

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 Its popularity is attested to by its now being out of print – it has also inevitably become out of date.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*.

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