The Open Force Field Consortium: Executive Summary

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Molecular modeling is widely used in diverse pharmaceutical discovery applications, but its utility and predictive power is limited by the accuracy of the underlying *molecular mechanics force field* used to compute the energetics of biomolecular systems. The *Open Force Field Consortium* (OpenFF) is an open industry-funded pre-competitive effort to build iteratively more accurate force fields to improve predictive design, along with the necessary infrastructure to make these force fields easier to build and use.

Why a new force field? Current molecular mechanics force fields are built on early modeling work largely performed in the 1980s and 1990s, and the software infrastructure for developing, refining, and applying them has remained largely unchanged since. While molecular modeling based on these force fields currently plays a key role in the pharmaceutical discovery pipeline, improved accuracy is needed to more effectively guide pharmaceutical discovery and design and to reduce costs and time to market, and a modern software infrastructure is needed to allow these force fields to be rapidly built, updated, and applied. The OpenFF effort breaks free of constraints imposed by legacy force field efforts while maintaining compatibility with all major molecular simulation packages used in today's workflows. The effort will take advantage of improved theoretical methods, modern maintainable software infrastructure, and vast increases in machine-readable physical property and quantum chemical data to develop new, more accurate, and easily extensible force fields that can be steadily improved to meet the needs of modern pharmaceutical R&D.

Aims: The OpenFF Initiative aims to (1) engineer a modern, open, sustainable, extensible, and well-supported framework for automated force field improvement and application; (2) use this to release rapid iteratively improved versions of an AMBER-compatible small molecule force field we have developed to take advantage of modern cheminformatics; (3) produce entirely new comprehensive force fields that break free of legacy accuracy limitations while maintaining compatibility with existing simulation software, providing dramatically improved accuracy for modeling predictions in diverse applications ranging from predictions of binding affinity, selectivity, and drug resistance, to partitioning, solubility, kinetics, and other properties; and (4) work closely with industry partners to ensure the development path follows that most relevant to R&D needs.

Open source, open data, open science: All software, code, data, and force fields will be open and freely available under Open Source Initiative and Creative Commons approved licenses, providing a foundation for further science beyond the scope and timescale of the formal initiative. Industry partners will be enabled to extend the force fields by adding proprietary data using open tools developed as part of this initiative, or build their own workflows based on these tools providing a pathway to sustainability.

Outlook: The Open Force Field Consortium is an exciting pre-competitive collaboration between academic and industry partners, working to build a shared open infrastructure and ecosystem that will aid discovery.