

Physical Principles of Protein Behavior in the Cell

Proteins are involved in essentially all of the biochemical reactions that take place in living organisms, including those required for the control of gene expression, metabolism, transport, and enzymatic catalysis. The mechanisms of protein regulation are being elucidated at an increasing pace, and many advances have been made in our understanding of how protein concentrations, localizations, and interactions are controlled within living cells. The introduction of novel, experimental, high-throughput techniques and of theoretical analysis methods has enabled the initial study of the networks of interacting molecules. These molecules function in myriad biological pathways through which cells maintain homeostasis and promote development.

An upcoming meeting, "Physical Principles of Protein Behavior in the Cell" (PhPPBC09), at the Max Planck Institute for the Physics of Complex Systems in Dresden, Germany (October 26–30, 2009; www.pks.mpg.de/~phppbc09/), will bring together researchers from the major areas that are relevant to understanding protein behavior in the cell, including protein expression, localization, function, folding, misfolding, and aggregation. Synergies among experimental, theoretical, computational, and statistical approaches are anticipated to lead to results on two main fronts: to improve our understanding of the physicochemical basis of protein behavior, and to suggest new methods for predicting and modulating it. Achieving these synergies will help provide an integrated view of the subject, and this workshop will stimulate such developments by exploring the connections between different fields and by providing a suitable framework for exchanging ideas and methods. The primary aim of the PhPPBC09 meeting will be to probe in depth the idea that further understanding of the physical principles that underlie protein behavior in the cell can greatly improve existing methods for characterizing and predicting structures, interactions, and functions of proteins; for modeling their evolution; and, ultimately, for suggesting new rational approaches for treating human diseases.

Galileo, one of the first modern scientists, suggested that the laws of nature are "written in the language of mathematics". This perspective has enabled tremendous progress to be made, particularly in physics and chemistry, and we are now beginning to extend it to formulate the mathematical laws that define the behavior of molecules and cells. Approaches in which *in vivo* biochemical reactions are described by systems of coupled differential equations are revealing a modular architecture and

a network organization. These insights enable researchers to carry out quantitative analyses on the factors that influence how an organism responds to environmental variations. A rather detailed characterization, for example, has already been provided about the way in which bacterial chemotaxis is orchestrated through a specific set of coupled biochemical reactions. Another example is the understanding of how molecular chaperones are tightly regulated to respond to stress conditions.

Physical approaches are also enabling advances to be made through the development of bioinformatics methods for the analysis of the vast amounts of data that are being generated at the genomic and proteomic levels. These types of analyses are revealing the hidden relationships between the various components of cellular machines and providing a way to start unraveling the tremendous complexity of the organization of the cell. Increasingly, researchers are recognizing that quantitative predictions of protein behavior may be made on the basis of the physicochemical properties of the amino acid components of proteins. For example, links have been revealed between the electrostatic charge and the hydrophobicity of polypeptide chains and their propensity to form some of the toxic aggregates associated with neurological disorders, such as Alzheimer's and Parkinson's diseases. Investigators also are determining how these same properties are related to protein concentration and expression, thus, revealing links between different aspects of protein behavior in the cell.

All of these themes will be discussed at the upcoming PhPPBC09 meeting, which is envisaged to bring to light even more connections between physics and biology. We expect that these developments will enable quantitative approaches to be formulated to increase our ability to understand and modulate the biochemical reactions taking place in the cell.

MARKUS PORTO

*Institut für Festkörperphysik, Technische Universität
 Darmstadt (Germany)*

H. EDUARDO ROMAN

Dipartimento di Fisica, Università di Milano-Bicocca (Italy)

MICHELE VENDRUSCOLO

Department of Chemistry, University of Cambridge (U.K.)