

Editorial

Biomolecular Systems Interactions, Dynamics, and Allostery: Reflections and New Directions

This issue presents a selection of articles from the Biophysical Society Thematic Meeting held in Istanbul, in September 2015, a meeting co-sponsored by the Biophysical Society, Koc University (Istanbul, Turkey), and the University of Pittsburgh (Pittsburgh, PA). The meeting aimed at bringing together experimental and computational researchers and providing a forum for exchanging views and sharing progress on a fundamental problem spanning multiple scales: mechanistic understanding of biomolecular systems interactions, dynamics, and allostery.

The invited manuscripts submitted in response to the call for articles related to this meeting provide a wide range of information on all aspects of the subject: some emphasize the technical aspects of computational modeling of biomolecular systems and interactions, while others carefully dissect the relationships between often sophisticated biophysical techniques and results, and the models that are designed to rationalize them. The inclusion of allostery in the mix has produced some of the most insightful and thought-provoking contributions, as many authors explore the implications of a modernized view of allostery that takes into account the dynamics and motional aspects of biomolecular interactions. The Eaton laboratory connects experimental results in hemoglobin in single crystals and silica gels to theoretical allosteric models and bridges ideas from one of the first model systems explored in terms of allostery to the latest theories of allostery. A “New & Notable” by Brunori highlights the continuity of these ideas through the evolution of our thinking on allostery. A bioinformatic analysis of the evolution of protein binding sites from the Panchenko lab provides fascinating insights into the ancestry of important protein-protein interactions. The Haliloglu laboratory draws attention to the significant effect of mutations at hinge sites in modulating substrate-binding dynamics. Greger and co-workers show how the clamshell motions at the N-terminal domain of AMPA and NMDA receptors are allosterically coupled to the rearrangements of the ligand-binding and transmembrane domains to impact receptor interactions in a synaptic environment. Walkinshaw, Erman, and co-workers show that binding of fructose 2,6-bisphosphate allosterically traps the pyruvate kinase from *Leishmania mexicana* in its enzymatically

active state. The Perahia lab shows the ability of cyclin/CDKs complexes to switch from active to inactive states upon excitation of the starting conformation along the lowest frequency mode accessible to the complexes. Horovitz and Levy combine experiments and theory to show that the binding of the *Drosophila melanogaster* Engrailed Homeodomain transcription factor to enhanced green fluorescent protein allosterically destabilizes the Engrailed Homeodomain transcription factor, inviting attention to such side effects of GFP tagging commonly used in cell biology.

An emerging trend is to understand the cellular ramifications of molecular interactions as well as their role in disease development. An article from the Nussinov lab addresses important questions about the mechanism of regulation of the Toll-like receptors and illustrates how disease-causing mutations can act to disrupt important protein-protein interactions in the pathways of these receptors. Klein-Seetharaman and co-workers focus on another class of interactions, those between cardiolipin molecules and proteins, toward a systematic characterization of the binding mechanisms and cellular effects of mitochondrial cardiolipin-protein complex formation. Gursoy and colleagues combine structural modeling with in vivo experiments to show how the assembly of glucocorticoid receptors with SWI/SNF chromatin remodeling complex and transcription factor C/EBP may modify transcriptional response. In another fascinating study, Luthey-Schulten and co-workers present the largest simulation of in vivo ribosome biogenesis to date, using a combination of lattice microbe framework and molecular dynamics simulations for *Escherichia coli*. Krishnamurthy and co-workers present a nice example of allosteric modulation of kinase activity detected by H/D exchange mass spectrometry, when a cAMP analog and a phosphodiesterase alter the conformational dynamics of PKA regulatory subunit. The Ozkan lab highlights the role of conformational dynamics and allostery in disease development of human ferritin.

Finally, three perspectives/reviews complete the issue: Janet M. Thornton and co-workers present a review of contemporary thinking on enzyme evolution and draw attention to the promiscuity of many enzymes as well as their evolvability to adapt to new reaction profiles. A perspective from the Bahar lab on the application of elastic network models to protein complexes emphasizes the functional significance of structure-encoded dynamics and suggests future studies on the evolutionary conservation of dynamics.

Submitted August 5, 2015, and accepted for publication August 7, 2015.

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Editor: Leslie Loew.

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0006-3495/15/09/0001/2

<http://dx.doi.org/10.1016/j.bpj.2015.08.005>



Shoshana Wodak and co-workers highlight the structural and mechanistic aspects of intertwined associations in homo-oligomeric proteins, as well as their biological relevance and involvement in disease-related aggregation processes.

As a whole, this special issue of the *Biophysical Journal* contains something for everyone, and well represents the excellence of the contributions to the conference from which it was derived.

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