

Binding Free Energy Redefined: Accurate, Fast and Affordable

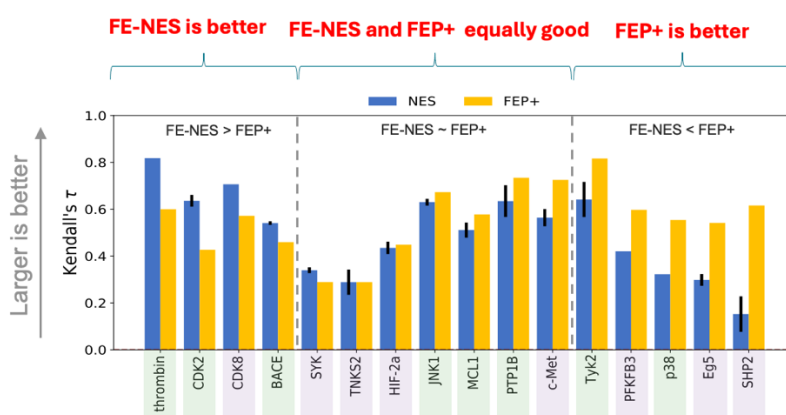
Chris Neale, Gaetano Calabró, Agnes Huang, and Lukas Eberlein

OpenEye, Cadence Molecular Sciences, 9 Bisbee Court Suite D, Santa Fe, NM 87508

Summary:

- Free Energy Nonequilibrium Switching (FE-NES) accurately ranks ligands by their relative binding free energies to accelerate lead optimization.
- Results with up to 10x higher throughput through FE-NES and cloud-scale parallelization.
- Evaluate more analogs and lower compute costs with efficient simulations.

Product Keywords: Orion®, MD, Free Energy Nonequilibrium Switching (FE-NES)



OpenEye's FE-NES delivers market-leading accuracy, though free energy results can vary by system and should be evaluated on a case-by-case basis. Data sets originally curated in [1, 2].

Computational estimation of ligand-protein binding free energies is essential in the lead optimization phase of drug discovery. Industry scientists have reported that OpenEye's Free Energy Nonequilibrium Switching (FE-NES) offers a 5-10X higher throughput and 2-5X more cost-effective alternative to traditional methods like free energy perturbation or thermodynamic integration, which typically require extensive sampling near equilibrium.

Our FE-NES implementation on the Orion® molecular design cloud platform provides automated calculations, even for large ligand sets, in just a few hours.

FE-NES delivers accuracy on par with industry-leading solutions, making it an ideal tool for daily lead optimization tasks.

Users can adjust FE-NES parameters to balance accuracy and throughput, enabling cost-effective ranking of hundreds or thousands of molecules in precise results for lead optimization. With various map types (including efficient star maps and networked OELOMAPs with cycle closure) and an interactive interface, users can leverage their expertise while keeping costs low and accuracy high, ensuring maximum value.

[1] Wang et al., 2015, *J. Am. Chem. Soc.*, 137: 2695.

[2] Schindler et al., 2020, *J. Chem. Inf. Model.*, 60: 5457