

Preface

The 2006 Nobel Prize in Physiology or Medicine was awarded to the discoverers of RNA interference, Andrew Fire and Craig Mello. This prize, which follows “RNA” Nobels for splicing and RNA catalysis, highlights just one class of recently discovered non-protein coding RNAs. Remarkably, non-coding RNAs are thought to outnumber protein coding genes in mammals by perhaps as much as four-fold. In fact, it appears that the complexity of an organism correlates with the fraction of its genome devoted to non-protein coding RNAs. Essential biological processes as diverse as cell differentiation, suppression of infecting viruses and parasitic transposons, higher-level organization of eukaryotic chromosomes, and gene expression are found to be largely directed by non-protein coding RNAs.

Currently, bioinformatic, high-throughput sequencing, and biochemical approaches are identifying an increasing number of these RNAs. Unfortunately, our ability to characterize the molecular details of these RNAs is significantly lacking. The biophysical study of these RNAs is an emergent field that is unraveling the molecular underpinnings of how RNA fulfills its multitude of roles in sustaining cellular life. The resulting understanding of the physical and chemical processes at the molecular level is critical to our ability to harness RNA for use in biotechnology and human therapy, a prospect that has recently spawned a multi-billion dollar industry.

This book assembles chapters from some of the experts in Biophysics of RNA to provide a snapshot of the current status of this dynamic field. While by necessity incomplete, this book aims to survey a number of the better characterized non-protein coding RNAs and the biophysical techniques used to study them. It is written for students and researchers at all levels of accomplishment interested in understanding how non-protein coding RNAs work and how biophysical and computational approaches can be used to delineate the molecular underpinnings of RNA function. Many topics are approached with the goal of describing how biophysical tools and techniques have been used to address fundamental questions in the biology of non-protein coding RNAs, rather than a description of RNAs themselves. In this light, we hope that the book will be of particular use to junior scientists seeking to tackle new problems in RNA biology from the vantage of biophysics.

Following a foreword featuring a general overview of the lessons from the biophysical study of RNA, the first three chapters aim to describe how theory, simulation, and experimental probing can be used to unveil the thermodynamics and kinetics governing RNA folding and dynamics. Chapters 4–6 are devoted to small self-cleaving ribozymes, as understood through the lens of X-ray crystallography, ensemble and single molecule fluorescence, and chemical probing. Subsequent chapters tackle increasingly complex RNAs and their protein complexes. In particular, Chaps. 7–9 focus upon large ribozymes that use more sophisticated mechanisms of catalysis and even recruit proteins to facilitate function in the cellular environment. As genetic regulation appears to be an increasingly important role for non-coding RNAs, Chaps. 10 and 11 concentrate on how X-ray crystallography, NMR spectroscopy, and fluorescence techniques have revealed how riboswitches specifically recognize small molecule metabolites to affect gene expression. Many modern non-protein coding RNAs are assembled into large ribonucleoprotein complexes (RNPs) and Chaps. 12–14 yield insights into how these particles are assembled to form a functional complex. These large RNP machines are by necessity highly dynamic entities that must adopt a number of conformations, as revealed in studies of the ribosome by cryo-electron microscopy in Chap. 15. Finally, non-coding RNAs often interact with other cellular machineries to enable their function, as discussed in Chaps. 16 and 17. We hope that our selection of topics is both timely and stimulating for the rapidly growing RNA community and beyond.

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