Title: Development of property-dependent alignment-free spectral fingerprint for predicting molecular properties

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Abstract

Understanding molecular interactions at the molecular surface is fundamental for predicting physicochemical properties in computational chemistry. Three-dimensional quantitative Structure-Activity Relationship (3D-QSAR) predicts the activity or properties of compounds by correlating structural features (such as shape, electrostatics, or hydrophobicity) with experimental/computational data. Traditional 3D-QSAR approaches often rely on alignment-based techniques that are typically based on classical or non-quantum mechanical features. These methods can fail to accurately capture the intricacies of molecular surface shape and surface properties, such as electrostatics, and their influence on intermolecular interactions. In this seminar, we introduce a versatile, property-dependent, and alignment-free spectral method that effectively captures molecular surface features and the distribution of properties across these surfaces, providing a novel descriptor to address key challenges in molecular property prediction.

We demonstrate the success of our method in predicting both computational and experimental hydration-free energies, achieving state-of-the-art accuracy for computational and experimental accuracy for empirical data. Additionally, we highlight the method's capability to detect topological changes in electron density resulting from bond dissociation and to cluster specific protein families based on shared structural and electrostatic characteristics. We will discuss strategies to overcome computational bottlenecks, including GPU acceleration and innovative mathematical approaches, such as information-theoretic fitting for highly accurate atomic densities and spectrum-slicing techniques for efficiently solving high-dimensional eigenvalue problems.