RESEARCH INTERESTS

Alexandra CHAVEZ-ROSS

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My main research interests lie in the mathematical models of different kinds of physiological systems and its possible applications. I am interested in developing and understanding nonlinear deterministic models, which reflect the basic features of a variety of physiological phenomena. The first motivations come from determining how these processes fail and lead to undesirable diseases.

Due to the growing complexity of physiological models, a thorough analysis of the behaviour and interaction of its basic components is crucial. Often, these models, albeit of many plausible simplifications, become too complex to be understood using basic mathematics. Therefore, applications of sophisticated mathematical tools and techniques is an invaluable asset for a thorough analysis. Working in an interdisciplinary environment has lead me into collaborations with biologists and mathematicians, bridging the gap between these two basic and important sciences.

As a complement to analytical techniques, I am also interested in a variety of numerical methods and its practical implementations. I have a broad numerical experience in solving systems of ordinary differential equations and the use of sophisticated software for the solutions of ordinary and partial differentials equations. I believe that the cross-fertilization between theoretical and numerical analysis converges in a fascinating tool for the understanding of complex biological models.

Here I include a brief description of the main projects I have lately been involved in.

Modelling the inflammatory response in Alzheimer's disease:

In the last few centuries human life expectancy has reached an age where degenerative diseases of the brain have become very common. Alzheimer's disease (AD) is one of the most devastating ones affecting a growing number of elderly people (around 70 years old). One of the symptoms of AD is formation of abnormal foci in the brain called "senile plaques", containing a substance called β-amyloid.

A complex biochemical feedback mechanism is thought to be involved resulting in aggregation of β-amyloid forming such plaques. In particular, chemotactic effects of β-amyloid protein on the migration and accumulation of "immune" brain cells (glia cells) are analysed. These characteristic brain cells in turn promote chemicals associated with inflammation, and also lead to further production of β-amyloid by stressed neurons. In order to understand how glia cells interact with such chemicals, L. Keshet, M. Luca, A. Spiros and myself are developing a mathematical model based on the Keller-Segel (K-S) one dimensional chemotaxis system. This model is cast in terms of two coupled partial differential equations with cross-diffusion terms. By means of a linear analysis, it is possible to predict when aggregates of cells and protein emerge for the K-S system. We are currently investigating the stability of such aggregates using adaptive mesh numerical techniques capable of accurately following sharp spike concentrations. In order to produce a more realistic model, we have incorporated cell proliferation and death to the K-S system. We are also considering to introduce two types of glia cells which are believed to be involved in the inflammation process. As an important validation of our models we are involved in extracting realistic values for the relevant parameters from data collected on different cells and chemicals in the human brain.

Control of Ovulation and Polycystic Ovary Syndrome:

The production of eggs is a remarkable wasteful process within the reproduction system in mammals. From millions of eggs produced by the fetal life of the mammal, only around 0.2% are released from the ovary for eventual fertilisation. During its life in the ovary, an egg is within a follicular unit which nourishes it and protects it. J. Stark and myself, in collaboration with biologists S. Franks, H.D. Mason and K. Hardy, have been interested in understanding the mechanisms that control the number of follicles ovulated each cycle. In humans, a failure of such control mechanisms can lead to Polycystic Ovary Syndrome (PCOS), which accounts for a substantial fraction of all cases of anovulatory infertility found in women of reproductive age. Although some treatment is currently available for women suffering from PCOS related infertility, the better understanding of the selection process in both normal and "abnormal" circumstances is crucial for future treatment improvement.

The primary mechanism controlling ovulation in mammals is believed to rely on a competitive process between a group of developing follicles during the terminal phase of the ovarian cycle. Such competition is mediated through a hormonal feedback loop involving the pituitary gland. Nonlinear mathematical models have been developed to analyse and simulate such a competitive feedback mechanism. The most simplified model able to simulate the feedback system and follicle growth is the one proposed by M. Lacker. From a series of assumptions he suggested a manageable system of ODEs that simulates the basic features of the first half of the menstrual cycle. We have therefore, generalised the model in various ways, which has lead us to more interesting and realistic dynamics. These generalisations have complicated the system, but just to an extent where a thorough theoretical and numerical analysis are still viable.

Disorders in auditory systems:

Within normal circumstances and in the absence of sound, the auditory neurons fire spontaneously and randomly. Under acoustic stimulation, the firing becomes temporally correlated. The mechanisms for which some hearing disorders (such as tinnitus, a perceived ringing or buzzing in the ear), resulting from spontaneous correlation without stimuli are still to be fully understood.

Together with R. Miura, I. Ran, D. Schwarz and E. Puil, we are developing a model of membrane electrical activity in auditory neurons. The model will identify mechanisms promoting correlated firing. Our findings are simultaneously validated by extensive laboratory experiments. With the current-clamp technique on gerbils thalamic tissue, we are currently measuring membrane electrical properties. We are also interested in identifying possible types of neurotransmitters thought to induce hyperexitablilty in these type of neurons. We believe, hyperexcitable thalamic neurons induce correlated firing. The ultimate goal is to design drugs for treating abnormal auditory conditions which in extreme features have lead to severe human depression cases.