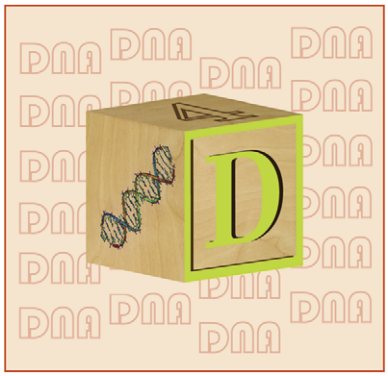
In This Issue

A scientist scratches his forehead and frowns. In front him, carefully laid over the entire surface of his lab bench, is a seemingly impenetrable schematic with a jungle of connectors criss-crossing the sheet, bridging arrays of diodes, sensors, actuators and forming logic gates and memory storage units. And yet, regardless of its appearance, this is not a plan for a new ultra-advanced facility for examining the far reaches of the universe. The schematic is how an emerging field of synthetic biology views a cell, cellular communities, and organisms. The view stems from the set mission of synthetic biology to engineer artificial biological parts and systems as well as reengineer existing ones in programmable fashion to achieve the desired outcomes. In this issue of *Chemistry & Biology*, through a collection of Review and Crosstalk articles, we take a look at interdisciplinary approaches used to improve our understanding of biological processes and at how this information is used to equip cells with new capabilities or create alternative living systems with unique properties.

Before I proceed with more details on the topics covered in the 2009 Special Issue of *Chemistry & Biology*, I would like to thank, on a behalf of entire editorial group, the authors who contributed their exciting articles, all reviewers who provided valuable feedback, and the many other scientists consulted during the preparations of this issue, as well as to emphasize that this special issue is the result of a true collaborative effort between the numerous researchers thus involved.



Dial D for DNA

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The realization that DNA is the carrier of genetic information and the revelation that the information is encoded by the four nucleic acid bases were revolutionary developments of the mid-20th century. Andrew Krueger and Eric Kool now discuss the most recent explorations into the world of nonnatural, synthetic, chemically designed bases and base pair structures. They elaborate on new opportunities for the use of alternative nonnatural base pair strategies for biotechnological applications as well as highlight the ways these chemical approaches provide an extension of our understanding of fundamental principles governing DNA structure and replication.

Sending Signals Up and Down Pathways

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Cells are endowed with a remarkable diversity of signaling networks that are essential for cellular existence. Information is received from the outside and transmitted via numerous carriers and hubs to final response regulators that trigger events which lead to changes in cell behavior. Here, Peter Pryciak describes recent efforts that aim to produce new signaling pathways not occurring in nature. The reported accomplishments indicate that modularity of signaling proteins provides a foundation for rewiring signaling pathways by domain swapping. The author argues that, in addition to producing synthetic cellular behaviors, innovative ways employed to redirect traffic up and down cellular signaling highways lead to critical discoveries about cellular function as well as pave the way for the advancement of new research tools.

From Chemistry Mimicking Biology

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In biological systems, enzymes protect unstable intermediates of enzymatic reactions by occluding them within the enzyme interior. This process is mostly driven by establishing specific interactions with the transient species that stabilize it. Functional cavitands are synthetic receptors that share properties of biological systems and provide the environment for trapping and stabilizing labile intermediates of chemical reactions, thus enabling their direct observation. Pioneering work on cavitands was done by Julius Rebek, Jr., and in their review, Richard Hooley and Julius Rebek, Jr., describe these fascinating systems and discuss an intriguing analogy between synthetic systems produced in organic laboratory and enzymatic systems existing in nature.

Evolution of Synthetic Polymers

PAGE 265

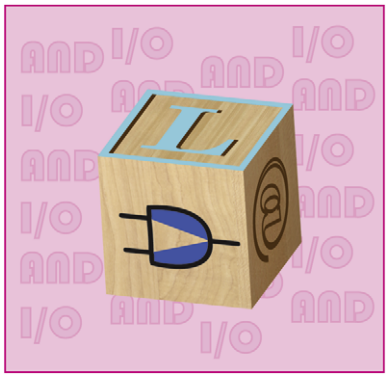
The function and structure of any living system depends on the presence and interplay of numerous polymers, such as proteins, built of amino acids, and DNA or RNA, built of nucleic acids. Their domination over the living system is at least partially due to their ability to evolve. Yevgeny Brudno and David Liu examine what happens when evolutionary principles are applied to the production of sequence-defined synthetic polymers. Their review dissects both enzymatic and nonenzymatic templated polymerization approaches for creating nonnatural polymers and explores the directed evolution of sequence-defined synthetic polymers.

Engineering Metabolism: In Synthesis Veritas

PAGE 277

Industrial scale production of antibiotics depends on the use of microbes and the exploitation of their diverse metabolic pathways for production of large quantities of medicinally useful compounds. Every metabolic pathway orchestrates a cascade of highly evolved biocatalysts, enzymes, each able to act at the specific time in the pathway and perform specific chemical transformation. The absence from the nature-provided arsenal of a specific pathway or a specific enzyme no longer poses an obstacle en route to a desired compound, as discussed in a review by Collin Martin, David Nielsen, Kevin Solomon, and Kristala Jones Prather.

Mammalian Genetic Circuits Just Might Ring Up



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An additional level of complexity that synthetic biology has recently got under its belt is the ability to design synthetic mammalian gene circuits. Here, Wilfried Weber and Martin Fussenegger provide an overview of the latest mammalian synthetic biology devices assembled into regulatory cascades, logic evaluators, hysteretic circuits, epigenetic toggle switches, time-keeping components, and even transmitter/receptor systems not unlike cell phones. Expanding these applications further could lead to higher level of functional control, as in an example of a synthetic ecosystem with layers of complexity maintained through dynamic interspecies communication.

RNA in Control

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Synthetic biology is a multidisciplinary endeavour to engineer biological systems to perform defined tasks by using a set of standardized components and establishing an appropriate set of connections between them. From Maung Nyan Win, Joe Liang, and Christina Smolke we learn what role RNA programming in living systems has in these efforts. Their review presents a discussion of design principle for creating functional RNA molecules with ever-increasing complexity. They also address issues surrounding integration of designed RNA molecules into cellular circuitry and provide a framework for building RNA parts and devices.

DNA with Muscles: Finding a Needle in a Haystack

PAGE 311

The double helix, two anti-parallel strands of DNA in an intimate contact with one another, is the first thing that springs to mind when we think about this fascinating macromolecule. However, DNA molecules can easily be synthesized outside the biological context as single-stranded polymers and designed to fold into different structures. This review by Kenny Schlosser and Yingfu Li focuses on a specific class of catalytic DNA molecules, or DNAzymes. Although the functional repertoire of DNAzymes is remarkable, the authors provide informative discussion of the success and limitation of in vitro selection methods used for navigating through DNA sequence space in a search for activity.

When 20 Is Just Not Enough

PAGE 323

Nature had it all penned out for billions of years. Using 20 amino acids, in most cases, it was able to produce the incredible structural and functional diversity of the current protein world. But 20 is no longer enough, as explained by Qian Wang, Angela Parrish, and Lei Wang in their review article. They review the process by which researchers have so far been able to incorporate upwards of 40 different nonnatural amino acids and thus produce custom-made proteins. The methodology has had a steady success in *E. coli* and fares well in lower eukaryotes. The special emphasis in this review is placed on eukaryotic expression systems as the new frontier.

Synthetic Genomes: From Fiction to Science

PAGE 337

Once, sequencing the human genome was part of scientific dreams and then, at the dawn of the 21st century, it became reality. De novo gene and genome synthesis re not far behind. With the ability to create genes and genomes at will, scientists will be given an unprecedented freedom to manipulate life, and societal questions are justifiably to be expected. In the concluding review of this special issue, Steffen Mueller, J. Robert Coleman, and Eckard Wimmer discuss both the technical challenges long DNA synthesis faces as well as the societal implications of synthetic biology.

As scientists make strides to extend the ability to control, dissect, and rebuild cellular processes, *Chemistry & Biology* is glad to be in a position to offer this collection of Review and Crosstalk articles in the hope that they might serve as catalysts for future discoveries.

Milka Kostic

