2nd BCAM Workshop on Nonlinear Dynamics in Biological Systems

Thursday 01 - Friday 02 September 2016
Basque Center for Applied Mathematics
Bilbao, Spain

Book of Abstracts

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Program

Thursday 01 September 2016

Registration - (09:00-09:50)

Welcome words - Seminar Room (09:50-10:00)

Cell Motility and Active Particles - Seminar Room (10:00-12:00)
Chair: Dr. Echebarria, Blas
10:00 Migratory behaviour of Physarum polycephalum microplasmodia
HAUSER, Marcus
10:30 Large-scales patterns of position-based interacting active particles: incidental leaders, nematic patterns, and aggregates
PERUANI, Fernando
11:00 Coffee Break
11:30 A Bacterial Swimmer with Two Alternating Speeds of Propagation. Motility in Open and Confined Geometries
BETA, Carsten

Complex Networks - Seminar Room (12:00-13:00)
Chair: Dr. Hauser, Marcus
12:00 Self-organizing cultured neural networks
SENDIÑA NADAL, Irene
12:30 Competition in evolutionary systems modeled as complex networks
AGUIRRE, Jacobo

Lunch - Pintxos at BCAM Hall (13:00-14:30)

Complex Chemical Systems - Seminar Room (14:30-15:30)
Chair: Dr. Hochberg, David
14:30 Conditions for spontaneous mirror symmetry breaking in cooperative polymerization of chiral species
STICH, Michael
15:00 Time scales in a coagulation-fragmentation model
YVINEC, Romain

Coffee Break - (15:30-16:00)

Complex Chemical Systems - Seminar Room (16:00-17:00)
Chair: Dr. Beta, Carsten
16:00 Fusion, fragmentation and spontaneous mirror symmetry breaking in nucleated enantioselective polymerization
HOCHBERG, David
16:30 Design of Dynamical Chemical Reaction Networks
PLASSON, Raphaël

Poster session (17:00-18:45)
Personalized Simulation of Cortical Spreading Depression
KROOS, Julia
Mathematical challenge: modelling human β-cell in both healthy and diabetic patients
MARINELLI, Isabella
Development of a computational model of calcium signaling in cardiac cells at the submicron scale
MARCHENA, Miquel
Survival curve analysis: beyond the Kaplan-Meier estimator
MULLA, Suhayl
Influence of gap junction dynamics on the stability of reentrant waves in cardiac tissue
HAWKS, Claudia
Effective cooperativity in Ryanodine Receptor clusters. Relevance for calcium alternans
SANCHIS, Guillem
Multiscale coupling of Electrophysiology and Metabolism in the Neuron-Astrocyte complex
CAPO RANGL, Gabriela
Genotypic shifts in microbial populations viewed as a competition in the genome network
YUBERO, Pablo
An hybrid automaton approach of a multi-scale hemoglobin production model
FORETS, Marcelo
Friday 2nd September 2016

Heart Dynamics - Seminar Room (09:30-11:00)
Chair: Dr. Alvarez, Enrique

09:30  Pro-arrhythmic effects of cardiac contraction  
       ECHEBARRIA, Blas
10:00  Comparison of defibrillation protocols through a simple cardiac  
       dynamic model  
       BRAGARD, Jean
10:30  Computational modeling for assessing the incidence of steam pops  
       and thrombus during radiofrequency cardiac catheter ablation  
       GONZÁLEZ SUÁREZ, Ana

Coffee Break - (11:00-11:30)

Heart Dynamics - Seminar Room (11:30-13:00)
Chair: Dr. Gerardo-Giorda, Luca

11:30  A Mechanism for QRS Amplitude Alternans in Electrocardiograms  
       and the Initiation of Spatiotemporal Chaos  
       FENTON, Flavio
12:00  Wave control by cooperative excitation of cardiac tissue and the  
       emergence of chimera states  
       NIEDERMAYER, Thomas
12:30  Modelling structural heterogeneity via space-fractional differential 
       equations  
       CUSIMANO, Nicole

Lunch at Larruzz restaurant - (13:00-15:00)

Cell Dynamics and Communication - Seminar Room (15:00-16:30)
Chair: Dr. Stich, Michael

15:00  Onset of mechanochemical pattern formation in simple models of  
       viscoelastic active cytoplasm  
       ALONSO, Sergio
15:30  Complexity in Electrophysiological Dynamics. Emergence and  
       measures of organization  
       PONT, Oriol
16:00  Turing patterns without diffusion: how immobile pigment cells can  
       color the skin of zebrafish  
       BULLARA, Domenico
Cell Motility and Active Particles

Migratory behaviour of Physarum polycephalum microplasmodia

Thursday, 1 September 2016 10:00 (0:30)

Dr. HAUSER, Marcus

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The motility of amoeboid cells of the plasmodial slime mould Physarum polycephalum was studied experimentally. Analysis of their trajectories and of their mean square displacements reveal two characteristic types of behaviour that depend on the time interval $\tau$ between any pair of points along the trajectory. Whereas free migration of cells is observed for time intervals $\tau > 300$ s, at short time intervals (of up to $\tau \approx 100$ s) the motility is due to changes in the cell shape induced by the peristaltic pumping of protoplasm through the cell. Freely migrating cells display persistent random motion with very long persistence times of up to $\approx 1.5$ h. Superdiffusive motion typically lasts for $\approx 5$ h, while at longer times the dynamics becomes diffusive. Whereas symmetric velocity distributions are found for short time intervals $\tau$, the typical velocity distributions from freely migrating cells show an asymmetric component, which reflects the long-lasting persistent motions. We observed that high propagation velocities are correlated with both, episodes of straight motion and an elongated cell shape. Furthermore, the patterns of cell thickness oscillations (that provide for the intracellular peristaltic pumping of protoplasm) also changed as a function of the propagation velocity of the cell.
Cell Motility and Active Particles

Large-scales patterns of position-based interacting active particles: incidental leaders, nematic patterns, and aggregates

Thursday, 1 September 2016 10:30 (0:30)

Dr. PERUANI, Fernando

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We study systems of active particles that interact by a short-ranged, position-based, attractive force that acts inside a vision cone (VC) and lack velocity-velocity alignment. We show that this active system can exhibit – due to the VC that breaks Newton’s third law – various complex, large-scale, self-organized patterns. Depending on parameter values, we observe the emergence of aggregates or milling-like patterns, the formation of moving (polar) files with particles at the front of these structures acting as effective leaders, and the self-organization of particles into macroscopic nematic structures leading to long-ranged nematic order. Combining simulations and non-linear field equations, we show that position-based active models represent a new class of active systems fundamentally different from other active systems, including velocity-alignment-based flocking systems. The reported results are of prime importance in the study, interpretation, and modeling of collective motion patterns in living and non-living active systems.
Cell Motility and Active Particles

A Bacterial Swimmer with Two Alternating Speeds of Propagation. Motility in Open and Confined Geometries

*Thursday, 1 September 2016 11:30 (0:30)*

Dr. BETA, Carsten¹

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Bacterial swimming is among the most prominent forms of motility in the living world. It typically follows a run-and-turn strategy, where episodes of persistent motion (runs) are interrupted by abrupt changes in the swimming direction (turns). Here, we report an in-depth analysis of swimming trajectories of the soil bacterium Pseudomonas putida. We observed that the majority of the turning events display a turning angle of 180° (reversals). To a lesser extent, also turning angles of 0° are found (pausing events). Remarkably, we observed that, upon a reversal, the swimming speed changes by a factor of two on average - a prominent feature of the motion pattern that, to our knowledge, has not been reported for any other bacterial swimmer before. In narrow microfluidic channels, P. putida displays more frequent reversals in swimming direction and swims faster but the qualitative features of the swimming pattern are preserved. Additionally, we observed that run segments are no longer straight and cells swim on circular trajectories, which can be attributed to a hydrodynamic wall effect. We also analysed the movement of P. putida in more complex micro-environments, dominated by cylindrical obstacles of different diameters and spacings. A theoretical model, based on the experimental values for the average run time and the rotational diffusion, recovers the mean-square displacement of P. putida if the two distinct swimming speeds are taken into account. Compared to a swimmer that moves with a constant intermediate speed, the mean-square displacement is strongly enhanced.
Complex Networks

Self-organizing cultured neural networks

Thursday, 1 September 2016 12:00 (0:30)

Dr. SENDIÑA NADAL, Irene

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We analysed the morphological evolution of assemblies of living neurons from locust ganglia, as they self-organize from collections of separated cells into elaborated, clustered, networks. In particular, we designed and implemented a graph-based unsupervised image segmentation algorithm with a very low computational cost. The processing automatically retrieves the whole network structure from large scale phase-contrast images taken at high resolution throughout the entire life of a cultured neuronal network. The network structure is represented by a mathematical object (the adjacency matrix) in which nodes are identified neurons or neurons’ clusters, and links are the reconstructed connections between them. The algorithm is also able to extract all other relevant morphological information characterizing neurons and neurites. More importantly and at variance with other segmentation methods that require fluorescence imaging from immunocytochemistry techniques, our measures are non invasive and entitled us to carry out a fully longitudinal analysis during the maturation of a single culture. In turn, a systematic statistical analysis of a group of topological observables grants us the possibility of quantifying and tracking the progression of the main networks characteristics during the self-organization process of the culture. Our results point to the existence of a particular state corresponding to a small-world network configuration, in which several relevant graphs’ micro- and meso-scale properties emerge. Finally, we identified the main physical processes taking place during the cultures morphological transformations, and embedded them into a simplified growth model that quantitatively reproduces the overall set of experimental observations.
Complex Networks

Competition in evolutionary systems modeled as complex networks

Thursday, 1 September 2016 12:30 (0:30)

Dr. AGUIRRE, Jacobo

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Competitive interactions represent one of the driving forces behind evolution and natural selection in biological, sociological and technological systems. For example, animals in an ecosystem may vie for food or mates; sensory stimuli may compete for limited neural resources in order to enter the focus of attention; web pages compete for absorbing the largest possible number of internauts...

In summary, many of the complex systems that evolve in nature are based on competing in environments for limited resources, and a wide variety of them are modelled as networks. In addition, the environments in which these competitions take place are not always static. The biosphere is changing and faces continuous and often severe challenges. These affect systems that evolve at all levels, from the world of genomes to whole cities. From this perspective, an open question of great interest is the understanding of the mechanisms and factors that induce competitors to succeed or fail in adapting to these time-depending conditions. In this talk, I will address: (i) The possibility of establishing a general framework for analysing processes in which different agents organized as networks compete for resources, either in constant or changing environments. (ii) The actual usefulness of this theory in biological problems of real interest for society.

Complex Chemical Systems

Conditions for spontaneous mirror symmetry breaking in cooperative polymerization of chiral species

Dr. STICH, Michael

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To explain the origin of biological homochirality is still a theoretical and experimental challenge, even after many decades of research. At the same time, supramolecular polymerization systems provide a rapidly growing field for testing ideas about how spontaneous symmetry breaking can arise. In this presentation, we investigate a simple model of cooperative polymerization (nucleation, elongation, dissociation and fragmentation) for two enantiomers, coupled through a racemization process, and try to find with analytical techniques under which circumstances symmetry breaking can be expected.
Complex Chemical Systems

Time scales in a coagulation-fragmentation model

Dr. YVINEC, Romain

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This work is motivated by protein aggregation phenomena in neurodegenerative diseases. A key observation of in-vitro polymerization experiments of prion protein is the large variability of the so-called 'nucleation time', which is experimentally defined as the lag time before the polymerization of proteins truly starts (typically several hours in a 10 hours experiment).

In this context, we study a stochastic version of a well-known nucleation model in physics, namely the Becker-Döring model. In this model, aggregates may increase or decrease their size one-by-one, by capturing or shedding a single particle. We will present numerical and analytical investigation of the nucleation time defined as a first passage time problem.[1,2]

Finally, we will present limit theorem techniques to study the link from the discrete size Becker-Döring model to a continuous size version (the Lifshitz-Slyozov model), which may be of importance to study large size aggregates formation. For general coefficients and initial data, we introduce a scaling parameter and show that the empirical measure associated to the Becker-Döring system converges in some sense to the Lifshitz-Slyozov equation when the scaling parameter goes to 0. [3] When the aggregation is favorable, we derive a mean-field transport PDE limit together with an entrant boundary condition, leading to an effective reduced dynamical model. When the aggregation is initially unfavorable, we shed light on metastable behavior and the phase transition phenomena can be appropriately described by large deviation techniques.

Complex Chemical Systems

Fusion, fragmentation and spontaneous mirror symmetry breaking in nucleated enantioselective polymerization

Thursday, 1 September 2016 16:00 (0:30)

Dr. HOCHBERG, David

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Understanding how biological homochirality may have emerged remains a challenge for origin of life research. In line with this goal, we introduce and solve numerically a kinetic rate equation model of nucleated enantioselective polymerization in closed mass systems. The microreversible scheme involves: (1) solution phase racemization of the monomer building blocks, (2) linear chain growth by stepwise monomer addition, (3) chain fusion or annealing. Mechanically induced breakage of the longer chains maintains the system out of equilibrium. Spontaneous mirror symmetry breaking can be achieved starting from small initial enantiomeric excesses due to the inherent statistical fluctuations about the racemic composition, confirming the model’s capacity for absolute asymmetric synthesis, and in the absence of chiral inhibition.
A striking singularity of biological systems is the strong dynamical organization of the chemical reactions network sustaining their activity. In order to maintain their metabolism from an energy source, living cells rely on chains of energy transfer involving functionally identified components and organizations. However, propagation of a sustained energy flux through a cascade of reaction cycles has only recently reproduced as a steady state in simple chemical systems. As observed in living cells, the spontaneous onset of energy-transfer chains notably drives local generation of singular dissipative chemical structures: continuous matter fluxes are dynamically maintained at boundaries between spatially and chemically segregated zones, but in absence of any membrane or predetermined material structure [1].

The first system is the design of an artificial photoactivated proton pump [2]. Inspired by photosynthesis, a mechanism in which light can locally set out-of-chemical equilibrium a reaction involving a “blind” reactant. A chain of energy transfer was setup relying on a photoacid transducer, for which light absorption leads to energy storage upon conversion to a state of higher free energy via exchange of protons as “hub” reactants. The stored chemical energy was further propagated to slow proton-exchanging components, resulting in the photogeneration of nontrivial proton concentration profiles, and sustained dynamic cycles of reaction diffusion of protons in solution.

The last system is the design of a temperature gradient-driven polymerization system [3]. The escalated polymerization of oligonucleotide could be generated by setting-up a chemical environment that would be typically observed in porous materials of hydrothermal vents. A water pore is open at the top and exposed to a solution of monomers engaged in reversible reaction of polymerization. A temperature gradient is applied to this system, leading to the establishment of thermal convection, combined to the thermophoresis of monomers. The combination of these effects leads to the accumulation of the monomers at the bottom of the pores, and their subsequent reversible polymerization. As a result, a temperature-gradient driven cycle of polymerization/depolymerization is obtained in a dynamical steady-state.

Heart Dynamics

Pro-arrhythmic effects of cardiac contraction

*Friday, 2 September 2016 09:30 (0:30)*

Dr. ECHEBARRIA, Blas

**Co-author(s):** RADSZUWEIT, M. ² ; ALVAREZ-LACALLE, E. ¹ ; BÄR, M. ³

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In this talk we present a simplified model of cardiac excitation-contraction coupling to study the effect of tissue deformation on the dynamics of alternans, i.e., alternations in the duration of the cardiac action potential, that occur at fast pacing rates and are known to be proarrhythmic. We show that small stretch-activated currents can produce large effects and cause a transition from in-phase to off-phase alternations (i.e., from concordant to discordant alternans) and to conduction blocks. We demonstrate numerically and analytically that this effect is the result of a generic change in the slope of the conduction velocity restitution curve due to electromechanical coupling. Thus, excitation-contraction coupling can potentially play a relevant role in the transition to reentry and fibrillation.
Heart Dynamics

Comparison of defibrillation protocols through a simple cardiac dynamic model

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Defibrillation is the standard clinical treatment used to terminate ventricular fibrillation. An electrical device delivers via a pair of electrodes a controlled amount of electrical energy in order to reestablish the normal heart rate. However, in order for the shock to be successful it is necessary to apply high energies, typically around 150 Joules for the transthoracic defibrillation. These high energy shocks have several side effects. There have been numerous attempts to reduce the defibrillation thresholds by, e.g., reversing the polarity of the shock during the defibrillation and optimizing the reversal time, waveform and duration of the shock. In this talk we propose to evaluate the efficiency of different standard and non-standard protocols for defibrillation. To do this, we have used a simple numerical model. The model consists of a one-dimensional ring of cardiac tissue. The electrical behavior of the cardiac tissue is modeled through the bidomain model and a modified Beeler-Reuter system of differential equations are used for modeling the active properties of the cell membrane. The mechanisms of successful defibrillation were also analyzed and they revealed that the biphasic shocks were more efficient than monophasic shocks due to the higher level of tissue activation at high energy level.

References:
J. Bragard et al., Chaos 23 (4), 043119, 2013.
J. Bragard et al., PRE 92 (6), 062919, 2015.
Heart Dynamics

Computational modeling for assessing the incidence of steam pops and thrombus during radiofrequency cardiac catheter ablation

Friday, 2 September 2016 10:30 (0:30)

Dr. GONZÁLEZ SUÁREZ, Ana

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Radiofrequency catheter ablation (RFCA) is a well-established minimally invasive medical procedure intended to destroy thermally cardiac tissue fragments causing arrhythmias. Although globally a pretty safe procedure, it may present some risk. Thrombus formation can occur during RFCA at the electrode-tissue interface when the temperature exceeds 80°C. Open-irrigated electrodes have been developed to reduce the risk of thrombus formation by cooling the electrode-tissue interface, allowing higher RF power delivery and the creation of larger lesions. On the other hand, higher RF power delivery increases the risk of steam pops occurrence, a rather serious complication. Steam pops are caused by tissue overheating above 89°C, and may cause explosive rupture of myocardium. If the steam pop occurs sufficiently deep in the tissue, or if the RFCA is performed on atria, whose walls are thinner that the ones of the ventricles, such explosive rupture may actually result in a perforation of the cardiac chamber wall, and in dramatic hemorrhagic events. To date, it is still very complicated to predict the occurrence and location of steam pops into the tissue during RFCA. A three-dimensional model for RFCA with open-irrigated electrode, validated against in vitro experiments, is here presented to show its potential for accurate spatio-temporal prediction of steam pop and thrombus formation.
Heart Dynamics

A Mechanism for QRS Amplitude Alternans in Electrocardiograms and the Initiation of Spatiotemporal Chaos

Friday, 2 September 2016 11:30 (0:30)

Dr. FENTON, Flavio¹

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It is widely believed that the life-threatening transition to chaotic fibrillation occurs via spiral-wave breakup that is preceded by spatiotemporal dispersion of refractoriness due to alternations in the duration of the cardiac action potential (AP). However, recent clinical and experimental evidence suggests that other characteristics of the AP may contribute to, and perhaps drive, this dangerous dynamical instability. To identify the relative roles of AP characteristics, we performed experiments in rabbit hearts under conditions to minimize AP duration dynamics which unmasked pronounced AP amplitude alternans just before the onset of fibrillation. We used a simplified ionic cell model to derive a return map and a stability condition that elucidates a novel underlying mechanism for AP alternans and spiral wave breakup. We found that inactivation of the sodium current is key to develop amplitude alternans and which is directly connected to conduction block and initiation of arrhythmias. Simulations in 2D in which AP amplitude (APA) alternation led to turbulence confirm our hypothesis. Our results suggest novel approaches for preventing the dangerous transition to fibrillation.
Heart Dynamics

Wave control by cooperative excitation of cardiac tissue and the emergence of chimera states

Friday, 2 September 2016 12:00 (0:30)

Dr. NIEDERMAYER, Thomas

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Rotating excitation waves and electrical turbulence in cardiac tissue have been associated with arrhythmias like the life-threatening ventricular fibrillation. The application of an electrical shock (defibrillation) is an effective therapy, as it globally excites the tissue resulting in termination of all excitation waves, but also causes severe side effects. Recent experimental studies have shown that a sequence of electrical pulses is able terminate fibrillation more gently than a single pulse. Only tissue at major conduction heterogeneities, such as large coronary arteries, may be activated by each of these very weak pulses. Therefore, global tissue activation and wave termination originates from few localized activation sites. In order to decipher the interplay of the individual pulses, we performed extensive simulations of cardiac tissue perforated by blood vessels. The pulses appear to be highly cooperative. The period between pulses turns out to be crucial for the defibrillation success, with the optimal period being similar to the dominant excitation period of the tissue. The characterization of electrical turbulence by a simple model allows us to elucidate these findings.

In the last part of the talk, the emergence of chimera states in a biological system is discussed. Such chimeras are intriguing dynamical states in networks of identical oscillators and are characterized by the coexistence of coherence and incoherence. It turns out that a simple, yet realistic, model for hydrodynamic interactions of flagella and cilia, thread-like projections of eukaryotic cells, comprises all necessary and sufficient conditions for chimera formation. The flexibility of cilia might function as a switch between coherent and incoherent dynamical states. We believe that chimeras have unknowingly been observed in experimental and computational studies of large cilia arrays.
Heart Dynamics

Modelling structural heterogeneity via space-fractional differential equations

Friday, 2 September 2016 12:30 (0:30)

Dr. CUSIMANO, Nicole

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Mathematical models of electrical propagation in excitable media are typically developed via the homogenisation principle, that is, under the assumption that microscopic inhomogeneities in the medium have a negligible effect on the transport phenomena observed at the macroscopic scale. For highly heterogeneous structures, such as cardiac or neural tissue, this hypothesis is questionable and alternative modeling strategies might provide better suited approaches in these settings. In this talk, I will discuss the use of non-local models in space and fractional order operators to characterise structural complexity and model electrical pulse propagation in heterogeneous biological tissue. I will provide some numerical results and focus on important aspects of both the modeling and the implementation of the considered mathematical problem.
Cell Dynamics and Communication

Onset of mechanochemical pattern formation in simple models of viscoelastic active cytoplasm

Friday, 2 September 2016 15:00 (0:30)

Dr. ALONSO, Sergio

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The interior of living cells is a blend of macromolecules, filaments of different sizes, and small molecules in solution with water. The whole mixture is alive and active, and produces active cytoplasmatic motion. The displacement of molecules from one side to the other of the cell is accompanied with a viscoelastic deformation of the cell. The viscoelasticity in the interior of the cell has been studied with simple linear viscoelastic models. There are different linear models of viscoelasticity and the choice of the viscoelastic model extremely depends on the particular study and on the type of cell.

First, we compare and characterize different types of linear viscoelastic models together with a simple active gel model for the actomyosin cytoskeleton. The type of instabilities obtained from the linear stability analysis of the resulting equations depends on the viscoelastic model employed. Next, we incorporate the active stress into a two-phase model of the cytoplasm which accounts for the spatiotemporal dynamics of the cytoskeleton and the cytosol. The cytoskeleton is described as a solid matrix that together with the cytosol as an interstitial fluid constitutes a poroelastic material.

Finally, we extend the active poroelastic model by the use of a qualitative chemical reaction-diffusion model that describes the regulation of the inhibitor by another biochemical species. The biochemical reaction enhances the formation of mechanochemical waves if the reaction rates and input concentrations are near or inside an oscillatory regime. The period of the waves is found to be controlled by the characteristic oscillation period of the chemical system, whereas their wavelength is set by mechanical parameters.
Cell Dynamics and Communication

Complexity in Electrophysiological Dynamics. Emergence and measures of organization.

Friday, 2 September 2016 15:30 (0:30)

Dr. PONT, Oriol\(^1\)

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Action potentials play an important role in the dynamics of cell-cell communication and they are thus of key relevance in neural tissues. They evidence the intrinsic dynamics of intracellular and membrane exchanges, and transmit nerve impulses both at gap junctions (through direct ionic exchange) and synapses (by initiating neurotransmission).

In practice, action potential impulse trains exhibit a complex dynamics. Each impulse is highly anharmonic, and the shapes and amplitudes of impulses evolve continuously with regulation-based modulation. Additionally, the signal is quasi-periodic, and period fluctuations are far from random: They are highly structured across scales and follow what appears as non-Markovian dynamics.

We propose to characterize anharmonicity in the signal as smooth perturbations of harmonicity, by introducing multiple symmetry breaks of variable strength at given phase axes. P. Hanusse has shown that the resulting framework is analytically treatable with a generalization of pseudo-trigonometric functions that include a shape factor as anharmonicity parameter \( r \). These generalizations are defined up to an order \( n \) of convolutions,

\[
pcos_n(x) = \sum_{k=0}^{n} k^{-n} r^{k-1} \cos(kx).
\]

Order 1 can be solved and it corresponds to a phase equation defined as a fraction of trigonometric polynomials.

We show that typical real-world electrophysiological signals, with smooth deviations from harmonicity, are typically well described with just the first few terms and result in a rather compact, sparse representation. In particular, we have done an analysis of FitzHugh-Nagumo impulse trains; we have found that 3 anharmonic terms reconstruct better than an equivalent 8-term Fourier representation, with less than half the PSNR and no artifacts from Gibbs phenomenon.

Reference:
P. Hanusse, Rencontres du Non-Linéaire (2010)
Cell Dynamics and Communication

Turing patterns without diffusion: how immobile pigment cells can color the skin of zebrafish

Friday, 2 September 2016 16:00 (0:30)

Dr. BULLARA, Domenico¹

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The core mechanism of pattern formation on zebrafish skin seems affected by an apparent intrinsic contradiction: the patterns behave like Turing patterns, but evidence shows the absence of cellular diffusion, which rules out the possibility of a reaction-diffusion mechanism. Here we show a minimal model based on the available experimental information, which is able to produce stationary patterns with intrinsic wavelength via a Turing instability, without diffusion or any other kind of cellular motion. This model unveils a completely new mechanism for the zebrafish pattern formation, which we name “differential growth”. Differential growth induces a nontrivial redistribution of cellular populations in space through birth and death processes fostered by opportune short-range and long-range biological interactions between the cells.
Poster session / 1

Personalized Simulation of Cortical Spreading Depression

KROOS, Julia

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Migraine is a prevailing disease in present day population. Cortical Spreading Depression (CSD) is a depolarisation wave that originates in the visual region and propagates across the cortex to the peripheral areas in about 20 minutes. CSD has been suggested, by several studies, as a correlate of visual aura, a neurological phenomenon preceding migraine and causing perceptual disturbance. As of today, little is known about the mechanisms that can trigger or stop such phenomenon and possible curative treatments. However, the complex and highly individual characteristics of the brain cortex suggest that the geometry might have a significant impact in supporting or contrasting the propagation of CSD. Accurate patient-specific computational models are thus fundamental to cope with the high variability in cortical geometries among individuals, but also with the conduction anisotropy induced in a given cortex by the complex neuronal organisation in the grey matter. In order to study the role the geometry has in shaping CSD, we introduce a mean field model for neural excitation, distributed over a personalized brain geometry obtained from MRI imaging. Patient-specific conductivity tensors are derived locally from Diffusion Tensor Imaging (DTI) data. Our computational results are two-fold: first, we found significant differences in the propagation traveling patterns of CSD, both intra and inter-hemispherically, revealing important asymmetries in the propagation profile. Second, we identify computable Quantities of Interest (QoIs) able to identify brain regions featuring a peculiar behavior during CSD propagation. Our study reveals dynamical aspects of CSD, which, if applied to subject-specific cortical geometry, might shed some light on how to differentiate between healthy subjects and those suffering migraine.

Poster session / 2

Estimation of age-specific rates of reactivation and immune boosting of the varicella zoster virus

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Studies into the impact of vaccination against the varicella zoster virus (VZV) have increasingly focused on herpes zoster (HZ), which is believed to be increasing in vaccinated populations with decreasing infection pressure. This idea can be traced back to Hope-Simpson’s hypothesis, in which a person’s immune status determines the likelihood that he/she will develop HZ. Immunity decreases over time, and can be boosted by contact with a person experiencing varicella (exogenous boosting) or by a reactivation attempt of the virus (endogenous boosting). Here we use transmission models to estimate age-specific rates of reactivation and immune boosting, exogenous as well as endogenous, using zoster incidence data from the Netherlands (2002-2011, \( n = 7,026 \)). The boosting and reactivation rates are estimated with splines, enabling these quantities to be optimally informed by the data. The analyses show that models with high levels of exogenous boosting and estimated or zero endogenous boosting, constant rate of loss of immunity, and reactivation rate increasing with age (to more than 5% per year in the elderly) give the best fit to the data. Estimates of the rates of immune boosting and reactivation are strongly correlated. This has important implications as these parameters determine the fraction of the population with waned immunity. We conclude that independent evidence on rates of immune boosting and reactivation in persons with waned immunity are needed to robustly predict the impact of varicella vaccination on the incidence of HZ.
Development of a computational model of calcium signaling in cardiac cells at the submicron scale

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Atrial fibrillation (AF) is the most common arrhythmia. It affects 1-2% of the general population, and increases gradually with age from 0.5% in people aged 50-59 to 9% in octogenarians. Clinically, AF duplicates the mortality rate and increases the risk of ictus 5-fold. In spite of this the treatment of AF remains deficient or inefficient, because of the incomplete knowledge of the complex pathophysiology of this disease. Often, this arrhythmia has been linked to a disregulation in the dynamics of intracellular calcium, the messenger that signals the contraction of cardiac cells. In the cell, calcium is mostly encountered within a bag, called the sarcoplasmic reticulum (SR), and is released to the intracellular medium through calcium sensitive channels (RyR) attached to the membrane of the SR. We have developed a model for the dynamics of intracellular calcium in auricular myocytes at the submicron scale, incorporating data from the size and geometry in the distribution of clusters of RyRs, and apply it to proarrhythmic situations, such as calcium waves or cardiac alternans.

Survival curve analysis: beyond the Kaplan-Meier estimator

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Purpose: Although the Kaplan-Meier estimator is a widely used statistic to assess survival probability, it is not designed to recognise how survival curves differ from one another. This project proposes a novel analysis through parametric fitting of survival data to a mathematical function.

Methods: Caenorhabditis elegans lifespan assays were conducted on wild-type (N2) and hif-1(ia4) mutants at 15°C and 20°C. We investigated numerous existing survival models which have previously been used to analyse survival curves and additionally developed a novel 5-parameter model to fit C. elegans survival data.

Results: Existing models were not sufficiently accurate in fitting our data series and did not account for the biphasic distribution of C. elegans survival. Our 5-parameter model fitted data more accurately and allowed us to model survival with biologically interpretable parameters, namely two time phases, two death rates and the weight between the two phases. Statistical analysis show that only 3 parameters vary significantly for the sampled data. Log-rank analysis shows that worms cultured at 15°C have a significantly extended lifespan to those at 20°C (p:<0.05). Additionally, our model shows that temperature significantly changes parameters, indicating an adaptation which prolongs 2nd phase mortality (t2) (p:<0.0001). hif-1(ia4) mutants show a significantly extended lifespan compared to N2 at 20°C due to changes in t2 (p:<0.05).

Conclusion: We have created and validated a model which can be used to fit survival data from C. elegans in different conditions (temperature and mutation). This now allows us to investigate how survival curves differ and quantitatively determine differences between curves.
**Influence of gap junction dynamics on the stability of reentrant waves in cardiac tissue**

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**Aims:** In the literature, simple models assuming constant conductivities often model the electrical connection between cardiac cells. However, experimental studies have shown that gap junctions (GJ) actually connect adjacent cardiac myocytes. These GJ are complex proteins of the connexin family (Cx40; Cx43; Cx45 being the most commonly found in human cardiac tissue). These GJ possess their own dynamics and this dynamics interacts with the propagating action potential (AP) by remodeling the conductivities of the cardiac tissue (in analogy to the plastic behavior of the brain cells). The aim of the present paper is to study the influence of the GJ dynamics on the stability of the AP.

**Methods:** The model that we have used is a one-dimensional ring of cardiac tissue of size L (size is varied between 6 to 10 cm) where the electrical activity is modeled by the bidomain formulation. In addition, the Beeler-Reuter model and the Peñaranda et al. model [1] for the active properties of the membrane have been used. The GJ dynamics is described following the works of Lin [2] and Desplantez [3]. The bidomain model has been reformulated in terms of the intra- and extra-cellular electrical potential in order to model more accurately the GJ dynamics.

**Conclusions:** The addition of the GJ dynamics in the model of cardiac propagation has modified the stability producing alternans dynamics rather than regular dynamics observed in the case of constant conductivity. We have also observed the appearance of conduction block when the AP was stable in the constant conductivity case.

**References:**


Multiscale coupling of Electrophysiology and Metabolism in the Neuron-Astrocyte complex

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Several mathematical models have been developed in the recent years to describe the brain activity. The latter is a complex interaction between several dynamics that coexist in a working brain. In particular, we highlight the electrophysiological activity of the neurons, the metabolic cycle of the neuron-astrocyte complex that provides the neurons with the energy needed to produce action potentials, the nutrient supply through the Brain Blood Barrier from the capillaries that irrigate the cerebral tissue, and the blood flow in the circulatory system. These dynamics have been individually the topic of a vast research activity in the last decades, and a large amount of literature is available. A common feature of these studies is a deep analysis on only one of the aforementioned cerebral activities, with only a marginal interest in the others, despite the strongly intertwined roles of these dynamics. We introduce here a lumped model that combines electrophysiology of a neuron-astrocyte complex, its energy metabolism, and the supply of nutrients and oxygen from capillaries. The link between the two models is the energy balance between ATP production by the metabolic network and the energy consumption by the pump action of the sodium-potassium ATPase. The main difficulty in coupling the two models resides in their dramatically different time scales (milliseconds for the electrophysiology and minutes for the metabolism). The electrophysiology acts as a fast time scale driver for the metabolism which represents a slow time scale feedback. We will present the mathematical and computational aspects of the model, and we will show the behaviour of the coupled model for different scenarios: a prolonged resting state, a sustained neuronal activity followed by a return to resting state, and an ischemic episode.

Effective cooperativity in Ryanodine Receptor clusters. Relevance for calcium alternans

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Cardiac alternans is an arrhythmia characterized by a beat-to-beat alternation in the strength of the heart contraction. At the moment, the mechanism through which alternans arises is not well understood. It is known to be associated by an alternation in the levels of intracellular calcium, although it has also found to be related to an instability in the electrical propagation through the tissue; In particular, the role of Ryanodine Receptors (RyR2) in alternans is a current topic of debate. In cardiac cells, the contraction is driven by the release of Ca\textsuperscript{2+} ions from the sarcoplasmic reticulum in thousands of RyR2 clusters that release calcium from the Sarcoplasmic Reticulum (SR) in response to a signal in the membrane in the form of an action potential. This action potential triggers the entrance of a small quantity of calcium through the membrane which binds to the RyR2 cooperatively. Upon binding, the receptors open and calcium stored in the SR is massively release. The objective of this work is to implement a stochastic model of the cluster to compute how the probability of a local calcium release to occur, in the form of a local spark, depends on a variety of biophysical parameters related with the dynamics of intracellular calcium and the stochastic configuration transitions of the protein channels. The resulting probability curves present an effective cooperative larger that the binding cooperativity of the receptor. The obtained probability functions are used in a simplified coupled return maps model of a cardiac cell to explore the cooperativity levels required to generate calcium alternans.
Genotypic shifts in microbial populations viewed as a competition in the genome network

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In the biosphere, species and populations are in constant adaptation to an ever changing environment. In the past decades different studies have reported that even with smooth variations, sudden changes of state occur[1-2]. This naturally raised concerns on the proximity of planetary tipping points that we might be reaching, with a resulting emphasis on the study of early warning signals.

In this context, sudden state changes were recently analyzed in the study of the genotype composition of populations of fast growing and mutation-prone species such as viruses and bacteria [3]. The study put forward that population shifts are a generic property of such systems in a time varying environment, provided there is some heterogeneity.

The present work seeks for a deeper theoretical explanation of these critical transitions. A complex network approach was used under the hypothesis that the drastic population shifts are related to the links between two interconnected sub-networks embedded in the space of genomes [4]. The Kauffman NK-model provided the mapping of two fitness landscapes to our set of genotypes. The smooth environment change was modeled with a linear transformation from the initial to the final landscape.

Our results reflect that it is indeed the way in which these two sub-networks are linked in the space of genomes that rules the abruptness of the transition. The sequences that act as connector nodes between both sub-networks become of much interest, leading to the study of a new set of early warning signals related to this novel approach that could be of experimental applicability.

References:

An hybrid automaton approach of a multi-scale hemoglobin production model

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We consider a multi-scale model of hemoglobin production. Representing the physical model as an hybrid automaton, we search for optimal parameter values with respect to experimental measures at different time-scales. Instead of a blind search, an optimal control approach is proposed, and the numerical solution is explored by applying state-of-the-art semi-definite programming relaxation methods.