Chemists develop 'looking glass' for spotting sound molecular structures

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New York University chemists have developed a computational approach for determining the viability and suitability of complex molecular structures—an advancement that could aid in the development of pharmaceuticals as well as a range of other materials.

"Understanding how molecules interact and achieve stable conformations in different environments is vital to many industries," says Mark Tuckerman, a professor in NYU's Department of Chemistry and the senior author of the study, which appears in the journal *Proceedings of the National Academy of Sciences*. "However, the number of possible configurations is enormous, and the pathways leading to the most stable ones are complex, which makes these favored structures difficult to nail down in computational searches."

"Our results offer an approach that can aid in predicting these optimal structures, providing the potential to enhance the production of everything from over-the-counter drugs to new LED materials," adds Tuckerman, also a professor at NYU's Courant Institute of Mathematical Sciences and the NYU-East China Normal University Center for Computational Chemistry at NYU Shanghai.

Manufacturers need to know how to choose chemical compounds for a given function from a vast space of all possible compounds—dissolving once ingested, and not in the bottle, in the case of pharmaceuticals, or maintaining their form under harsh weather conditions in the case of construction materials.

In order to understand the how best to go about predicting these structures, researchers rely on a construct called the free energy surface, a multidimensional mathematical object that reveals optimal spatial or geometrical configurations of a given system—whether it pertains to pharmaceuticals or computer chips. However, because the molecular constituents of such systems of interest and their interactions are often remarkably complex, elucidating these multi-dimensional free energy surfaces in order to derive the best "molecular answers" has presented significant challenges to scientists.

To help overcome this, the NYU team focused on a particular aspect of free energy surfaces: landmarks, which are considered, chemically and/or structurally, the most important features of these extremely complex, or high-dimensional, surfaces.

Specifically, relying on a computer simulation of free energy surfaces, they developed an algorithm designed to spot these landmarks while "seeing over" the terrain's high dimensionality.

The method, Tuckerman explains, "gives a rendering of a complex terrain that is computationally tractable by generating the most important and useful facets of free energy surfaces. From these facets, we can ultimately determine not only the most favored conformations of the constituent molecules and their spatial arrangements, but also the relative stability of these conformations and the likelihood of random conversions between them."

More information: Locating landmarks on high-dimensional free energy surfaces, Ming Chen, *PNAS*, DOI: 10.1073/pnas.1418241112

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