Roumen Tsanev Plenary Lecture

Biomathematical Approaches in Protein Studies

Nevena Ilieva

Institute of Information and Communication Technologies
Bulgarian Academy of Sciences, Sofia
nevena.ilieva@parallel.bas.bg

Roumen Tsanev was the founder of molecular biology research in Bulgaria. Among his many achievements is the creation of gene-engineered human interferon-gamma. With our contributions to recent developments in the study and modulation of the activity of this important biomolecule by means of modern biomathematical approaches we also pay tribute to this outstanding scientist for pioneering biomathematics and bioinformatics research in Bulgaria with one of the first mathematical models of cell differentiation in the early 70es of the 20th century, together with Blagovest Sendov another renowned Bulgarian scientist.

Problems in model studies of biological molecules and complexes result from the size of the systems on the one hand (a large number of elements – atoms or atomic complexes in the picometer range) and the time scale of the running processes– from femtoseconds to hours and even days on the other. Due to the nature of interactions in which biomolecules are involved (short as well as long-range interactions), simply increasing the computing power of modern supercomputers is not enough to solve them. Efforts are concentrated on the development of enhanced phase-space sampling methods or alternative (coarse-grained in one sense or another) representations of the studied systems, but foremost on expanding the boundaries of the existing modeling techniques through synergetic protocols of complementary approaches. The aim is to create multilevel multiscale approaches to understanding biomolecular structure and dynamics [1] for modeling of natural biological molecules [2, 3], as well as for design and analysis of synthetic ones, with predefined features and behavior [4, 5], in the context of mutually supportive interplay between mathematics and biology [6, 7], as one of the pillars of the highly exciting field of mathematical biology.

At the core of all these methods is molecular dynamics a powerful approach for de novo and even ab initio modeling of multiparticle-system dynamics able to provide information on their equilibrium and transport properties often inaccessible to today's experimental technique [8]. This underlies the interpretation of

molecular dynamics simulations as in silico experiments. A variety of biomathematical approaches involving molecular dynamics applications – stand-alone [9], augmented by enhanced sampling techniques [10] or as part of multi-level approaches combining deterministic and stochastic elements [11] – will be presented on examples ranging from investigations of immunoactive biomolecular complexes (human interferon-gamma with its receptors [12] and major histocompatibility complex [13]), through the search for alternatives in case of bacterial multi-resistance (antimicrobial peptides [14]) and to the analysis of the structure and folding of proteins [15]. We shall also address the need for development of new approaches to extract and analyze structural information on proteins from the available data as well as its visualization [16, 17].

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nevena.ilieva@parallel.bas.bg