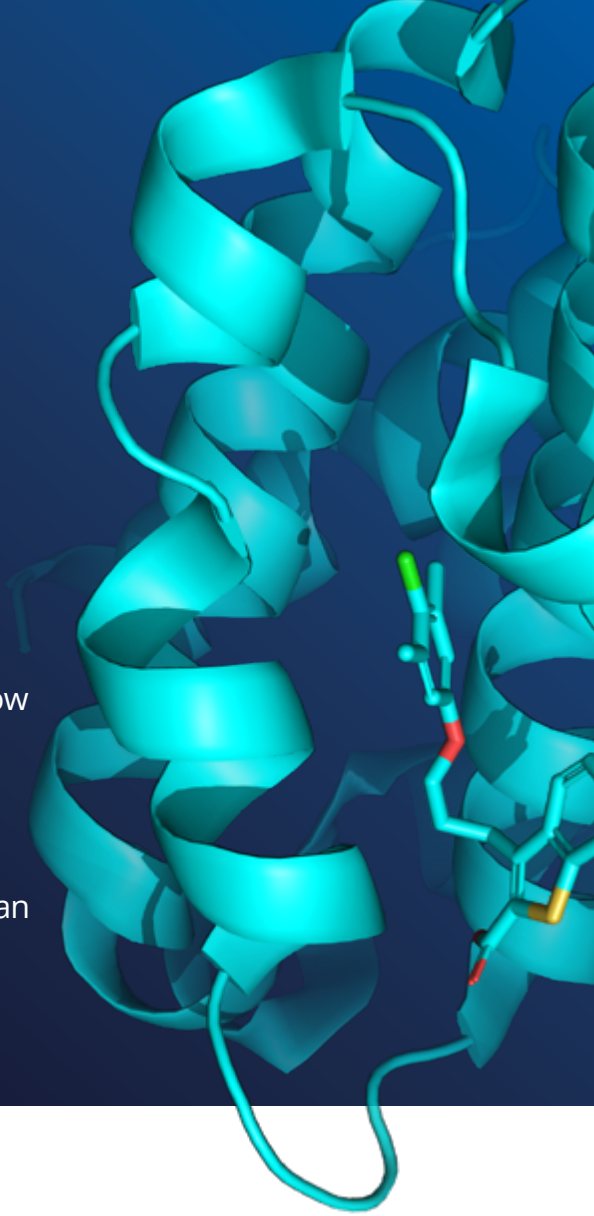
FEP Protocol Builder



Spend more time on your science and less time fine-tuning protocol settings for challenging systems

FEP Protocol Builder is an automated machine learning workflow for FEP+ model optimization. This workflow is designed for systems with insufficient predictive accuracy using default settings or after initial manual protocol optimization attempts. FEP Protocol Builder saves researcher time and increases the chances of successfully enabling FEP+ by efficiently identifying an optimized predictive model for your system of interest.

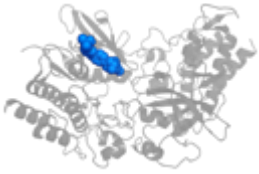
Save time with a fully automated workflow to identify an optimized FEP+ model

Enable FEP+ for challenging targets through efficient exploration of parameter space

Proceed with confidence to use FEP+ prospectively in your program

Schrödinger

Expedite FEP+ use for challenging systems with a fully automated workflow



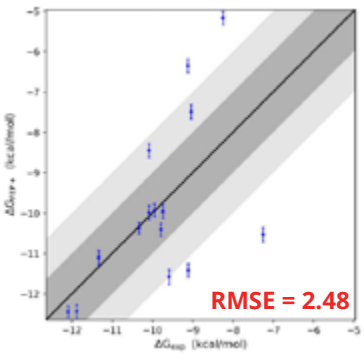
System

Target: RET

X-ray crystal structure

15 congeneric ligands

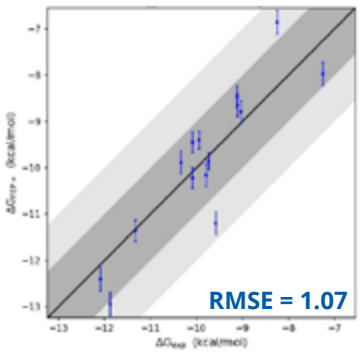
Default Protocol



FEP-PB

Fully Automated FEP-PB Protocol
Run time 7 days on approximately 25 GPUs

Fully Automated FEP-PB



Protocol	ASN879 rotamer	ASP892 charge state	Water model	Reference ligands	REST residues	Pairwise RMSE (kcal/mol)
Default	Flipped	ASP	SPC	4887, 4897	–	2.48
FEP-PB	Not Flipped	ASH	TIP4PD	4898, 4901	A:LEU 772 A:PHE 893	1.07

Fully automated FEP Protocol Builder generated optimized FEP protocol with improved pairwise RMSE compared to default model. All protocols were performed with the same 15 congeneric ligands with modifications at 2 R-groups with known affinity data from PDB ID: 2IVV. FEP Protocol Builder was applied to quickly and rigorously validate the amenability of the target to the Schrödinger platform.

Recommended inputs

- At least one experimental protein-ligand structure or a computationally-generated protein-ligand binding mode hypothesis
- At least 10 congeneric ligands (≥20 preferred) with known affinity data (with a dynamic range of at least 2 to 3 orders of magnitude)

Available as software or a service

Leverage your internal resources or work with Schrödinger's team of experts and large-scale compute power to optimize your next FEP+ model.

CONTACT US

Publications

- FEP Protocol Builder: Optimization of free energy perturbation protocols using active learning. de Oliveira C, et al. *J. Chem. Inf. Model*. 2023, 63, 17, 5592–5603.
- Advancing drug discovery through enhanced free energy calculations. Abel R, et al. *Acc. Chem. Res.* 2017, 50, 7, 1625–1632.

Speak with an expert to get started

Contact us: sales@schrodinger.com
Learn more: https://www.schrodinger.com/platform/products/fep/fep-protocol-builder

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