Chemistry: A Way to the Roots of Biology**

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"Chemistry meets Biology" was the title of a recent editorial in *ChemBioChem* which sketched the research landscape at the interface between chemistry and biology and thus pointed to a possible perspective for articles that may be in covered in *ChemBioChem*. Briefly, it was outlined that the marriage of chemistry and biology takes place in an interfacial discipline which is commonly regarded as bioorganic chemistry. The field has been renamed in some institutions, to be known as "chemical biology" today. Creating synthetic tools for the study of biological phenomena at all levels of biological organisation was envisioned as the major focus of the field. The message to the synthetic organic chemist was not to concentrate too much on the synthesis of intellectually challenging molecules such as the complex natural products seen as molecular summits, but to take a closer look into the classes of problems that are elaborated in the lab of his collegue from the biology department, or better yet, to learn biology and do the biological studies himself.

Well, this direction of research is, of course, a possible roadmap for synthetic chemistry and I do fully appreciate advice of the authors in terms of education programs for chemistry students. In fact, this has been done already in many universities and for many years, and it is rather easy to foresee that the trend will become a stable one over the next few years. However, there is much more to do and the interface between chemistry and biology is much broader than sketched by the authors. First of all, there are three major disciplines in chemistry—not only organic chemistry, but also inorganic and physical chemistry—and all of them have been stimulated and guided into new directions by leading discoveries in biology. For example, biophysical chemistry became a well-established discipline in many chemical departments, long before the currently observable massive opening up of bioorganic chemistry took place. Secondly, although organic chemistry is firmly based on the development and application of synthetic methods—also in the context of developing tools for biology—it is and ever was more than that. The mechanistic approach of physical organic chemistry was of greatest importance for our understanding of organic reactions, their control, their design and their application in situations, where selectivity is the demanding factor. Today, synthetic chemistry faces the challenge not only to develop more efficient methods for covalent synthesis, but also to learn how the principles of control can be expanded into the design and application of strategies of noncovalent synthesis. The fundamental research underlying this approach comes from supramolecular chemistry, a multidisciplinary endeavour in which bioorganic chemistry is certainly a key player. As such, the link between supramolecular chemistry and biological nanotechnology grows fastest at the interface between chemistry and biology. Thirdly, a well-conceived goal of bioorganic chemistry is to mimic chemical activities in biological systems, such as binding, catalysis, compartimentation and transport. This mimicry aims towards the reduction of biological complexity to a level that can be understood, conceived and explained on a fully chemical basis. Even if the reductionist's approach—or the reductionist's agenda to use the words of John Maddox—does not necessarily lead to something that is better than the biological prototype or help to speed up biological discoveries, it does help to understand the meaning and perhaps even the origin of the biological function or process—from a chemist's perspective. As such, reduction and mimicry of biological functions and processes means learning **chem**istry from **bio**logy with **chem**ical means. This is, in my view, something that has a value in its own right and should not escape the attention of a journal like *ChemBioChem*.

Chemistry is today at the age of having its midlife crisis. As with every midlife crisis, the fascination from viewing new horizons becomes the major issue in life and the value of the former achievements is questioned as never before. Indeed, the crisis itself may be the result of the way that chemistry self-organized as a science. Up to the end of the eighties there was no need for a rethinking, as chemistry was a *leading industry*. Perhaps, even, the crisis of chemistry developed because of the latter. Gradually, chemical achievements were mainly looked at as boring technical achievements by the public, and the fascination of pure chemical problems consequently became barely communicable to a nonchemist. The intellectual challenger biology won the race of public acknowledgement. Chemistry was about to perceive its future role as a kind of technical support to speed up even more the success of its "competitor". Furthermore, the socioeconomical signal of unemployed chemists was read by potential students of chemistry and the crisis also began to take over the academic chemical research. But any successful midlife crisis should result in something that is called "spiritual completion". What could this mean to chemistry facing the future?

Every natural science has questions, whose fascination does not necessarily result from the daily action taking place in the particular field. The origin of the universe and the big bang, for example, do attract the mind of the young student, regardless of whether he or she could

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ever conceive a routine job in front of a computer located in a huge physics laboratory for high-energy particle acceleration. The big bang itself radiates the fascination that is necessary to set up the student's mind to go into this direction and to study physics. Of course, there are also economical prospects. But if two fields have the same attraction with respect to the latter, the field with the higher fascination has a better chance of winning the competition. Chemistry, unlike physics, has generally never asked such big questions, as there were always enough problems of daily urgency. Increasing the lifespan and the quality of human life was urgent enough not to confuse oneself with "irrelevant" questions. But in the saturated western world, the intellectual human mind is curious and demands more from chemistry as a science.

The genomic revolution in biology continues to decipher the tree of life and it is forseeable that every species of the whole biota of our planet will be stored as digital strings quite soon. Functional genomics is beginning to decipher the meaning of genetic information on a molecular level today and the speed of harvesting and analyzing biological information in the language of molecules and their interactions is expected to increase tremendously. Several new meta-languages will appear that are no longer related to molecules and their actions, but to families and systems of molecules organized in dynamic networks, meta-languages describing different hierarchical levels of biological organization, meta-languages that do not even exist today. If this prediction is correct, the language of molecules will sooner or later become less important in understanding biology. Chemistry, nevertheless, should contribute to this exciting development. But it should also begin to ask more seriously those questions that were considered as irrelevant before.

Clearly, the origin of life on Earth and elsewhere in the universe is such a question, perhaps the most challenging that can be ever asked in chemistry. The reconstruction of the tree of life can be only followed back to the last universal common ancestor. What came before? How did life start on Earth? If not on earth, how did it start elsewhere? Does it exist elsewhere in the universe? Does it even exist elsewhere in our solar system? Can life be synthesized in the laboratory? What are the conditions to sustain a "chemical", that is, synthetically created biology? These are questions that are taken seriously enough in the US to be funded by society. The NASA Astrobiology Institute (NAI) now spans a network of 11 world-renowned institutions, among which Harvard and Scripps are members. In 2003 we will celebrate the 50th birthday of two major discoveries: the discovery of the double-helical structure of DNA by Watson and Crick, and the discovery by Miller that amino acids, some of the building blocks of life, emerge spontaneously under simulated prebiotic conditions. It is my hope that the European community will accept the challenge and form a conjunction between the top-down approach of molecular biology and the bottom-up approach of prebiological chemistry, an approach that could result in finding the roots of biology.