same time, a visiting scientist in the group, François Pierre, who is on leave from the elementary particle physics department at Saclay, in France, was going over data himself. Within a few days, both had independently found evidence for the new particle. (One day on the way to lunch, each said to the other, "By the way, I have something to show you!")

Since then, the entire LBL-SLAC team has collected about 200 events, half with a decay into a K meson and a $\pi$ meson and half into a K meson and three $\pi$ mesons. According to Roy Schwitters at SLAC, a multihadronic decay event is detected about once a minute, and, in about 1 percent of these, researchers find the new particle.

Evidence for a second charmed meson produced in association with the first has also been obtained. Lack of such evidence would have been highly damaging to the charm model, since the mesons must be produced in pairs to conserve charm. The evidence rests on what is called a recoil mass spectrum. Knowing the energy and momentum that went into the collision and subtracting the energy and momentum of one of the products, the researchers can determine the energy and momentum of the "rest." It turns out that the mass of the "rest" is centered in a region between 2 and 2.2 Gev, indicating that the second particle has a mass different from the first. More data has to be accumulated, however, before the LBL-SLAC investigators will estimate the energy more precisely.

Less cautious in their interpretation are others who have seen the recoil data, which appears to show two peaks at 2 and 2.15 Gev. Glashow and his associates at Harvard say the apparent structure is consistent with the simultaneous production of a charmed meson in either a 1.865-Gev ground state or a 2-Gev excited state and a second charmed meson in the excited state. Rapid decay of an excited charmed particle into its ground state could give rise to the particle observed in the invariant mass distribution.

The particles that the investigators found are electrically neutral. There should also be a charged meson with charm at about the same mass as the neutral meson and a second charged meson at a mass (in the ground state) of about 2 Gev. Neither of these particles has been observed as yet. Theorist Michael Chanowitz at LBL points out that they could be detected by their characteristic decays, but because the charged particles should be produced much less frequently than the neutral ones, much more data must be accumulated before a statistically valid identification could be made.

### Checking Charm's Consequences

Glashow, who is coinventor of the charm model, is obviously happy with the particle discovery, as well he might be. Charm was first postulated more than 10 years ago on what can fairly be described as esthetic grounds. Later on, the model was extended to explain certain discrepancies in the decay by weak interactions of strange particles, such as the K meson. It has to be regarded as deeply satisfying, argues Chanowitz, if a concept proposed years before for altogether different reasons should now be the key to understanding the surprises in elementary particles that have occurred in the last 2 years.

The task now is to verify the several predictions of the charm model that have not as yet been observed. If, as SLAC's Sidney Drell points out, the LBL-SLAC group's experiment is by far the most convincing piece of evidence for charm up to now, until all its consequences are checked out, scientists must retain an open-minded skepticism.

For one thing, other decay routes of the neutral particle besides K-$\pi$ and K-3$\pi$ ought to be seen, observers agree. One important example of these, according to theorist Fred Gilman of SLAC, is called a semileptonic decay via the weak interaction in which charm is not conserved (none of the decay products have charm). In the semileptonic decay mode, the putative charmed meson should often decay into hadrons (including a K meson), a charged lepton (an electron, a positron, a muon, or a antimuon), and a neutrino.

The only other laboratory in the world able to duplicate the SPEAR experiment is DESY. In particular, the scientists there have a particle detector that is particularly suited for picking out electrons and positrons from other charged particles. Verification of the semileptonic decay might therefore come from DESY. Bjorn Wiik, a group leader at DESY, has reported that his group has seen electrons under the expected conditions. But, he cautions, it will be a few more weeks before enough data is in hand to ascertain whether the electrons are coming from the decay of the particle seen at SPEAR or from some other source.—ARTHUR L. ROBINSON

G. Kolata (1976)

# Water Structure and Ion Binding: A Role in Cell Physiology?

A major difference between living and dead cells is that living cells selectively retain certain ions, such as potassium, and exclude others, such as sodium. Ion concentrations in dead cells reflect those in the solutions surrounding them. For more than 15 years, a small group of researchers has challenged the conventional explanation of this effect. Most physiologists believe that it is due to ion "pumps" in membranes. The pumps are said to use cell energy to transport some ions into and others out of the cell. The dissident group, however, contends that the pumps do not exist and that, instead, ions are excluded from cells on the basis of their low solubilities in cellular water, except when specific charged sites with which the ions can associate are available. Cell water, they maintain, has a different structure than either liquid water or ice, and this special structure affects the solubility of various ions in it.

Dialogue between advocates of pumps and of structured water and ion binding has been strained (see box). Each side believes it has steadily accumulated evidence that the other side is wrong. Recently, however, some crucial experiments and calculations have been performed that provide strong evidence for the existence of pumps. These results do not rule out the possibility that structured water still plays a role in cell physiology, but the details of such a role remain to be determined.

The structured water and ion binding theory is based on the following argument. First, its advocates believe they have evidence that ion pumps are thermodynamically impossible—they would require more energy than is available to the cell. This means that there must be some other explanation for selective ion retention and exclusion. Next, its advocates point to their use of nuclear magnetic resonance (NMR) to probe the structure of cell water. Results of NMR studies, they claim, demonstrate that cell water is more structured than liquid water and less structured than ice. This would affect the solubilities of ions in the cell and could account for selective ion exclusions.

Two results have been published that structured water advocates interpret as demonstrating the impossibility of ion pumps. In 1952 Gilbert Ling, now at Pennsylvania Hospital, poisoned muscle cells so that they could have no energy sources other than two energy-yielding compounds, adenosine triphosphate (ATP) and creatine phosphate, already present in the cells. Under these circumstances, the cells still accumulate potassium and exclude sodium for about 8 hours. After poisoning the cells, Ling measured the average fall in the concentrations of ATP, adenosine diphosphate, and creatine phosphate so that he knew how much energy the cells used. Concurrently, he measured the rate at which sodium ions were excluded from the cells to determine how much energy would be required by a sodium pump, if such a pump existed. Ling concluded that a sodium pump, operating at 100 percent efficiency, would require at least 15 to 30 times as much energy as was available.

In 1973 Raymond Damadian and Lawrence Minkoff of the State University of New York Downstate Medical Center in Brooklyn performed an experiment similar to Ling's and obtained a similar result. However, they used bacteria rather than muscle cells and studied the transport of six substances rather than one. They also differed from Ling in the way they measured the amount of energy used by the cells after access to any new energy sources was prevented. Minkoff and Damadian measured the rate at which ATP was hydrolyzed (providing energy) by seeing how quickly radioactively labeled phosphate present outside the cells was taken up by the cells and incorporated into the terminal phosphate of ATP.

The experiments by Ling and by Min-

## Structured Water Advocates Air Complaints

The controversy between proponents of the structured water theory and the vast majority of physiologists and biophysicists who do not advocate that theory does not seem to be entirely based on scientific differences. The structured water advocates claim that their theory of the behavior of water and ions in living cells is summarily dismissed by mainstream scientists and that they are often prevented from receiving grants and from publishing. They testified in Congress last year about their lack of funds and recently began a campaign to protest their treatment by the editor and council of the Biophysical Society.

One of the leading spokesmen for the structured water theorists is Freeman Cope of the Naval Air Development Center in Warminster, Pennsylvania. It was Cope who testified at the congressional hearings that Representative John B. Conlan (R–Ariz.) held on National Science Foundation (NSF) funding—a move that many physiologists contend hindered more than helped the cause of the structured water advocates.

Cope called for a cessation of grant support for research on the opposing pump theory and asked that the present administrators in the biomedical division of the NSF be replaced. And although most investigators believe that the pump theory is valid, Cope dismissed it in his testimony. He said the NSF "has been wasting tax money funding research on a scientific hypothesis which has been disproven, and which has not and is unlikely ever to be of any practical use to anybody." Cope's testimony, he claims, was brushed off by the NSF. It served, however, to alienate many advocates of the pump theory.

In addition to castigating the NSF, Cope and his supporters recently launched an attack on the leaders of the Biophysical Society. They allege that they have had great difficulty publishing in the *Biophysical Journal* in the 2 years that Frederick Dodge has been editor of that journal, although Dodge has published criticisms of their theory. Moreover, they say he did not permit them equal space to reply. To try to open the ranks of the Biophysical Society to proponents of structured water, Cope wrote a letter to all members of the society asking that they vote for his colleague, Carleton Hazlewood of Baylor University, for a position on the council of the Biophysical Society. Hazlewood, however, was narrowly defeated.

On 5 March 1976, 2 months after writing his original letter, Cope wrote a second letter to members of the Biophysical Society asking that Dodge resign. In this letter Cope stated that Dodge's refusal to publish replies to criticisms of structured water advocates "was a misuse of editorial power by Dr. Dodge to suppress publication of work which threatened his self-esteem, professional reputation and grants, which depend on maintaining the illusion of validity of old concepts of salt and water biophysics upon which the professional reputations of Dr. Dodge and his friends are built." Cope then asked that the members of the Biophysical Society join a new society that he and his colleagues were founding (and thereby subscribe to a new journal). Concurrently, Gilbert Ling of Pennsylvania Hospital, who is a founder of the structured water theory, sent a letter to members of the council accusing Dodge of censorship.

In response to these repeated attacks by Cope and his group, Dodge, who is at IBM's Thomas J. Watson Research Center in Yorktown Heights, New York, says he wishes to stay aloof. He explains that, unlike his predecessors, he chose not to let proponents of the structured water theory review each other's papers. Consequently, they now find it difficult to publish in the *Biophysical Journal*. Although Dodge refused to be quoted, he made it clear, in a conversation with *Science*, that, in his opinion, there is no truth or substance to allegations of conspiracies among the editors of the *Biophysical Journal* against papers by the structured water group.

The bitterness and frustration expressed by members of the structured water group have made peaceful coexistence with their opponents impossible, and they are becoming increasingly isolated from other physiologists and biophysicists. As one observer notes, "there is paranoia on one side [the structured water advocates] and contempt on the other [the pump advocates]." Thus the communications gap between the structured water advocates and mainstream scientists seems likely to continue in the foreseeable future.—G.B.K.

koff and Damadian are central to the contention that pumps cannot exist. Soon after the work of Minkoff and Damadian appeared in print, however, two letters were published criticizing it and, although they defended their work, most physiologists believe the criticisms have held up. The problem, according to these critics, is that Minkoff and Damadian greatly underestimated the amount of energy available to the bacterial cells because Minkoff and Damadian failed to account for the large intracellular pool of phosphate in those cells. This pool would limit the rate at which the labeled phosphate would be taken up by the cells.

Although the criticisms of the experiments by Minkoff and Damadian cast some doubt on their conclusions, the older work of Ling was, until recently, either ignored or unquestioned. Now, however, two investigators—Jeffrey Freedman of Yale University and Christopher Miller of Cornell University—have discovered that Ling's data are compatible with a much lower rate of sodium efflux from the cells than Ling estimated. They report that Ling's analysis of his data led him to assume that sodium was being transported out of the muscle cells at least 20 times faster than the rate accepted by muscle physiologists. Thus in neither muscle nor bacteria cells, if these critics are correct, are pumps thermodynamically infeasible.

If pumps are possible, the next question is, Do they exist? One way to answer this would be to see whether isolated intact cell membranes, without the components of cell interiors, still accumulate potassium and exclude sodium. This would test the pump theory because such membranes could not enclose structured water.

Structured water advocates maintain that cell water interacts with charged macromolecules inside cells. Water molecules act as dipoles and line up against these charged molecules, the positively charged ends of the water molecules against the negatively charged sites on the macromolecules. Then another layer of water molecules lines up against the initial layer and so on, resulting in concentric layers of oriented water molecules about a macromolecule. As the distance from a charged macromolecule increases, order in the water layers decreases.

Freedman recently showed that sealed red cell membranes that enclose virtually no cytoplasm—referred to as red blood cell ghosts—exclude sodium and accumulate potassium. He points out that these ghosts have almost no proteins inside them to orient water molecules. Almost all (98 percent) of red blood cell proteins are hemoglobin molecules, and the ghosts contain less than 5 percent of their original hemoglobin molecules. It could be argued that the ghosts bind potassium to charged sites on their membranes, but this argument cannot hold for sodium. Thus Freedman concludes that pumps may exist and structured water and selective ion binding by cellular macromolecules may not be the sole explanation for selective ion accumulations and exclusions. (Experiments similar to Freedman's were done previously by others but those investigators did not rigorously exclude the possibility that some whole red blood cells were present among the ghosts. Freedman ruled out this possibility.)

Other evidence consistent with the idea that pumps exist has been obtained by investigators who reconstituted artificial membranes. For example, Shirely Hilden and Lowell Hokin of the University of Wisconsin Medical School added enzymes thought to be sodium and potassium pumps to phospholipids. The resulting vesicles, they found, transport sodium and potassium if they are supplied with energy in the form of ATP. Efraim Racker of Cornell University obtained similar results with an artificial membrane containing an enzyme thought to act as a calcium pump. Moreover, the transport of sodium, potassium, and calcium through these artificial membranes did not appear to require inordinate amounts of energy.

Many investigators, including advocates of pumps, agree, however, that cell water may have some ordered structure that makes it different from liquid water. Water molecules are known to line up against charged surfaces of macromolecules, and NMR relaxation times of water molecules in cells are different from those of liquid water. These relaxation times provide a measure of the environment of water molecules and, specifically, how much freedom of motion they have. Most investigators, then, do not question that cell water is likely to be structured but ask to what extent it is structured and what the physiological importance of this structure is.

Asking how much cell water is structured often leads to semantic arguments, according to Samuel Horowitz of the Michigan Cancer Foundation in Detroit. Horowitz claims that the terms "remain undefined and ambiguous." Thus investigators come up with vastly different interpretations of similar data, making debate meaningless.

The more important question of the physiological importance of structured water remains unanswered, although there is evidence that the water does not exclude various ions and compounds such as sodium and certain sugars to the extent postulated by the structured water advocates. Freedman asked whether sugars that are not metabolized by cells will be excluded from them. He found that six such sugars had concentrations inside cells that were within 10 percent of their concentrations outside the cells. The structured water advocates would predict that these nonelectrolytic substances should be excluded from the cells.

Horowitz and Philip Paine recently performed an experiment designed to bypass the complexities introduced by the cell membrane. These investigators first injected a small pool of liquid gelatin into oocytes and allowed it to gel in place. This pool represented a solvent inside the cells whose properties had been studied outside cells and which was known to resemble ordinary water. They then injected radioactively labeled sucrose into the cells, allowed it to come to equilibrium, and measured its concentration in both the cytoplasm and the gelatin. They found that significantly less sucrose was present in the cytoplasm than in the gelatin, indicating that the water of the cytoplasm was not as good a solvent as the water of the gelatin or, by extension, ordinary water.

As the experiment by Horowitz and Paine demonstrates, the possibility that structured water may be important to cell physiology remains open. Investigators have shown, moreover, that some properties of cell water apparently change with the states of cells. Damadian reported that cancer cells can be distinguished from most normal cells by their NMR relaxation times, indicating that at least some properties of their water may be altered. (Other investigators, however, contend that Damadian is detecting cells with increased amounts of water in them, which does not necessarily mean they are cancerous.) Paula Bell and Carleton Hazlewood of Baylor College of Medicine in Houston together with Potu Rao of the M. D. Anderson Hospital and Tumor Institute in Houston found that NMR relaxation times of HeLa cells change during the cell cycle. Thus, although the role of water structure and selective ion association in cell physiology may not be as great as structured water advocates claim, the nature, extent, and possible functions of the association of ions and water with cell macromolecules may be worthy of further study.—GINA BARI KOLATA