J. exp. Biol. (1979), **81**, 3–5
Printed in Great Britain

PREFACE

Waddington (1957) summarized a central property of biological systems with the observation that 'the main respect in which the biological picture is more complicated than the physical one is the way time is involved in it'. There are few examples of temporal ordering in biological systems that are as puzzling and as intriguing as the sustained autonomous oscillations that are observed in so many biological systems.

Certainly the first biological oscillator to attract the speculation of classical science was the heart. The problem was compounded by Harvey's demonstration that even very small sections of eel heart continue to contract rhythmically. Some scientists of the seventeenth and eighteenth centuries regarded the autonomy of the cardiac pacemaker as a definitive demonstration of the validity of vitalist theories that postulated the necessity of vital forces unique to biological systems. With the rise of modern mechanistic philosophies in the second half of the nineteenth century these views fell into general disfavour, but the problem of biological oscillations was largely neglected rather than resolved. It came to be generally supposed that periodic behaviour was in some sense pathological and confined to a very small number of tissues. Indeed in 1973 Bünning wrote: 'As recently as 15 to 20 years ago, to proclaim the existence of an endogenous diurnal rhythm was regarded, even by some well known biologists, as subscribing to a mystical or metaphysical notion.' In the past fifteen years, however, the perspectives of the biological community concerning pacemaker behaviour have been subjected to major revisions. To a large extent this has occurred as the result of developments in two very different subjects: theoretical thermodynamics and experimental physical chemistry.

Early experimental reports of periodic chemical reactions (Bray, 1921) were largely ignored as were early theoretical papers (Hirniak, 1910; Lotka, 1910, 1920) on the subject. It was commonly thought that all chemically reacting systems invariably evolve to a static state where constituents are uniformly distributed in both time and space. This seeming contradiction was resolved only after several researchers (Schrödinger, 1945; Prigogine, 1961) recognized and stressed the important distinction between thermodynamically open and closed systems. The importance of this distinction for oscillations is concerned with the generation of entropy. In a thermodynamically open system, the net production of entropy consists of two distinct components: (i) the generation of entropy within the system, and (ii) the exchange of entropy between the system and its surroundings. This entropy flow may be either positive or negative. In a thermodynamically open system, negative entropy flow can more than compensate for local entropy production. This exchange of entropy is essential for oscillations. A further distinction that was found to be important for a thermodynamic understanding of oscillations was the distinction between a steady state and an equilibrium. Prigogine & Balescue (1955, 1956) demonstrated that oscillations are impossible in regions near an equilibrium state whenever fairly general technical requirements are met (the validity of the Onsager relations). However, if a steady state is sufficiently far from equilibrium, it is possible for a chemical system to oscillate about that steady state indefinitely. No violation of thermodynamic laws occurs. These theoretical developments were accompanied by a series of experimental discoveries. In 1958, Belousov reported that the oxidation of citric acid by bromate did not proceed to equilibrium monotonically but rather displayed sustained oscillations between a yellow and colourless state. Unlike earlier isolated reports of periodic chemical phenomena, Belousov's work attracted the attention of several colleagues in the Soviet Union. Further, the possible implications for biological systems were immediately recognized and reports appeared in the biological literature (Zhabotinskii, 1964). A synthesis of the biological, biochemical and thermodynamic programmes occurred at meetings held in Prague in 1968, in Finland in 1969 and in the resulting volume (Chance *et al.* 1973).

Interest in biological oscillations also expanded as the result of improved bioelectrical recording techniques. As electrophysiology moved from classical preparations such as nerve and muscle fibres to other cell-types, it was found that oscillatory behaviour that had been previously supposed to be the exclusive property of 'excitable' cells could in fact be observed in a wide range of non-excitable tissues as well.

All of these developments have contributed to the growing realization that rhythmicity is not an aberrant behaviour confined to a small class of highly specialized cell types. Oscillations are not exceptional but constitute the response of many biological systems to normal physiological conditions. The number of confirmed bio-oscillations is now so large that it proved impossible to survey the entire spectrum of rhythmic activity in a single volume. Because long-period oscillations (notably the 24-hour circadian rhythms) have been discussed in detail in specialized monographs (Bünning, 1973; Conroy & Mills, 1970; Hastings & Schweiger, 1976) they have not been considered here. In this volume attention is directed to those higher-frequency oscillators where it is possible to construct theories which describe the generation of the oscillation at the cellular level. Throughout the contributions three questions have been considered. (i) What kinds of periodic behaviour can be observed in biochemical and physiological systems? (ii) What instability generates the oscillations? (iii) What functional advantages are conferred by oscillatory control (i.e. why is the oscillation there?)?

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