

Foreword

It was just 62 years ago that we finally learned that DNA was the genetic material – the master blueprint of life. Since then, the nucleic acids DNA and RNA have been studied in exquisite detail and both their chemical and biochemical properties are firmly established. Indeed, the double helical structure of DNA has become an icon of our time appearing widely not only in the scientific literature, but also in the popular press and most recently as jewelry. A thorough knowledge of nucleic acids and their properties is now a key ingredient in the education of both biologists and chemists. Ten years ago the second edition of “Blackburn & Gait” was published and seemed sufficiently comprehensive that only small additions would be needed if it were ever to be rewritten. Its popularity is attested to by its now being out of print – it has also inevitably become out of date. Much has changed in the last 10 years and a new edition is now both necessary and most welcome.

One major discovery within the biological arena has been the phenomenon of RNA interference, which was not even mentioned in the last edition, and yet at this time several companies have been formed to capitalize on it and at least one product is heading into clinical trials. We also now know that short micro-RNAs play key roles in development and are probably of ubiquitous importance in controlling gene expression. These and other small RNAs are likely to play a much more critical and subtle role in the lives of cells than we might ever have imagined. I find this personally very satisfying, since, when we discovered split genes and RNA splicing in 1977, the introns were almost immediately labeled “junk”. It now seems that at least some of these intronic sequences play positive roles in controlling gene expression and their involvement in other processes may still await discovery. Studies of small RNAs in eukaryotes are proceeding quickly and I eagerly await the results from similar studies in bacteria and archaea. It seems likely that great discoveries lie ahead although new methods may be required to make them. The development of such methods will be greatly facilitated by a thorough knowledge of the chemistry and biology of nucleic acids – the subject of this book.

Among the great technical achievements of the last 10 years have been several breakthroughs in the scale of DNA sequencing. First came the complete sequence of a simple bacterium, *Haemophilus influenzae*, quickly followed by that of the first archaea, *Methanocaldococcus jannaschii*. A key feature of these projects was the use whole-genome shotgun sequencing pioneered by Craig Venter. These “small” genomes were soon followed by draft sequences for a number of eukaryotic genomes including, of course, the draft human genome sequence announced in 2003 and coinciding with the 50th anniversary of the determination of the structure of DNA by Jim Watson and Francis Crick. With more recent advances in sequencing technologies that use highly parallel methodology, one machine can now generate enough data for a small bacterial genome in a few hours, at a quite reasonable price. We can anticipate an even more massive influx of new data in the next few years. The accumulation of sequence data far exceeds our experimental capacity to probe it. Fortunately, bioinformatics stands ready to help and with appropriate experimental input, should allow us to make sense of the terabases (10^{12}) of DNA sequence data that will soon be present in GenBank. In parallel with these improvements in DNA sequence determination, techniques for DNA synthesis have progressed rapidly. It has now become so simple and inexpensive that many laboratories find it more expedient to have the genes of interest synthesized rather than to clone them. Among other things, this allows the introduction of desirable codons tailored to the expression system to be used.

All of this new work serves to highlight the intertwining of chemistry and biology that has taken place over the last 50 years. Those wishing to understand this interrelationship and appreciate the excitement currently present in the field can do no better than browse the many excellent chapters in this third edition of *Nucleic Acids in Chemistry and Biology*.

Richard J. Roberts

Preface

The first edition of *Nucleic Acids in Chemistry and Biology* in 1990 met the pressing need for a single volume that integrated the chemistry and biology of nucleic acids in an introductory yet authoritative text. That book was so very well received that in 1996 we produced the second edition, which was completely revised and rewritten by very much the same team of international experts.

Ten years on we have responded to the still growing need for this book with a fully revised and updated third edition. Two irresistible pressures have driven this activity. First, the expansion in the chemistry and biology of nucleic acids continues unabated. The human and numerous lesser genomes have been fully sequenced since we presented the second edition and there has been a veritable explosion in the chemistry and biology of RNA. Many exciting crystal and NMR structures of nucleic acids and their protein complexes, including the ribosome, have been published. Changes of such magnitude have inevitably made significant parts of the 1996 text out of date. We have addressed these issues by expansion of the appropriate sections of the book and also by new authorship. Second, the second edition sold out several years ago. Indeed second-hand copies are occasionally available on the web at a handsome premium!

In planning this third edition, we first expanded the team of editors to include two younger colleagues, David Loakes and David Williams. We then changed publishing house to move under the roof of the Royal Society of Chemistry. For a variety of reasons it has been necessary to make changes to the team of principal authors and we thank especially Stephanie Allen, Martin Egli, Julie Fisher, Andy Flavell, Ihtshamul Haq, Charles Laughton, Ben Luisi, Anna Marie Pyle, Elliott Stollar, and Nick Williams for their essential and scholarly contributions. With the active support of the Royal Society of Chemistry and its commissioning and production teams, we have made significant changes in the style of presentation of this new edition. It now has a bibliography of primary and secondary sources that are referenced throughout the text. While we have maintained a number of multi-colour illustrations in addition to our standard two-colour format, we have abandoned the use of stereo-pair illustrations and the end-of-section summaries. These changes have created space for some expansion – but not enough for our needs: the third edition has grown substantially compared to its predecessor! This has enabled the authors to introduce a great deal of new material. In doing so, we have retained the essential core of chemistry and biology that has made this book so effective as a teaching resource at every level of study and an initiation into the molecular basics of nucleic acids. A selection of figures that may have value for course teachers are available electronically at the following website: <http://www.rsc.org/books/nucleicacids>

Above all, we have endeavoured to maintain the quality of the earlier editions, both of which have been widely appreciated for their easy readability, simplicity of exposition, clarity of illustration, and uniformity of style. That has underpinned our efforts to deliver a new edition that once again fulfils the needs of students and new research workers, primarily those having a chemical and biochemical background who seek to understand this great subject at a molecular level. Indeed, we know that *Nucleic Acids in Chemistry and*

Biology has become the course-book of choice in universities across three continents. At the same time, from many favourable comments on editions 1 and 2 we know that this book has also reached out to more senior scientists across many disciplines.

G Michael Blackburn

Michael J Gait

David Loakes

David M Williams