### Interdisciplinary Complex Systems: Theoretical Physics Methods in Medicine.

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# **1** Topics

- Reaction-diffusion equations
- Turbulence in vortex dynamics
- Heat Transfer in excitable tissues
- Mechano-electric Feedback
- Computational Cardiology
- Mathematical Models of Tumor Growth

#### 1 Topics

# 2 Participants

#### 2.1 ICRANet participants

- Donato Bini (IAC, CNR, Rome, Italy)
- Christian Cherubini (University Campus Bio-Medico, Rome, Italy)
- Simonetta Filippi, project leader (University Campus Bio-Medico, Rome, Italy)

### 2.2 External Collaborations

- Valentin Krinsky(INLN,CNRS, Nice, France)
- Alain Pumir(INLN,CNRS, Nice, France)
- Luciano Teresi (University Roma 3, Rome, Italy)
- Paola Nardinocchi (University Roma 1, Rome, Italy)

### 2.3 Students

Alessio Gizzi (University Campus Bio-Medico, Rome, Italy)

#### 2 Participants

### **3** Brief description

This group has started recently the study of problems of nonlinear dynamics of complex systems focusing on biological problems using a theoretical physics approach. The term "biophysics" is today changing in its meaning and appears not to be sufficient to contain areas like "theoretical biology", "living matter physics" of "complex biological systems". On the other hand, the term "Theoretical Physics applied to biological systems" appears to be wide enough to describe very different areas. It is well established both numerically and experimentally that nonlinear systems involving diffusion, chemotaxis, and/or convection mechanisms can generate complicated timedependent patterns. Specific examples include the Belousov-Zhabotinskii reaction ,the oxidation of carbon monoxide on platinum surfaces, slime mold, the cardiac muscle, nerve fibres and more in general excitable media. Because this phenomenon is global in nature, obtaining a quantitative mathematical characterization that to some extent records or preserves the geometric structures of the complex patterns is difficult.

Following Landau's course in theoretical physics, we have worked in Theoretical Biophysics focusing our studies on pathological physiology of cardiac and neural tissues. Finite element simulations of electro-thermo-visco-elastic models describing heart and neural tissue dynamics in 1D and 2D have been performed ([1],[2]), finding a possible experimental way to evidence the topological defects which drive the spiral associated with typical arrythmias (Figure 1), typical of reaction diffusion equations, whose prototype, with two variables for the sake of simplicity, is shown below

$$V_t = D_1 \nabla^2 V + f(U, V) U_t = D_2 \nabla^2 U + g(U, V),$$
 (3.0.1)

where the V variable refers to an activator and the U variable to the inhibitor respectively. The f and g terms are typically highly nonlinear in U and V. We have analyzed [3] in particular the coupling of the reaction-diffusion equations governing the electric dynamics of the tissue with finite elasticity (see Figures 2, 3 and 4). The problem, due to the free boundary conditions, must be formulated in weak form (integral form) of deformable domains, and requires massive use of differential geometry and numerical techniques like finite elements methods. The experience obtained in this field will be adapted in future studies for problems of self-gravitating systems and cosmology. Moreover computational cardiology and neurology for cancer research in 3D



Figure 3.1: Spiral wave in the temperature domain at a given time.

using NMR imported real heart geometries have been studied ([4]-[6]) (Figures 5,6 and 7). More in detail the RMN import of a real brain geometry in Comsol Multiphysics (a powerful finite element PDEs solver) via an interpolating function has been performed. The physical property associated with the greyscale is the diffusivity tensor, assumed to be isotropic but inhomogeneous. Applications to antitumoral drug delivery and cancer growth processes have been presented.



Figure 3.2: 2D Evolution of a spiral wave in voltage domain coupled to finite elastic deformations at a given time.



Figure 3.3: 3D spiral wave coupled to strong mechanical deformations.



Figure 3.4: 3D spiral waves iso-voltage lines embedded in a mechanically deformed domain.



Figure 3.5: Voltage distribution at a given time on a real 3D NMR imported heart geometry.



Figure 3.6: 3D NMR imported brain geometry associated with a diffusion tensor.



Figure 3.7: Mathematical model of tumor growth on the reconstructed brain geometry.

## 4 Publications (2005-2008)

 Cherubini C., Filippi S., Nardinocchi P., Teresi L., "An electromechanical model of cardiac tissue: Constitutive issues and electrophysiological effects," Progress in Biophysics and Molecular Biology vol. 97, 562–573 (2008)

Abstract: We present an electromechanical model of myocardium tissue coupling a modified FitzHughNagumo type system, describing the electrical activity of the excitable media, with finite elasticity, endowed with the capability of describing muscle contractions. The high degree of deformability of the medium makes it mandatory to set the diffusion process in a moving domain, thereby producing a direct influence of the deformation on the electrical activity. Various mechanoelectric effects concerning the propagation of cylindrical waves, the rotating spiral waves, and the spiral breakups are discussed

2. Bini D., Cherubini C., Filippi S., "Heat Transfer in FitzHugh-Nagumo models," Physical Review E, Vol. 74 041905 (2006).

Abstract: An extended FitzHugh-Nagumo model coupled with dynamic al heat transfer in tissue, as described by a bioheat equation, is derived and confronted with experiments. The main outcome of this analysis is that traveling pulses and spiral waves of electric activity produce temperature variations on the order of tens of C. In particular, the model predicts that a spiral wave's tip, heating the surrounding medium as a consequence of the Joule effect, leads to characteristic hot spots. This process could possibly be used to have a direct visualization of the tip's position by using thermal detectors

3. Bini D., Cherubini C., Filippi S., "Viscoelastic FitzHugh-Nagumo models," Physical Review E, Vol. 72 041929 (2005).

Abstract: An extended Fitzhugh-Nagumo model including linear viscoelastici ty is derived in general and studied in detail in the one-dimensional case. The equations of the theory are numerically integrated in two situations: i) a free insulated fiber activated by an initial Gaussian distribution of action potential, and ii) a clamped fiber stimulated by two counter phased currents, located at both ends of the space domain. The former case accounts for a description of the physiological experiments on biological samples in which a fiber contracts because of the spread of action potential, and then relaxes. The latter case, instead, is introduced to extend recent models discussing a strongly electrically stimulated fiber so that nodal structures associated on quasistanding waves are produced. Results are qualitatively in agreement with physiological behavior of cardiac fibers. Modifications induced on the action potential of a standard Fitzhugh-Nagumo model appear to be very small even when strong external electric stimulations are activated. On the other hand, elastic backreaction is evident in the model

- 4. S.Filippi, C.Cherubini, Electrical Signals in a Heart, Comsol Multiphysics Model Library, Sept. p.106-116.(2005)
- 5. S.Filippi, C.Cherubini, Models of Biological System, Proceedings of COMSOL Conference, Milan (2006). Abstract: This article discusses the RMN import of a brain geometry in Comsol Multiphysics via an interpolating function. The physical property associated with the grayscale is the diffusivity tensor, assumed here to be isotropic but inhomogeneous. Applications to antitumoral drug delivery and cancer growth processes are discussed.
- 6. C.Cherubini, S.Filippi, A.Gizzi, Diffusion processes in Human Brain using Comsol Multiphysics, Proceedings of COMSOL Conference, Milan (2006).

Abstract: This article presents different applications of Comsol Multiphysics in the context of mathematical modeling of biological systems. Simulations of excitable media like cardiac and neural tissues are discussed.