

MASTER IN BIOPHYSICS



ALPHABETIC LIST OF MASTER PROFESSORS OFFERING TOPICS FOR FINAL PROJECTS

The student must contact the professor responsible of the project and obtain his/her approval.

Alternatively, the student can propose a different project supervised by a professor from an external research institution. The project must be approved by the Master coordination committee for its execution.

Prof. Jordi Alcaraz Casademunt (jalcaraz@ub.edu)
Unitat de Biofísica i Bioenginyeria. Universitat de Barcelona.

JA. Effects of abnormal tissue hardening in lung fibrosis studied with 3D cultures and nanotechnologies.

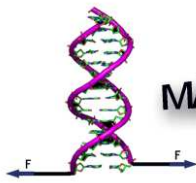
Prof. Raúl Benitez Iglesias (raul.benitez@upc.es)
Departament d'Enginyeria de Sistemes, Automàtica i Informàtica Industrial. UPC

RB1. Nonlinear time-series analysis of physiological systems.

Many of the basic properties of complex physiological systems can be studied with a dynamical systems approach. Indeed, their dynamics is often characterized by its non-linear behavior, the interplay of several biophysical mechanisms at different scales and the presence of noise. This approach combines methods from interdisciplinary fields such as artificial intelligence, statistical data processing, information theory or nonlinear time series analysis. The aim of this project is to use non-linear time series analysis in order to study the heart rate dynamics under different clinical and experimental conditions.

RB2. Probabilistic methods for the analysis and processing of physiological signals.

Biomedical and electrophysiological signals typically reflect the complex interplay between different underlying physiological systems.



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Within this framework, probabilistic methods are especially suitable for the analysis and processing of these signals since they provide a better characterization of the non-deterministic features of the data.

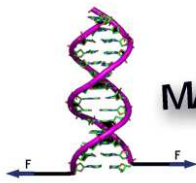
The aim of this project is to use statistical methods in order to analyze different biomedical signals and images. The resulting techniques should be useful for the automatic and semi-automatic diagnosis of clinical conditions.

Prof. Javier Buceta Fernández (javier.buceta@pcb.ub.es)
Parc Científic de Barcelona

JB1. Computational geometry applied to tissue or membrane dynamics: computational geometry offers a number of tools and techniques to deal with geometrical properties of spatial structures. These tools, as the so-called Voronoi tessellation, have been used in a number of biological problems where the overall properties depend on the dynamics of interacting elements as tissue dynamics, ecology, and tumor growth among others. In this project you will have to apply those tools to problems as tissue regeneration or raft dynamics in membranes.

JB2. Analysis of expression-activity landscapes in network motifs: the complexity of transcriptional networks can be reduced in many cases to simple structures called motifs that implement specific functionalities to the cell. For example, the so-called incoherent 1 and coherent 1 feed forward loops in *E. coli* represent more than 60% of its transcriptional network. The functionality of these structures have been analyzed from the point of view of the expression level but full characterization requires an expression-activity analysis. In this project you will have to analyze network motifs in *E. coli* using that approach. In addition you will have to analyze from a statistical thermodynamic approach those motifs by studying the operator dynamics.

JB3. Engineering circuits in biology: networks of interacting genes can be translated into Boolean logic where functions as OR, NAND, or XOR have a can be implemented. In this project you will have to explore how robust are these logical structures to molecular noise and also to combine them for developing complex circuits.



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Prof. Jaume Casademunt Viader (jaume.casademunt@ub.edu)

Departament Estructura i Constituents de Matèria, Facultat de Física, UB

JC1. Cooperative effects of processive molecular motors pulling on fluid-like cargoes.

The goal is to study the collective dynamics of small clusters of motors pulling on vesicles or membrane tubes. Different aspects that can be developed include numerical simulation of Langevin equations for ratchet-like motors, Monte Carlo simulation of discrete random walkers and analytical calculations in different approximations. The proposed work builds on previous results that have revealed nontrivial cooperativity of motors (J. Brugués and J. Casademunt, Phys. Rev. Lett. (2009), in press), in the direction of including force-dependent kinetics and a realistic modeling of monomeric kinesin, a motor which is known to work collectively for long-range, efficient transport in axons. The results may have implications for the motor traffic disorders that are associated to most neurodegenerative diseases.

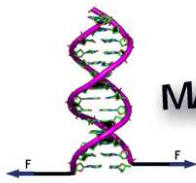
JC2. Bleb formation and dynamics.

In many circumstances the pressure inside the cell is sufficiently large to locally break the membrane-cytoskeleton linkers, thus forming a bleb, that is a protrusion of the membrane which is detached from the actine cortex. In this circumstances, the pressure drives the flow of cytosol into the bleb. The dynamical balance between this flow and the rebuilding of the actin cortex to retract the bleb yields an interesting mechanism of cell deformation which is used by ameboid cells for propulsion on substrates, and provides also a mechanism for cell migration within tissues (as in cancer malignant tumours). Other biological functions such as apoptosis are also closely related to blebbing activity. The aim of this work is to study the dynamics of bleb nucleation through an instability of the cell membrane-adhesion.

A statistical model of adhesion will be studied both analytically and numerically to establish the conditions for membrane detachment and the statistics of blebbing events (see Jan Brugués doctoral thesis, UB 2009).

JC3. Dynamic stability of mitotic spindles.

The dynamical stability of the mitotic spindles involves a careful balance between force-dependent kinetics of cross linking molecular motors and of polymerization/depolymerization activity of microtubules.



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Recently, a nonlinear model has been proposed (O. Campàs, J. Casademunt, I. Pagonabarraga, *Biophysical Journal* (2008)) to account for this process in antiparallel assemblies of microtubules. This model will be generalized and studied to elucidate the role of different physical parameters on the overall stability and structure of the mitotic spindle. A second step will be to study numerically the dynamics of the system including fluctuations in the numbers of cross linking motors.

JC4. *Dynamics of tissue growth.*

A numerical simulation of the growth of epithelial tissues will be set up and tested, along the lines of previous works that include elastic, adhesive and contractile stresses at the cell membranes (R. Farhadifar et al, *Current Biology* 17, 2095 (2007)). The focus will be on the relationship between growth anisotropy, cell division and morphology of the growing tissue. We will also apply the formalism to cases where two different types of cells are present, with focus on the dynamics of cell domains in the context of a growing tissue.

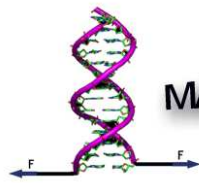
Prof. Blas Echevarria Domínguez (blas@fa.upc.edu)
Departament de Física Aplicada, UPC

BE1. *Mathematical modeling of intracellular calcium dynamics in human atrial cells.*

The goal is to develop a mathematical model of intracellular calcium dynamics, based on the experimental data obtained by Dr. Leif Hove-Madsen (Centro de Investigación Cardiovascular CSIC-ICCC), and use it for the study of electro-mechanical alternans.

BE2. *Model of Brugada syndrome.*

Brugada syndrome is an anomaly in the ECG, known to be related with occurrences of sudden cardiac death. At physiological level, it is due to a mutation that results in malfunctioning of the sodium channels. In the present work, a detailed Markov model of the sodium channel will be considered, to study the effect of this mutation in the probability of reentry.



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BE3. *Excitation-contraction coupling.*

The propagation of the cellular action potential induces the mechanical contraction of the heart. But this, in turn, affects the action potential through stretch-activated channels. This feedback can give rise to autonomous excitations and instability of rotors. We plan to develop simplified models that take into account the basic ingredients of this feedback to explain the observed phenomena.

Prof. Ramón Farré Ventura (rfarre@ub.edu)

Unitat de Biofísica i Bioenginyeria. Universitat de Barcelona -
Institut d'Investigacions Biomèdiques August Pi Sunyer.

RF. *Effects of mechanical stimuli on stem cell differentiation.*

Prof. Aurora Hernández-Machado (a.hernandezmachado@gmail.com)

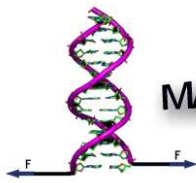
Departament Estructura i Constituents de Matèria, Facultat de Física, UB

AHM1. *Membrane domains, cellular division and hydrodynamic effects in red blood cells.*

We will apply a curvature-driven phase-field model to study the shapes of membrane domains rich in cholesterol and proteins and to cellular division induced by line tension. We will also consider the effects of hydrodynamics on a red blood cell in a vessel.

AHM2. *Flow of biological fluids in microchannels.*

We will study experimentally the flow of Newtonian and viscoelastic biological fluids in microchannels under the presence of an oscillatory pressure. We will obtain the permeability of the flow and we will compare with a three dimensional dynamic model.



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AHM3. *Patterns in cellular differentiation.*

Cell differentiation depends on gene expression. In the project we will study the interaction of the genetic networks of different cells that are located in neighboring sites in space. We will obtain a spatial distribution of different cells and we will compare our model to experiments in plants and the initial development of embryos.

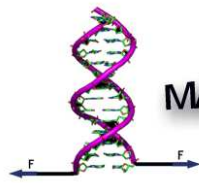
Prof. Marta Ibañes Miguez (marta.ibanes@gmail.com)

Departament Estructura i Constituents de Matèria, Facultat de Física, UB

MI1. *Stochastic pattern formation for embryonic development.*

During the development of an embryo, cells acquire distinct traits and functions (become differentiated) and exhibit different patterns of gene expression. An important question in embryonic development is how spatiotemporal organized patterns of gene expression arise. This pattern formation process involves in many cases complex nonlinear dynamics. In addition, there are several examples in the literature of gene expression patterns in embryos which are stochastic but still have a global order. Understanding and characterizing these stochastic processes pose a challenge both from a theoretical and experimental perspective. In this Master project a theoretical (computational and analytical) study is proposed to study stochastic pattern formation.

The student is expected to learn mathematical modeling and computational analysis of stochastic processes in terms of Langevin and Fokker-Planck equations, as well as the biology involved in the process of pattern formation under study.



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Prof. Alvaro Mata Chavarría (amata@pcb.ub.cat)
Nanotechnology Platform
Parc Científic Barcelona.

AM1. *Micro and nanofabricated substrates to control enzyme mediated molecular self-assembly.*

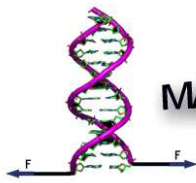
This project aims to develop surfaces with specific topographical and biochemical patterns designed to precisely position enzymes and control the assembly of small Fmoc-based molecules into well-defined nanofibers. The project would require the use of nanofabrication techniques, soft lithographic techniques, the use of the Dip Pen Nanolithography, and small molecule manipulation.

AM2. *Peptide-based materials for tissue engineering or regenerative medicine.*

This project consists in using recombinant elastin-like peptides (ELPs) comprising specific bioactive epitopes such as arginine-glycine-aspartic acid-serine (RGDS) to design and develop scaffolds for controlling cellular behavior (adhesion, migration, differentiation). We are currently using micro and nanofabrication techniques to create 2D or 3D scaffolds with specific physical and chemical properties. We are exploring the use of these materials as 3D or 2D self-assembling scaffold for either *in vitro* or *in vivo* applications. This project involves the manipulation of small molecules and peptides, the use of hydrogels and microfabrication techniques, and some cell culture work.

AM3. *Surface engineering to investigate and modulate material-protein-cell interactions.*

This project looks to take advantage of nanofabrication and analytical equipment present in our laboratory to investigate the independent and synergistic effects of surface nanotopography and wettability on protein deposition, adhesion, and conformation. By controlling the properties of the adhered protein layer it may be possible to control and modulate downstream cellular effects. The overall objective of this project is to design implant, scaffold, or device surfaces that can produce specific biological reactions, enhancing or diminishing specific biological processes, and controlling the overall biological response. This project relies heavily on nanofabrication techniques to create nanostructure surfaces and on the use of atomic force microscope to analyze protein-surface interactions.



MASTER IN BIOPHYSICS



Prof. Daniel Navajas Navarro (dnavajas@ub.edu)

Unitat de Biofísica i Bioenginyeria. Universitat de Barcelona -
Institut de Bioenginyeria de Catalunya.

DN. Nanomechanics of inflammatory cells in acute lung injury.

Prof. Ignacio Pagonabarraga Mora (ipagonabarraga@ub.edu)

Departament Física Fonamental, Facultat de Física, UB

IP1. Mechanical properties and rheology of model active gels.

The objective is the analysis of a simple model which captures the basic ingredients of an active solid, and the possibility to understand the basic behavior of active and passive microrheological techniques.

IP2. Cell mechanosensing.

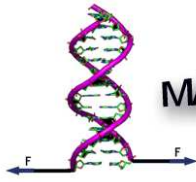
Analyze the collective response of cells which interact through the active stresses which generate on the solid sustaining medium

IP3. Self organized patterns in interacting cells.

The objective of this project is to analyze the physical mechanisms underlying. The effective interactions between model microorganisms as a result of the hydrodynamic flows they originate and the possibility to excrete and sense specific chemicals. The insight gained will be useful to understand the physical mechanisms underlying the dynamics of quorum sensing.

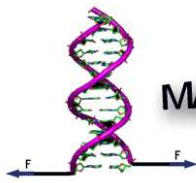
IP4. Electrodynamics effects in membranes.

Use of coarse grained models of lipid bilayers including electrostatic charges to analyze the impact the latter has in the conformation and dynamical responses of membranes on the relevant length and time scales in which they evolve.



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Prof. Matteo Palassini (matteo.palassini@gmail.com)
Departament Física Fonamental, Facultat de Física, UB

MP1. Stochastic dynamics of genetic and epigenetic regulation.

Abstract:

This project consists in the stochastic modeling of gene regulatory networks. There are two possible subjects: 1) the nonequilibrium dynamics in small regulatory networks; 2) chromatin dynamics and epigenetic signals. The work involves both analytical aspects, stochastic computer simulations, and comparison with experiments. Two previous students of the Master have graduated with a Final Project on related topics.

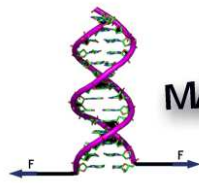
MP2. Using next generation sequencing technologies to dissect the epigenome of human insulin producing cells.

Prof. Jorge Ferrer Marrades (jferrer@clinic.ub.es), Genomic Regulation of Beta Cells, Endocrinology, Hospital Clínic de Barcelona, CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Institut d'Investigacions Biomediques August Pi i Sunyer, Barcelona.

In collaboration with Matteo Palassini

Summary

Diabetes, which is one of leading causes of death, blindness, and kidney failure, results from the destruction or altered function of beta-cells. Our lab is interested in understanding the regulation of the genome in pancreatic insulin-producing beta-cells. In particular we would like to understand how variants of the genomic DNA sequence that are commonly encountered among different individuals might influence the state of the genome (its *epigenome*) in pancreatic beta-cells. This is of interest among other reasons because many common DNA sequence variants have been implicated in the development of human diabetes, but the reasons remain unclear. We are using novel high throughput sequencing technologies (Illumina Solexa platform) to build genome-wide charts of *epigenome* features in human pancreatic beta-cells. The lab takes a multidisciplinary approach to the analysis of these datasets, and collaborates with Dr Matteo Palassini from Dept de Física Fonamental in the development of new analytical approaches. Several specific projects are available in this area, including a) the development of computational and mathematical approaches to define and characterize epigenomic features identified through Nextgen sequencing, and b) implement statistical approaches to study the effects of common human genetic variation on chromatin and transcriptional activity in the human genome.



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Recent publications:

Gauthier BR, Wiederkehr A, Baquié M, Dai C, Powers AC, Kerr-Conte J, Pattou F, MacDonald RJ, Ferrer J, Wollheim CB. “A new link between PDX1 and TFAM explains mitochondrial dysfunction in a beta-cell model of MODY4”, *Cell Metabolism* 2009.

Servitja JM, Pignatelli M, Maestro MA, Cardalda C, Boj SF, Lozano J, Blanco E, Lafuente A, McCarthy MI, Sumoy L, Guigó R, Ferrer J. “Hnf1alpha (MODY3) controls tissue-specific transcriptional programs and exerts opposed effects on cell growth in pancreatic islets and liver”, *Mol Cell Biol.* 2009 Mar 16. PMID: 19289501.

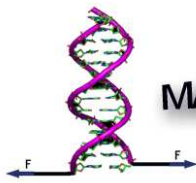
Boj SF, Servitja JM, Martin D, Rios M, Talianidis I, Guigo R, Ferrer J. “The functional targets of the monogenic diabetes transcription factors HNF1{alpha} and HNF4{alpha} are highly conserved between mice and humans”, *Diabetes.* 2009 Feb 10. PMID: 19188435

Luco RF, Maestro MA, Sadoni N, Zink D, Ferrer J. “Deficiency of the transcriptional activator Hnf1a causes altered subnuclear positioning of genomic targets”, *PLoS Genetics*, 2008 May 23;4(5):e1000079.

MP3. Protein-ligand binding energy studies.

Master project with joint supervision of Victor Guallar (Barcelona Supercomputer Center) and Matteo Palassini (Dep. Fundamental Physics).

The main objective is to develop computational techniques to obtain protein-ligand binding free energies. We aim to find novel algorithms capable of (with respect to the present techniques): obtaining a more accurate binding free energy, and 2) speed up its calculation. For this purpose we propose the combination of two distinct techniques. First we will map the binding pathway by means of PELE, a novel Monte Carlo algorithm recently developed at the BSC [1,2]. Secondly, we will guide non equilibrium dynamics along this pathway, computing the binding free energy by means of the Jarzinsky equality. The project has a high impact in pharmacology and in biomedical inhibition mechanistic studies.



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Prof. Fèlix Ritort Farran (fritort@gmail.com)

Departament Física Fonamental, Facultat de Física, UB

FR1. *Modeling single molecule experiments.*

The project consists in theoretical modeling of results obtained in single molecule experiments carried out in the Small Biosystems lab. Potential subjects are: DNA and RNA unzipping, DNA-protein interactions, fluctuation relations and molecular (DNA, RNA or proteins) folding.

FR2. *Antigen-antibody interactions.*

This project consists in studying the affinity and kinetics of ligand-receptor binding. A key part of the project is data analysis and doing optical tweezers experiments.

FR3. *Improving molecular synthesis protocols.*

This project consists in devising optimized synthesis protocols for nucleic acids and proteins for later manipulation using single molecule technology (optical tweezers and AFM). Major parts will be to design novel chemistry for labeling single molecules and purification of enzymes (e.g. to carry out molecular motor experiments).

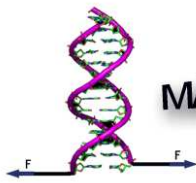
Prof. José María Sancho Herrero (josemariasancho@ub.edu)

Departament Estructura i Constituents de Matèria, Facultat de Física, UB

JMS1. Stochastic simulations of Langevin equations to study transport, diffusion and reaction at molecular scale.

JMS2. Numerical simulations and theoretical analysis of ratchet models to study molecular machines. The student can choose a particular device such: channels, pumps, motors, etc.

JMS3. Study of bacterial pattern formation due to chemotaxis by the use of Langevin equations with multiplicative noise.



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Prof. Jordi Soriano Fradera (jsfradera@gmail.com)

Departament Estructura i Constituents de Matèria, Facultat de Física, UB

Prof. Jordi Soriano carries out experimental research in neuroscience and developmental biology. Projects that can be developed in the following years include:

Neuroscience:

JSF1. Patterned neural networks. In the last years there have been an increasing interest in the development of neural cultures with defined topology, where neurons are confined to specific regions and their connections grow along predefined directions. For instance, neurons that grow along a thin, long line form a one-dimensional neural culture. The scope of the project would be to advance in the development of such cultures and in the study of network-scale features, such as neural activity or velocity of propagating fronts.

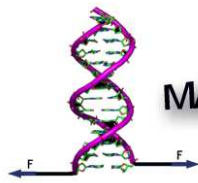
JSF2. Soft lithography applied to neural culturing. Recent advances in nanotechnology and microfabrication permit the placement of single neurons in physical traps made of resin or PDMS molds. The project is oriented to the learning and application of such techniques to prepare neural cultures “on a chip”.

JSF3. Electric stimulation of neural cultures. As a follow up of recent experimental results, the project will study the effects of an electric stimulation on neural response and excitability, and on network connectivity.

JSF4. Neural activity and calcium imaging. The project will focus on the study of neural activity on cultures using calcium sensitive dyes. From a technical point of view, the scope of the project is to characterize the applicability of different dyes. From a biophysical perspective, the project will use calcium imaging techniques to characterize propagation fronts in neural cultures.

Developmental biology:

JSF5. Hydra regeneration from cell aggregates. The freshwater polyp Hydra is characterized by its astonishing regeneration capabilities. The animal is able to regenerate from either a small fragment of tissue or from an aggregate of dissociated cells. The scope of the project would be to characterize the



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regeneration of big aggregates, where multiple animals form simultaneously. The project also includes the learning of animal and tissue culturing.

Prof. Xavier Trepats Guixer (xtrepats@ub.edu)

Unitat de Biofísica i Bioenginyeria. Universitat de Barcelona -
Institut de Bioenginyeria de Catalunya.

XT. Dynamic study of force transmission during collective cell migration.
