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FROM PHYSICS TO BIOLOGY

851
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FROM PHYSICS TO BIOLOGY

The Interface between Experiment and Computation

BIFI 2006 II International Congress

Zaragoza, Spain 8 – 11 February 2006

EDITORS
Jesús Clemente-Gallardo
Yamir Moreno
José Félix Sáenz Lorenzo
Adrián Velázquez-Campoy

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FROM PHYSICS TO BIOLOGY


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II INTERNATIONAL CONGRESS

From Physics to Biology:

The Interface between Experiment and Computation

ZARAGOZA, SPAIN
FEBRUARY 8-11, 2006.

INVITED SPEAKERS

- M. Amzel (Johns Hopkins, *USA*)
- C. Cavasotto (Molsoft LLC, *USA*)
- S. Cocco (Ecole Normale Supérieure, *France*)
- E. Freire (Johns Hopkins, *USA* and BIFI)
- M. Karplus (Strasbourg and Harvard, *USA*)
- S. Leibler (Rockefeller, *USA*)
- A. Perczel (Eotvos, *Hungary*)
- A. Tramontano (La Sapienza, *Italy*)
- G. Waksman (Institute of Structural Molecular Biology, *UK*)
- M. E. Wall (Los Alamos National Laboratory, *USA*)
- E. Westhof (Strasbourg, *France*)

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UNIVERSIDAD DE ZARAGOZA

INSTITUTE FOR BIOCOMPUTATION AND PHYSICS OF COMPLEX SYSTEMS.

The Organizing Committee promotes a call for contributions. There will be 11 invited lectures and around 16 short oral contributions to be selected among those presented as a poster when they are best suited for a talk. Please see the web page of the conference for instructions and further information.

http://bifi.unizar.es

IMPORTANT DATES

Deadlines:
Early registration:
October 15, 2005

Last day to complete registration:
November 15, 2005

Poster abstract submission:
January 5, 2006.

MORE INFORMATION:
http://bifi.unizar.es

Dates and venue:
February 8 - 11 2006
Auditorium of Zaragoza

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University of Zaragoza, Spain

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Foreword

Just a few lines as Director of the BIFI to thank all the participants of the Second International Conference BIFI2006 “From Physics to Biology: the interface between experiment and computation”.

One of the main aims of our Institute is the interdisciplinary collaboration of chemists, physicists and biologists, of theoreticians and experimentalists. With this goal in mind we organize an International Conference every two years, in this occasion on the interface of Physics and Biology.

The Conference of this year has accomplished most of its goals, first with the excellent interventions of the Invited speakers, whom I would like to thank for their help and for having made easier our task as organizers. I would like also to thanks the rest of participants for their great presentations and the enlightening debates which followed both the oral communications and the poster sessions. All this together ensured the scientific success of the Conference. Let this volume be a humble tribute to all the participants, for their interest and their search for knowledge.

Finally I also want to thank the members of the Institute who generously offered their efforts and time to organize this event: theirs is a major part of the success of the Conference.

José Felix Sáenz Lorenzo
Director of BIFI

Preface

During the last several years, molecular and cell biology have attracted the attention of both biologists and physicists and they have moved from the study of individual components toward the modeling and understanding of many interacting components. On the other hand, the complexity of biomolecules and their collective behavior make necessary the interaction between those researchers devoted to experimental and theoretical studies. The aim of the BIFI2006 Conference was therefore to bring together researchers working at the interface between Physics and Biology from both the theoretical and experimental point of views. It was held by the Institute of Biocomputation and Complex Systems Physics (BIFI), at the University of Zaragoza, Spain. There were three main topics at the conference: Nucleic Acids, Proteins and Peptides, and Collective Behavior of Biomolecules. Specifically, the subjects covered included:

- Mechanical properties of DNA and RNA: unzipping and stretching of single molecules.
- Structure and folding of RNA.
- Non canonical forms of DNA.
- Docking of virtual ligand libraries containing millions of molecules.
- Conformational flexibility and ligand docking.
- Energy landscapes and ligand binding.
- Protein-protein interactions: the interactome.
- Signal networks and disease.
- Macromolecule folding with emphasis in structure prediction.
- Biomolecular interactions and their analysis with theoretical/computational approaches of relevance for ligand and drug design.
- Studies into the collective behavior of interacting biomolecules and the modeling of biological networks.
- Self -assembly of DNA structures and proteins.
- Cell Signaling.
- Ab initio and DFT molecular computations.
- Disordered systems and molecular and neural networks.
- Solvation energy.
- Energy functions.

The Conference attracted more than 120 scientists coming from many different countries and ran over 4 days. The list of invited speakers included leading scientists from all over the world: M. Amzel (Johns Hopkins University), C. Cavasotto (Molsoft LLC), S. Cocco (Ecole Normale Supérieure, Paris), E. Freire (Johns Hopkins University and BIFI), M. Karplus (Strasbourg and Harvard Universities), S. Leibler (Rockefeller University), A. Perczel (Eötvos University), A. Tramontano (University of Rome), G. Waksman (Institute of Structural Molecular Biology, UK), M.E. Wall (Los Alamos National Laboratory), and E. Westhof (Strasbourg University). They all

gave lectures where the main directions of the aforementioned subjects were reviewed as well as outlined current trends in biological experimentation and theoretical and numerical modeling.

The present issue of the AIP Conference Proceedings aims to provide a glimpse of what kind of works were discussed during the Conference.

Cavelier & Amzel describe a computational study, using a combination of Quantum Mechanics and Molecular Mechanics, intended to elucidate the electron transfer mechanism catalyzed by the redox enzyme quinone reductase, emphasizing the critical role of dynamics and fluctuations. Wall contributes with a manuscript that is at the forefront of current theoretical research in the subjects of ligand binding, protein fluctuations and allosteric free energy. Cavasotto contributes with a very well-taken manuscript where the current knowledge and the last developments in virtual screening are thoroughly explained, pointing out also the strong and weak points. Cocco & Monasson present the modeling and characterization of mechanical unzipping of single nucleic acid and the effect of the nucleotide sequence; by simulating the experimental output, they explain how to approach the inverse problem: how to predict the sequence from the monitored signal. Giorgetti et al. review some of the current challenges in protein structure prediction.

Junier et al. shortly review the protein folding problem in small proteins in a work that may represent a good introduction to the beginners in the field and goes over different techniques, both experimental and theoretical, with emphasis in single molecule experiments; state of the art of models (at different length scales) as well as numerical work (mostly simulations) done on them are also addressed. Tortosa & Jaramillo have made an effort to communicate in a short contribution several technical aspects on computational protein design, in particular, the design of active sites into protein scaffolds which can be validated experimentally. The benefits from the interaction of biologists and physicists is illustrated in the work presented by Danenberg, who studies different energetic strengths and cooperativity of H-bonds in peptides by means of a technique borrowed from the physical sciences, namely, Density Functional Theory. Along the same lines, Echenique et al. analyze the effects of constraints in the conformational equilibrium distribution of peptides through quantum mechanical calculations, the definition of an appropriate set of internal coordinates for branched molecules, and a statistical measure of differences between different levels of potential energy approximations. Zaman performs a multiscale modeling of cell migration landscapes at various length and time scales. Sanchez-Ruiz presents a summary of some new visions on protein folding thermodynamics constructed from experimental evidences of downhill protein folding, focusing on deviations from the classical two-state behavior that are not due to intermediates, but to very low, or even absent barriers.

Hernandez et al. present a summary of recent findings on a very interesting and appealing issue: the complex regulatory mechanism of a protein, FurA, involved in iron regulation; the experimental methodology and tools, as well as open questions, are pointed out. A simple elastic model, the Gaussian Network Model, is used as a tool to study the differential looseness of different regions of the apoflavodoxin protein by

Bruscolini et al.; the model, upon introduction of the possibility of breaking contacts, is capable of reproducing the thermodynamics of the unfolding process, in particular, the presence of an intermediate during thermal unfolding. Moreno et al. review several topological and dynamical aspects of recent studies concerning the highly topical subject of biological networks at both molecular and cellular levels. Velázquez-Campoy describes the implementation of the McGhee-von Hippel theory for ligand binding to linear macromolecules with overlapping binding sites in isothermal titration calorimetry. Gracia et al. pay attention to ligand docking with consideration of the target flexibility at the side-chain and backbone level making use of NMR solution structures that would represent the different conformations adopted by the target. Schubert et al. report in a detailed and clear contribution a phylogenetic analysis of FAD synthetase aimed to identify key residues essential for substrate binding and catalysis. Samsonov et al. reports on the expression of the Ctr1 gene in specific tissues and propose an in silico model of the protein produced by this gene. Basdevant et al. deal with a model of solvation at an intermediate level between implicit and explicit methods. Finally, the characterization of the interaction between protein and metal ions, employing thermodynamic and structural tools and techniques, and the physiologic role of metal in regulating the function of the DtxR repressor are addressed by D'Aquino and Ringe.

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We would like to acknowledge all the sponsors of the Conference, and in particular, to *Universidad de Zaragoza*, *Diputación General de Aragón*, *IberCaja*, *Ministerio de Educación y Ciencia*, and *Megware Computer GmbH*. Heartfelt thanks also go to the Organizing Committee (specially to José L. Alonso), to all invited speakers that generously accepted our invitation, to the participants for sharing their results and for creating a scientifically rich environment and to the conference secretaries (Conchita Carbó, Mercedes Fatás and Isabel Vidal) whose hard work and efforts made possible this successful meeting.

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