



Invited Review

Bifurcation/Chaos and Their Practical Relevance to Chemical and Biological Systems

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ABSTRACT

Bifurcation and chaos are important phenomena affecting many physical and chemical systems. They are also related to the stability/instability and multiplicity phenomena associated with these systems. The phenomena are not only of theoretical/mathematical interest but are also important for laboratory, pilot plant and commercial units. This paper concentrates on 3 systems:

1. The novel auto-thermic Circulating Fluidized Membrane Steam Reformer (CFBMSR) for the efficient production of the clean fuel hydrogen and which shows multiplicity of the steady state (static bifurcation)
2. A novel fermentor for the efficient production of bio-ethanol that shows static/dynamic bifurcation as well as chaotic behaviour
3. The neurocycle of the acetylcholine transmitter in the brain using diffusion-reaction models in order to gain insight into their possible connection to Alzheimer and Parkinson Diseases (AD/PD); these are preliminary efforts to investigate the bifurcation and chaotic behaviour of this neurocycle.

Keywords: Bifurcation, multiplicity, chaos, CFBMSR, chemical/biological reaction engineering, neuro-cycle, Alzheimer and Parkinson Diseases (AD/PD)

INTRODUCTION

Multiplicity of steady states in chemically reactive systems was first observed by Liljernoth (1919). However, it was not until the 1950s that great interest in this phenomenon was generated, inspired by the

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Minnesota school of Aris, Amundson and others (1958) and their students (e.g. Balakotaiah & Luss, 1981; 1983). Uppal, Ray and Poore (1974), Ipsen and Schreiber (2000) and Melo *et al.* (2001) added on to the basic knowledge and understanding regarding these phenomena. The bifurcation behaviour of non-isothermal bubbling fluidized bed catalytic reactors has been extensively investigated by Elnashaie and co-workers (1973; 1977; 1989; 1980; 1996). Earnshaw and Keener (2010) investigated in a more general manner the global asymptotic stability of non-autonomous master equations, while Danforth (2013) investigated chaos of atmosphere hanging in a wall. Dingqi *et al.* (2011) studied in some detail the combustion of coal based on the chaos theory. For more general applications, Werndl (2009) investigated the implications of chaos on unpredictability and Jua'rez (2011) investigated health and prediction applications.

Excellent reviews on the subject were published by Ray (1977), Bailey (1977, 1998), Gray and Scott (1994), Elnashaie and Elshishini (1996) and Epstein and Pojman (1998). Important mathematical principles are given by Golubitsky and Schaeffer in their book published in 1985. These important phenomena do not receive proper attention in chemical and biological engineering education and research. This state of affairs is perhaps due to lack of understanding regarding the practical importance and implications of these phenomena (Elnashaie & Elshishini, 1996). In this review, three chemical and biological reaction engineering systems are presented which are strongly affected by these phenomena. There are other systems also affected by these phenomena, such as Fluid Catalytic Cracking (FCC) for the production of high-octane-number gasoline (Elnashaie & Elshishini, 1996), UNIPOL process for the production of polyethylene and polypropylene (e.g. Choi & Ray, 1985) as well as other polymerisation reaction engineering systems (e.g. Teymour & Ray, 1992) as well as catalytic carbon mono-oxide oxidation (e.g. Razon & Schmitz, 1986), just to mention a few. This paper concentrates on only three main systems; two are related to clean fuel production and the third is related to modeling of the brain's neurocycle transmission process. The first mathematical reporting of period doubling to chaos was by Feigenbaum on 1980.

The first system considered in this paper is efficient production of hydrogen in the novel auto-thermic CFBMSR; the second is efficient production of the clean fuel ethanol by fermentation; and the third is the reaction-diffusion modeling of the behaviour of the acetylcholine neurotransmitter in the brain.

Hydrogen is becoming a promising clean energy source for the future (Goltsov & Veziroglu, 2002; Ohi, 2002; Elnashaie, 2005); it is mainly produced by the steam reforming of hydrocarbons (Tottrup, 1982; Elnashaie & Elshishini, 1993; Christensen, 1996). However, the conventional fixed bed steam reforming process is inefficient, highly polluting and suffers from catalyst deactivation (Rostrup-Nielsen, 1977; Elnashaie *et al.*, 1988; Twigg, 1989; Elnashaie & Elshishini, 1993). One of the main bottlenecks in this classical configuration is the extremely low catalyst effectiveness factor in the range of 0.001-0.01 (Elnashaie & Elshishini, 1993). The catalyst effectiveness factor has been considerably improved using fine catalyst particles in the bubbling fluidized bed (Elnashaie & Adris, 1989; Adris *et al.*, 1991, 1994a, b, 1997, 2002). The second main bottleneck is the thermodynamic equilibrium limitation associated with the reversibility of the reactions. This limitation has been "broken" using permeable hydrogen membranes (Elnashaie & Adris, 1989; Adris *et al.*, 1991; 1994a,

b; 1997; 2002). Recently, a novel CFBMSR has been shown to be more efficient and more flexible for pure hydrogen production, through which a wide range of hydrocarbons such as natural gas, naphtha, gasoline, diesel and bio-oils can be processed for use as feedstock (Chen & Elnashaie, 2002; Prasad & Elnashaie, 2002; Chen *et al.*, 2003a & b). The third bottleneck is associated with the inefficiency of heat supply to the highly endothermic reforming reactions through the huge top/side-fired furnaces (Twigg, 1989; Elnashaie & Elshishini, 1993). This limitation is "broken" using auto-thermal operation in a reaction-regeneration process, which "breaks" not only the heat transfer limitation, but also the carbon formation/catalyst regeneration limitation (Chen & Elnashaie, 2005; Elnashaie *et al.*, 2005). However, auto-thermal operation is associated with complex static and dynamic bifurcation behaviour (Elnashaie & Elshishini, 1996). Deep understanding of this complex phenomenon is essential for efficient design and safe operation/control of this process. In the hydrogen production part of this process, the static bifurcation behaviour and its practical implications are explored for two auto-thermal reforming configurations, as shown in Fig. 1a and Fig. 1b.

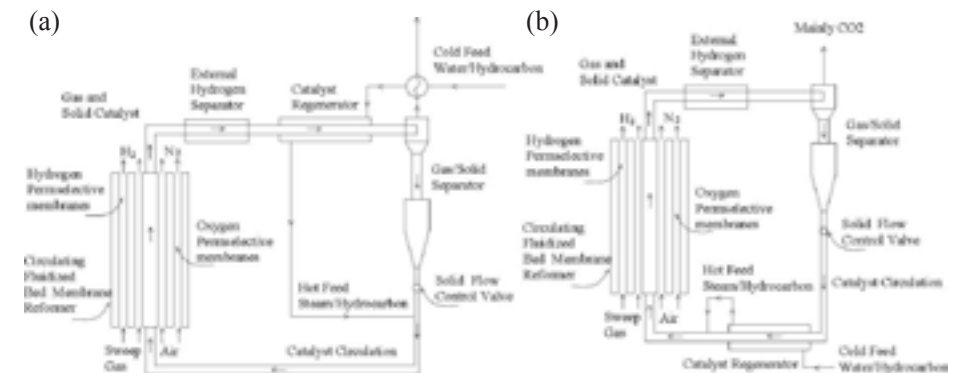


Fig. 1: The novel auto-thermal CFBMSR with continuous catalyst regeneration (a) before (b) and after the gas-solid separation

Kari *et al.*, (2009) investigated the effect of chaos on the control of the nonlinear chaotic reactor. Pyror *et al.* (2008) used the chaos theory to investigate into the probabilities and possibilities that may have their implications on all types of system.

In the first configuration the catalyst regeneration is carried out before the gas-solid separation (Fig. 1a), while in the second configuration it is carried out after the gas-solid separation (Fig. 1b). Heptane is used as a model component of heavy hydrocarbons. A number of palladium-based hydrogen permselective membranes and dense perovskite oxygen permselective membranes are used inside the reformer for hydrogen removal and oxygen supply respectively. For the efficient production of hydrogen, the remaining hydrogen exiting from the riser reformer is further removed in an external hydrogen separator. In the first configuration, the carbon deposited on the nickel reforming catalyst is burned off by excess air in the catalyst regenerator as well as the combustion of flammable gases such as un-reacted heptane and the by-products, methane and carbon monoxide. The regenerated catalyst is separated from the gases using a gas-solid separator and then recycled to the riser reformer. In the second configuration,

the solid catalyst is first separated from the gases and then the carbon deposited on the nickel catalyst is burned off in the regenerator. This is followed by separating the regenerated catalyst from the carbon dioxide. Exit hydrocarbons and carbon monoxide are used together with carbon dioxide from the catalyst regenerator as part of the feed to a novel CO₂ dry reformer (Prasad & Elnashaie, 2002). The regenerated catalyst is recycled to the riser reformer.

Both nature and modern industry, as well as its associated trends, generate huge amounts of lignocelluloses that can be useful as raw materials for a wide spectrum of products (Kaylen *et al.*, 1999; So & Brown, 1999). The most important among the spectrum of useful products to be produced from this abundant lignocellulose raw material is ethanol, a clean fuel, an important solvent and a source of other important chemicals and fine chemicals. The production of ethanol from lignocellulose can be a difficult task, with the level of difficulty depending on the choice of raw materials. The primary step in the production of ethanol from the lignocellulose is the separation of lignin from lignocellulose, a process now called lignocellulose fractionation that is seeing extensive research and development. Sugars are produced by the hydrolysis of biomass and other cellulosic sources. Various hydrolysis technologies for cellulosic feedstock always produce a mixture of sugars (glucose, xylose, arabinose etc.). These two steps of the process have been the subjects of extensive research (Sun & Cheng, 2002; Mais *et al.*, 2002; Iranmahboob *et al.*, 2002; Krishnan *et al.*, 1997; Ho *et al.*, 2000). In this part of the review the focus is on the process of bioconversion i.e. fermentation, with the aim of efficiently fermenting the sugars produced by hydrolysis and obtaining better productivity and yield of ethanol. Ethanol derived from renewable sources such as lignocellulose wastes/materials is an attractive clean fuel to limit air pollution and reduce dependence on fossil fuels (Kralik *et al.*, 2001; Newton, 2003). Interest in biofuels has been regained since the Kyoto Protocol which binds industrialised countries that signed this treaty to reduce their carbon dioxide emissions and other greenhouse gas production. Improvements over conventional fermentation processes have been proposed to increase the sugar conversion, ethanol yield and productivity of the process. Continuous ethanol removal using different methods are useful in reducing the ethanol inhibition on the biocatalyst (Jeong *et al.*, 1991; O'Brien & Craig, 1996; Ikegami *et al.*, 1997; Nomura & Nakao, 2002). Another method of reducing the initial inoculation amount of microorganisms and of increasing the rate of fermentation is to recycle the microorganisms back to the fermentor (Roca & Olsson, 2003; Lang *et al.*, 2001; Giridhar & Srivastava, 2001; Giorno *et al.*, 2002; Lalue *et al.*, 2002). For the fermentor it is important to notice that stability and consistency of bioprocesses has become more important with the development of new biological products and the tighter regulations on product quality. This in turn requires a quantitative knowledge of the bio-culture stability and dynamics to understand, control and optimise the process (Davey *et al.*, 1996). In fermentation processes, many investigators have reported the presence of sustained oscillations in experimental fermentors and they have developed suitable mathematical relations to model these fermentors (Ghommidh *et al.*, 1989; Daugulis *et al.*, 1997; McLellan *et al.*, 1999; Jobses *et al.*, 1985; 1986a; Jobses, 1986b).

This review summarises the rich static/dynamic bifurcation behaviour of the ethanol fermentor system (Garhyan *et al.*, 2003; Garhyan & Elnashaie, 2004a, 2004b, 2004c, 2004d, 2005; Mahecha-Botero *et al.*, 2005). It also shows that these oscillations can be complex, leading to chaotic behaviour, and that these periodic and chaotic attractors can be useful. Using

an experimentally verified mathematical model, it is shown that the average conversion of sugar and average yield/productivity of ethanol is sometimes higher for periodic and chaotic attractors than for the corresponding steady states. The results have been confirmed experimentally (Garhyan & Elnashaie, 2005).

In the case of the fluidized bed membrane reactor, bifurcation studies are limited to "static bifurcation" because it is formed of coupled distribute systems, with complicated dynamic characteristics which have not been studied yet, while in the case of the fermentor both "static and dynamic" are studied since the fermentor is described by lumped system, and this has been studied. The dynamics of the fluidized bed membrane reformer is not any less important than that of the fermentor, and a dynamic model should be developed and dynamic experiments carried out.

From the environmental point of view, efficient production of the clean fuels, hydrogen and ethanol represents an important contribution towards achieving a cleaner environment and radically reducing carbon footprints of modern societies. From a sustainable-development point of view these advanced technologies (together with the production of biodiesel) that have adopted the use of renewable raw materials such as biomass represent an important step towards freeing modern societies of over-dependence on non-renewable fossil fuels with all their economical, environmental and political disadvantages.

The third example is dealing with the acetylcholine neurotransmitter in the brain. The chemical synapse is a highly specialised structure that has evolved for exquisitely controlled voltage-dependent secretion. The chemical messengers, stored in vesicles, are released from the pre-synaptic cell following the arrival of an action potential that triggers the vesicular release into the pre-synaptic terminal (Quinn *et al.*, 1995). Once released from the vesicles, the transmitter diffuses across a narrow synaptic cleft and binds to specific receptors on the postsynaptic cell. This initiates an action potential event on the nerve-muscle cell membrane triggering muscle contractions (Quinn *et al.*, 1995; Llinas, 1999; Paez & Fayad, 1999; Guyton & Hall, 2000; Tucek, 1978). Acetylcholine (ACh) plays a well-recognised role in nerve excitation (Quinn, 1995; Llinas, 1999; Guyton and Hall, 2000; Tucek, 1978; Barman, 1969). It is found in cholinergic synapses that provide a stimulatory transmission in the nervous system. Its complete neurocycle constitutes a coupled two-enzyme system. The two-enzyme/two-compartment model shown in this review paper differs from other membrane excitation models such as the Rose-Hindmarsh model of action potential (Hindmarsh & Rose, 1982; 1984) which is a modification of the Fitzhugh model (Fitzhugh, 1985). This later model was developed to simulate the repetitive, patterned and irregular activity seen in molluscan neurons.

With the above motivations and extending the earlier investigation completed by Elnashaie and coworkers (El-Rifaie *et al.*, 1980, Elnashaie *et al.*, 1983a; Elnashaie *et al.*, 1983b; Elnashaie *et al.*, 1984; Elnashaie *et al.*, 1995; Ibrahim & Elnashaie, 1997; Ibrahim *et al.*, 1995;), a novel diffusion-reaction model is formulated using the non-linear dynamic approach to simulate and study the synaptic gap.

HYDROGEN PRODUCTION

The reactions and kinetics for the riser reformer are summarised in earlier work by many researchers e.g. Elnashaie and Elshishini (1996), Paradeep and Elnashaie (2002) and Chen and Elnashaie (2005). For the first configuration, because the gases exiting the external hydrogen separator contains some flammable gases such as un-reacted heptane, the by-products methane and carbon monoxide, and with the excess air feed in the catalyst regenerator, combustion of these gases take place.

For the second configuration, however, only the burning of carbon takes place. For modeling, only the heat produced in the catalyst regenerator and its thermal effects on the entire system are considered. For the sake of simplicity, we assume plug flow in both the reaction side and permeable membrane tubes. Then the riser reformer is modeled as a plug-flow reactor with no gas-solid slip because of high gas velocity (~ 3 m/s) and the use of fine catalyst particles (186 μm) (Patience *et al.*, 1992). The other main assumptions are as follows:

- (1) Steady-state operation
- (2) There is no heat loss for the entire adiabatic process.
- (3) There is no oxidation of hydrogen or carbon monoxide over the nickel-reforming catalyst, which is based on reported experimental investigation that oxygen can be safely and successfully introduced into a catalytic steam reformer (Roy *et al.*, 1999).
- (4) The palladium based hydrogen membranes and dense perovskite oxygen membranes are 100% selective for the permeation of hydrogen and oxygen, respectively (Shu *et al.*, 1994; Barbieri & Di Maio, 1997; Tsai, 1997).
- (5) The heat capacities of the components and the heat of reactions are constant.
- (6) The pressures in the riser reformer, hydrogen and oxygen membrane tubes are constant.
- (7) The performances of hydrogen and oxygen permselective membranes are not affected by carbon deposition.
- (8) The heat of reactions in the catalyst regenerator are used to preheat the cold feed water to generate steam, the heptane and the regenerated catalyst before recycling to the riser reformer, in which the necessary heat for the endothermic steam reforming reactions is supplied.

The steady state model equations for this CFBMSR form a set of initial value non-linear ordinary differential equations. The reported maximum operating temperatures of current palladium-based hydrogen membranes are in the order of 900 K (Shu *et al.*, 1994; Barbieri & Di Maio, 1997). Unless otherwise specified, the results presented are under a set of standard parameters and reaction conditions, e.g. Elnashaie & Elshishini (1996), Paradeep and Elnashaie (2002) and Chen and Elnashaie (2005). It is important to notice that under auto-thermal operation, the feed temperature to the riser reformer is a system variable rather than a feed parameter. Heptane conversion is defined as the total moles of heptane converted per mole of heptane fed. The hydrogen yield is defined as the total moles of hydrogen produced per mole

of heptane fed. Under auto-thermal operation, there is no external heat supply and therefore it is also the same as the net hydrogen yield.

RESULTS AND DISCUSSION

Detailed bifurcation results for the two configurations using different parameters as bifurcation parameters are presented. and they show very clearly the importance of the bifurcation phenomena on design, optimisation and operation of these novel reformers (Chen & Elnashaie, 2005). In this paper we give only a sample of these results for the case where the steam-to-carbon (of heptane) feed ratio is used as the bifurcation parameter.

Bifurcation behaviour of Configuration I of CFBMSR: Catalyst is regenerated before the gas-solid separation

Fig.2 (a-d) shows the bifurcation behaviour when steam to carbon (S/C) feed ratio is used as the bifurcation parameter. The base value of S/C= 2.0 mol/mol. When the S/C feed ratio is lower than 1.44 mol/mol, only one steady state exists in the auto-thermal CFB membrane reformer. In this region low S/C feed ratio is used and thus, the extent of steam reforming (i.e. the fraction of heptane which reacts with steam) is small. On the other hand, for this low S/C, the carbon formation competes for the reactant heptane. The higher the reformer exit carbon flow rate, the higher the amount of carbon deposited on the catalyst and the higher the heat generation in the catalyst regenerator. As a result, the auto-thermal circulating feed temperature to the reformer i.e. the temperature of the stream fed to the reformer is high. For S/C feed ratios below 1.15 mol/mol, the auto-thermal circulating feed temperature increases sharply, as shown in Fig. 2a. Although the bifurcation behaviour discussed in this review is limited to static bifurcation, however, based on the bifurcation theory (Elnashaie & Elshishini, 1996), any decrease in the steam-to-carbon ratio (or increase in the temperature) will lead to thermal "runaway". When the S/C feed ratio is between 1.44 and 2.25 mol/mol, multiplicity with three steady states occurs, which are usually classified into lower, middle and upper steady states according to the feed temperature to the reformer, respectively (Fig. 2a). For example, at the S/C feed ratio of 2.0 mol/mol, three steady states exist with circulating reformer feed temperatures of 688, 702 and 740 K, respectively. Fig.2c shows that at the middle and upper steady states the conversion of heptane is 100%, while at the lower steady state the conversion of heptane is between 81.6 and 95.8%. The conversion of heptane on this lower steady state branch decreases with the increases in the S/C feed ratio. This is the opposite of the usual operation where the reformer performance increases when the S/C feed ratio increases. The reason for this behaviour is that the reformer exit carbon flow rate shown in Fig. 2b is low on this lower steady state branch, making the heat generation from the burning of carbon in the regenerator low. On the other hand, the heat consumption for preheating the cold feed water and heptane increases when the S/C feed ratio increases. In order to balance the heat supply and heat consumption in the reformer-regenerator system, the conversion of heptane under auto-thermal operation has to decrease with the increase in the S/C feed ratio. In the multiplicity region, the higher the reformer exit carbon flow rate (net carbon deposition on the catalyst), the higher the auto-thermal feed temperature to the reformer. But the trend of net hydrogen

yield is totally reversed. As shown in Fig. 2d, the higher the auto-thermal feed temperature to the reformer, the lower the net hydrogen yield. For example, at the S/C feed ratio of 2 mol/mol, the net hydrogen yield is 14.4 at the upper-feed temperature 740 K, while it is 14.6 at the middle-feed temperature of 702 K and 14.66 at the lower-feed temperature of 688K. This reverse relationship between the net hydrogen yield and the auto-thermal circulating feed temperature is due to the carbon formation-burning process in the auto-thermal system. Steam reforming does not only extract hydrogen from hydrocarbons but also extracts hydrogen from steam, while carbon formation only extracts hydrogen from hydrocarbons. Therefore, the larger the fraction of heptane cracking for carbon formation, the more the carbon generation, the higher the auto-thermal circulating feed temperature and the lower the net hydrogen yield. According to the bifurcation theory (Elnashaie & Elshishini, 1996), only the lower and upper steady states are stable, while the middle steady state is an unstable saddle-type state. When the S/C feed ratio is higher than 2.25 mol/mol, the auto-thermal circulating feed temperatures and the reformer exit carbon flow rates are almost constant while the conversion of heptane is decreasing. This is due to the fact that the higher the steam feed, the higher the reaction extents of endothermic steam reforming (of heptane and methane) and the mildly exothermic water gas shift reaction. In order to keep the system operating auto-thermally, the conversion of heptane has to be relatively low in order to provide enough “fuel” to generate heat in the catalyst regenerator to supply the necessary heat for the endothermic steam reforming in the riser reformer. As a result, the auto-thermal circulating feed temperature to the riser reformer is low and the conversion of heptane is low. For example, at the steam-to-carbon feed ratio of 2.5 mol/mol, the conversion of heptane is 78.1%, the reformer exit carbon flow rate is 0.9 kg/h and the auto-thermal circulating feed temperature is 694 K. Because the net hydrogen yield is defined as the amount of hydrogen produced per mole of heptane fed, the longer the feed heptane is burned in the regenerator, the smaller the net hydrogen yield (Fig. 2d). For example, at a high S/C feed ratio of 2.5 mol/mol, the net hydrogen yield is 13.8 moles of hydrogen per mole of heptane fed. In this set of results the maximum net hydrogen yield is about 15.6 moles of hydrogen per mole of heptane fed at the lower steady state when the steam-to-carbon feed ratio is close to 1.44 mol/mol, as shown in the left-hand bifurcation point in Fig. 2d. It is about 70.8% of the theoretical maximum hydrogen yield of 22 when the final reforming products are carbon dioxide and hydrogen.

Bifurcation behavior of configuration II: Catalyst regenerated after the gas-solid separation

In the second configuration only the burning of carbon deposited on the nickel catalyst supplies the heat for the endothermic reforming reactions and for the vaporisation of cold feed water and heptane. Because steam reforming of heptane is a highly endothermic reaction, the heat supply requirement from the burning of carbon in the catalyst regenerator is high. In order to generate enough carbon on the catalyst as an energy source for an auto-thermal operation, the steam-to-carbon (S/C) feed ratio is much lower than in the usual processes. The standard S/C feed ratio is in mol/mol. In order to keep the same total feed rate to the riser reformer, the base feed flow rates of heptane and steam for configuration 2 (Fig. 1b) is S/C=1. Similar behaviour

to this is observed in Figs. 2 (a-d). In this case the S/C feed ratio is the bifurcation parameter. In this configuration the multiplicity is over a very narrow region from the S/C feed ratio of 0.994 to 1.023 mol/mol. For a practical operation, the control for the accurate S/C feed ratio is very important. In this case the auto-thermal circulating feed temperature to the reformer increases with the increase in the S/C feed ratio on the lower and upper steady state branches, while there is a decrease on the middle steady state branch. However, this case shows that the reformer exit carbon flow rate increases slightly with the increase in the S/C feed ratio on the lower and middle steady state branches, but a decrease on the upper steady state branch. The conversion of heptane is always 100%; the yield of by-product methane decreases on the lower and upper steady state branches but increases on the middle steady state branch with an increase in the S/C feed ratio. The net hydrogen yield in Fig. 3d increases to the multiplicity region from the S/C feed ratio of 0.975 mol/mol. Then it is almost constant when S/C feed ratio is in the range of 1.023 to 1.05 mol/mol. In the multiplicity region the order of reformer exit carbon flow rate or the order of methane yield from high to low is the lower, middle and upper steady states, while the order of net hydrogen yield from high to low is the middle, upper and lower steady states, respectively. For example, at the S/C feed ratio of 1.02 mol/mol, the reformer exit carbon flow rates are 42.1, 41.5 and 39.1 kg/h at the lower, middle and upper steady states, respectively. The methane yields are 0.15, 0.080 and 0.008 moles of methane per mole of heptane fed. The net hydrogen yields are 14.26, 14.41 and 14.35 moles of hydrogen per mole of heptane fed at these three steady states. The order of net hydrogen yield is middle>upper>lower steady states, and this yields a curve that bends and crosses itself at the right bifurcation point close to the S/C ratio of 1.023 mol/mol.

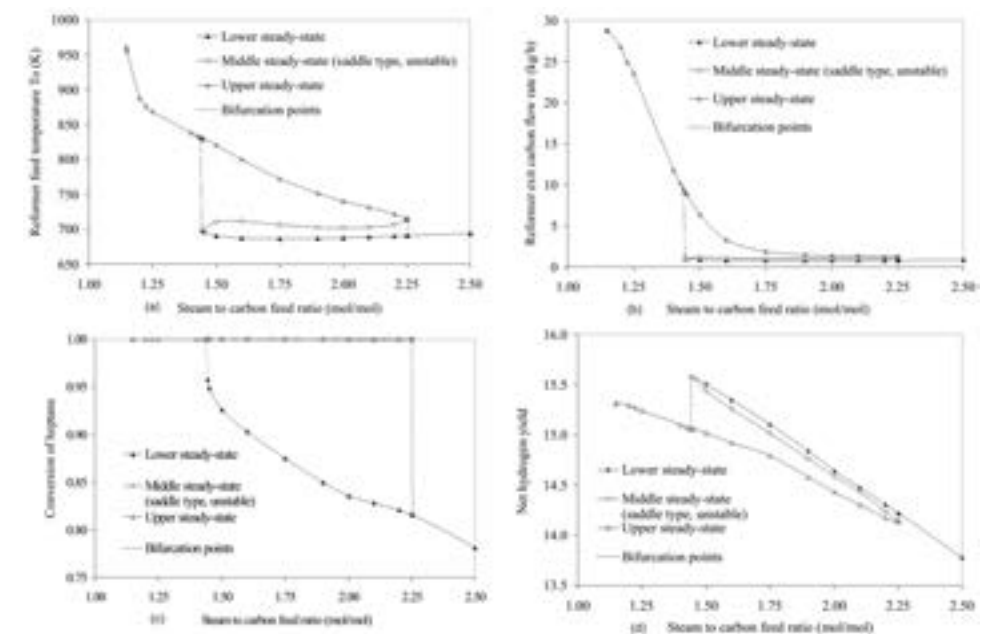


Fig.2: Bifurcation behaviour with steam-to-carbon feed ratio as the bifurcation parameter in the auto-thermal CFBMSR when catalyst is regenerated before gas-solid separation (Fig. 1a) and after gas-solid separation (Fig. 1b)

BIOETHANOL PRODUCTION

In the preceding case of hydrogen production, the novelty is the configuration itself; bifurcation occurs when the process is thermally intensified to get the highest hydrogen yield and productivity with minimum energy consumption. In the following case of fermentor for the production of bio-ethanol, the process configuration remains simple but novel modes of operation are explored: periodic and chaotic. This approach for the bio-ethanol production using an unstable mode of operation of a CSTR fermentor exploits the bifurcation and chaos theories to maximise ethanol yield and productivity. The research work reviewed in the following sections consists of: developing a reliable and relatively simple model to describe the fermentation process, verifying the model used in bifurcation and chaos analysis work and then using these results to guide experimental investigation of bifurcation and chaos and their implications on improving ethanol yield and productivity. Verification of the model results against experimental results (Garhyan *et al.*, 2003; Garhyan & Elnashaie, 2004a, 2004b, 2004c, 2004d, 2005; Mahecha-Botero *et al.*, 2005) is essential to validate the model. Bifurcation analysis was carried out for configuration where continuous in-situ ethanol removal using an ethanol selective membrane was reported by Garhyan and co-workers (2004a; 2005). Detailed bifurcation analysis was also reported for more complicated configurations consisting of multiple fermentors with continuous ethanol removal and cell recycle (Garhyan & Elnashaie, 2004c).

MODEL DEVELOPMENT AND DISCUSSION

Biochemical reactors can be viewed as highly complex dynamical systems in which various chemical components are present in the intracellular and extracellular spaces and each cell has unique properties. A rigorous model accounting for the above complexities is called a structured-segregated model (Cazzador *et al.*, 1987; Eakman *et al.*, 1966; Srienc & Dien, 1992); this model is difficult to formulate and analyse. The presence of oscillations within cellular systems has been observed and mathematically described, such as glycolytic oscillations and oscillations in intracellular calcium concentrations in different types of cells (Goldbeter, 1996). More simplified models can be formulated either by neglecting the intracellular chemical variations (unstructured models) (Bellgardt, 1994; Duboc & von Stockar, 2000; Hjortso & Nielsen, 1994) or by neglecting the heterogeneity of the cell population (un-segregated models) (Cazzador, 1991; Jones & Kompala, 1999; Ramkrishna *et al.*, 1987). The simplest models are unstructured-un-segregated models (Daugulis *et al.*, 1997). The structured-un-segregated bio-kinetic model describing the continuous fermentation of glucose to ethanol in a continuously stirred fermentor can be described by a set of four differential equations (Garhyan *et al.*, 2003). This model has four state variables, namely, the concentrations of sugar (C_S), ethanol (C_P) and microorganism (C_X), and an internal key component (C_e). This cellular component “e” is essential for both growth and product formation and has a non-linear dependence on ethanol concentration. Hence the inhibition by ethanol does not directly influence the specific growth rate of the culture, but the effect is indirect (Jobses *et al.*, 1985, 1986a, b). The term E is the ratio of the internal key component concentration to the microorganism concentration ($E = C_e/C_X$). The model is expressed in the form of four coupled non-linear differential

equations (Garhyan *et al.*, 2003; Garhyan & Elnashaie, 2004b). For the steady state, the set of four differential equations reduces to a set of four coupled non-linear algebraic equations, which can only be solved simultaneously. Jobses *et al.* (1985; 1986a, b) used successfully this four-dimensional model to simulate the oscillatory behaviour of an experimental continuous fermentor in the high-feed sugar concentration region. This model has been used to explore the different possible complex static/dynamic bifurcation behaviours of this system in the two-dimensional [D (dilution rate = $(1/\text{residence time})$) - C_{S0} (feed concentration of substrate, sugar)] parameter space, and to review the investigations into the implications of these phenomena on substrate conversion and ethanol yield and productivity. The system parameters for one of the experimental runs of Jobses *et al.* (1986a, b) showing oscillatory behaviour is used as the base set of parameters (Garhyan *et al.*, 2003).

PRESENTATION TECHNIQUES AND NUMERICAL TOOLS

The bifurcation diagrams are obtained using the software package AUTO97 (Doedel *et al.*, 1997). This package is able to perform both steady state and dynamic bifurcation analysis, including the determination of entire periodic solution branches using the efficient continuation techniques (Kubicek & Marek, 1983). The DIVPAG subroutine available with IMSL Libraries for FORTRAN with automatic step size to ensure accuracy for stiff differential equations is usually used for numerical simulation of periodic as well as chaotic attractors. FORTRAN programmes are written for plotting the Poincare plots. MATLAB can also be used instead of FORTRAN. The classical time trace and phase plane for the dynamics are used. However, for high periodicity and chaotic attractors these techniques are not sufficient. Therefore, other presentation techniques are used. These techniques are based upon the plotting of discrete points of intersection (return points) between the trajectories and a hyper-surface (Poincare surface) chosen at a constant value of the state variable (e.g. $C_X = 1.55 \text{ kg/m}^3$ in fermentation processes, where C_X is the concentration of the microorganism). These discrete points of intersection are taken such that the trajectories intersect the hyper-plane transversally and cross it in the same direction. The return points are used to construct a number of important diagrams namely: Poincare one parameter bifurcation diagram, which is a plot of one of the co-ordinates of the return points (e.g. C_S) versus a bifurcation parameter (e.g. D) and return point histogram, which is a plot of one of the co-ordinates of the return points [e.g. C_S , substrate (sugar concentration)] versus time.

RESULTS AND DISCUSSION

A detailed static/dynamic and chaotic analysis has been carried out for this system and will be reviewed. However, in this review we give only samples of these non-linear dynamics analysis results. Fig.3 is a two-parameter continuation diagram of D vs. C_{S0} showing the loci of Static Limit Points (SLPs) and Hopf Bifurcation (HB) points. Two-parameter bifurcation diagrams are usually constructed by taking a fixed value of all parameters and having the bifurcation diagram between two parameters, e.g. Fig.3 shows the two parameters, D and C_{S0} bifurcation diagrams. The one-parameter bifurcation diagram keeps one of the two parameters constant and takes a state-variable-vs.-the-other-bifurcation parameter. In order to evaluate the performance of the

fermentor as an alcohol producer, the following variables are calculated from state variables and feed conditions: conversion of substrate, the product (ethanol) yield and its productivity according to the simple relations incorporated in the computer programme. Substrate (sugar conversion), $X_s = (C_{s0} - C_s)/C_{s0}$; Ethanol Yield = $Y_p = (C_p - C_{p0})/C_{s0}$ or $\bar{Y}_p = (C_p - C_{p0})/(C_{s0} \cdot X_s)$.

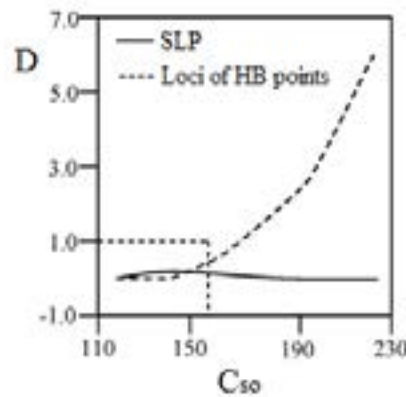


Fig.3: Two parameters continuation diagram of C_{s0} vs. D

Ethanol productivity (production rate per unit volume, $\text{kg}/\text{m}^3 \cdot \text{hr}$) of the fermentor is $P_p = C_p \cdot D$. For the oscillatory and chaotic cases, the average conversion \bar{X}_s , average yield \bar{Y}_p and the average production rate \bar{P}_p as well as the average ethanol concentration \bar{C}_p are computed. They are defined as, $\bar{X}_s = \left| \int_0^\tau X_s \cdot dt / \tau \right|$, $\bar{Y}_p = \left| \int_0^\tau Y_p \cdot dt / \tau \right|$, $\bar{P}_p = \left| \int_0^\tau P_p \cdot dt / \tau \right|$, $\bar{C}_p = \left| \int_0^\tau C_p \cdot dt / \tau \right|$, where the τ values in the periodic cases represent one period of the oscillations, and in the chaotic cases, they are taken long enough to be reasonable representation of the “average” behaviour of the chaotic attractor.

Sample case, dilution rate D as the bifurcation parameter with $C_{s0} = 140 \text{ kg}/\text{m}^3$. Jobses *et al.* (1986a, b) use this value of C_{s0} in their experiments together with a dilution rate of $D = 0.022 \text{ hr}^{-1}$. Their model results represent the experimental results very well. Details of static and dynamic bifurcation behaviour for this case are shown in Fig.4(A-D), with the dilution rate D as the bifurcation parameter. Fig.4A shows the bifurcation diagram for substrate concentration (C_s) with clear demarcations between the different regions using dotted vertical lines. It is clear that the static bifurcation diagram is an incomplete S-shape hysteresis type with a Static Limit Point (SLP) at very low value of $D = 0.0035 \text{ hr}^{-1}$. The dynamic bifurcation shows a Hopf Bifurcation (HB) at $D_{HB} = 0.05 \text{ hr}^{-1}$ with a periodic branch emanating from it. The region in the neighbourhood of the SLP is enlarged in Fig.6b. The periodic branch emanating from HB terminates homoclinically (with infinite period) when it touches the saddle point very close to the SLP at $D_{HT} = 0.0035 \text{ hr}^{-1}$. Fig.4c is the bifurcation diagram for the ethanol concentration (C_p). It is clear from Fig. 6c that the average ethanol concentrations for the periodic attractors are higher than those corresponding to the unstable steady states. Figures 6d show the bifurcation diagrams for ethanol yield (Y_p) where the average yield (Y_p) for the periodic branch are shown

as diamond-shaped points and it is clear that the average yield of the periodic attractor is higher than the unsteady state. The same applies for productivity which is not shown here. The period of oscillations increases as the periodic branch approaches the homoclinical bifurcation point; the period tends to infinity indicating homoclinical termination of the periodic attractor at $D_{HT} = 0.0035 \text{ hr}^{-1}$. The region (Region1) with three point attractors ($D < D_{HT}$) is characterised by the fact that two of them are unstable and only the steady state with the highest conversion is stable. The highest conversion (almost complete conversion) occurs in this region for the upper stable steady state. This steady state also gives the highest ethanol yield which is equal to 0.51 (Fig. 4d). On the other hand, this region has the lowest ethanol production rate due to the low values of the D (a given fermentor active volume corresponds to a very low flow rate). Region 2 of $D_{HB} > D > D_{HT}$ is characterised by a unique periodic attractor (surrounding the unstable steady state), which starts at the HB point and terminates homoclinically at a point very close to SLP as shown in Figs 4a and 4b. It is clear that in this region, the average of the oscillations for the periodic attractor gives (as shown in Figs 4c, d) a higher C_p , Y_p and P_p than that of the corresponding steady states, which means that the operation of the fermentor under periodic conditions is not only more productive but will also give higher ethanol concentrations by achieving a higher sugar conversion. A comparison between the static branch and the average of the periodic branch in this region (e.g. at $D = 0.045 \text{ hr}^{-1}$) shows that the percentage improvements are as follows: for C_p it is 9.34%, for X_s it is 9.66%, for Y_p it is 8.67% and for P_p it is 9.84%. Therefore, the best production policy for ethanol concentration, yield and productivity for this case is a periodic attractor.

It is fundamentally and practically important to notice that conversion, yield and productivity are very sensitive to D changes in the neighbourhood of the HB point. This sensitivity is not only qualitative regarding the birth of oscillations for $D < D_{HB}$ but also quantitative comparing the conversion, yield and productivity for $D > D_{HB}$ and their average values for $D < D_{HB}$. The further decrease in D beyond D_{HB} causes the average values of conversion, yield and productivity to increase. Region 3 is characterised by the existence of a unique stable steady state having the conversion, yield and productivity characteristics very close to those of the unstable steady state in region 2. In general, there is a trade-off between concentration and productivity, which requires economic optimisation to determine the optimum D . The phenomenon of possible increase in conversion, yield and productivity through deliberate unsteady state operation has been known for some time (Douglas, 1972). Deliberate unsteady operation is associated with non-autonomous (externally forced) systems. In the present work, the unsteady state operation of the system (periodic operation) is an intrinsic characteristic of the system in certain regions of the parameters. Moreover, this system intrinsically shows not only periodic attractors but also chaotic attractors. Static and dynamic bifurcation and chaotic behaviour are due to the non-linear coupling of the system (Elnashaie & Elshishini, 1996). This non-linear coupling is the cause of all the phenomena including the possibility of higher conversion, yield and productivity. Physically it is associated with the unequal excursion of the dynamic trajectory (periodic or chaotic) above and below the unstable steady state as shown in Fig. 5 (Garhyan *et al.*, 2003).

CONCLUSIONS AND RECOMMENDATIONS FOR THE FERMENTATION PROCESS

Extensive non-linear analysis of an ethanol fermentor is investigated and the published results show the complex static and dynamic bifurcation. The mathematical investigations have been used as a guide to carry out experimental work to substantiate the analysis. The investigations reveal rich static and dynamic bifurcation behaviour of the fermentation system, which includes bi-stability, incomplete period doubling cascade, period doubling to banded chaos and homoclinical (infinite period) bifurcation (Keener, 1981) for periodic as well as chaotic attractors. The investigations concentrate on the effect of the different values of the dilution rate and substrate feed concentration on the bifurcation/chaotic behaviour of the system. Special emphasis is given to the implication of these phenomena on the sugar conversion, ethanol yield and productivity of the fermentation process. It is well known from the dynamical system theory that these experimentally observed and mathematically simulated oscillations must start and end at certain critical points (Elnashaie & Elshishini, 1996). Therefore, the models are used to investigate the rich static and dynamic bifurcation behaviour of such experimental fermentors over a wide range of parameters. Bifurcation analysis provides insight into the possible utilisation of periodic attractors to enhance the conversion, yield and productivity of the fermentation process. It is seen in the continuous experiments that the experimental values of the state variables closely match the simulated values, thus confirming that the simplified structured-un-segregated models are suitable for the description of the fermentation process. Different configurations are also explored with in-situ ethanol removal with continuous recycle of the product stream and microorganisms (Garhyan & Elnashaie, 2004a-c). It is clear from the literature that the continuous in-situ removal of ethanol stabilises the oscillations and increases the sugar conversion due to alleviation of product inhibition. Experiments were carried out to show that a change in bifurcation parameter (dilution rate, D hr⁻¹) results in sustained oscillations. Moreover, when the dilution rate is above the HB value, the oscillations disappear to give a steady-state value. It has been clearly established that periodic and chaotic attractors can give higher average ethanol yield and productivity than the corresponding steady state. Some earlier work in chemical synthesis report the conversion and yield improvements by operating the chemical reactor under unstable oscillating conditions (Douglas & Rippin, 1966; Douglas, 1972).

BIFURCATION AND CHAOTIC BEHAVIOUR OF ACETYLCHOLINESTERASE AND CHOLINE ACETYLTRANSFERASE ENZYMES SYSTEMS: MODELING THE CHEMICAL SYNAPSE TOWARDS AN UNDERSTANDING OF ALZHEIMER AND PARKINSON DISEASES

Although the causes of Alzheimer and Parkinson Diseases are still unknown, extensive multidisciplinary research is still being carried out in order to uncover the causes. Chemical reaction engineering tools can be used to simulate the chemical synapse as an enzymatic diffusion-reaction system. This approach may be useful in obtaining some insight into the dynamic behaviour of neural transmission and contribute to the efforts in treating these diseases.

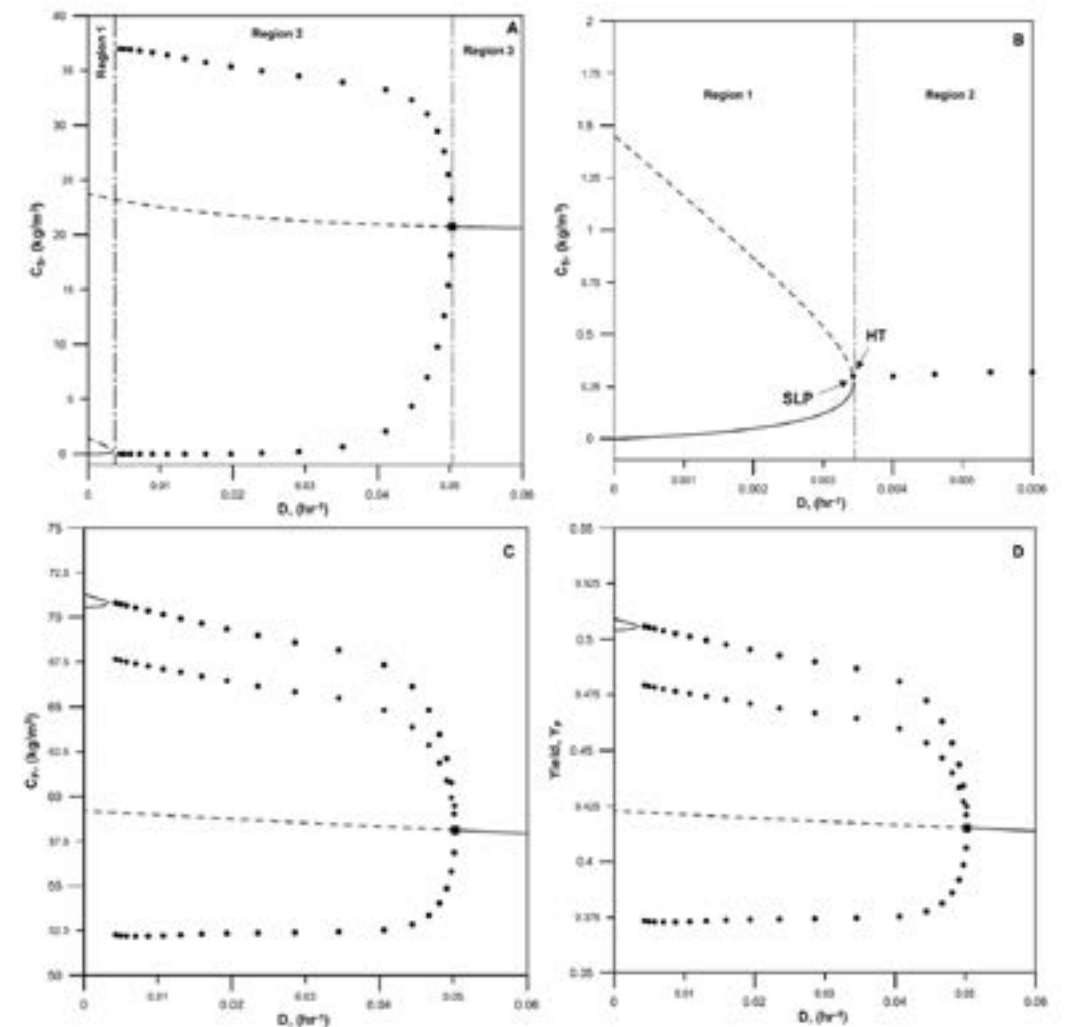


Fig.4: Bifurcation diagrams at $C_{S0} = 140$ kg/m³ with D as bifurcation parameter. Steady state branch (____ stable, ---- unstable), Periodic branch (•••• stable, ♦♦♦♦ unstable, average of oscillations)

Alzheimer Disease (AD)

AD is a degenerative disease of nerve cells on the cerebral cortex that progressively deteriorates memory and ability to learn, reason, communicate and perform daily activities and, at some point, results in failure to recognise loved ones. The accumulation of protein clusters in the brain is associated with AD, but their role is still unclear. The clumps of protein are composed of beta-amyloid proteins and form what are called neuritic plaques and neurofibrillary tangles, taking place outside and inside neurons respectively. AD is also associated with the poor performance of the neurotransmitter acetylcholine (Braunwald *et al.*, 2001; Alzheimer's Association, 2006; Alzheimer's disease Education and Referral Center, 2006).

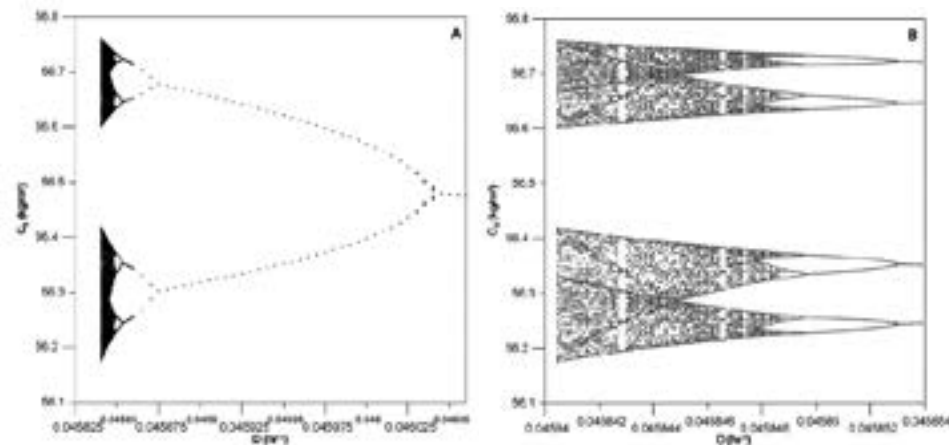


Fig.5: Dynamic characteristics at $C_{SO} = 200 \text{ kg/m}^3$ and $D = 0.04584 \text{ hr}^{-1}$, A) One dimensional Poincare bifurcation diagram, B) Enlargement of (A)

Parkinson Disease (PD)

PD is a neurodegenerative disorder of the central nervous system. It causes a progressive loss of nerve cell function in the part of the brain that controls muscle movement. As a part of the brain called the substantia nigra becomes impaired, tremors, rigidity, slow movement, stiffness in arms and legs and balance problems, and difficulty walking are seen to manifest; these characteristics are the common symptoms of this disease. PD is also associated with the poor performance of the neurotransmitter dopamine and an imbalance between dopaminergic and cholinergic systems (National Parkinson Foundation, 2006; Parkinson's Information, 2006).

The Chemical Synapse

The chemical synapse is a highly specialised structure that evolved for exquisitely controlled voltage-dependent secretion. Different chemical messengers, stored in vesicles, are released from the presynaptic cell following the arrival of an action potential that triggers the vesicular release into the presynaptic terminal (Llinas, 1999). Once released from the vesicles the transmitter diffuses across a narrow synaptic cleft (Paez & Fayad, 1999) and binds to specific receptors in the postsynaptic cell and initiates an action potential event in the nerve-muscle cell membrane triggering muscle contractions (Llinas, 1999). Acetylcholine plays a recognised role in nerve excitation (Guyton & Hall, 2000). It is found in cholinergic synapses that provide a stimulatory transmission in the nervous system. Its complete neurocycle implies a coupled two-enzyme/two-compartment model with two strongly coupled events as follows:

The activation event. Acetylcholine (S) is synthesised from Choline and Acetyl Coenzyme A (Acetyl-CoA) by the enzyme Choline Acetyl-transferase (ChAT) (Barman, 1969; Tucek, 1978) and is immediately stored in small vesicular compartments closely attached to the cytoplasmic side of the presynaptic membranes.

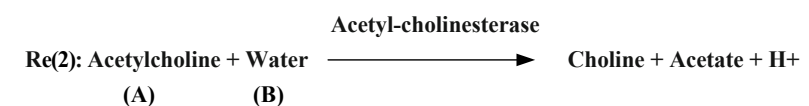
The degradation event. Once Acetylcholine has completed its activation duty, the synaptic cleft degradation begins removing the remaining Acetylcholine (Soreq & Xakut, 1993). This occurs through the destruction (hydrolysis) of Acetylcholine by the Acetylcholinesterase enzyme (AChE) to form Choline and acetic acid (Barman, 1969). Diseases such as Alzheimer (Alzheimer, 1906) and Parkinson (Parkinson, 1817) are the result of an imbalance of the cholinergic system considered above, with devastating consequences on human health. The above simplified sequence of events suggests that one can obtain some insight into such a cycle using a simple diffusion-reaction model (Naka *et al.*, 1997; Naka & Sakamoto, 2001) simulating the non-linear interaction between these events. Other modeling details can be found elsewhere (Mahecha-Botero *et al.*, 2004, 2005).

SIMPLIFIED DIFFUSION-REACTION MODELING FOR THE ACETYLCHOLINE NEUROCYCLE

The complete neurocycle of the Acetylcholine as a neurotransmitter may be simulated as a simplified two-enzyme/two-compartment system. Each compartment may be described as a constant flow, constant volume, isothermal, continuous stirred tank reactor (CSTR). The presynaptic and postsynaptic cells are represented by these two compartments separated by a permeable membrane as shown in Fig.6. Assuming that all the events are homogeneous in all the vesicles, and using the proper dimensionless state variables and parameters, the behaviour is considered for a single synaptic vesicle as described by this simple two-compartment system. Using dynamic mole balances for the chemical species involved in the enzymatic neurocycle of the neurotransmitter obtained is represented by a set of differential equations describing the system. Nonlinear analysis of this set of highly non-linear balance equations gives preliminary insight into the dynamic/static, bifurcation and chaotic behaviour of this complex biological system. From an enzyme kinetics point of view, the most general case is usually considered, where both enzymes have non-monotonic dependence upon substrate and hydrogen ions concentrations. It is usually assumed that Acetylcholine is synthesised in the presynaptic cell by the enzyme Choline Acetyl-transferase due to an activation reaction (where the stimulatory neurotransmitter Acetylcholine is synthesised) as follows:



Acetylcholine is destroyed (hydrolysed) in the postsynaptic cell by the enzyme Acetylcholinesterase through a degradation reaction (where the stimulatory neurotransmitter Acetylcholine is degraded) as follows:



Using the approach described above, static and dynamic simulations are usually carried out for different parameter values, obtaining many static and dynamic characteristics of the system. Some of results are shown in Figs 7-9. Figure 7 shows static bifurcation behaviour with the Acetyl-cholinesterase enzyme activity as the bifurcation parameter. S is the dimensionless concentration of the substrate Acetylcholine and SB_1 and SB_2 are the two static bifurcation points. It is clear that the behaviour is strongly dominated by hysteresis and multiplicity phenomena. This means that if for any reason (any external disturbance as an inhibitor, denaturalisation of the enzyme or a cholinergic disease) the Acetyl-cholinesterase enzyme activity is affected, then the 'normal' concentrations of all components could change dramatically. For example, if we observe the transmitted Acetylcholine at the postsynaptic cell and assume that the Acetyl-cholinesterase enzyme activity increases, the neurotransmitter should show a change in its concentration from 2.4×10^{-7} (kmol/m³) to 1.2×10^{-5} (kmol/m³). This means that its concentration increases by a factor bigger than 50. It is possible that some phenomena like the one described here could be the cause of Alzheimer Disease.

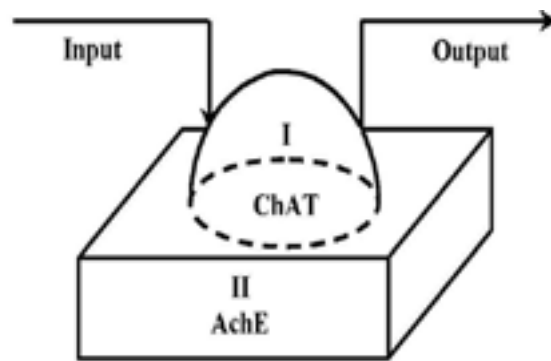


Fig.6: Two enzyme/two-compartment model

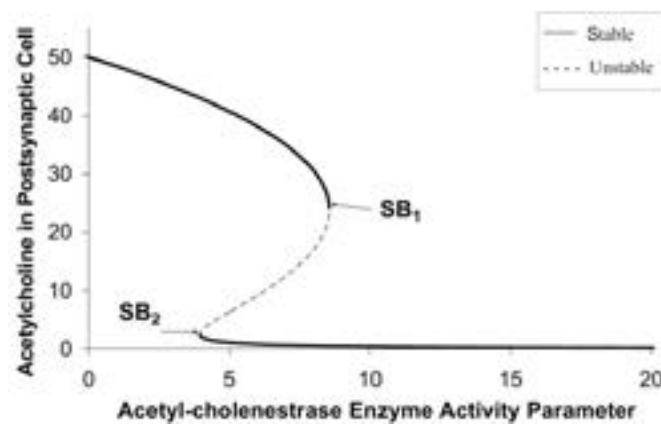


Fig.7: Bifurcation diagram as the Acetyl-cholinesterase enzyme activity is varied. Effect on the neurotransmitter in the postsynaptic cell. Steady state branches. SB: Static Bifurcation.

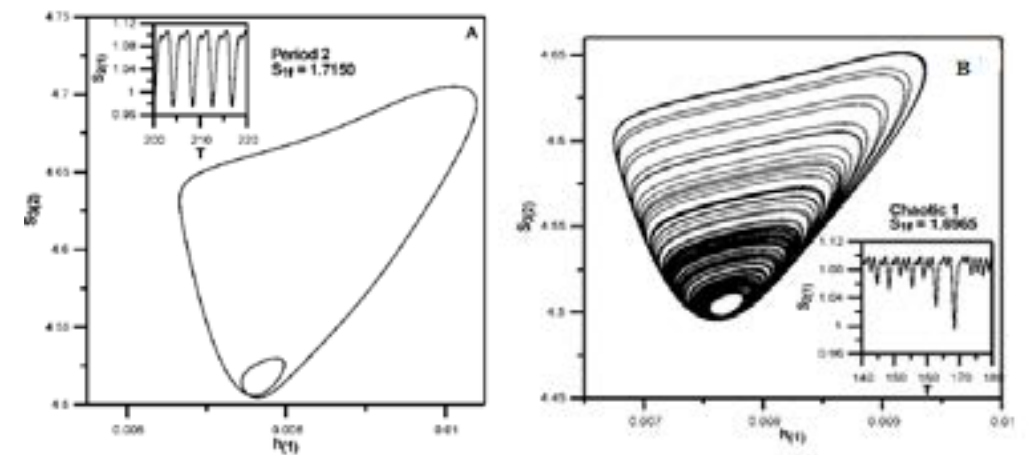


Fig.8. Dynamic simulations show region of periodic/chaotic behaviour. (A) Periodic, and (B) Chaotic

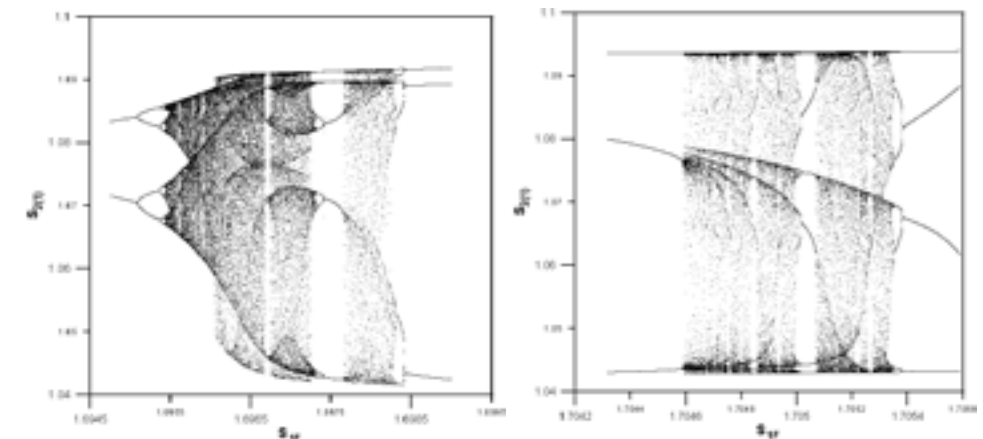


Fig.9: Poincaré maps show period doubling to chaos and enlargement of region of chaotic behaviour.

Fig.8 shows the strong sensitivity of the behaviour to a very small change in S_{1f} (dimensionless acetylcholine concentration in the feed), changing the behaviour from periodic to chaotic. Simulation results of the concentrations of chemical species in both the presynaptic and postsynaptic cells show a period doubling mechanism to chaos (Fig.8, Fig.9); S_1 is dimensionless acetylcholine concentration; S_2 is dimensionless choline concentration and S_3 is dimensionless acetate concentration; h is the dimensionless hydrogen concentration. Between brackets 1 is compartment 1 and between brackets 2 is compartment 2. Subscript f is the feed. Oscillating values from periodic and chaotic attractors of chemical species concentrations fairly agree with measured data from rat and guinea pig data found in the literature. It is interesting to notice that some state variables correspond to the physiological expected values in some regions. This may open the door for future experimental research in order to use the model for simulating real physiological behaviour.

CONCLUSION: THE NEUROCYCLE

A review of the modeling of an acetylcholine neurocycle is presented. Bifurcation and chaotic dynamics dominate the behaviour of the system. Extensive multidisciplinary research in neurosciences is required to develop a deeper understanding of the human brain. Furthermore, chemical reaction engineering modeling techniques may be useful to unveil the behaviour of complex systems such as the chemical synapses. The type of work presented in this review leads towards a better understanding of the complex behaviour of the human brain. This will help to direct new research on neurodegenerative diseases such as Alzheimer and Parkinson.

NUMERICAL TECHNIQUES

Almost all bifurcation and chaos phenomena are associated with non-linear systems, two point boundary value differential equations and non-monotonic behaviour of the non-linear functions. Therefore, the investigation of these phenomena strongly depends upon the use of numerical techniques to solve these non-linear equations (Elnashaie & Elshishi, 1996; Elnashaie & Garhyan, 2003; Elnashaie & Uhlig, 2007). Because bifurcation and chaos do not only involve solving the non-linear equations but also present it in the form of bifurcation and chaos diagrams, special techniques are needed to do them (Elnashaie & Elshishini, 1996; Elnashaie & Uhlig, 2007). Such models describing realistic chemical engineering systems exhibit as explained above very complex bifurcation and chaos behaviour due to the strong coupling between the transport processes and the nonlinear dependence of the reaction rates on temperature and concentration. During the past 50 years, they have proved to be an inexhaustible source for the development and testing of various local bifurcation and chaos techniques. Chemical reacting systems are the richest among these systems, unlike the Navier-Stokes equations, which are partial differential equations in time and two/three spatial coordinates, models of chemical reactors and reacting flows vary from a pair of ordinary differential equations describing the behaviour of a continuous flow stirred tank reactor with a single exothermic reaction to several PDEs, which describe combustion problems in which the fluid flow is strongly coupled to heat and mass diffusion and complex chemistry. Another distinguishing feature of reactor models is that the number of dimensionless parameters that appear is usually large, typically four to 15 for a single reaction. Hence, a comprehensive numerical study of the behaviour of a given model is impractical without some theoretical guidance. [Balakotaiah](#) and [Khinast](#) (2000) present an excellent such guide of numerical techniques for bifurcation analysis. Other numerical techniques for bifurcation and chaos analysis are presented by excellent authors in books and papers (e.g. Wiley, 2000; Nikolay *et al.*, 2002; Eugene, 2003)

GENERAL CONCLUSIONS: BIFURCATION AND CHAOS IN CHEMICAL AND BIOLOGICAL SYSTEMS

Static/dynamic bifurcation and chaos are fundamentally very important phenomena that every chemical and biological engineering engineer should know about as an essential part of their training (Elnashaie & Garhyan, 2003). These phenomena are widespread in many chemical and biological engineering systems and have important practical implications on

the behaviour of those systems. Understanding and analysing these phenomena is essential for the rational design, optimisation, operation and control of these chemical and biological engineering processes. These phenomena can sometimes be dangerous and harmful; in such cases engineers and researchers should have the techniques to avoid them (e.g. the relatively modern field of Chaos Control), in some other cases they can be beneficial and it should be possible to exploit them (e.g. the fermentor presented in this review). In other cases they are neither harmful nor beneficial but they need to be analysed and utilised to understand certain complex behaviour especially in biological systems. The source of these phenomena is mainly non-linearity and synergetic non-linear coupling. However non-linearity is not sufficient; it seems that at least one of the processes dependent upon at least one of the state variable needs to be non-monotonic. Coupling between reaction and diffusion seems also to be a necessary condition for the occurrence of these phenomena. For example non-monotonic processes when taking place in homogeneous plug flow reactors do not show any of these phenomena; however, as soon as diffusion comes into the picture, through axial dispersion in a homogeneous system and/or solid-gas interaction in a heterogeneous system these phenomena start to become a part of the characteristics of the system. Another important point is what may be called feedback of information, like counter-current operation, recycle or continuous circulation (e.g. the novel CFBMSR review), this can also give rise to bifurcation and chaos. These simple intuitive arguments apply mainly to chemical and biological reaction engineering systems. For other systems like fluid flow systems the source of bifurcation and chaos can be quite different. It is well established now that the transition from laminar flow to turbulent flow is actually a transition from non-chaotic to chaotic behaviour. The synergetic interaction between hydrodynamically induced bifurcation and chaos and that resulting from chemical and biological reaction/diffusion is not well understood and calls for extensive multidisciplinary research efforts.

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