

Model systems

This year's model

Editorial overview

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Model systems have an odd status among biologically oriented chemists. An understanding of complex chemical processes found in living organisms (e.g. enzymatic reaction mechanisms) is often most productively pursued, at least in early stages, by examining simplified and purely synthetic model systems. Yet, the preparation and study of model systems often involves technical skills that are quite different from those required for analysis of the ‘real thing’, and it can happen that chemists who delve deeply into model studies do not make the transition to studying the biological systems that initially inspired the chemical simplification. In such cases, the later stages of model studies can seem to be disconnected from the original problem. Accordingly, at various historical points in several subdisciplines of biological chemistry, model studies have come to be seen as a bit superfluous.

Current Opinion in Chemical Biology is to be commended for devoting an issue each year to *Model systems*. Despite the checkered history alluded to above, the distillation of complex biological phenomena to simple chemical models can provide high impact and value. In particular, this research strategy frequently leads to the elucidation of new chemical principles that can transcend the original biological problem, and provides a basis for incisive experimental design and proper data interpretation in the biological context.

The excellent set of reviews in this issue shows how vibrant and productive the model-based approach remains. Reviews by Regen (pp 729–735) and by Waters (pp 736–741) describe synthetic models that represent new tools for study of noncovalent recognition in biological structures. In Regen’s case, the questions involve how lipids in a biological membrane choose their neighbors, and the experimental approach involves the clever use of synthetic lipid vesicles with thiol-modified constituents. Waters’s review focuses on the enduring problem of understanding the role of aromatic–aromatic interactions in biomolecular phenomena.

Reviews by Cloninger (pp 742–748) and by Boon and Smith (pp 749–756) present recent advances in the development of biologically inspired chemical entities that have considerable promise for biomedical applications. In Cloninger’s case, the subject is dendrimers, and applications include delivery of genes and small drug molecules. In Smith’s case, the topic is synthetic agents that facilitate the flipping of lipids between bilayer leaflets or delivery of water-soluble cargo across bilayers. The review by Fujita *et al.* (pp 757–764) deals with a more abstract kind of modeling, in which the complexity of biomolecular structure and function is translated into an entirely new chemical medium.

In eukaryotic cells, DNA transcription is controlled by protein modules. The review by Ansari and Mapp (pp 765–772) describes how these modules have inspired the creation of synthetic transcription factors, which offer a powerful new tool for functional genomics as well as potential chemotherapeutics. As DNA

transcription is controlled by protein modules, so polyketide biosynthesis is accomplished by enzyme modules. The review by Pohl (pp 773–778) focuses on the power of these modules, especially on exciting opportunities to exploit their tolerance for non-natural substrates to introduce molecular diversity. Nitric oxide transmits signals in biological systems. Thionitrites (SNO species) serve as both natural reservoirs of biological nitric oxide and potential chemotherapeutics. The review by Stamler and Toone (pp 779–785) describes current ideas (and controversies) regarding the chemical and biochemical mechanisms by which thionitrites decompose to form nitric oxide.

Reviews by Lazar and Walker (pp 786–793) and by Mrksich (pp 794–797) focus on the surface of cells. Many important antibiotics target the enzymes that synthesize the peptidoglycan layers of the bacterial cell wall. Lazar and Walker describe recent progress in the synthesis of peptidoglycan intermediates and their use as mechanistic probes for these target enzymes. The extracellular matrix (ECM) of animals provides a scaffold for cell adhesion and migration. Mrksich reviews the use of chemistry to create synthetic surfaces that mimic critical aspects of the cell–ECM interaction.

A feature of this issue of *Current Opinion in Chemical Biology* is the range of experience among its contributors.

Well-established authors who have played major roles in inventing the subjects they review (Fujita, Mrksich, Regen, Smith, Stamler, Toone and Walker) are balanced by new voices who bring fresh perspectives to active fields (Ansari, Cloninger, Mapp, Pohl and Waters). The established authors will be (or should be) well known to readers, but the younger contributors deserve an introduction. Ansari, at the University of Wisconsin–Madison, is using biochemical and genomic/proteomic tools to reveal the mechanistic events that culminate in the expression of specific genes. Cloninger, at Montana State University, is taking a creative approach to the synthesis of dendrimer displays of carbohydrate arrays with defined geometry and density, for exploration of protein–carbohydrate recognition. Mapp, at the University of Michigan, is developing a molecular-level picture of gene expression in eukaryotic cells by using novel synthetic organic molecules as mechanistic probes. Pohl, at Iowa State University, is creating new biosynthetic pathways to orchestrate the synthesis of complex carbohydrates and other molecules. Waters, at the University of North Carolina at Chapel Hill, has recently provided several exciting advances in the study of interactions involving aromatic moieties. Together, these contributing authors highlight with alacrity and insight the variety of contributions that the ‘model’ impulse can make in the hands of skilled chemists.