Biomimetic chemistry: a frontier at the chemistry/biology interface

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Chemistry is only in part a natural science. There is of course continuing interest in exploring and understanding the chemistry of life, and this is certainly natural science and a major part of the chemistry/biology interface. Most chemistry, however, is concerned with unnatural compounds and reactions — those invented by chemists. Medicinal chemists invent new pharmaceuticals and they certainly work at the chemistry/biology interface. There is also a large and increasing field, however, for which we have coined the name 'biomimetic chemistry' [1]. This is the field in which chemists invent new substances and reactions that imitate biological chemistry.

In part such imitation is done to put the biological compounds and properties in a general context. For example, after we had elucidated the special chemistry of thiamine pyrophosphate that explained its ability to act as a coenzyme [2], we varied the chemical structure to see why Nature had selected such a complex molecule for its function [3]. Similarly, we [4] and others [5,6] have synthesized various analogs of natural DNA to try to understand the relevance of the natural structure to its function. This type of activity can be thought of as 'Nature appreciation'.

The intellectual flow in such work is mostly from chemistry to biology. The purpose is to learn something new about biology using chemistry as the tool — of course some new chemistry is also often learned. In biomimetic chemistry, however, there is another field in which the intellectual flow is from biology into chemistry, having the purpose of expanding the scope of chemistry itself.

When chemists survey the marvellous chemical processes involved in life, they cannot fail to be amazed and inspired: amazed at the spectacular chemistry that Nature is using and inspired to learn from it so as to invent chemistry that is better than what chemists have achieved to date. The challenges are not simply intellectual, since many of the practical applications of modern chemistry could be much improved if some biomimetic goals could be achieved.

For example, the ability of antibodies to bind antigens with high affinities and high shape selectivities — or the related ability of biological molecular receptors such as those that function in taste and smell — has inspired the field called 'molecular recognition', in which chemists synthesize nonprotein analogs of antibodies. Some interesting receptors that bind hydrophobic molecules with shape recognition and high affinity have been created [7], as well as others that bind peptides with sequence recognition [8–10]. Such molecular receptors have useful potential as tools in clinical analysis, for instance, or as medicinal compounds.

Of course selective binding also plays a role in the interaction of enzymes with their substrates. One of the most interesting biomimetic challenges is the creation of artificial enzymes, especially those not based on proteins at all [11,12]. Such catalysts should incorporate a binding site along with catalytic groups. The goal is to achieve both fast rates and high selectivities; in some senses enhancing the selectivity would be the most interesting aim.

In the biosynthesis of cholesterol, there are enzymes that can selectively oxidize particular methyl groups attached to saturated carbon while leaving double bonds untouched. Normal chemical reactivities are the reverse, but there is no mystery about how enzymes achieve such selectivities. The substrate is bound to the enzyme in such a way that only the otherwise unreactive atom is within reach of the catalytic groups, so it is attacked. We have been pursuing such reactions over many years [12], and the word 'biomimetic' was originally coined to refer to such efforts [1]. Recently, some catalysts have been created that indeed imitate the ability of enzymes to carry out selective oxidation of otherwise unreactive positions in steroids and other molecules because of their specific binding geometry to the artificial enzymes [13].

Biological membranes have inspired chemists to generalize their structures, and to try to incorporate novel channels for passive and active transport of molecules across such membranes. The goal is to imitate some of the most interesting functions of living cells, and eventually to imitate a form of life, including self-reproduction. The driving force is, in part, simple scientific curiosity but there is no doubt that artificial cells that have the ability to imitate life to some extent would greatly expand chemistry and its applications. Such a goal is part of the general interest in changing chemistry from a reductionist to an integrationist approach. We are moving from exploring and understanding simple systems to learning the properties of interacting systems. A living cell is an excellent example of a system that has properties achieved only because of the interaction of many different chemical paths and substances.

What can we expect in the future? Synthetic molecular receptors will be created for use in the analysis of clinically important biological substances, and as medicinal compounds to regulate biological processes. Chemists will make increasingly sophisticated enzyme mimics that catalyze important reactions with high rates and selectivities. These will be used as catalysts in the manufacture of useful chemicals, working in environmentally friendly solvents such as water and with high yield so that little waste product is produced and little energy is consumed. Artificial membranes incorporating active and passive transport channels will be used to construct mimics of cells, first as scientific curiosities and later as miniature devices to perform useful functions.

There is no doubt that learning the detailed chemistry of life is important, and it is one of the frontiers of the chemistry/biology interface. Learning to imitate and generalize that chemistry, however, is also one of the frontiers, and it has tremendous promise for the future. Just as the tools of chemistry will help us understand life processes in detail, the information and inspiration from biology promises to help chemistry move to a new plateau. Chemistry now is one of the most useful and practical sciences — the basis of a large part of modern technology [14]. As chemical research incorporates the subtlety of Nature's own chemistry, it should be able to make even greater contributions to human welfare.

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