Edmond Henri Fischer
Biochemistry without boundaries

Biochemist at the University of Washington in Seattle, he won a share of the 1992 Nobel Prize in Physiology or Medicine for discoveries concerning reversible phosphorylation: a regulatory mechanism that activates and deactivates enzymes in the vast majority of living cells. Fischer was born in Shanghai, China, in 1920.

Do you keep abreast of advances in protein phosphorylation? What excites you these days?
Protein phosphorylation is involved in a number of diseases directly, including: Alzheimer's disease; Parkinson's disease; diabetes; myelogenous leukaemia; viral and bacterial infections such as smallpox, cholera and plague; and cancer. A lot of biotechnology and pharmaceutical companies are working on protein phosphorylation — on enzymes that add phosphates (kinases) and those that take them off (phosphatases). Too little work on phosphatases in my opinion, particularly as certain ones, like PTEN, act as tumour suppressors. However, very little has come out yet regarding drugs that target phosphatases.

A lot of science is quite reductionist. Is this better than taking a systematic, top-down view?
No, one of the beauties of science is that you never know when the next big breakthrough will happen. You approach it systematically. Science builds on science. Every result pertains to the next questions, and every question suggests the next experiment. You cannot predict when the next big breakthrough will happen.

Research fields emerge unpredictably. Take protein phosphorylation — that was our luck. We found a very simple reaction — embarrassingly simple — which turned out to be absolutely crucial for the regulation of cellular processes. For years it was considered to be the most prevalent mechanism of cellular regulation, and then all of a sudden ubiquitination popped up (co-discovered by Nobel laureate Aaron Ciechanover; see page S4) and now that has taken the centre stage.

In the 1950s it was all about enzymes. We had little information on enzymes or on the 3-dimensional structure of proteins until Max Perutz and John Kendrew (recipients of the 1962 Nobel Prize in Chemistry) used X-ray crystallography to determine the structures of myoglobin and haemoglobin.

Has working on proteins for so long given you a particular view on life?
Life is an inevitable phenomenon and it exists all over the universe. There is very good evidence that there are 500 million planets similar to Earth in the Milky Way. The probability that life does not exist on one of these other planets approaches zero. What kind of life, nobody knows.

A self-replicating system was established 3.5 billion years ago. At first, evolution was slow, becoming more rapid in the past 550 million years as single-cell organisms coalesced to form multicellular organisms. Before that, single cells had to compete with one another for food, light, micronutrients, etc. But the moment cells began to associate with one another to form specific tissues and organs, they had to cooperate: to speak with one another, synchronize growth and behaviour for the good of the whole.

The main criteria for life are self-duplication and conversion of foreign molecules into molecules identical to you. So crystallization is not life. Putting a crystal of copper sulphate in solution so that it grows is not life. Some people think the first self-duplicating molecule was a protein, but other people think it might be nucleic acid.

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Nature Video of Fischer advising a young researcher:
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Your Nobel prize is for physiology or medicine. How do these areas relate to each other?
Medicine is not only clinical, it also covers molecular biology, biochemistry, physiology, pathology, neurobiology and more. These days, medicine extends from the molecule to the organism.

To most researchers, it doesn't make any difference if they are in the department of biochemistry or the department of neurobiology or pathology or microbiology. The amount of new information that is being gathered in the biomedicine arena is such that it is almost inconceivable that people could work in isolation. Collaboration is totally indispensible if one wants medicine and biology to progress. We have all the tools; people communicate very easily now.

If you compare what you had planned at the very beginning of your career, and where you are right now, are they similar?
When I was a kid I didn't want to be a biochemist, I wanted to be a microbiologist. When I started at the University of Geneva in Switzerland I sought advice from the professor of microbiology. He said if I wanted to be a research biologist, I should study chemistry first. "One uses test tubes more than microscopes these days," he said. So I became an organic chemist, but always with one eye on living systems. That is why my thesis was on enzymes. I have always been interested in basic research. The only thing that has changed is that I used to lack the systematic approach needed to solve problems. ■

Fischer's response implies that new scientific discoveries affect the ontological paradigms in play, and that these vary. I wonder: does this suggest that what is considered a fundamental scale at one point of investigation becomes superseded by a more complex set of things in the next?

Amanda Parr, former philosophy student and now a public servant in Canada, who posed the original question on lindau.nature.com.