift in the 24-hour photosynthesis rhythm of the bean plant and in the 24-hour bioluminescence rhythm of dinoflagellates, suggesting that ion passage through the membrane is intimately linked with biological rhythms. Other cellular rhythms, such as respiration and movement toward light, could also depend directly on ion variations.

The model accounts for the effect of the major phase-shifter of biological rhythms: light.

In mammals, light is known to change the permeability of the retinal cell membrane to ions. Thus light could alter the amount of ions passing through the retinal cell membrane. This perturbation could exert a feedback effect on new ions entering the cell and hence phase-shift the ion oscillations. Hormones might then serve as messengers between retinal cells and other cells in the body.

In lower animals and plants, light could work comparable changes in ion gates in membranes. When a phytochrome—a pigment that helps plants respond to light—was placed in an arti-



Njus: Looking for mutant rhythms.

ficial membrane, ion movement through the membrane changed.

If the cell membrane is indeed the site of the biological clock, which components of the membrane might serve as mediators of ions passing through? The Harvard biologists propose that ion fluxes, both passive and active, would probably be mediated by proteins in the membrane. But the properties of the proteins in turn probably depend on the fluidity of lipids in the membrane. Since circadium rhythms are temperature-compensated—the rhythms change little with any change in temperature—and since lipids in membranes are known to adapt to temperature, membrane lipids could well be the ultimate key to the biological clock.

The Harvard biological team is now trying to test their model experimentally. They agree that it's a tough challenge. Cell structures and functions can often be studied or measured by grinding cells up. But biological rhythms are neither structures nor functions, but a phenomenon. "As soon as we grind up the cell, the rhythms are gone," Njus laments. So they are taking another tack: isolating dinoflagellates whose biological rhythms deviate from the norm, then looking to see whether the mutants have mutated proteins in their membranes. "If isolated mutants have similar changes in their membrane structures," says Njus, "then it might be a key to the clock." □

. . . Plastics

available to researchers, they were able to use it as an intermediate in an important cancer drug.

"I think the guys down in Washington just get law happy. We in the chemical business, especially the small company, think this thing can be taken care of by voluntary means."

Small chemical companies generally don't have testing facilities and budgets comparable to larger companies, but some critics feel the dangers warrant increased spending and vigilance. A Providence, Md., physician, Pietro U. Capurro, recently made public his research (and growing alarm) about the high death rate in that town from similar cancers since a small chemical company opened there in 1961. Residents (presumably affected by air pollution) as well as plant workers have died in larger than expected numbers.

While disagreement and inactivity continue on amending Government regulation, there is a consensus on the need for more research on new and existing components of plastic manufacture. Several Government and university scientists made eloquent statements at a recent NIEHS meeting in North Carolina on the need for more research funds and more toxicologists. NIEHS Director David P. Raul says flatly, "The Government has just not allocated enough of its scarce resources to environmental research." OSHA health division administrator John P. O'Neill says his agency is now considering additional standards for several plastics components based on toxicology research, but "priorities have to be set for developing these standards because of limited administrative and research funds. The program will be greatly assisted as more data are available. When the standards were first written for the implementation of OSHA, it became evident that there were very little data available on the impact of chemicals on workers. Actually, much of the data we would need to establish effective standards lie in industry. They have experience with different control methods and workable standards, and these data are necessary if we are to avoid setting ivory tower standards.

"At this point," says O'Neill, "I think it would behoove the chemical industry to establish some strict exposure standards for themselves. Just because a chemical is not known to be toxic or deleterious at the time, there is no reason industry should permit unlimited exposure to the workers as is now done in some cases. They should take information from the list of hazardous chemicals already established by NIOSH, examine these chemicals in their own plants and control them now, and not wait for laws to be passed or for workers' health to be impaired." □