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Editorial

The future is predictable: exploring the boundaries of free energy simulations

Chin-Hung Lai*

Department of Medical Applied Chemistry, Chung Shan Medical University, Taichung 40241, Taiwan

* **Correspondence:** Email: chlai125@csmu.edu.tw; Tel: +88642473002212224.

Molecular dynamics (MD) and free energy calculations have profoundly altered our strategies for exploring biological and chemical systems at the atomic scale. These computational approaches present a distinctive lens through which to view processes that are frequently unattainable by experimental observation alone, including the prediction of ligand-protein binding affinities and the study of the dynamics of sophisticated biomachinery.

In our examination of the complexities surrounding molecular interactions, it is evident that the challenges we face extend beyond mere technical obstacles and present opportunities for innovation. The task of sampling rare events, the substantial computational costs associated with simulating biologically relevant timescales, and the limitations of current empirical potentials for non-standard molecules are just a few of the hurdles that researchers must navigate. Moreover, the simulation of large, multi-component systems, such as membrane environments or entire cellular machineries, introduces additional complexities that require the development of novel approaches and methodologies.

This special issue will facilitate readers' understanding of the vigorous advancements and innovative developments in molecular dynamics and free energy calculations. It gathers top experts who will directly address these challenges, shedding light on the pathway to the next generation of simulation methodologies. The discussions will include AI-driven strategies, automated workflows, and cloud computing platforms, all of which are on the verge of transforming the field.

The contributions featured in this special issue clearly demonstrate a domain that is experiencing dynamic and innovative growth. The 'current limits' are not merely being tolerated; instead, they are being dismantled through a wave of methodological progress. As we look ahead, the combination of physics-based models with data-driven artificial intelligence, supported by ever more powerful

computing resources, signals the dawn of a new era in predictive simulation. The effort to make the computation of intricate molecular events as routine as reading a sequence is already underway, with the advancements showcased here laying the groundwork for a deeper comprehension of molecular systems.

Use of generative-AI tools declaration

Grammarly was employed solely for proofreading and enhancing the readability of this editorial. All ideas, and conclusions remain the authors' own work.

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Conflict of interest

The author declare no competing financial interests in this editorial.

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