van der Waals Energy Modeling: a Comparative Study of Empirical and Physical Approaches

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Understanding molecular recognition, crystal packing, protein-ligand binding and macromolecular structure all depend on accurate modeling of non-covalent interactions. In this study, we introduce and evaluate two complementary — empirical and physically grounded — for computing exchange-repulsion, and dispersion energies. Once combined, these two terms form van der Waals (vdW) potentials allowing the computation of total vdW interaction energies. A set of 21 atom-type-specific vdW parameters of a buffered 7-14 potential was derived via a least-squares optimization using the SciPy library and implemented in the MoProSuite software[1]. The empirical model yields highly accurate interaction energies, exhibiting a strong correlation (R = 0.990) with reference Symmetry-Adapted Perturbation Theory (SAPT) values from the extensive NENCI-2021 dataset comprising 6,000 diverse small-molecule dimers[2].
The physical model utilizes transferred electron density and anisotropic atomic polarizabilities from the ELMAM2 electron density database[4] to estimate exchange-repulsion and dispersion energies, respectively. The vdW energies determined using the physical model exhibit a significant correlation, R = 0.956, with SAPT data. The physical model further emphasizes the significance of accurate electron density and polarizability parameters for correct vdW interaction estimation, without the need of ad-hoc fitted atomic parameters. Validation against a benchmark of protein side chain–side chain interactions (SSI) confirmed that both models effectively capture key non-covalent interactions in biologically important molecular systems[4].

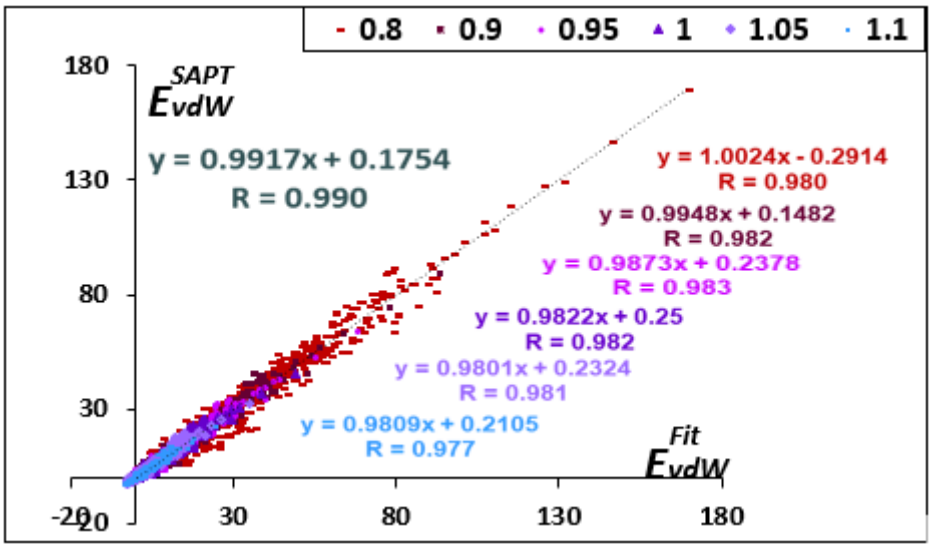

Figure 1: Fitted and SAPT values of empirical Evdw energy for 6,000 diverse small-molecule dimers.

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