Special Session 25: Dynamics in Complex Biological Systems

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Many biological systems such as neuronal systems, immune systems and gene regulatory systems have highly nonlinear elements and form complex networks that may feature nontrivial coupling(feedback) and architectures. Experimentally, they have been observed for generating complex spatio-temporal activity patterns. Understanding the mechanisms underlying such dynamic patterns, as well as their transient behavior that may emerge in these networks, represents a mathematical challenge of current interest. The aim of this special session is to survey some recent results in which dynamical systems theory or computational and statistical methods have been developed and applied to these dynamical patterns, examples of which include oscillation, bursting and other neuronal activities in complex neuron circuits, dynamical patterns in complex inflammatory systems that are related to wound healing, immune reactions, and cell differentiations in gene regulations. The common themes of these dynamics include many excitatory/inhibitory coupling or in general positive and negative feedbacks, and their effects on the overall dynamics; the influence of stochastic noise may be another significant contributor that are not only as act as perturbations to these dynamics patterns, but also give rise to new dynamics altogether.

This special session offers a forum for new viewpoints and results related to this rapidly developing field. The aim is to foster and encourage communication and interaction between researchers in these interesting directions. The topics include mathematical models and theoretical analysis, computational and statistical methods of dynamical systems and differential equations, as well as applications, in neurodynamics, biological circuitry, biophysics and biochemistry, in several scales.

The topics may include but not restrict to: 1. Neuronal dynamics: Mathematical modeling and dynamical analysis of biological neurons, synapses, neuronal networks and brain, especially with effects of time delay and noise; Nervous signal generation, encoding and transduction; Cognitive information processing, learning and memory functions in brain; Mathematical and computational analyses in artificial intelligence and other biological and medical applications; 2. Immune dynamics: Modeling biomedical processes including tumor growth, cardio-vascular disease, infection, and healing are mediated by immunologic mechanisms; Nonlinear differential equations arises in immunology and medical applications; Analysis of mathematical models for features of solutions such as instabilities, bifurcations, symmetries, and blow-up that provide insight into the nature of the underlying bio-physical mechanisms; 3.Systems Biology: Dynamical system models in Gene regulation, expression, identification and network; Computational evolutionary biology; Algorithms, models, software, and tools in Bioinformatics.

A mathematical model for the origin of left-handedness

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An overwhelming majority of humans are right-handed. Numerous explanations for individual handedness have been proposed, but this population-level handedness remains puzzling. I will present a novel mathematical model and use it to test the idea that population-level hand preference represents a balance between selective costs and benefits arising from cooperation and competition in human evolutionary history. I will also present evidence of atypical handedness distributions among elite athletes, and show how our model can quantitatively account for these distributions within and across many professional sports. The model predicts strong lateralization for social species with limited combative interaction, and elucidates the absence of consistent population-level "pawedness" in many animal species.

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Investigating bacteria-immune dynamics in premature infants

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Necrotizing enterocolitis (NEC) is a severe disease of the gastrointestinal tract in premature infants characterized by an impaired epithelium and exaggerated inflammatory response. Toll-like receptors-4 (TLR4) are located on epithelial cells and function in sensing bacteria and protecting against bacterial translocation. However, TLR4 activation can also lead to an uncontrolled inflammatory response and has been identified as a key contributor to the development of NEC. Toll-like receptors-9 (TLR9) can suppress TLR4 activation and potentially reduce inflammation, but they may also compromise the beneficial antibacterial effects of TLR4. A mathematical model of bacteria-immune interactions within the intestine is developed here to analyze conditions in which inhibiting TLR4 activation may regulate inflammation and prevent tissue invasion by bacteria. The model offers a means for exploring the competing effects of TLR4 and TLR9 and the influence of therapeutic intervention on system dynamics. In particular, model predictions are used to suggest three interventions for NEC: reducing bacteria in the mucus layer, administering probiotic treatment, and blocking TLR4 activation. Situations in which the proposed treatments would be most helpful or potentially harmful are identified using the model.

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Determining the conductance for a neuronal cable model defined on a tree graph via a boundary control method

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Dendrites of nerve cells can be expected to have non-uniform conductances that one would like to determine. Can this be done by boundary measurements? Motivated by this question, we solve the inverse problem of recovering a single spatially distributed conductance parameter in a cable equation model defined on a finite tree graph that represents a dendritic tree of a neuron. We employ a boundary control method that gives a unique reconstruction and an algorithmic approach.

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Dynamics of sleep-wake states: a stochastic process, random graph model

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We pass our lives alternating behavioral states of sleep and wakefulness. Underlying this alternation are two interacting neuronal networks: wake-active cells and sleep active cells. Moreover, for many mammals the dynamics of the state oscillation are those of a renewal process such that the distribution of wake episodes is power-law distributed while the distribution of durations of sleep episodes is exponentially distributed. In order to study how these dynamics may arise from interacting networks, we consider a directed random graph model consisting of excitatory wake- and sleep-active clusters that compete via inhibitory inter-cluster connections. Each node (neuron) can be in any of three states: basal, excited or inhibited. Activity spreads as a stochastic process on the full network, and the clusters alternate periods of high activity. We apply both standard and novel probabilistic approximations to analyze the resulting dynamics.

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Complex immune responses: modeling & control

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Host-pathogen interactions consist of a complex cascade of events involving a multitude of immune cells and molecules concentrated on the goal of eliminating the offending agent and restoring equilibrium. The immune response cannot always restore homeostasis on its own, and appropriate interventions are needed. However, the administration of therapeutics helping to guide desirable outcomes is not as precise as one might think. Tools such as Model Predictive Control (MPC) have been suggested as a way to systematically determine the correct timing and amount of therapies to achieve a specified health goal. In this talk I will give an overview of modeling immune event cascades to various pathogens and introduce the MPC methodology applied to a four dimensional ordinary differential equations model of systemic inflammation.

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Bursting oscillation in the pre-BÖtzinger complex

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In this talk, we study and classify the bursting in a two-cell network of excitatory neuron within thepre-Bötzinger complex of the mammalian brain stem. We investigated the effects of different parameters on the bursting generation and pattern transitions in the two-cell model network with synaptic coupling by the fast-slow decomposition and bifurcation analysis approach. Comparing the firing patterns of the uncoupled and coupled cells, we found that the bursting patterns are the same both for a single and two-cell model network with the parameter g_{Na} changed, while they are different with the parameter g_K changed. Our results show the ions Na^+ and K^+ have different effects on the complex firing activities in the network when the single cells coupled by excitatory synapse.

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Bifurcations and chaos in a three dimensional discrete time Lotka-Volterra model

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Three dimensional discrete time competitive Lotka-Volterra map was studied by Gardini et al.. Bischi et al. extended their results to discrete time prey predator model. Bischi et al. investigated some local and global behaviors of this three dimensional map by numerical explorations. In this paper, this three dimensional map will be further studied from another point of view. Specifically speaking, the conditions of existence for flip bifurcation and Neimark-Sacker bifurcation are derived using the center manifold theorem and the bifurcation theory. In addition, we prove that there exists chaotic behavior in the sense of Marotto's definition of chaos. And numerical simulations show the consistence with the theoretical analysis.

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Standing and travelling patterns in a neural field model

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We study both standing and traveling patterns in a firing rate model with 'Mexican hat' type of synaptic couplings and non-saturated firing rate functions. We present an intrinsic relationship between the underlying integral equation and a system of ODEs. Then we establish the existence of standing and travelling solutions through the system of ODEs. We further analyze the linear stability of the traveling patterns. We also analyze the coexistence and bifurcations of thestanding and traveling solutions.

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Equilbria and linearization of the one-dimensional Forchheimer equation for incompressible two-phase flows

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We derive the 1-D Forchheimer equation for incompressible two-phase fluid flows in porous media in the presence of capillary forces. This type of equation is used to model dynamics of different biological system. The original problem is reduced to an initial value problem for a non-linear system of parabolic equations. We find six classes of equilibria and present their qualitative analyses. We show that for appropriate capillary forces and relative permeability these equilibrium states are linearly stable.

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Neutrophil dynamics in response to chemotherapy and G-CSF

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We have used a mathematical model of the combined dynamics of the hematopoietic stem cells and the differentiated neutrophil progeny to examine the effects of periodic chemotherapy in generating neutropenia, and the corresponding response of this system to granulocyte colony stimulating factor given to counteract the neutropenia. We find that there is a significant period of chemotherapy delivery that induces resonance in the system (at a period twice the average neutrophil lifespan from commitment to death) and a corresponding neutropenia suggesting that myelosuppressive protocols should avoid this period to minimize hematopoietic damage. The response to G-CSF is highly variable.

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Bursting dynamics of pancreatic beta-cells with electrical and chemical couplings

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Pancreatic beta-cells located in islets of Langerhans in the pancreas are responsible for the synthesis and secretion of insulin in response to a glucose challenge. Bursting electrical activity is also important for pancreatic beta-cells as it leads to oscillations in the intracellular free calcium concentration, which in turn leads to oscillations in insulin secretion. The minimal model for a single pancreatic beta-cell was extended by introducing one additional ionic current was considered. The synchronization behaviors of two identical pancreatic beta-cells connected by electrical (gap-junction) and chemical (synaptic) couplings, respectively, are investigated based on bifurcation analysis by extending the fast-slow dynamics from single cell to coupled cells. Various firing patterns are produced in coupled cells under proper coupling strength when a single cell exhibits tonic spiking or square-wave bursting individually, no matter the cells are connected by electrical or chemical coupling. The above analysis of bursting types and the transition may provide us with better insight into understanding the role of coupling in the dynamic behaviors of pancreatic beta-cells.

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Foam cell formation in atherogenesis

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The onset of atherosclerosis is characterized by the uptake of lipids by immune cells within the arterial wall. Once lipid laden, these immune cells are dysfunctional and runaway inflammation may occur. We consider a model of the formation of foam cells(lipid laden macrophages) with the view that aggregation corresponds to a mathematical instability. The disease mitigating effects of anti-oxidant and high density lipoproteins are investigated.

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Using a mathematical model to analyze the treatment of a wound infection with oxygen therapy

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A mathematical model was developed to treat a wound with a bacterial infection using oxygen therapy. The model describes the relationship among neutrophils, bacteria, oxygen, cytokines, and reactive oxygen species. A quasi-steady-state assumption was introduced to reduce the model down systems of two and three equations. A mathematical analysis on the reduced model and simulation results will be presented in this talk.

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1. Control of attractors in nonlinear dynamical systems using external noise/ 2. Effects of noise on synchronization phenomena

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Synchronization phenomena as a result of the occurrence of cooperative ones are ubiquitous in nonequilibrium physical and biological systems and are of vital importance in information processing in the brain. Those systems are , in general, subjected to various kinds of noise. While in equilibrium thermodynamic systems external Langevin noise is considered to play the role of heat bath in terms of temperature, few systematic study has been conducted to explore effects of noise on large degrees of nonlinear dynamical systems exhibiting limit cycle oscillations and chaotic motions, due to their complexity. Considering nonlinear models as simple as possible that allow rigorous analyses based on use of nonlinear -Fokker-Planck equations, we have conducted systematic studies to observe effects of noise and changes in types of attractors with changes in several kinds of parameters characterising mean-field coupled oscillator and (or) excitable element ensembles. The first title deals with general aspects shown by our models and the second one specialises understanding of results of noise effects in terms of phase diagrams to show the appearance and disappearance of synchonization of limit cycle oscillations.

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Complexity in a Leslie-Gower delayed prey-predator model

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The complex dynamics is explored in a prey predator system with multiple delays. The predator dynamics is governed by Leslie-Gower scheme. The existence of periodic solutions via Hopf-bifurcation with respect to delay parameters are established. To substantiate analytical findings, numerical simulations are performed. The system shows rich dynamic behavior including chaos and limit cycles.

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A model for foreign body and its stability analysis

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Implanted medical devices often trigger immunological and inflammatory reactions from surrounding tissues. The foreign body-mediated tissue responses may result in varying degrees of fibrotic tissue formation. There is an intensive research interest in the area of wound healing modeling, and quantitative methods are proposed to systematically study the behavior of this complex system of multiple cells, proteins and enzymes. This paper introduces a kinetics-based model for analyzing reactions of various cells/proteins and biochemical processes as well as their transient behavior during the implant healing in 2 dimensional space. In particular, we provide a detailed modeling study of different roles of Macrophages (MΦ) and their effects on fibrotic reactions. The main mathematical result indicates that the stability of the chronically inflamed state depends primarily on the reaction dynamics of the system, spatial diffusion and chemotaxis can not de-stabilize an equilibrium which is stable in the reaction-only system. However if the equilibrium is unstable by its reaction-only system, the spatial diffusion and chemotactic effects can help to stabilize when the model is dominated by classical and regulatory macrophages over the inflammatory macrophages. The mathematical proof and counter examples are given for these conclusions.

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Mathematical modeling of immune response to influenza infection

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Influenza is a contagious acute respiratory disease caused by a highly cytopathic virus attacking the epithelium cells of the respiratory tract. Human body responds to the infection by initiating a spectrum of immune responses, ranging from innate to adaptive cellular and antibody, which are regulated by an intricate network of signaling interactions that have not yet been completely characterized. Although in most cases the disease is mild and results in a full recovery, in some cases complications may lead to severe trauma or death. In the talk I will outline a series of simplified models that provide qualitative and quantitative prediction of the time course of the disease, aid in understanding of the mechanisms of the immune response, and have been utilized in the study the effects of an antiviral drug treatment. Our latest effort has been focused on ensemble models that reflects the uncertainty about parameter values, data sparseness, and the likely variation of the disease outcome across a population exposed to IAV. The technique is useful when the model contains many unknown parameters, such as reaction rate constants of biochemical processes, which are poorly constrained and their direct measurement in vivo is not feasible.

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Eye/head movement dynamics satisfying the Donders' law

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The problem of head movement has been studied in conjunction with the eye movement problem for well over hundred years and the names of Helmholtz, Donders and Listing are associated with it. The basic problem is that the eye and the head movement can be looked at as a rotational dynamics on the space SO(3) with constraints that has to do with the axis of rotation. In general, Donders' Law specifies that the axis of rotation has a small torsional component that can be expressed as a function of the horizontal and vertical components. In this research, head movement dynamics is constructed by writing down a suitable Riemannian Metric on the constrained space of rotation matrices, together with a suitable form of "coordinate free" potential energy and a damping term.

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Effect of the channel block on the spatiotemporal dynamics in stochastic Hodgkin-Huxley neuronal networks

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The influence of sodium and/or potassium ion channel blocking on the evolution of spiral wave is investigated in a stochastic two-dimensional network of Hodgkin-Huxley neurons. Some interesting results are approached. (1) With the decreasing of factor for sodium ion channel block, the mean interspike interval of action potential and the wave length increase, and the conductive velocity keeps stable for a lager membrane patch size, however, the evolution trends of spiral wave are almost unchanged, for a smaller membrane patch size. The result confirms that the evolution of the spiral waves is dependent on the sodium ion channel block in the neural network with weak strength noise being considered. As a result, the noise weakens the influence of the sodium ion channel poisoning on the evolution of spatiotemporal pattern in neural network. (2) In the case of potassium ion channel is blocked, no matter how large the patch sizes are, the spiral waves become denser and denser with the factor of poisoning decreasing, and mean interspike interval of action potential of a single neuron decrease. As the factor of poisoning decreases, the trends of the mean interspike interval of action potential, the wave length and the conductive velocity in neural network with a lager membrane patch size are similar with the trends in the system with a smaller membrane patch size. In other words, the influence of potassium ion poisoning on the evolution of spatiotemporal pattern is independent of the strength of noise. Furthermore, the effect of noise on the evolution of spatiotemporal patterns in the neural network is analyzed by calculating the firing possibility and the factor of synchronization.

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Oscillatory dynamics induced by time delay in an internet congestion control model with a ring topology

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Internet is one of the most complex artificial systems and congestion control is among the major tasks of designing this system. In this paper, an n-dimensional congestion control model with ring topology is considered to study the oscillation induced by time delay via Hopf bifurcation. Firstly, time delay is difficult to design or estimate, therefore its influence is of major concern. Secondly, ring topology can be used to model the rapidly developing Ethernet ring as well as some local and campus area network systems, therefore it is worth attention. Then, given the assumption that the variance of hops of all the transmissions is zero, the expression of the possible critical delay for Hopf bifurcation is obtained by analyzing the linear part of the system around the equilibrium and verified by the numerical simulation. Based on that, the method of multiple scales is employed to obtain the quantitative relation between the delay and the oscillation induced by it. The analytical results agree well with those obtained by numerical method. Furthermore, the effects of other parameters are studied either. The discussions reveal that excessive hops may cause the oscillation and increasing the link capacity can control this unexpected dynamics.

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Multiscale analysis of bacterial chemotaxis

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Chemotaxis is the active movement of cells or organisms in response to external chemical signals. The chemotactic movement of bacteria such as E. coli has been described using both continuum models and cell-based models. In continuum models, the evolution of cell density is described by partial differential equations (PDEs), such as the classical Patlak-Keller-Segel (PKS) chemotaxis equations. However, these models are phenomenological and their relation to mechanistic cellular processes such as signal transduction and movement is not well understood. In contrast, cell-based models can integrate great details of fundamental cellular mechanisms and address population behavior. However, for problems that involve large numbers of cells, they are computationally intensive and time-consuming. In this talk, I will elucidate the connections between continuum/phenomenological models and cell-based/mechanistic models of bacterial chemotaxis in shallow and steep signal gradient. The derived macroscopic PDEs show good agreement with the stochastic simulations of the cell-based models.

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Different bursting patterns in two-parameter bifurcation plane of fast subsystem

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Firing activities during insulin secretion in pancreatic islets are principally characterized by bursts of action potentials. In view of diversities of electrical bursting patterns in pancreatic β-cell, a simple but representative Vries-Sherman model with fast and slow time scales is considered to study different existing regions of different bursting patterns and transition mechanism between them by means of two-parameter bifurcation analysis of fast subsystem with respect to a kinetic parameter and a slow variable in a varying range of the slow variable. Since the number and types of bifurcation curves are different in different regions in two-parameter bifurcation plane, topological types and dynamic behaviors of different bursting patterns in the different regions are revealed by fast/slow analysis with respect to the slow variable. Summarily, codimension-1 and -2 bifurcation analysis is very important to explore dynamic behavior of different electrical bursting and transition mechanism between them, moreover, it can also provide a theoretical basis for physiological experiment design.

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Robustness of global dynamics for reversible Schnackenberg equations

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Schnackenberg equations originally introduced as a simplified model for some tri-molecular autocatalytic biochemical reactions, including pattern formations in embryogenesis. This talk will focus on the global dynamics of the reversible Schnackenberg equations on a bounded 3D domain. The robustness of the global attractors for the family of solution semiflows with respect to the reverse reaction rate as it converges to zero will be shown.

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