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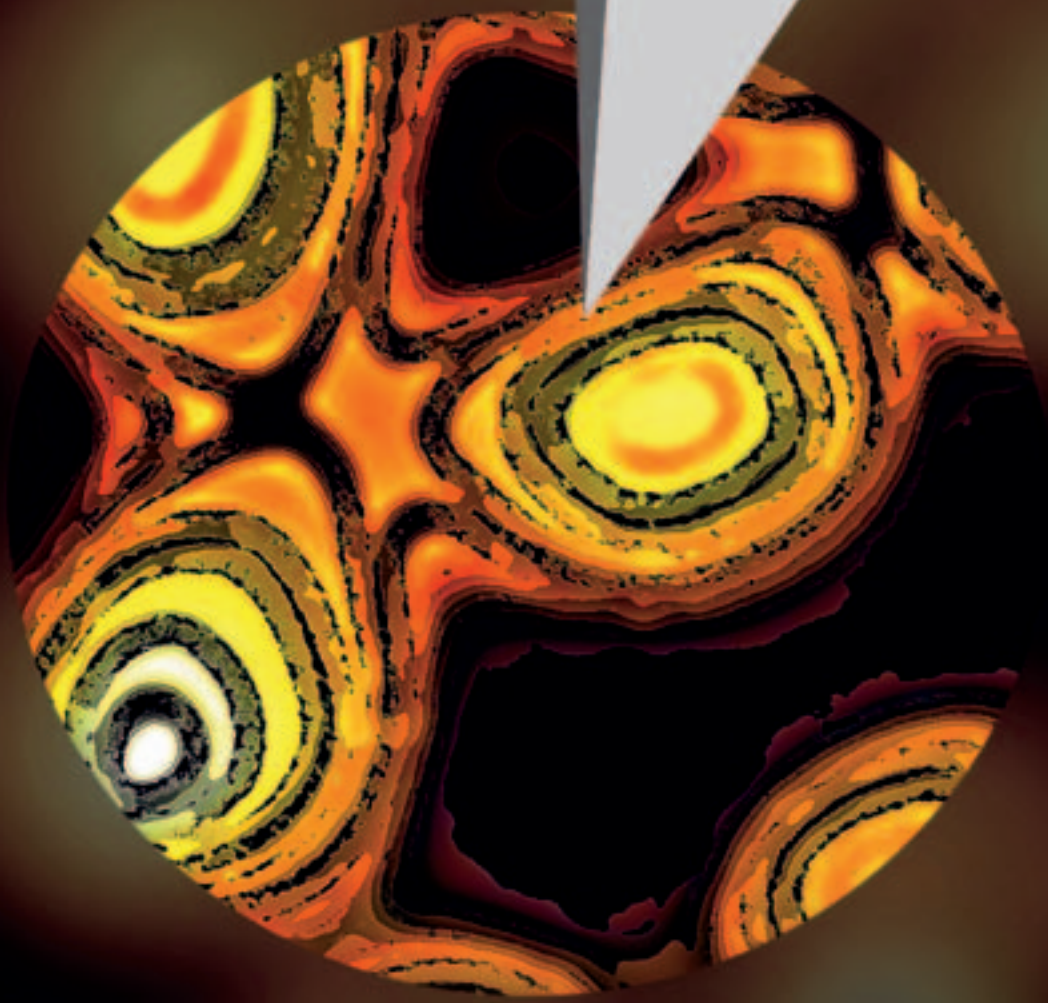

Scientific Report **2009**

Scientific Report
2009

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Foreword

The following pages contain a summary of the current research lines at the Unidad de Biofísica, together with the list of staff, students and visitors, and our recent publications and other activities. This Annual Report intends to serve a two-fold purpose, providing the reader with information about our activities, and supplying our sponsors with the necessary data about the end-product of their funding. We shall be glad to answer any questions or provide further information, and would be delighted to welcome you personally in our laboratory.

Presentación

Las páginas que siguen contienen un resumen de las líneas de investigación en marcha en la Unidad de Biofísica, junto con la relación de trabajadores, estudiantes y visitantes, y nuestras publicaciones y actividades recientes. Esta Memoria anual tiene un doble propósito, proporcionar información sobre nuestras actividades a los lectores en general, y transmitir en particular a nuestros patrocinadores los datos necesarios sobre los resultados producto de su generosidad. Con mucho gusto responderemos a cualquier pregunta y proporcionaremos información complementaria, y por supuesto estaremos encantados de recibirles personalmente.

Aurkezpena

Hurrengo orrietan Biofisika Unitatean gaur egun dauden ikerketa lerroen laburpena, ikertzaile, ikasle eta bisitarien zerrenda, eta gure argitarapen eta ekintzen berri eskaintzen da. Urteroko txosten honek helburu bikoitza du: irakurle orori gure ekintzen berri ematea, eta bereziki, gure laguntzaileei beraien eskuzabaltasunari esker lortutako datuak jakinaraztea. Atsegin handiz, edozein galdera erantzuteko, informazio osagarria eskaintzeko, edota pertsonalki errezibitzeko prest gaude.

News 2009

- Two new scientists, supported by Ikerbasque www.ikerbasque.net joined our Institute. They are **Marcelo Guerin**, from Argentina, formerly at Colorado State University (Fort Collins, CO, USA) and **Vadim Frolov**, from Russia, formerly at the National Institutes of Health (Bethesda, MD, USA).

- Mr. Ignacio Murguía Mañas started working as Managing Director in charge of both the Fundación Biofísica Bizkaia and the *Unidad de Biofísica*.

- The Spanish Ministry of Science and Innovation (MICINN) granted the *Unidad de Biofísica*, through the University of the Basque Country, the amount of five million euros as a special contribution for the new building of the Institute.

- The *Unidad de Biofísica* received, through the *Fundación Biofísica Bizkaia*, one of the special grants (2009-2012) from the Department of Education of the Basque Government, aimed to support the Basic and Excellence Research Centres in the Basque Country.

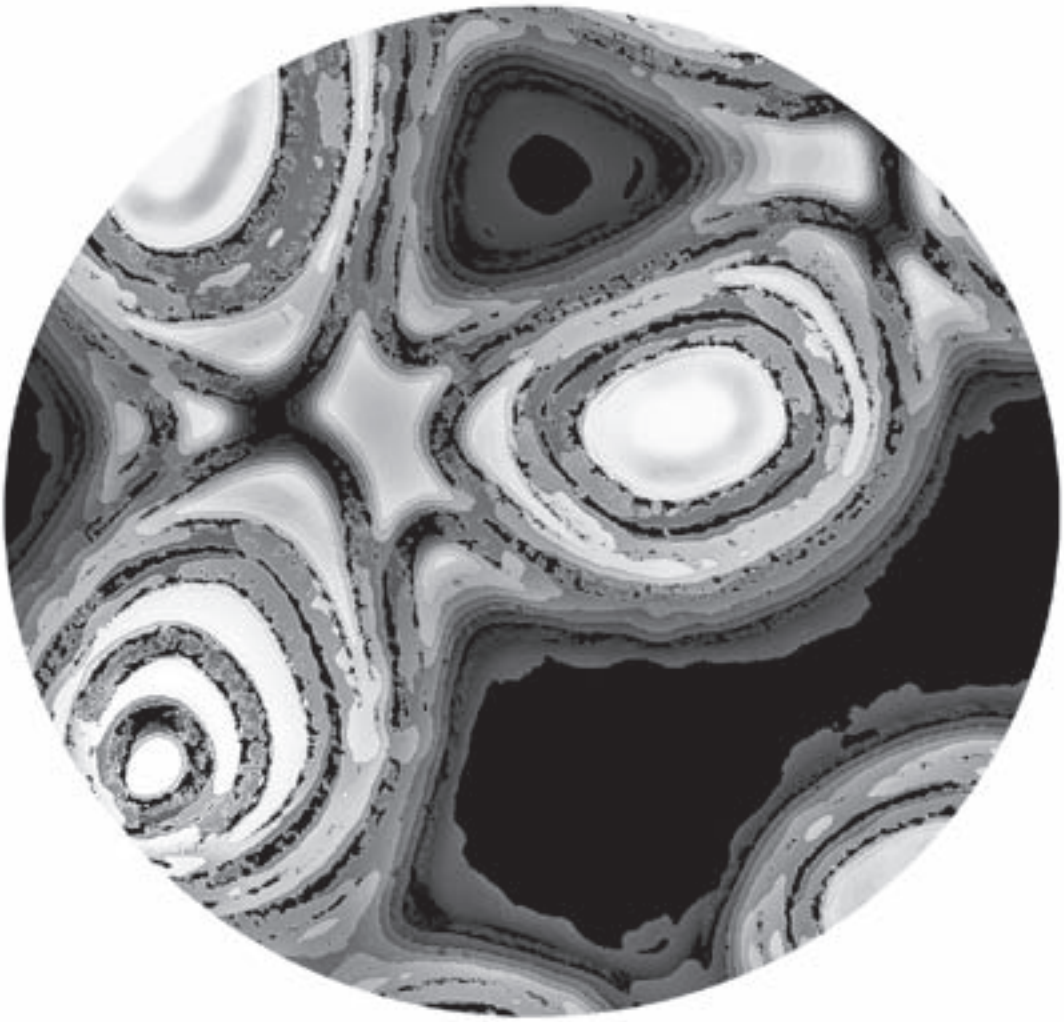
- The *Unidad de Biofísica* got a record number of pre-doctoral and post-doctoral contracts from the Basque Government, eight in total. Congratulations to all of them!

- Two former Ph.D. students from our Institute were granted the Special Ph.D. Prize (*Premio Extraordinario de Doctorado*) awarded by the University to the best theses presented in the academic year 2005-06. They are **Jesús Sot** and **Maier Lorizate.**

- **INNOPROT** a spin-off company of the *Unidad de Biofísica* obtained the **Gaztedi Award** from the Basque Enterprise Founding and Developing Agency (*DEMA*).

- On November 7-9 the Unidad de Biofísica hosted a special meeting on *Frontiers in Biophysics*. Fourteen first-class biophysicists discussed the hottest topics of current Biophysics, and gave us useful advice on the future developments of our Centre.

- One of the prestigious CONSOLIDER grants from the Spanish Ministry of Science and Innovation was awarded to a multi-lab consortium, of which Drs. I. Alkorta, D.M. Guérin and Á. Villarroel, from the *Unidad de Biofísica*, are partners. The grant aims to support the “Spanish Ion Channel Initiative” (SICI).



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Lines of Research 2008/2009

Sphingolipids, "rafts" and membrane domains

(A. Alonso, F.M. Goñi)

In recent years the interest for membrane domains has increased, in particular transient domains known as rafts. The hypothesis of "rafts" suggests that these microdomains are enriched in sphingolipids and in cholesterol. Sphingomyelinases are enzymes that break down sphingomyelin into ceramides and water soluble products. Ceramides are membrane lipids, but their activity is mainly seen through cytosolic proteins. Our group studies, on the one hand, the characteristics of sphingomyelinases, and on the other hand, the changes induced by ceramides in the physical properties of membranes, in order to identify the molecular bases of the physiological activity of ceramides. We are also analysing the tendency of various different sphingolipids (ceramides, sphingosine) to form domains in the lipid bilayer plane.

References:

"Cholesterol displacement by ceramide in sphingomyelin-containing liquid-ordered domains, and generation of gel regions in giant lipidic vesicles". J. Sot, M. Ibarguren, J Busto, L.-R. Montes, F.M. Goñi and A. Alonso. *FEBS Lett.* **582**, 3230-3236 (2008).

"Sphingosine-1-phosphate as an amphipathic metabolite: its properties in aqueous and membrane environments" M. García-Pacios, M.I. Collado, J.V. Busto, J. Sot, A. Alonso, J.L.R. Arrondo and F.M. Goñi. *Biophys. J.* **97**, 1398-1407 (2009).

"Cis- versus trans-ceramides: effects of the double bond on conformation and H-bonding interactions" S.C. Phillips, G. Triola, G. Fabrias, F.M. Goñi, D. B. Dupré and M.C. Yappert. *J. Phys. Chem.* **113**, 15249-15255 (2009).

Membrane protein folding and stability. Structural motif engineering and design

(A.R. Viguera)

Protein folding has been the subject of intensive research. Well designed combinations of experimental and computational studies are enabling folding to be followed at atomic resolution, with the result that general rules are emerging. This insight, however, pertains to water-soluble proteins and it is unclear how the unifying mechanisms extend to the many proteins that reside in membranes. Understanding membrane protein folding in vitro will not only begin to overcome the problems of overexpression, purification and solubilization of membrane proteins, but also bring new techniques to membrane protein research. We have chosen the pore-forming fragment of colicin A as a model to study protein-lipid complex formation and stability. We investigate the kinetics and thermodynamics of folding aiming to obtain mechanistic detail, with an emphasis on α-helical proteins.

References:

"Par j 1 and Par j 2, the two major allergens in *Parietaria judaica*, bind preferentially to monoacylated negative lipids" R.González-Rioja, J.A.Asturias, A.Martínez, F.M.Goñi & A.R.Viguera. *FEBS J.* **276,** 1762-1775 (2009).

"NMR assignment and backbone dynamics of the pore-forming domain of colicin A" A.Ibañez de Opakua, T.Diercks, A.R.Viguera & F.J.Blanco. *Biomol NMR assign (published online 26 november 2009)*.

Structural studies of Biomolecules using IR spectroscopy

(J.L.R. Arrondo)

In the nineteen eighties, our laboratory pioneered the application of infrared spectroscopy to the study of the structure of lipids and proteins. Currently we are developing the new technology of two-dimensional IR spectroscopy, applying it to the analysis of the structure and conformational changes of proteins, lipids and their complexes.

The main areas on which we are currently focussing our attention are:

- Study of sphingomyelin-colesterol mixtures
- Membran proteins and lipoproteins
- Amyloidogenesis
- Protein-DNA interactions

References:

"Structure and dynamics of membrane proteins as studied by infrared spectroscopy". J.L.R. Arrondo y F.M. Goñi. *Prog*. *Biophys. Mol. Biol.* **72**, 367-405 (1999).

"Phosphorylation of the carboxy-terminal domain of histone H1: effects on secondary structure and DNA condensation" A. Roque, I. Ponte, J.L.R. Arrondo and P. Suau *Nucleic Acids Res.* 1-8 (2008).

Protein folding and the role of molecular chaperones

(A. Muga, A. Prado, F. Moro)

Molecular chaperones are proteins that take part in many processes that are essential for cell viability. Our group studies nuclear and cytosolic chaperones. Nucleoplasmin is a nuclear chaperone involved in the exchange of basic proteins bound to DNA, which regulates the condensation state of chromatin. In particular, we are interested in characterising the effect of phosphorylation on the structure and activity of this protein. The cytosolic chaperones currently being studied are *E.coli* heat shock proteins, the DnaK GroEL and ClpB system, which correspond to members of the Hsp70, Hsp60 and Hsp100 families respectively. We are trying to characterise the molecular mechanism by which the association of these chaperones enables protein aggregates to be reactivated under conditions of stress. These studies are carried out using a combination of biochemical (expression and purification of proteins), molecular biological (directed mutagenesis, hybrid proteins) and biophysical (fluorescence, IR spectroscopy, calorimetry among others) techniques.

References:

"Phosphorylation of both nucleoplasmin domains in required for activatio of its chromatin decondensation activity" S. Bañuelos, M.J. Omaetxebarria, I. Ramos, M.R. Larsen, I. Arregi, O.N. Jensen, J.M. Arizmendi, A. Prado and A. Muga *J. Biol. Chem.* **282**, 21213-21221 (2007).

"DnaJ recruits DnaK to protein aggregates" S.P. Acebrón, V. Fernández-Saiz, S.G. Taneva, F. Moro and A. Muga. *J. Biol. Chem.* **283**, 1381-1390 (2008).

"DnaK-mediated association of ClpB to protein aggregates. A bichaperone network at the aggregate surface" S.P. Acebrón, I. Martín, U. del Castillo, F. Moro and A. Muga. *FEBS Lett.* **583**, 2991-2996 (2009).

"Energetics of nucleotide-induced DnaK conformational states" S.G. Taneva, F. Moro, A. Velázquez-Campoy and A. Muga. *Biochemistry* **49**, 1338-1345 (2010).

Insights into the structure, function and nucleocytoplasmic traffic of nuclear proteins

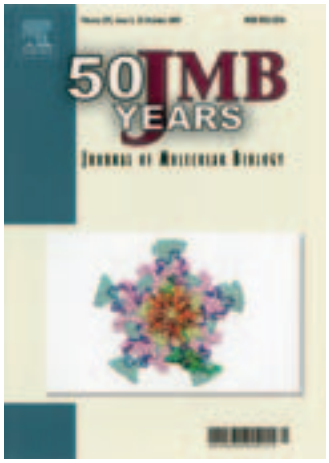
(M.A. Urbaneja, S. Bañuelos)

Nuclear chaperones are involved among other functions in the chromatin remodeling that takes place during various physiological processes such as fertilization (e.g. mediated by nucleoplasmin) and ribosome assembly and cell proliferation control (e.g. mediated by nucleophosmin). Like other nuclear proteins, they are synthesized in the cytoplasm and rely on carriers (in the case of nucleoplasmin / nucleophosmin family, importin α/β heterodimer carrier) to be imported into the cell nucleus. Nucleophosmin is a "shuttling" protein: it needs to be imported and exported continuously. Protein function is frequently regulated by cell localization, and failure in this traffic may trigger diseases. Nucleophosmin mislocalization and disfunction have been related to several types of human cancer. Based on biochemical, molecular biology and biophysical approaches we are studying nucleophosmin structure, function and interaction with nuclear transport receptors, trying to understand the basis of its pathogenic alterations

References:

"Activation of nucleoplasmin, an oligomeric histone chaperone, challenges its stability" S.G. Taneva, I.G. Munoz, G. Franco, J. Falces, I. Arregi, A. Muga, G. Montoya, M.A. Urbaneja & S. Banuelos. *Biochemistry* **47**, 13897-13906 (2008).

"A mechanism for histone chaperoning activity of nucleoplasmin: thermodynamic and structural models" S.G. Taneva, S. Banuelos, J. Falces, I. Arregi, A. Muga, P.V. Konarev, D.I. Svergun, A. Velazquez-Campoy & M.A. Urbaneja. *J. Mol. Biol.* **393**, 448-463 (2009).



References:

"Lipid phase coexistence favors membrane insertion of equinatoxin-II, a pore-forming toxin from *Actinia equina*" A. Barlic, I. Gutiérrez-Aguirre, J.M.M. Caaveiro, A. Cruz, M.B. Ruiz-Argüello, J. Pérez-Gil and J.M. González-Mañas *J. Biol. Chem.* **279**, 34209-34216 (2004).

"Pore formation by equinatoxin, a eukaryotic pore-forming toxin, requires a flexible N-terminal region and a stable β-sandwich" K. Kristan, Z. Podlesek, V. Hojnik, I. Gutiérrez-Aguirre, G. Guncar, D. Turk, J.M. González-Mañas, J.H. Lakey, P. Macek and G. Anderluh *J. Biol. Chem*. **279**, 46509-46517 (2004).

Inter-domain relationships in integral membrane proteins

(I. Alkorta, F.M. Goñi)

The purpose of this project is to determine the role of the various protein components that are part of the bacterial conjugation system of the R388 plasmid. In particular, we are interested in the membrane protein TrwB. This protein, the first member of the coupling family of proteins to be purified, is involved in the transfer of DNA from the donor to the recipient cell. Clarifing its role in the process of conjugation will contribute to solving the problem of antibiotic resistance shown by an increasing number of bacterial strains (in collaboration with F. De la Cruz, University of Cantabria).

References:

"Role of the transmembrane domain in the stability of TrwB, an integral protein involved in bacterial conjugation" I. Hormaeche, I. Iloro, J.L.R. Arrondo, F.M. Goñi, F. de la Cruz and I. Alkorta *J. Biol. Chem.* **279**, 10955-10961 (2004).

"The transmembrane domain provides nucleotide binding specificity to the bacterial conjugation protein TrwB" I. Hormaeche, R.L. Segura, A.J. Vecino, F.M. Goñi, F. de la Cruz and A. Alkorta *FEBS Lett.* **580**, 3075-3082 (2006).

Mechanisms for virus-induced membrane fusion

(J.L. Nieva)

Our objective is to determine the molecular mechanism by which membrane glycoproteins of some viruses (HIV, Ebola) induce the fusion of the cell and viral membranes. Prediction tools have been developed to detect the domains that are inserted into the target membrane. Specifically, we seek to understand their behaviour as antigenic determinants, and to develop inhibitory agents that would block their destabilizing interaction. A branch of this field consists of the characterisation of similar domains that may be involved in the infective power of the prion protein. In parallel, we are studying the mechanism of cell membrane permeabilisation, induced by certain viral products (viroporins) during infection (this work on viroporins is in collaboration with L. Carrasco, CBM, Madrid).

References:

"Distinct mechanisms of lipid bilayer perturbation induced by peptides derived from the membrane-proximal external region of HIV-1 gp41" B. Apellániz, S. Nir and J.L. Nieva. *Biochemistry*, **48,** 5320-5331 (2009).

"Structural constraints imposed by the conserved fusion peptide on the HIV-1 gp41 epitope recognized by the broadly neutralizing antibody 2F5" I. de la Arana, J.P. Julien, B.G. de la Torre, N. Huarte, D. Andreu, E.F. Pai, J.L.R. Arrondo and J.L. Nieva. *J. Phys. Chem*. **113**, 13626-13637 (2009).

Mitochondrial membranes, apoptosis and cancer

(G. Basañez)

During apoptosis, mitochondrial membranes undergo dramatic changes in permeability and morphology. The principal components involved in these processes are the BCL-2 family of proteins, with assistance from an increasing number of mitochondrial protein/lipid effectors. Despite the remarkable progress made in uncovering the molecular underpinnings of apoptotic cell death in the last decade, identification of the precise mechanisms by which BCL2 family proteins regulate the structure and functioning of mitochondrial membranes remains a key and controversial issue in the field of cell death. Given the inherent complexity of the cellular apoptotic network, we use in vitro reconstituted systems with physiologically relevant characteristics to try to elucidate the mode of action of specific members of the BCL2 family and/or their effectors at the membrane level, using a multidisciplinary approach based on biophysical techniques. Considering the important role played by BCL2 family proteins in tumorigenesis and in cellular responses to chemotherapy, the information gained in these studies may facilitate progress in the fight against cancer.

References:

"Unravelling the bcl-2 apoptosis code with a simple model system" G. Basañez and J.M. Hardwick *PLoS Biol.* **6,** 1148-1151 (2008).

"BIM and tBID are not mechanistically equivalent when assisting BAX to permeabilize bilayer membranes" O. Terrones, A. Etxebarria, A. Landajuela, O. Landeta, B. Antonsson and G. Basañez. *J. Biol. Chem.* **283,** 7790-803. (2008)

"Endophilin B1/Bif-1 stimulates BAX activation independently from its capacity to produce large scale membrane morphological rearrangements" A. Etxebarria, O. Terrones, H. Yamaguchi, A. Landajuela, O. Landeta, B. Antonsson, H.G. Wang and G. Basañez. *J. Biol. Chem.* **284,** 4200-12 (2009).

X-ray crystallography and crystallisation of proteins and virus

(D.M.A. Guérin)

Learning about the structure of macromolecules of biological interest (enzymes, receptors, large molecular aggregates such as viruses) enables the mechanisms of the biochemical functions they perform to be interpreted. Protein crystallography, currently the most advanced and powerful technique for determining atomic structures, is used by our group to study a wide range of macromolecules. We are currently working on the resolution of the structure of several proteins of interest in the Biophysics Unit (membrane protein Scramblase and some of its mutants) and we are collaborating with national and international centres on other crystallography projects (Triatoma virus, Potassium Channel KcsA and Acyl-CoA binding protein, among others). In parallel with this crystallography work, we are developing new experimental devices, using optical, x-ray and spectroscopic techniques, to characterise the process of nucleation during protein crystallization.

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Identification and characterization of proteins and lipids associated to regulators of cell excitability

(Á. Villarroel)

Among ionic channels, those that are potassium selective are, by far, the most diverse group. They play a key role in processes such as immune response, cell differentiation, excitability and cell death, among others. More than 60 genes for potassium channels are known in the human genome, which together with the fact that up to four different subunits can combine to form a channel, means that there are an large numbers of variants. Despite this impressive redundancy in "potassium permeation", mutations in some subunits cause hereditary diseases, indicating that the rest of the channels cannot substitute for them. These diseases are known as channelopathies. To date, around 10 potassium channelopathies have been identified and four of these are due to mutations in genes of the KCNQ family, the gene products of which are Kv7.1-Kv7.5.

Our research is focused on the molecular study of these proteins that regulate cell excitability. In humans, mutations of these proteins cause arrhythmia, epilepsy and deafness, depending on the isoform affected and their distribution within the tissue. Our objective is to identify the network of proteins associated with these channels, by analysing the physiological consequences of these interactions through mutagenesis-function studies, and the use of electrophysiological, imaging, biochemical and high-resolution biophysical techniques. In addition, we aim to determine the role played by lipids in the regulation of these channels. Currently, we are establishing the channel regions involved in biogenesis, assembly, membrane insertion and subcellular localization, as well as in the regulation by lipid second messangers. We hope to identify the proteins and lipids that interact specifically with each of these domains, and these may become targets for the therapeutic drug development. In the longer term, our objective is to determine the three-dimensional structure of these macro-complexes. As an intermediate stage, en route to future crystallization, we are going to investigate new strategies for high-yield production of large quantities of water-soluble, properly folded macro-complexes.

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Advanced techniques of fluorescence spectroscopic micro and nanoscopy

(J. Requejo)

The broad objective of the research carried out in the Imaging Laboratory is to extend our understanding of biochemical and biological phenomena by making quantitative spatio-temporal observations and manipulating them in controlled ways, as well as to develop new complex research tools for this purpose. Emphasis is placed on methodologies, using optical techniques, which enable in vivo studies to be carried out on micro- and nanometre scales.

Until recently, fluorescence imaging techniques only exploited one property of the fluorescence emission as a source of contrast. The simultaneous measurement of multiple properties of a single image (multidimensionality) provides information on both the chemical species and its environment with spatial resolution thanks to its spectroscopic properties. For this, it is essential to find new high-contrast fluorescent markers that minimise the disturbance of the native biological structure, and techniques of laser beam design which minimise the photo-damage. It will be very interesting to visualise individual molecules in samples with high densities of emitters directly and dynamically, either by reducing the area of fluorescence emission (STED) or by localization of individual fluorescent molecules on a nanometre scale, after reversible photo-induced deactivation of the surrounding medium (PALM, STORM). The instruments and methodological tools that developed in the imaging laboratory in the course of the project are applied to the study of the organization and dynamics of components of the cell membrane.

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Systems Biophysics and Computational Biology

(J. Vilar)

Our research activity is focused on computational and mathematical analysis of biological systems at their various levels of organization, from molecular properties to cell behaviour and the role these play in the cell population dynamics. The main objective is to deepen our understanding of the underlying mechanisms and to use this information for the controlling and designing cellular processes. For this, we use the latest computational technologies with a wide range of methods including molecular dynamics, structural bioinformatics, stochastic simulation algorithms and mathematical analysis of dynamic systems. Using these computational biophysical techniques, together with corresponding experimental results, we are studying proteins, nucleic acids and lipids, as well as their interactions, their collective properties and the dynamics of their macromolecular complexes in networks of gene expression and signal transduction.

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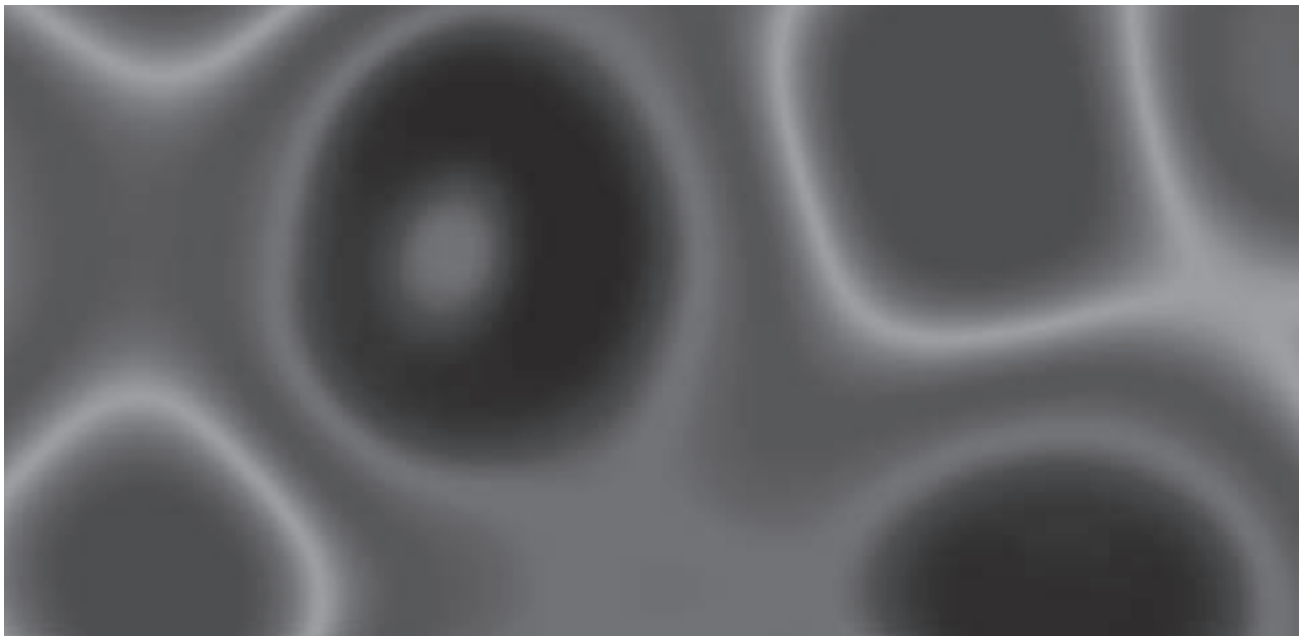

Structural Glycobiology

(M.E. Guerin)

Glycans are not only one of the major components of the cell but also are essential molecules that modulate a variety of important biological processes in all living organisms. These oligo- and polysaccharides are used primarily as energy storage and metabolic intermediates as well as being key structural components in bacteria and plants. Moreover, as a consequence of protein and lipid glycosylation, glycans generate a significant amount of structural diversity in biological systems. These structural features are particularly apparent in molecular recognition events including cell-cell, cell-matrix and cell-molecule interactions during critical stages of development, the immune response and host-pathogen interactions. Most of the enzymes encoded in eukaryotic/prokaryotic/archaeal genomes responsible for the biosynthesis of glycan structures are glycosyltransferases. The long-term goal of our research program is to understand how glycosyltransferases function to control health and disease at the molecular level. We are particularly interested in investigating the structural and mechanistic properties of glycosyltransferases with special emphasis on the study of integral and peripheral membrane-associated enzymes. To this end, we are using a multidisciplinary approach including molecular biology, protein biochemistry, protein biophysics and structural biology.

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Nanomechanics of cell membrane systems

(V. Frolov)

Morphological flexibility of cell membranes provides the foundation for the spatial organization of living cells. The signature morphologies of cellular endomembrane systems are created at the nanoscale where specialized proteolipid complexes assemble to control membrane curvature, shape and topology. Our main focus is on fundamental molecular mechanisms of membrane remodeling by such complexes operating at submicron scales, where pathways of membrane deformations are defined by forces applied by individual protein complexes, carefully organized in time and space, and elastic resistance of the lipid bilayer. We apply novel experimental approaches combining nanomanipulations, electrophysiology and time-resolved fluorescence, confocal and TIRF microscopy to characterize mechanical properties and dynamics of biomimetic and cell membranes at the nanoscale, with particular attention to topological membrane remodeling, fusion and fission, dynamics of the force- and geometry-induced demixing of membrane components and diffusion in complex media. We reconstitute the morphological activity of the prototype proteins controlling membrane remodeling, such as dynamin and matrix protein of enveloped viruses, using nanofabricated lipid templates to resolve subtle features of the proteolipid interactions, creation and sensing of membrane curvature by proteins, and dynamics of protein complexes on membrane surfaces.
Finally, we carry out theoretical analysis of the proteolipid interactions utilizing phenomenological membrane models and simulations.

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"Structural Studies of the Allosteric Communication Defective Chaperonins GroEL-E461K and GroEL-E434K" **Aintzane Cabo Bilbao;** Supervisor: Diego M.A. Guérin, 17 January 2008, with *summa cum laude*

"Estudios estructurales de lipoproteínas de baja densidad humanas por espectroscopia de infrarrojo" **José Ángel Fernández Higuero;** Supervisors: José Carlos González Milicua and José Luis Rodríguez Arrondo, 2 April 2008, with *summa cum laude.*

"Mecanismos que regulan la densidad en membrana de los canales KCNQ2" **Paloma Aivar Mateo;** Supervisor: Álvaro Villarroel Muñoz, 24 October 2008, with *summa cum laude.*

"Interacción de DnaK y ClpB con agregados protéicos" **Sergio Pérez Acebrón;** Supervisor: Arturo Muga Villate, 7 November 2008, with *summa cum laude.*

"Reconocimiento de epítopos insertos en membrana por los anticuerpos neutralizantes del VIH 2F5 y 4E10" **Nerea Huarte Arrayago;** Supervisor: José Luis Nieva Escandón, 12 December 2008, with *summa cum laude.*

"Mecanismos de regulación de proteínas BCL-2 por componentes de la maquinaría d fisión mitocondrial y por potenciales fármacos antitumorales" **Aitor Etxebarria Gallego;** Supervisor: Gorka Basañez Asúa, 20 February 2009, with *summa cum laude*.

"Actividades esfingomielinasa bacterianas y de mamíferos. Caracterización y efectos estructurales en membranas" **David López Jiménez**; Supervisor: Alicia Alonso Izquierdo, 23 March 2009, with *summa cum laude.*

"Toxinas bacterianas con actividad fosfolipasa C/esfingomielinasa. Interacciones con bicapas lipídicas" **Patricia Urbina Fernández;** Supervisor: Félix M. Goñi Urcelay, 24 March 2009, with *summa cum laude.*

"Structural basis of the stability, infectivity and (dis)assembly process of Triatoma Virus" **Jon Agirre Hernández;** Supervisor: Diego M.A. Guérin, 29 May 2009, with *summa cum laude*.

"Adenilato ciclasa de Bordetella pertussis. Estudio de su interacción con membranas" **Geraxane Gómez Bilbao**; Supervisors: Helena Ostolaza and César Martín, 17 July 2009, with *summa cum laude*.

"Structural studies of membrane proteins: The coupling protein TrwB of plasmid R388 and the pore-forming toxin FraC" **Ariel E. Mechaly García;** Supervisor: Diego M. Guérin, 11 September 2009, with *summa cum laude*.

"Fusión de membranas modelo inducida por fosfolipasas y por fluctuaciones térmicas" **Maitane Ibarguren Aizpitarte;** Supervisor: Félix M. Goñi, 22 September 2009, with *summa cum laude*.

"Estudios de formación de fibras amiloides por espectroscopía de infrarrojos" **Igor de la Arada Etxebarria;** Supervisor: José Luis Rodríguez Arrondo, 16 October 2009 with *summa cum laude*.

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Conferences and Courses

Organization of Meetings

The **Biophysics Unit** organised a workshop on "Open questions on the origins of life 2009", in collaboration with **UPV/EHU** and the **Information Autonomy Systems Research Group**, held in Donostia from 20 to 23 May 2009. **K. Ruiz-Mirazo** was a member of the Organizing Committee.

G. Basañez was a member of the Organizing Committee for the symposium: "Mitochondrial membranes, apoptosis and cancer" in the 34th Congress of the Federation of European Biochemical Societies, held in Prague, Czech Republic from 4 to 9 July 2009.

A. Alonso was a member of the Scientific Committee for the VII Iberoamerican Congress of Biophysics held in Buzios, Brasil, from 30 September to 3 October 2009.

F.M. Goñi was a member of the Scientific Committee for the 1st International Symposium on translational regenerative medicine, held in Vitoria-Gasteiz on 31 October 2009.

Invited Talks

Rincón. Puerto Rico, 20-22 February 2009.
National 2DCOS 2009 Symposium.

- **J.L.R. Arrondo.** "What we do with proteins and 2DCOS"

Boston, Massachusetts, USA, 28 February – 4 March 2009
53rd Annual Meeting of the Biophysical Society

- **F.M. Goñi, Co-Chair** "Membrane structure"
- **F.M. Goñi** "Cholesterol displacement by ceramide in sphingomyelin-containing liquid ordered domains, and generation of gel regions in giant lipidic vesicles"

Heidelberg, Germany, 19 May, 2009
SFB638 – Dynamics of macromolecular complexes in biosynthetic transport.

- **F.M. Goñi "**Phospholipases Eating their way through heterogeneous lipid membranes. Tender morsels and crusty leftovers**"**

Donostia-San Sebastián, 20-23 May 2009

Workshop Open Questions on the Origins of Life. Darwin and the origins of life. "El legado de Darwin en el marco de las teorías actuales sobre el origen de la organización biológica".

- **K. Ruiz-Mirazo** "A systems view on the problem of defining the origin of life boundaries"

Zamudio, Bizkaia, 4-5 June 2009.

3rd Workshop on Structural Biology at CIC bioGUNE "Viruses, miniaturized wonders".

- **D.M. Guérin."**Structural, Biochemical, Biological, and Technological Studies on the Insect Virus TrV"

Lisboa, Portugal, 19 June, 2009

Prieto's Fest: 20 years of Biophysics. A one-day symposium on the occasion of the 60th anniversary of Manuel J.E. Prieto.

- **F.M. Goñi** "Biophysics: Past, Present and Future"

Prague, Czech Republic, 4-9 July, 2009

34th FEBS Congress

- **G. Basañez** "Model membrane systems as valuable tools for mechanistic studies of BCL-2 family protein function**"**

Genova, Italy, 11-15 July 2009

European Biophysics Congress

- **A. Alonso (Chair) "**Lipid Biophysics 1"
- **A. Alonso** "Imaging phospholipase C/sphingomyelinase activity in vesicles containing coexisting ordered-disordered and gel-fluid domains"

Wroclaw, Poland, 5-7 August 2009

The fifth International Symposium on two-dimensional correlation spectroscopy (2DCOS5)

- **J.L.R. Arrondo*. "***Kinetics of fibril formation. An infrared 2DCOS study"

Palermo, Italy, 28 August - 2 September, 2009

XIII ECSBM

- **J.L.R. Arrondo *"***A 2DCOS study of the effect of radiation on tgase activity".

Bogotá, Colombia. 8-11 October 2009

Columbinan network of research incubators (RedColsi), "XII Encuentro Nacional y VI Internacional de Semilleros" Agustiniana University

- **D.M.A. Guérin.** "Formación de los investigadores en las universidades españolas en el contexto internacional: Un ejemplo relacionado con la enfermedad de Chagas"

Lake Balaton, Hungary, 18-23 October. 2009.
Workshop Systems Chemistry II: Evolution and Systems

- **K. Ruiz-Mirazo** "On the lipid-peptide minimal cell scenario"

Calgary, Canada, 11 December 2009
IBI Seminars. Institute for Biocomplexity and Informatics (Univ. Calgary)

- **K. Ruiz-Mirazo** "Modeling infra-biological systems: stochastic simulations of self-reproducing proto-cells"

Communications at Conferences

Various different members of the Biophysics Unit have presented communications at conferences, 40 at international and 11 at national events, among which we should highlight contributions at the 53rd Annual Meeting of the Biophysical Society, Boston, Massachusetts (USA), and the XXXII Congress of the Spanish Society for Biochemistry and Molecular Biology, SEBBM held in Oviedo, Spain.

Courses

"Técnicas de campo y de Laboratorio para la detección, aislamiento, identificación y caracterización molecular del virus TrV en triatominos del Perú" was organised and taught by **D.M. Guérin** at the Faculty of Biological Sciences, Pedro Ruíz Gallo National University, Lambayeque, Peru from 12 to 16 October 2009.

"Técnicas de laboratorio para la identificación, aislamiento y determinación de la infectividad en triatominos del virus TrV" was organised and taught by **D.M. Guérin** at the Faculty of Veterinary Sciences, National University of La Plata, La Plata, Argentina from 19 to 23 October, 2009.

Science Communication

The 2009 Health and Nutrition Series (*Nutrición y Salud)* organised by the BBVA Foundation and CIC bioGUNE in collaboration with the Biophysics Unit, UPV/EHU, the British Council, the Regional Government of Biscay and the Government of the Basque Country.

Bilbao, 5-25 February 2009

Celebrating Evolution – the 200th anniversary of the birth of Charles Darwin

- **Pilar Carbonero** "Evolución bajo dominio humano en el reino vegetal" **Chair**:
- **F.M. Goñi**

Donostia-San Sebastián, 28-30 September 2009

ATOM by ATOM into nanoscience

- **F.M. Goñi** "Lipidic nanoparticles: fat is beautiful"

Bilbao, 14-18 December 2009

Science Week 2009 in Miguel de Unamuno Secondary School.

- **F.M. Goñi** "Gripe A y enfermedades 'nuevas'"

A. Alonso has continued to be the organiser for the second series of BioForums (*BioForo*) through 2009 with participation of the following researchers:

- ***Francisco José Ayala*** *(University of California. Irvine, California)*
- ***Oriol Bachs*** *(University of Barcelona, Barcelona)*
- ***Mª Isabel Geli*** *(Molecular Biology Institute of Barcelona (IBMB), Barcelona)*
- ***Daniel Müller*** *(Biotechnology Center, Dresden University of Technology, Dresden, Germany)*
- ***José López Barneo*** *(Seville Biomedical Research Institute (IBIS), Virgen del Rocio University Hospital, CSIC, University of Sevilla, Sevilla)*
- ***Jesús Gil*** *(Cell Proliferation Group, MRC Clinical Sciences Centre, Faculty of Medicine, Imperial College, London, United Kingdom)*
- ***Teresa Giráldez Fernández*** *(Nuestra Señora de Candelaria University Hospital HUNSC, Tenerife)*
- ***Jose Rizo-Rey*** *(Department of Biochemistry University of Texas Southwestern Medical Center, Dallas, Texas)*
- ***Bernat Crosas*** *(Molecular Biology Institute of Barcelona (IBMB), Barcelona)*
- ***Gustavo Aguirre*** *(Faculty of Medicine, University of Philadelphia, USA)*
- ***William R. Gallaher*** *(Department of Microbiology, Immunology and Parasitology, Lousiana State University. Health Sciences Center, New Orlean,s USA)*
- ***Francisco Bezanilla*** *(University of Chicago. Emeritus Professor Dept. of Physiology, UCLA, CA, USA)*

- ***Francisco Real*** *(Spanish National Cancer Research Centre, Madrid)*
- ***Joan Seoane*** *(Institut de Reserca, Vall d´Hebrón Hospital)*
- ***Juan Carlos Lacal*** *("Alberto Sols" Biomedical Research Institute, Madrid)*
- ***Eduardo Díaz-Rubio*** *(San Carlos Clinical Hospital, Madrid)*
- ***Manel Esteller*** *(The Bellvitge Institute for Biomedical Research, Barcelona)*

The *Bioforo* activities included this year the special Workshop on "Advances in cancer research and treatment", held on December 15, 2009 at the *Facultad de Ciencia y Tecnología* (UPV/EHU).

Governing Bodies and Academic Committees

I. Alkorta became Vice-Dean of the *Facultad de Ciencia y Tecnología*, in charge of Communication, Image and Interactions with Society.

J.L. Nieva continued to serve as Director of the Department of Biochemistry and Molecular Biology.

H. Ostolaza continued to serve as the Secretary of the Department of Biochemistry and Molecular Biology.

J.L. R. Arrondo continued to serve as a Member of the UPV/EHU University Research Committee.

A. Muga continued to serve as Coordinator of the Degree in Biochemistry.

F.M. Goñi stepped down as Coordinator of the Master in Molecular Biology and Biomedicine (MBMB) and was appointed to the office of Doctoral Programme Coordinator in Molecular Biology and Biomedicine.

A. Alonso continued serving as President of the Commission for setting up the new Degree in Biochemistry and Molecular Biology (June 2008-).

A. Alonso was appointed as a Member of the Commission for Teaching Evaluation of the Spanish National Evaluation Agency ANECA in the area of Health (April 2009-).

I. Alkorta continued to serve as a Member of the Academic Affairs and of the Academic Exchange Committees of the Facultad de Ciencia y Tecnología.

Scientific Societies

F.M. Goñi continued to serve as the President of the FEBS Publications Committee.

A. Alonso continued to serve as the President of the Spanish Society of Biophysics.

A. Alonso and J.L. R. Arrondo continued to serve as members of the Spanish Committee of the International Union of Pure and Applied Biophysics (IUPAB).

A. Alonso continued to serve as a member of the Executive Committee of the International Union for Pure and Applied Biophysics (IUPAB). http://iupab.org/about/officers-and-council/

Scientific Journals

F.M. Goñi continued to serve as a member of the Editorial Advisory Board of the *Journal of Chemical Biology,* a journal published by Springer.

A. Alonso continued to serve as a member of the Editorial Committee of *Biochimica et Biophysica Acta-Biomembranes* and of *Biophysical Reviews.*

Other Activities

"Iñigo Álvarez de Toledo" Awards

F.M. Goñi was a member of the Evaluation Committee for Fundamental Research of the Iñigo Alvarez de Toledo Renal Foundation**.** (18 September 2009).

Novia Salcedo Foundation
F.M. Goñi is a member of its Governing Board and Working Committee**.**

Prize for outstanding thesis
J. Sot Sanz and **M. Lorizate Nogales** received this award in 2009.

European Science Foundation.
F.M. Goñi was appointed to serve as a member of the ESF Pool of Reviewers of the European Science Foundation.

Department of Innovation Science and Business

F.M. Goñi was appointed evaluator of international scientific and technical projects by the Agency for Quality Assurance in Higher Education and Research of Andalusia (Department of Innovation, Science and Business).

Irun 2020 Strategic Plan

F.M. Goñi collaborated in work carried out under the framework of the Irun 2020 Strategic Plan for the Irun City Council**.**Irun 2020 Strategic Plan

Visitors (2009)

Dr. **Arne Elofsson** from the Stockholm Bioinformatics Center, Stockholm University, Sweden, visited in January and February 2009.

Gabriel Piedrafita, of the Complutense University of Madrid, stays with us for short periods of time several times a year to carry out research in our laboratories.

During brief visits, the following researchers gave seminars:

José Abad Rodríguez (National Hospital for Paraplegics, Toledo, Spain)

Sandra B. Gabelly (John Hopkins University, Baltimore, USA)

Abelardo M. Silva (Structural Biology, Sequoia Pharmaceuticals, Gaithersburg, MD, USA)

Marcelo Guerin (Department of Microbiology, Immunology and Pathology, Colorado State University, USA)

Hugo Mónaco (Department of Biotechnology, University of Verona, Italy)

Werner Mäntele (Institute for Biophysics, University of Frankfurt, Germany)

Alberto Bokos (Innobasque, Zamudio, Biscay, Spain)

William R. Gallaher (Department of Microbiology, Immunology and Parasitology, Louisiana State University Health Sciences Center, New Orleans, USA)

Francisco Bezanilla (University of Chicago, Illinois, USA)

Funding

In 2009, the Biophysics Unit received funding from the following institutions (listed alphabetically).

- Areces Foundation
- European Union
- Government of the Basque Country (Department of Education, Universities and Research)
- Government of the Basque Country (Department of Industry, Commerce and Tourism)
- Ministry of Science and Innovation
- Regional Government of Biscay (*Diputación Foral de Bizkaia*, Department of Innovation and Economic Promotion)
- University of the Basque Country

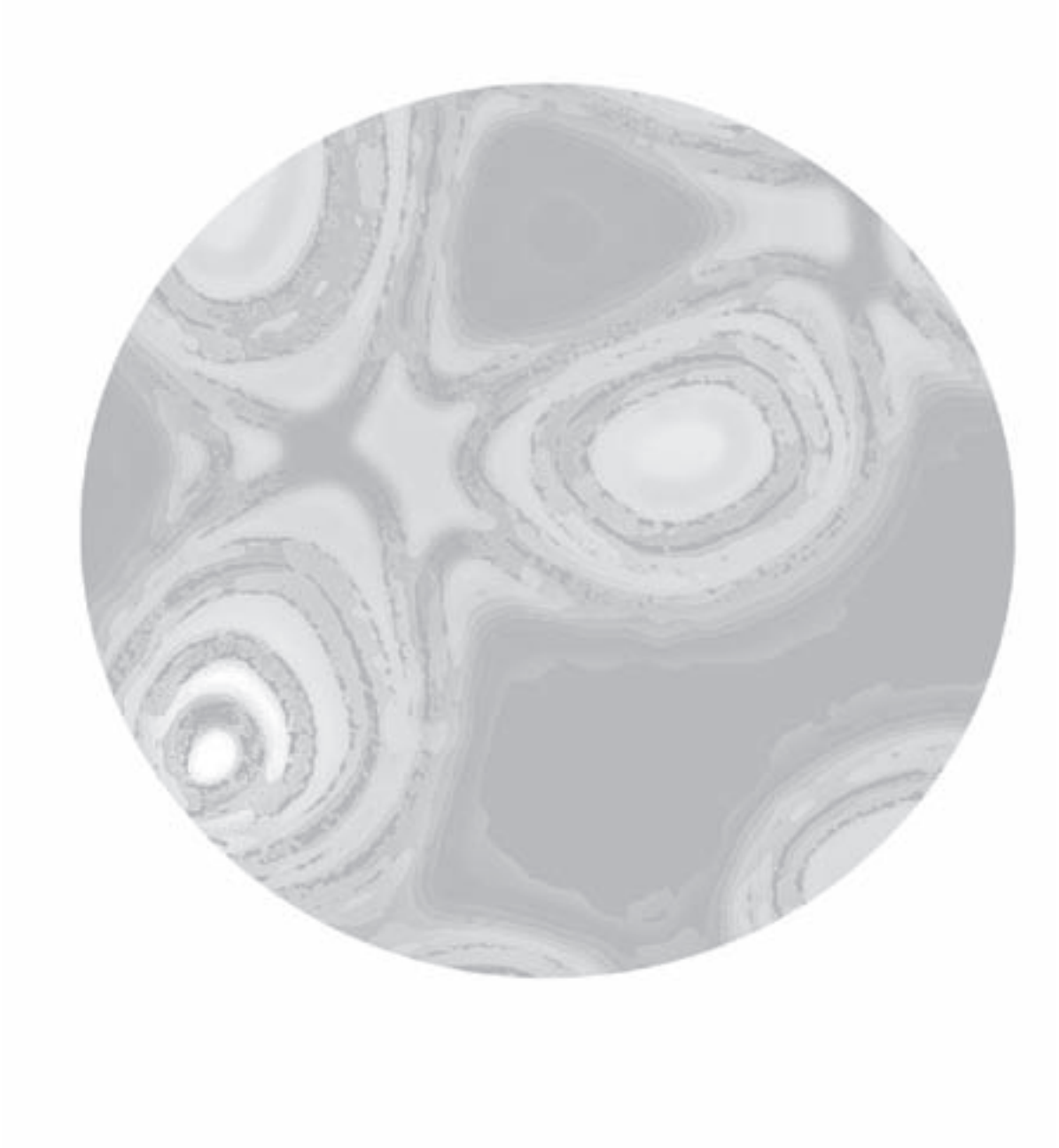
The Unit wish to thank to all of these backers for their generous funding and ongoing support.

PhD Theses from the Biophysics Unit.

(Until 1999, Biomembrane Group of the Department of Biochemistry, UPV/EHU)

- José Ignacio García Gurtubay (1979)
- Alicia Alonso Izquierdo (1981)
- Mª Carmen Barbero (1981)
- Mª Angeles Urbaneja Arrúe (1984)
- José María Valpuesta Moralejo (1985)
- Arturo Muga Villate (1988)
- Juan Manuel González Mañas (1989)
- María Aránzazu Partearroyo (1989)
- José Luis Nieva Escandón (1991)
- Ana Rosa Viguera Rincón (1992)
- José Castresana Villamor (1992)
- Helena Ostolaza Echabe (1992)
- Sonia Bañuelos Rodríguez (1995)
- Mª Asunción Requero Zabala (1995)
- Gorka Basañez Asua (1996)
- Fernando Moro (1996)
- Ana Soloaga Villoch (1997)
- Susana Rivas Cacho (1997)
- Izaskun Echabe Pérez (1997)
- Francisca Pereira Rios (1997)

- Mª Begoña Ruiz-Argüello (1998)
- José Manuel Martínez Caaveiro (1999)
- Mª Pilar Veiga Alameda (1999)
- Ana V. Villar Ramos (2000)
- Tatiana Suárez Cortés (2000)
- Asier Sáez Cirión (2001)
- Aitor Hierro Ayuela (2002)
- Aitziber López Cortajarena (2002)
- Aitziber Agirre Ruiz de Arkaute (2003)
- Asier Galán Cousillas (2003)
- Ion Gutiérrez Aguirre (2003)
- Itsaso Hormaeche Berciano (2003)
- Begoña Sot Sanz (2003)
- Ibon Iloro Manzano (2004)
- Xabier Coto Revuelta (2004)
- Jesús Sot Sanz (2005)
- Ruth Montes Burgos (2005)
- Vanesa Fernández Sáiz (2006)
- Isbaal Ramos Hernández (2006)
- Maier Lorizate Nogales (2006)
- Francesc-Xabier Contreras Gómez (2006)
- Silvia Sánchez Martínez (2007)
- Lissete Sánchez Magraner (2007)
- Marcos García Pacios (2007)
- Oihana Terrones Urio (2007)
- Aintzane Cabo Bilbao (2008)
- José Ángel Fernández Higuero (2008)
- Paloma Aivar Mateo (2008)
- Sergio Pérez Acebrón (2008)
- Nerea Huarte Arrayago (2008)
- Aitor Etxebarria Gallego (2009)
- David López Jiménez (2009)
- Patricia Urbina Fernández (2009)
- Jon Agirre Hernández (2009)
- Geraxane Gómez Bilbao (2009)
- Ariel E. Mechaly García (2009)
- Maitane Ibarguren Aizpitarte (2009)
- Igor de la Arada Etxebarria (2009)
- Ana Julia Vecino Ortega (2009)
- Jon Busto Vega (2009)



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