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New methods for freezing and storing at low temperatures might lead to many new potentialities for the human race, the most exciting of which would be the opportunity for dying individuals to avail themselves of future medical progress. Successful experiments have already been done with cells and lower animals, but many problems remain.

PHYSICS AND LIFE PROLONGATION

by Gerald Feinberg

SCIENCE AND TECHNOLOGY in the 20th century have made real many dreams of men in earlier ages. Among these are transmutation of elements and manned space flight. Another dream of many men in different places and times, that of elimination of aging and death, remains unfulfilled by us. Scientists who work on this problem do not know how to solve it or even whether it can be solved at all.[1] I cannot answer these questions here, and I believe that physics is somewhat peripheral to their solution. Instead what I shall do is to present a somewhat novel way of looking at the matter, based on an optimistic estimate of future scientific progress. In addition, I shall discuss how some results of low-temperature biology (cryobiology) open the possibility to those living of taking advantage of this progress before the problems of aging and death are solved. This possibility depends on development of reliable methods of freezing, storing at low temperatures and reviving humans.

Developing such methods would lead to many new potentialities for the human race. The most exciting of these seems to be that of being able to take advantage of future medical progress. The methods will probably involve coöperation among biology, medicine and physical science. This can be seen from a brief list of some key unsolved problems in this area: (a) developing more efficient methods of heat transfer for cooling and thawing, (b) better understanding of the mechanism of damage in freezing cells, (c) discovery of more effective protective agents against freeze damage and (d) study of possible harmful effects of long-term storage on animals.

These problems may not be easy to solve, but in view of the immense consequences of their successful solution, we should undertake a strong effort to solve them. I shall try to indicate the important role that physics has in this effort. The reasoning I shall present is not original although I find it compelling. It has been given by Jean Rostand, for example, in more detail by the physicist Robert Ettinger in his book[2] *The Prospect of Immortality* and by Leo Szilard, in a story "The Mark Gable Foundation."[3]

Future progress of science

It has become commonplace to note that most people who have ever worked in science are still alive. Furthermore, most of the known fields of science have short histories, measured in decades. In view of these facts and of the obviously great advances in science and technology in this century, it is reasonable to expect that many problems we can not now solve will be solved by future scientists and that many limitations of our present technology will not be limitations of future technology. Predictions by scientists of the future of science and technology do not usually recognize this and are therefore almost certain to be insufficiently imaginative or optimistic when compared wih actual developments.

I believe the opposite approach is better, and a good first approximation for such predictions is to assume that everything will be accomplished that does not violate known fundamental laws of science as well as many things that do violate these laws. This is not a statement within a field of science but a statement about science. The distinction is important because some of the very talents required for successful work within a science, for example, step-by-step logic and suppression of extreme speculation, may be disadvantages in predicting what will be accomplished by methods as yet unknown. This paradox is neatly summarized in Arthur Clarke's law,[4] which

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Temperature Change and Metabolic Rate

ΔE (kcal/mole)	T_1 (°K)	T_2 (°K)	$\frac{Rate\ (T_2)}{rate\ (T_1)}$
10	310	80	$\exp[-46] \approx 10^{-20}$
10	310	190	$\exp[-10] \approx 10^{-4}$
20	310	80	$\exp[-92] \approx 10^{-40}$
20	310	190	$\exp[-20] \approx 10^{-8}$

says, "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Although this law may not be universally true, it does suggest good advice for distinguished scientists.

The principle that everything possible will eventually be accomplished does not give any guide as to how long it will take to do any particular feat. Here again predictions are usually too pessimistic. Things we can think of today as possible, without knowing how to do, are the ones that will be done in a relatively short time. It is these things we cannot yet even imagine that will take longest to accomplish. I am inclined to put 200 years as an upper limit for the accomplishment of any possibility that we can imagine today.

Application of this view to progress in medical science leads to the conclusion that cures for all diseases that afflict man eventually will be found. This accomplishment would be just a step along the way toward regulating biological processes in living organisms on all levels from molecular to macroscopic. There seems to be no reason why macroscopic regulation should not be possible. Some biologists have already suggested steps that could be taken towards this goal.[5] If one accepts that aging is a particular set of chemical and physical changes that occur within living organisms, the logic of this argument suggests that it will eventually be controllable and reversible, even if the methods are as yet unknown. This seems to me a much safer bet than the opposite view.

If it is true that "tomorrow will be better," in the sense described above, there remains the question of how this is relevant to prolongation of life for those alive today and in the near future. After all, someone dying of pneumonia in 1920 was not materially helped by development of penicillin therapy 20 years later. There is an approach to this problem that holds out promise to those alive now of taking advantage of future medical advances. This approach does not involve any major revisions in physics such as travel through time or any immense practical difficulties such as would be involved in using relativistic time dilatation. It is based on the fact that biological processes are temperature dependent and that at sufficiently low temperatures, biological activity can be stopped for arbitrarily long periods, and then, in principle, and in many cases in practice, restored by rewarming. It is this possibility that will open the door to the future.

Cryobiology and the future

It has been known since Arrhenius that the rate of biochemical reactions depends on temperature in a relatively simple way. The dependence, not hard to derive,[6] is given by

$$\text{Rate} \propto \exp\left[-\frac{\Delta E}{RT}\right] \qquad (1)$$

(R is the gas constant $= 2$ cal/deg-mole, T is the absolute temperature and ΔE is a constant characterizing the reaction, called the "energy of activation"). ΔE can be taken as an empirical constant although some estimates of it can be given theoretically. For typical biochemical or biological processes, ΔE is 10 or 20 k cal/mole.

The rate equation holds not only for elementary biochemical reactions but even for such phenomena as human-heartbeat rate.[6] It is clear from the equation that a substantial temperature reduction from the ordinary temperatures of living organisms will produce an enormous slowdown in the rate of biological processes, as shown in the table.

The data indicate that a biological system maintained at low temperature would for all practical purposes not undergo any metabolic processes involved in life or aging. But can such a system be brought to and from such a temperature without destroying it?

This question has been affirmatively answered for such simple systems as bacteria, yeast and protozoa.[7] These have been frozen and stored at temperatures down to −190°C for periods up to years and then successfully rewarmed and revived. The deterioration rate of the stored organisms appears to follow the rate equation reasonably well.[8] Techniques for ensuring survival of the organism have been developed somewhat empirically and are not completely understood. For example, in yeast, survival is greatest when the yeast is cooled slowly (~ 1°C/min) and warmed rapidly. This is not, however, a uniform phenomenon for all cells.

Successful freezing and thawing of a wide variety of cells of different types and from different species of multicellular animals have also been accomplished.[7]

In general, such cells do not remain viable if they are simply cooled below −10°C and later thawed. In 1949 C. Polge, A. U. Smith and A. S. Parkes[9] discovered that avian spermatazoa in a 10% glycerol solution could be frozen, stored at −79°C, thawed and revived. It has since been found that glycerol has a similar protective effect on many other kinds of cells as do certain other agents such as dimethyl sulfoxide. There is no completely convincing theory as to how this protection occurs since it is not clear what causes damage to cells frozen without protection. One plausible theory, advanced by A. M. Karow and R. W. Webb,[10] is that damage in freezing occurs when the part of the water within a cell that is bound to the cellular protein freezes. This destroys the lattice of water molecules that helps to maintain the shape of protein molecules, and the protein then denatures. The function of the protective agent is then to strengthen the water lattices sufficiently that they are not destroyed in the freezing process. Other theories have also been suggested. This problem requires cooperation among physicists, chemists and biologists. With development of an understanding of freeze damage and protection, a more systematic search could be made for optimal protective agents, and it would not be surprising if better ones were found.

The next step to the freezing and preserving of organs over long periods has not quite been accomplished although partial successes have been reported in the journal *Cryobiology*.[11] There are obvious problems in freezing organs such as assuring reasonably uniform cooling, perfusion of the organ with cryoprotective agents and optimal methods of rewarming. It is also unclear whether the damage to the organs occurs during cooling, storage or rewarming. Here again collaboration between physics and biology appears called for.

Freezing mammals

In the meantime, interesting experiments have been done[7] involving cooling of small mammals to temperatures not far below 0°C. Experiments have been carried out with hibernating animals such as golden hamsters. In the most successful experiments hamsters were cooled so that their deep body temperature was about −2°C, and about 50% of their total body water had frozen. They could then be kept for up to an hour this way and then revived by diathermy rewarming. Approximately half of the hamsters so treated recovered and lived out their normal life span. Thus far it has not been possible to extend the storage period or lower the temperature and still revive the animals for a long period.

Recently this work has been extended to nonhibernating mammals, rats, by P. and V. P. Popovic.[12] They were able to maintain young rats at −1°C for up to an hour in a supercooled state (that is with their body water still liquid) before thawing and reviving them. Short-term survivals (up to 24-hr. after thawing) of frozen rabbits and primates (galagos) have also been achieved. It is not clear why these larger animals eventually die or whether more efficient rewarming methods would serve to increase these survivals. None of these experiments involved use of cryoprotective agents, which would have obvious advantages in view of the results with cells.

Smith in her book[7] concludes her section on mammals with the following comments. "So far no technique has been evolved for perfusing individual organs or the whole mammal with glycerol and removing it without damage. If this could be done, it might be possible to cool the intact mammal and resuscitate it from temperatures as low as −70°C. Long-term storage of frozen mammals might then be considered . . . . Progress along these lines may require a team of physiologists including experts in surgery, electronics and other disciplines." The experience of physicists working at low temperatures would be of great value in some of the technical problems in realizing this goal.

An interesting by-product of the experiments on cooling mammals came from work by R. K. Andjos et al,[13] who cooled rats to temperatures just above freezing and maintained them there for 1-2 hr. At such temperatures the rats show neither heartbeat nor electroencephalography. The rats, however, could be revived fairly easily by diathermy rewarming. Rats that had been trained to solve problems of finding food in a maze were cooled and revived in this way. They retained the memory of their training by still being able to solve the maze. This experiment shows that memory is stable under cooling and thawing of the animal and indicates that memory involves some kind of chemical imprint in molecules rather than circulating electric currents since the latter had presumably ceased at the temperature where the EEG trace vanished. This conclusion about the nature of memory is in harmony with other recent experiments.[14] The result is of vital importance for the prospect of freezing and long-term storage of humans at low temperature since the preservation of memory and personality would be the main reason for undertaking such storage.

Freezing humans

Successful methods for freezing, storing and reviving humans would evidently have widespread applications. One that has been considered by many

Engravings after Holbein

authors would be to make interstellar voyages possible; they would otherwise be rather difficult. Other technological problems, however, might delay this for some time. A much more important application would be to make it possible for people of the present to benefit by progress of the future. In our lives we make constant use of progress of past generations. Indeed civilization would be impossible if it had to be reinvented by each generation. With the advent of successful freezing techniques, we shall be able to rely on the future as well. Imagine a patient dying of a now incurable disease. If he could be frozen and stored indefinitely at low temperature, he could be revived when the cure for the disease is developed. He would then be in a position similar to someone born when the disease was curable. As an example, if freezing techniques had been available in 1920, a man then dying of pneumonia could have been frozen and stored and could now be thawed and treated successfully. In addition, he would be able to take advantage of whatever else the future has to offer.

It is quite possible that all diseases will eventually be curable, and aging may be avoidable and even reversible. When successful freezing techniques become available, no disease need be considered hopeless. A person dying of whatever cause could be frozen and stored in the hope that he could eventually be revived and cured. One can think of possible drawbacks to this for both individuals and society, but a great many people, and not only the incurably ill, would be quite willing to try it. Although PHYSICS TODAY is not the place to begin discussing the social consequences of a successful freezing program, it is perhaps worthwhile to remark that progressive increase of possibilities open to humanity has been one of the major contributions of science. In view of this increase and the 40 million people who die each year of diseases that will some day be curable, the need for an energetic program of research on cryobiology appears strikingly clear. It is hard to think of any scientific advance that would open greater possibilities. Yet relatively small amounts of money and few researchers are involved in this quest in the scientific world at the present time.

Ettinger, in his book, has carried the argument one step further. For the living it is necessary to await successful completion of freezing research before attempting to freeze them. For the newly dead this consideration is irrelevant since the dead have nothing to lose by being frozen, even by imperfect methods. Ettinger therefore proposes that even today bodies of those just dead, as determined by cessation of heartbeat, could be immediately frozen by whatever techniques are available. This freezing will cause some damage to cells, but we can hope that many of them, in particular brain cells, will be preserved by the cold before enough time has elapsed for them to have been damaged by deprival of oxygen and nutrients. After freezing, the body must be stored until scientists can both counteract the damage done in freezing and undo whatever led to the death of the person in the first place, such as a heart attack. It may seem unlikely that this combination will ever come to pass, especially with the primitive freezing techniques now available. Ettinger makes the point that damage done in thawing is not a problem for this approach since thawing will be done in the future only when that problem is solved. Furthermore a dead body is no deader for having been frozen and stored, and the expenses would not be orders of magnitude beyond those of ordinary funerals. Since many people might wish to take the small chance that they will some day be revived if they are frozen on their death now, it would seem reasonable to make this possibility available to some of these individuals. ■

References

1. B. L. Strehler, *Time, Cells and Aging*, Academic Press, New York (1962).
2. R. Ettinger, *The Prospect of Immortality*, Doubleday, Garden City (1964).
3. L. Szilard, "The Mark Gable Foundation," published in *The Voice of the Dolphins*, Simon and Schuster, New York (1961).
4. A. Clarke, *Profiles of the Future*, Harper and Row, New York (1963).
5. E. Tatum, reported in Science **153**, 443 (1966).
6. F. Johnson, H. Eyring, M. J. Polissar, *The Kinetic Basis of Molecular Biology*, J. Wiley, New York (1954).
7. A. U. Smith, *Biological Effects of Freezing and Supercooling*, Williams and Wilkins, Baltimore (1961).
8. N. D. Levine, F. L. Anderson, J. Protozoology **13**, 199 (1966).
9. C. Polge, A. U. Smith, A. S. Parkes, Nature **164**, 666 (1949).
10. A. M. Karow, R. W. Webb, Cryobiology **2**, 99 (1965).
11. Cryobiology **2**, 314-316 (1966).
12. P. Popovic, V. P. Popovic, Cryobiology **2**, 23 (1965).
13. R. K. Andjos, F. Knopfelmacher, R. W. Russell, A. U. Smith, Nature **176**, 1015 (1955).
14. F. R. Babich, A. L. Jacobson, S. Bubash, A. Jacobson, Science **149**, 656 (1965).