Functional Nucleic Acids for Analytical Applications

Yingfu Li • Yi Lu
Editors

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Editors
Yingfu Li
Department of Biochemistry and
Biomedical Sciences
McMaster University
Hamilton, Ontario
Canada
liying@mcmaster.ca

Yi Lu
Department of Chemistry
University of Illinois at Urbana-Champaign
Urbana, Illinois
USA
yi-lu@illinois.edu

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Preface

Nature long ago solved the problem of finding sequences that code for useful structures, through the endless iteration of the simple algorithm at the heart of Darwinian evolution: variation, selection, reproduction. The deliberate application of this algorithm to the laboratory evolution of useful molecules is a recent development, but the power of this approach is already evident. My introduction to this field came almost 20 years ago when I wanted to explore the rich biochemistry implicit in the strong version of the RNA world hypothesis. Attempting to evolve RNAs that could carry out the key functions of RNA-based life seemed ambitious, so Andrew Ellington and I decided to start with the simple project of selecting for sequences capable of recognizing a given target. In 1990 we showed that it was indeed possible to evolve new RNAs that could bind to and distinguish between closely related small molecules. This was incredibly exciting to us because it was clear that the selected RNAs had to fold into defined three-dimensional structures that contained highly specific ligand-binding sites. Moreover, these ligand-binding RNAs, which we called aptamers, had been selected from a small (only 10^{15}) sample of completely random RNA sequences, implying that functional RNAs were relatively common in sequence space, and that some day really useful aptamers might be evolved! In parallel with our work, Craig Tuerk and Larry Gold found that unexpected sequence variants of a stem-loop RNA had emerged from a randomized population selected for binding to an RNA-binding phage coat protein, and their subsequent work showed that RNAs could be evolved that would bind to almost any protein target. These early findings were soon followed by the evolution of DNA aptamers, novel ribozymes and DNAzymes, and allosterically controlled ribozymes ("aptazymes"). Since then there has been an explosion of work devoted to the evolution of increasingly sophisticated and useful aptamers and nucleic acid catalysts, collectively referred to as functional nucleic acids or FNAs. Perhaps the most scientifically interesting and surprising application of FNAs has been the exciting effort aimed at the development of biosensors and other analytical applications, such as bioseparations, signal amplification, and signal processing, and it is this work that is summarized in a series of thorough and insightful reviews in the present volume.

The book begins with three excellent reviews, the first (by the editors of this volume) introducing the analytical applications of FNAs that are discussed in detail in Parts II and III of the book, the second covering natural riboswitches (Nature's own

RNA-based biosensors) and ribozymes, and the third covering artificially evolved aptamers, ribozymes, and DNAzymes. In Part II we see the remarkable array of amplification and detection technologies that have been coupled to FNAs to allow accurate and sensitive detection of a vast range of target analytes. These methods include a variety of fluorescence and colorimetric and other optical methods, as well as electrochemistry and catalytic signal amplification. Part III on emerging analytical applications is the most forward-looking part of the book, covering diverse topics ranging from aptamer-based separations, to massively parallel microarray detectors, to computational devices and nanomachines built from functional nucleic acids. The myriad of clever ways in which FNAs are now being used is truly remarkable, and this volume provides a wonderful overview for the reader interested in the current state of the art in this rapidly developing field.

Massachusetts General Hospital, USA Jack W. Szostak

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