
PREFACE TO THE THIRD EDITION

Biologists work on systems that have evolved. This gives us hope that any given case can be understood reductively. Nature built the system in steps, each step making an improvement on the previous version and so, this line of thought goes, the investigator can take it apart, study it in bits, and, perhaps, see how it all fits together. These notions have proved apt in studying gene regulation in the bacterial virus lambda.

The first edition of this text (published in 1986) described a series of protein-protein and protein-DNA interactions that effect two alternative patterns of gene expression in phage lambda. This “genetic switch” (as we called it) ensures an efficient change from one pattern to the other in response to an environmental signal.

This new edition is prompted by discoveries (none due to my efforts) that add to, rather than reformulate, the earlier story. The most striking of these describes interactions between proteins binding to widely separated sites on DNA, and shows how these interactions make the switch even more efficient than we had thought. Others probe more deeply than before, showing us, in clear molecular terms, how an activator of transcription works. Other experiments begin to dissect how the complex lambda gene regulatory network might have evolved, and still another reveals an enzymatic function carried by the repressor itself.

These new developments are described here in a chapter (Chapter 5) added to a reprint, only slightly modified, of the first edition. Those already familiar with the original description of the switch can learn about these developments by going directly to the new chapter; others can learn the whole story by reading the complete book as it now stands. The extended discussion of gene regulation in eukaryotes, added as part of the second edition but omitted here, has been reformulated and placed in a larger context in the book *Genes and Signals* (Ptashne and Gann 2002 Cold Spring Harbor Laboratory Press). The preface to the second edition has also been omitted here.

The new chapter illustrates, as did the original text, that uncovering interactions between components of the switch, and assessing their biological significance, required combining genetic with biochemical studies, and in some cases

with biophysical and structural studies as well. Given how weak some of the interactions are—for example, those mediating cooperative binding of proteins to DNA—it is hard to see how any other approach would have worked. Our picture of the switch has been formulated by studying the component reactions in isolation and then piecing them together. The fact that a step-wise approach has produced a picture of such (seeming) completeness and coherence is in itself (it seems to me) remarkable.

Strictly speaking, this book was, and remains, mistitled—“An Epigenetic Switch” would be more appropriate. An epigenetic change in the state of gene expression is one that persists in the absence of the original signal (or event), and that involves no change in DNA sequence. The maintenance of lysogeny over many cell divisions following its establishment (see Chapter 3) is a classic example of epigenesis.

There are important matters of gene regulation in lambda, currently under study, that I do not discuss in the new chapter. The mechanisms of action of the “anti-terminators” N and Q (introduced in Chapter 3) are two examples. Systems biologists have applied quantitative modeling approaches to this or that aspect of the lambda lifestyles and the transition between them, but I have not attempted to review these matters either. References to some of these studies are to be found at the end of Chapter 5.

All the figures from this book (along with those from *Genes and Signals*) are available on the Web Site www.genesandsignals.com.

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MARK PTASHNE
New York, NY

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