# Simultaneous Learning of Static and Dynamic Charges for Biomolecular Interactions

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Electrostatics and long-range interactions play a central role in molecular recognition, solvation, and binding affinity in biomolecular systems, yet remain challenging to model accurately with atomistic machine learning. Static partial charges govern Coulomb interactions that shape protein–ligand binding, while dynamic charges—such as atomic polar tensors—capture polarization and electric response induced by heterogeneous environments, including binding pockets, solvent, and ions.

We compare strategies for learning both static and dynamic charges in a unified machine-learning framework: independent models; coupled learning with or without isotropic dielectric corrections; and coupled learning with environment-dependent screening. While screening corrections are essential in the coupled setting, assuming homogeneous, isotropic screening proves insufficient for heterogeneous biomolecular environments such as solvated clusters and interfacial regions. Learning a local, environment-dependent screening improves the description of dynamic charge response, highlighting the importance of spatially varying dielectric effects for modeling polarization in drug-like and biomolecular systems. However, this added complexity offers limited gains over independent models for static charges while increasing computational cost, underscoring key trade-offs in developing scalable, physically grounded ML models for electrostatics in drug design.