Preface

As Bünning (1973) noted in his prefatory remarks, to suggest the existence of an endogenous diurnal rhythm was generally regarded even as late as 1955 as subscribing to a mystical or metaphysical notion. One might argue justifiably that the field of biological rhythms emerged as a discipline (often designated as chronobiology) with the Symposium on Biological Clocks held in 1960 at Cold Spring Harbor, New York. The tens of thousands of papers that have been published since this important meeting attest to the fact that the periodic behavior of living systems, rather than being in some sense pathological—or at the very least abnormal—and confined to a very small number of organisms and tissues, is the normal state of affairs, the rule rather than the exception.

A particularly intriguing class of biological periodicity is reflected in the large number of well-documented persisting circadian rhythms, having periods of approximately 24 hours, that occur at every level of eukaryotic organization. Despite their importance, many reviews of rhythmic phenomena stop short of a detailed consideration of these characteristically longer-period rhythms, perhaps because a convincing explanation of this very same property, together with that of temperature compensation of the free-running period, has not as yet yielded to experimental analysis. Small wonder then that a lead editorial in *Nature* some years ago (231:97–98, 1971) somewhat plaintively queried why so little was known about the biological clock and suggested that it was time to wind it up. Present-day grant review panels, some 15 years later, seem to echo this theme even more stridently!

Nevertheless, progress has been made. The Dahlem Conference on The Molecular Basis of Circadian Rhythms, held in Berlin over a decade ago (Hastings and Schweiger, 1976), admirably summarized in its unique format the most exciting current trends at the time (membranes were hot) and is still quite useful as a reference work. This monograph attempts to update this treatment and consider some of the more provocative developments in the field (as, for example, those obtained with the powerful approach of molecular genetics). Its title, nevertheless, is a bit presumptuous. We still cannot clearly delineate the molecular basis of circadian rhythmicity,

and we will have to expand our treatment somewhat to include progress made at the cellular and biochemical levels as well.

The layout of the book emulates that of a kind of sextet; the outer two movements, consisting of a brief introduction to circadian rhythms and a final section treating general theoretical and applied aspects, flank an inner quartet of chapters comprising the core of the book. The first of these chapters (chapter 2) surveys circadian organization at the cellular level and describes the most important eukaryotic microorganisms that have served as experimental material for the biochemical and molecular analysis to follow. Chapter 3 discusses in some detail the interaction of cell division cycles and circadian oscillators. Chapter 4 treats the results obtained by several major experimental lines of attack on circadian clock mechanisms. Finally, the various biochemical and molecular models for circadian oscillators that have been constructed on the basis of the data presented earlier are outlined in chapter 5, along with their formal predictions and the degree to which they have been validated or disconfirmed.

Where appropriate, ultradian and other noncircadian periodicities are discussed (such as the glycolytic cycle—perhaps the best understood biochemical oscillator, and for that reason, instructive as a possible mechanism whereby longer periods might be generated), and parallels are drawn to the recent explosion of work on neuronal oscillators (Berridge et al., 1979; Carpenter, 1981, 1982). Although the chapters are designed to be read sequentially, particularly by the potential initiate to the field, it is unlikely that they can compete successfully with a good concert, movie, or home videotape. Consequently, those readers at least somewhat versed in this arcane area should also find it profitable to skip among the various sections. To this end, there is extensive cross-referencing and a rather large bibliography is appended (literature search ended June 1987) with name and date citations' being given in the text.

In a work of this scope, sins of omission and commission unfortunately are inevitable. I will appreciate learning of such errors, distortions and misinterpretations. I thank all those authors who have given me permission to use their published illustrations; Dr. Colin S. Pittendrigh, who introduced me to the field; the National Science Foundation, which has supported my own research throughout the years; Prof. Régis Calvayrac, Directeur de la Laboratoire des Membranes Biologiques, Université Paris VII, who provided a home away from home for the finishing touches on the manuscript; Dr. Charles F. Ehret, who read the entire work; and Dr. Danielle L. Lavel-Martin, who aided in the production of the manuscript. I am grateful to all my students in my course on Biological Clocks over the past 20 years who helped me justify my existence, particularly those special classes at the University of Tel Aviv and the Université Paris VII who endured shortened versions of this monograph during my tenure as visiting professor there.

Stony Brook, New York Leland N. Edmunds, Jr.