Exploiting physics-driven molecular evolution in solvation sciences

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Data science technology is rapidly changing the role of information technology in society and all economic sectors. This technology has now also widely impacted the field of molecular sciences. Particularly, the field of drug design and the design of functional materials (e.g.,photovoltaic semiconductors) has widely benefited from the utilization of large data via artificial intelligence (AI) approaches such as machine learning and directed evolution. AI's ability to expertly work with data analytics is the primary reason why artificial intelligence and big data are now seemingly inseparable. However, data-based molecular design becomes severely limited in scenarios where the access to experimental data is technologically not achievable or tractable. Alternative sampling and exploration of chemical or aminoacid space via high throughput molecular simulations enable unique and novel insights into the complex relationships between molecular structure and functionality, and has opened numerous perspectives for the design of novel drug therapeutics as well as functional materials. However, these methods rely on the screening of existing small molecule or peptide data bases consisting of up to several million molecules. Owing to the astronomical dimension of the small molecule universe 10^{60} as well as peptide sequence space 20^{30}, a minute of the available search space is actually being sampled. Therefore, the prevailing mission in the molecular fields is to extend sampling or screening far beyond the direct availability of experimental data. To this aim, we introduced the concept of physics-based molecular evolution: Evolution of molecules is based on the principle that most if not all of the physical driving forces that govern functionality are inherently encoded within the complexity of independently parameterized classical molecular force fields, particularly coarse-grained force-fields. This “a peek into the lab” course will introduce participants to the recently developed evolutionary molecular dynamics methodology [1,2] used to perform simulate molecular evolution as well as its application in solvation science.

[1] Methorst, J., van Hilten, N., & Risselada, H. J. (2021). Inverse design of cholesterol attracting transmembrane helices reveals a paradoxical role of hydrophobic length. *bioRxiv*, 2021-07.
[2] van Hilten, N., Methorst, J., Verwei, N., & Risselada, H. J. (2023). Physics-based generative model of curvature sensing peptides; distinguishing sensors from binders. *Science Advances*, *9*(11), eade8839.

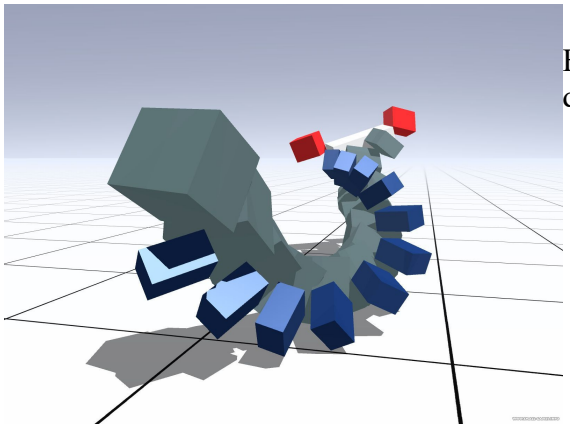

Fig 1. A virtual creature evolved from predefined design rules that are subject to the laws of physics.