

Preface

In writing a book on genetic recombination my aim is twofold. Firstly, I want to introduce the concepts and experimental strategies that underpin this field, in a form understandable by anyone with a basic knowledge of genetics and biochemistry. Secondly I want to write a book including homologous, site-specific, transpositional and illegitimate recombination to demonstrate how the different aspects of the subject are intertwined. Furthermore, from a historical perspective, a wider understanding of recombination is timely now that transgenic technology has become so powerful and gene therapy of somatic cells promises new approaches in medicine.

In order to facilitate this, I explicitly discuss some experimental strategies. This is because our knowledge is based on such experiments and no real understanding can be complete without the ability to follow such experiments. However, to facilitate the assimilation of these experimental approaches, I have reduced the technical and system-specific details to a minimum. What is left are the experimental strategies themselves, and the reader is referred to the original papers to learn the details.

The classification of recombination reactions as homologous, site-specific, transpositional or illegitimate is the standard way of generating a logical subdivision of the field. I have therefore retained this system of classification, but I hope that the reader will develop an understanding that many recombination reactions utilize more than one of these mechanisms. For example, the transposition of Tn10 and P involves transpositional and homologous recombination; immunoglobulin VDJ-joining involves site-specific recognition and a reaction resembling illegitimate end-joining; mating-type interconversion involves site-specific cleavage and homologous recombination; and certain eukaryotic transposon-mediated genome rearrangements may be due to transposition coupled to illegitimate end-joining. I have used the term 'strand-transfer' in the sense that it is used by those working in the fields of transposition and site-specific recombination. I believe that this is novel when applied to homologous and illegitimate recombination, but creates a conceptual framework that is useful for describing all recombination reactions.

I have limited the use of references to specific experiments described in the figures and to figures adapted from other publications. There are no references in the main text but I provide suggestions for further reading at

the end of each chapter. The ideas, interpretations and models presented here are all based on the significant contributions of others but, within the context of a book of this kind, I am unable to acknowledge all of these contributions individually. I apologize for this and refer the reader to the reviews listed. What I have done is to present my understanding of the field and this has involved some novel ways of representing recombination reactions.

I have been fortunate to have worked directly in three of the four areas of recombination described in this book. My PhD studies with Neville Symonds were on bacteriophage Mu transposition. I then worked on homologous recombination with Frank Stahl and finally I find myself investigating palindromic sequences that are unstable due to illegitimate recombination. Neville Symonds and Frank Stahl have undoubtedly contributed significantly to my understanding of this field. Neville Symonds has actively promoted an interdisciplinary approach to recombination by organizing, with Robin Holliday, the EMBO workshops on genetic recombination that were mostly held at Nethybridge in the Scottish highlands. These meetings have continued to be organized by Alain Nicholas and Steve West at Seillac in France and have contributed significantly to this book. Neville Symonds had a rule of no more than three slides per talk so that listeners could concentrate on understanding concepts, experimental design and conclusions instead of being presented with an indigestible amount of data. This book attempts to continue in this spirit.

I wish to thank Martin Boocock, David Brock, Raymond Devoret, Marty Gellert, Jim Haber, Hideo Ikeda, Roger Kemp, Ichizo Kobayashi, Steve Kowalczykowski, Noreen Murray, Charles Radding, Jim Shapiro, Dave Sherratt, Gerry Smith and Frank Stahl. Their advice, comments, criticism and support have made this venture possible. I have attempted to correct as many errors and omissions as possible but I take full responsibility for any that remain. The book is dedicated to the memory of my colleagues Ahmad Bukhari and John Scaife. I first met Ahmad on the train from Perth to Nethybridge in 1976 when I was a PhD student travelling to my first EMBO recombination workshop and was immediately captivated by his infectious excitement about Mu transposition. I became a colleague of John Scaife's when I joined the Molecular Biology department in Edinburgh in 1982. His wide range of interests never diminished the clarity of his vision and I had the pleasure of editing *Genetics of Bacteria* with him. Finally, I would like to thank Judith, Jonathan and Justine, for their love, support and forbearance throughout this project.