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COMMENTARY

Overview of the *Biomolecular Association and Dynamics* session at the 20th IUPAB congress, 45th Brazilian congress of SBBF, and the 50th annual meeting of SBBq

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Abstract
In this session, experts in molecular biophysics described the dynamics of biopolymers across a wide range of length and time scales. This discussion highlighted numerous techniques that span from highly detailed simulations, to coarse-grained theoretical models, as well as high-resolution structural analysis. The topics were equally diverse, where there was discussion of biological processes at small (individual atoms), intermediate (assemblies) and very large scales (phase separation).

The ability of biomolecules to reliably associate and dissociate with partner molecules/atoms is central to every aspect of cellular life. For example, these dynamic properties are required for the formation of complex assemblies, binding of substrates during chemical catalysis, signal processing, and gene expression. Within this context, efforts over the last several decades have provided incredible insights into the energetics of these biomolecular processes. The pursuit of theoretical questions has led to the adoption and application of statistical mechanical principles (i.e., energy landscape descriptions). With exponential increases in computational resources, simulation techniques have been pushed to increasing spatial and time scales. Similarly, revolutionary advances in experimental design have enabled time-resolved measures of individual molecules, as well as high-resolution (angstrom-scale) structural insights into large and complex assemblies. In the session "Biomolecular association and dynamics," leading experts in molecular biophysics represented a cross-section of the field, spanning from atomic-level descriptions of ions to large-scale phase separation dynamics (Figure 1). These talks described major achievements of the field, in addition to presenting a range of outstanding challenges.

Dr. Pablo D. Dans (Regional University Center, Uruguay) began his discussion with a historical account of the study of DNA dynamics. His efforts to develop and assess all-atom models for the study of nucleic acids (Dans et al. 2019, 2017) have provided precise descriptions of DNA energetics, which includes the influence of weakly interacting ions. Despite the critical dependence of nucleic acid structure on ionic composition, experimental and theoretical efforts have found it challenging to describe their transient interactions. To this end, Dr. Dans presented simulation-based analysis of the interplay between ions and DNA dynamics. A particularly interesting result was the predicted impact of individual monovalent ions on specific conformational changes in DNA. This finding raises questions about the limits of implicit-ion models, while also providing a concrete example for how ions may contribute to higher-level organization of DNA.

Moving to a larger spatial scale, Dr. Yaakov Levy (Weizmann Institute, Israel) presented his group's pioneering efforts to understand the dynamics of transcription factors (TFs). These proteins are responsible for rapidly "scanning" DNA, in order to find their binding sites (Leven and Levy 2019). Such binding events lead to the eventual expression of our genetic code. The ability of TFs to effectively search a chromosome requires these interactions to be short-lived. Using a range of coarse-grained models developed by his group, Dr. Levy's studies have revealed a range of mechanisms by which the search process may be facilitated. TFs may diffuse along the DNA, or they may hop between regions of DNA that are distant in sequence. This work has also shown how disordered regions can control TF dynamics by allowing for interesting maneuvers, such as the

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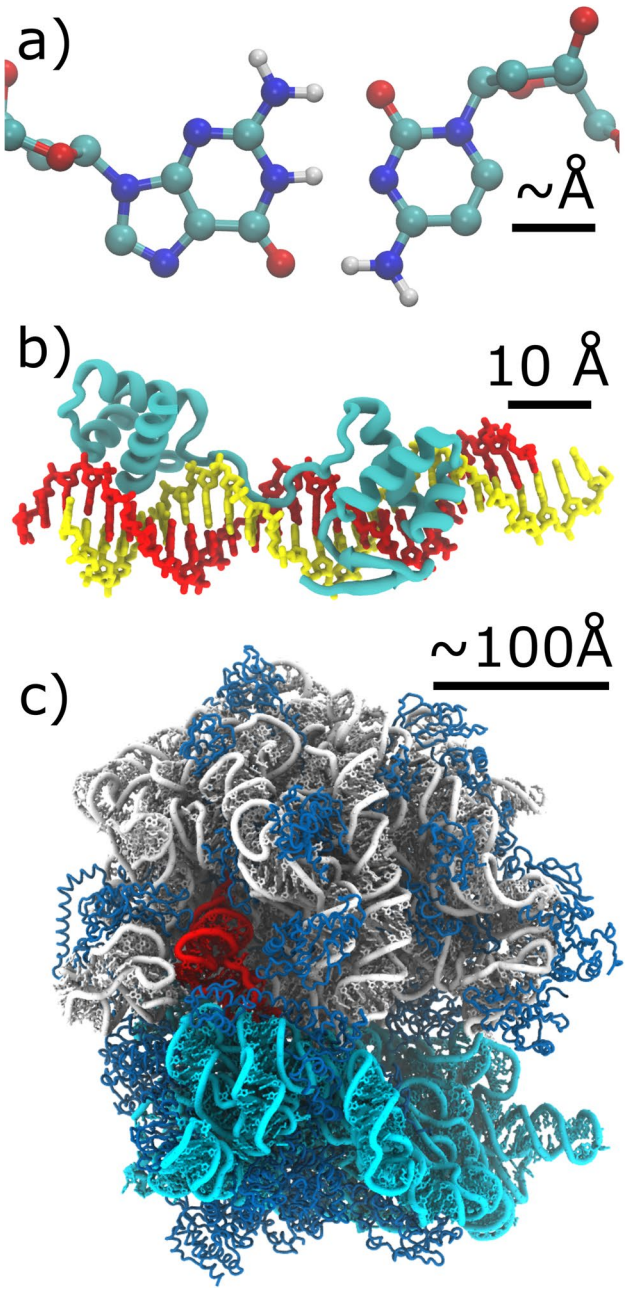

Figure 1: This session highlighted the vast range of biomolecular processes that govern cellular dynamics. Presentations described theoretical and experimental studies of individual DNA bases (panel **a**), interactions between transcription factors and DNA (panel **b**; PDB ID: 6PAX (Xu et al. 1999)), the ribosome (panel **c**; PDB ID: 6wd1 (Loveland et al. 2020)), and larger-scale phase separation dynamics associated with compartmentalization

"monkey-bar mechanism" (Vuzman et al. 2010), where the protein can "swing" between different regions of the DNA.

While transcription factors initiate the process of gene expression, Dr. Andrei Korostelev (UMass Medical School, USA) presented how expression is completed by the ribosome. Since his post-doctoral studies, where he determined some of the early high-resolution crystallographic structures of the ribosome, Dr. Korostelev has continued to push the limits of structural biological techniques. In his presentation, he discussed how recent advances in cryo-EM imaging have allowed for the broad functional landscape of the ribosome to be mapped. In this presentation, he focused on the process by which the ribosome reads and then proofreads an mRNA sequence (Loveland et al. 2020; Loveland et al. 2017). In addition to describing the molecular details of the ribosome, there was also discussion of technological advances that are allowing the experimental community to move towards continuous descriptions of the dynamics. In the coming years, it will be very exciting to see how these descriptions may directly interface with energy-landscape approaches that have been developed within the theoretical community (Levi et al. 2019).

Dr. Hue Sun Chan (University of Toronto, Canada) described the largest-scale dynamics of the session: liquid-liquid phase separation. There is now mounting evidence that these phase-separation processes may allow novel modes of compartmentalization in the cell. That is, rather than separating cellular components solely through the use of membranes, it is thought that liquid-liquid phase separation may be a driving factor. While the experimental evidence of these processes is rapidly accumulating, the principles that govern liquid-liquid phase separation are only beginning to be developed (Das et al. 2020; Pal et al. 2021). In this presentation, Dr. Chan described his group's recent efforts to expand theoretical concepts used in the study of protein folding and function to understand this emerging phenomenon.

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Declarations

Conflict of interest The authors declare no competing interests.

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