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How Atoms Interact Within Molecules

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Fundamental understanding of interatomic forces in molecules must emerge from quantum mechanics, yet widely used empirical force fields rely on simplified mechanistic approximations that often fail to capture the complexity of many-body systems. Here we employ recent developments in quantum field theory (QFT) for long-range electron correlation and machine learning force fields (MLFFs) to directly compute the depth and scatter of interatomic forces for molecular systems containing hundreds of atoms. We find that while the average interaction strength decays polynomially with interatomic separation, the interaction scatter remains robust and exhibits substantial anisotropy. Both QFT and MLFFs demonstrate that increasing the molecular size further amplifies this scatter and anisotropy – a phenomenon not considered in traditional textbook empirical models. These results provide new benchmarks for force models, shift the focus from interacting atoms to interacting "hotspots" that might determine the folding pathways of (bio)polymers, and rationalize why MLFFs are uniquely successful in capturing the nuances of complex molecular systems. Our findings offer a roadmap for the development of more accurate and quantum-aware molecular force fields.