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Hyperchaos in Acetylcholinesterase Enzyme Systems

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Abstract—Burst generation via a complex bifurcation scenario is discussed using a two compartments model of an enzyme system with substrate inhibition kinetics affected by the production of hydrogen ions accompanying the reaction (e.g. acetylcholinesterase enzyme system). Evidences are given to support the existence of homoclinicity associated with this complex dynamics, including the generalised criterion developed by Rossler *et al.* [1] for the application of Sil'nikov's theorem in the case of four-dimensional systems. Complex bi-stabilities are observed in certain regions, and the structure of some attracting sets occurring near homoclinic orbits are discussed. The results support the use of such fundamental models for different dynamical modes generation and analysis. The results relate to the transition of small and large frequency oscillations to periodic bursting and vice versa in excitable cells and many biophysical systems. © 1997 Elsevier Science Ltd

1. INTRODUCTION

Simple static and dynamic bifurcation behaviour of an enzyme system inhibited by substrate and affected by the production of hydrogen ions accompanying the reaction was investigated by Elnashaie *et al.* [2–4] almost twelve years ago. In the light of the recent advances in fundamental knowledge and techniques regarding the discovery of chaotic behaviour in the dynamics of different mechanical, physical, chemical, biological and physiological systems [5–14], a part of the complex dynamic characteristics of this enzyme system has been investigated recently [15] using a relatively simple phenomenological two compartments model. The previous investigation [15], which was restricted to cases without static limit points (unique steady-state solutions over the entire range of parameters investigated), has uncovered a good part of the rich dynamic characteristics of the enzyme system, including Hopf bifurcation giving rise to periodic solutions, period doubling sequences leading to chaos, banded and fully developed chaos, interior crises, tangent bifurcation leading to intermittency, periodic windows interrupting chaotic regions and alternating periodic chaotic sequences. In the present investigation, cases with static limit points (multiplicity of the steady-states) are investigated. For these cases the existence of static limit points (SLPs) together with the Hopf bifurcation (HB) points gives rise to one of the most important non-local bifurcation mechanisms, namely, homoclinic bifurcation. This situation also gives rise to an important bifurcation mechanism to chaos, namely, homoclinic chaos [16].

An example of such an enzyme is acetylcholinesterase which catalyses the production of choline and acetic acid (where the later is fully ionised to acetate and hydrogen ions) from

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acetylcholine substrate. This enzyme plays a recognized role in nerve excitation, in many different neurones that enervate skeletal muscles, and in some important brain functions [17]. In most cases, acetylcholine has excitatory effects. The potential differences resulting from acetylcholine when injected on one side of an artificial acetylcholinesterase membrane exhibit a similar electrical response to the behaviour observed with excitable membranes [18].

The understanding of excitable membranes behaviour is strongly enhanced by the advances in the mathematical theory of bifurcation as well as the advances in chemical, biochemical and biological engineering research in this field. One of the interesting dynamical modes of the excitable cells is the so-called 'bursting'. This is a term used to describe the behaviour of certain neurophysiological and chemical systems in which there is a period of rapid spiking followed by a quiescent (resting) period. It is often in this form of excitable membrane activity that cells in the biological nervous systems are involved in various rhythmic behaviour, such as central pattern generations in invertebrates or pacemakers of brain waves in mammalian cortex [19, 20]. It is therefore a question of biological interest to ask how a rhythm (or bursting) can come about [21]. An individual cell capable of bursting may be at rest or merely exhibit continuous firing of action potentials, when it is subjected to different stimuli. This obvious biophysical fact provides a main ingredient to theoretical models of bursting in excitable cells [21], where bursting oscillations are viewed as switching back and forth between a continuous spiking state and a quiescent state. The work of Holden and Fan [22–25] on the dynamic behaviour of membrane excitation using a non-phenomenological three variables model of action potential show clearly the existence of different dynamic modes, including simple periodic, bursting periodic and chaotic behaviour. A wealth of transition mechanisms between different types of behaviour has been discovered by Holden and Fan [22–25]. These mechanisms include period doubling, boundary crises, period adding, saddle-node tangent bifurcation as well as saddle-node non-tangent bifurcation. One of the interesting observations noticed is that many of the dynamic phenomena discovered by Holden and Fan [22–25] using the three-dimensional non-phenomenological action potential model are also obtained using the present phenomenological two compartments model with membrane separating the two compartments [15]. Interestingly enough, similar behaviour has been observed for a completely different system, namely, the fluidized bed catalytic reactors with highly exothermic consecutive reactions [26].

Further exploration of the enzyme system under investigation is introduced in this paper for cases with SLPs, in order to uncover some of the richness of the dynamical phenomena characterizing this enzyme system. Our attention will be focused on the burst generation near some homoclinic orbits. This focusing is motivated by the generalized criterion of homoclinicity developed by Rossler *et al.* [1] for the application of Sil'nikov's theorem [27] to four-dimensional systems in addition to the fact that complex behaviour usually occurs in the vicinity of degenerate Hopf bifurcation points where the strict definition of Hopf bifurcation is violated [28].

2. MODEL EQUATIONS

The problem investigated is that of the enzymatic reaction

$$S \xrightarrow{E} P_1 + P_2^- + H^+$$

where, in the case of acetylcholinesterase,

S denotes acetylcholine $\{CH_3CO{\cdot}O(CH_2)_2N^+(CH_3)_3\}$
P_1^- denotes choline $\{HO(CH_2)_2N^+(CH_3)_3\}$
P_2^- denotes acetate $\{CH_3COO^-\}$