CAN WE OUTLIVE METHUSELAH?
MATTHIAS WABL

No one wants to be old, but most of us want to get old. The two questions that interest many of us in this respect are: Can we stop the process of aging? And, can we live much longer than hundred years? These two questions probably are related to each other, but they need not to be.

It seems natural that, barring accidents and disease, we die of "old age". Death is viewed as the end of a body in decline. Could we explain aging, it seems, we would not have to explain death. For human beings this view has some merit. However, at the same time, in the language of everyday life we talk about the "clock" of life, which runs down. This metaphor does not imply that we have to age in order to die. All the parts of a clock that has run out may still be in mint condition and thus functional, and the clock may be wound up again. In contrast to this, at the time we die from, say, heart failure, the heart and also most other parts of our organism are generally in pretty bad shape.

Death has many meanings, but for our purpose here, we think of it as termination of existence of a particular human being, i.e., the desintegration of a multicellular organism. We all consist of many cells; although many of these cells die every day, the death of these cells does not imply death of the individual. On the contrary, cell death is even required for the continuation of life of the individual. Thus, cells that are infected by pathogens are killed by our immune system. And the cells of the outer layer of the skin, as many other cells of different type, die off to be replaced by new ones. When this normal, programmed, cell death is not sustained, tumors may result that eventually may kill the whole organism. In such a case, the individual cells live much longer than they are supposed to and they may even outlive the person they have been part of: for example, the cancer cells from a woman who died forty years ago are still cultured and thus alive today in many laboratories all over the world.

We replace our parts of the organism systematically and when needed; in that we resemble the gothic cathedrals that are built of sand stones, which have to be continually replaced over the centuries so that almost no stone of today has been part of the original structure. Why, then, do we not look always the same, as the cathedrals do? The reason for this is that to the builder it is obvious how a stone has to be replaced, and for rebuilding after a major catastrophy the blueprint for the cathedral is kept unchanged in the parsonage. But for the cells there is nothing obvious; and the blueprint for us is kept inside of the very same cells that are to be replaced. Before the cells are replaced, the blueprint has to be copied and it is at this moment that sometimes innocuous, sometimes serious, errors are introduced. When errors are introduced, the new cells might even be "better off" than the old ones; for example, they might grow faster. In general, however, this will be detrimental to the organism as a whole: in our example of faster growth a tumor may result. Proofreading the copies of the blueprints can reduce the rate of error, but cannot do away with each and every error. This fact is a consequence of a famous law of thermodynamics, one of the pillars of today's physics. The accumulation of errors over time brings incremental changes in the architecture of our organism, and, as explained above, unlikely to its advantage; the result is aging.

How then, can we ever be young? We, as homo sapiens, have been around for more than hundred thousand years, during which many errors in our blueprints must have occurred. The answer to this question is selection. As individuals, we all start from the fertilized egg, which is a single cell. This egg has one blueprint, which is tested over and over again during the development of the embryo. Many embryos do not make it and abort. And if serious errors become apparent during childhood, the afflicted person may never reach the sexual maturity and social acceptance needed to pass his blueprint onto the next generation of children.

Physics tell us that it is impossible to copy the blueprints of our many cells in an error-free way, and thus it is impossible for us to stay in this world forever. But how long could we live? A thousand years instead of our hundred years? The average life span appears to be a characteristic of the species: for example, a mouse lives about two years, a dog twenty years, and redwood trees can live a thousand years. Our question now becomes: what determines the average lifespan of an individual of a given species? Obviously, the fidelity with which the blueprints of the cells are copied has to be a factor, perhaps even the most important one. This fidelity is achieved by a number of proofreading systems inside the cells. The proofreading systems are inherited by the very same blueprint that is present in all cells; they consist of several enzymes, which are biocatalysts. If we were able to make our proofreading systems better, or to transplant better proofreading systems from other species onto us, we might live much longer.

It is conceivable that we transplant onto us biocatalysts that may prolong life by slowing down aging? In principle, the procedures to introduce foreign blueprints for any biocatalyst into our organism are in place; they are provided by the so-called recombinant DNA-techniques, and their final application to the (hopefully volunteering) person does not amount to much more than a shot similar to vaccination. That is not to say that we could substantially prolong life today or tomorrow. But there is no a priori reason why this could not be done in some time from now, and we may well be able to outlive Methuselah, who made it to 969 years. Let us discuss this issue again in a thousand years or so!