Binding Free Energy Redefined: Speed, Economy, and Accuracy

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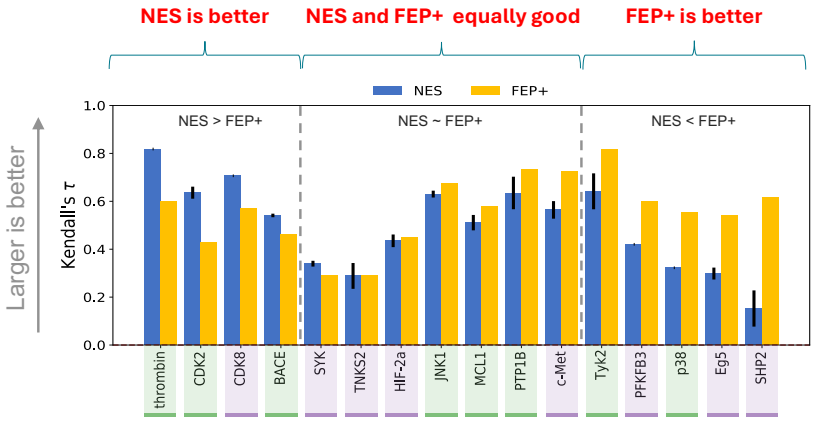
Summary:

- OpenEye Non-Equilibrium Switching (NES) predicts, within hours, ligand affinities with useful rank-order relations
- NES matches market-leading accuracy with superior computational efficiency
- NES evaluates more analogs at a lower computational cost than equilibrium methods

Product Keywords: Orion®, OE Affinity, MD, Non-Equilibrium Switching (NES)



OpenEye's NES matches market-leading accuracy, but free energy calculations vary by system, requiring case-by-case evaluation. 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 for both industry and academia. Industry scientists have reported that Non-Equilibrium Switching (NES) offers a 5-10X faster and 2-5X more cost-effective alternative to traditional methods like free energy perturbation and thermodynamic integration, which typically require extensive sampling near equilibrium.

OpenEye's NES implementation on the Orion® platform provides a ready-to-use solution. This enables automated calculations, even for large ligand sets, in just a few hours. It is an ideal tool for daily lead optimization tasks.

To evaluate free energy prediction accuracy, we use the Kendall's tau rank-order correlation coefficient, which measures how closely predicted results align with experimental data. NES delivers accuracy on par with industry-leading solutions.

Users can adjust NES switches to balance accuracy and throughput, enabling cost-effective ranking of hundreds of molecules or precise results for lead optimization. With various map types (OELOMAP, multi-star map, etc.) 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

Source: OpenEye CUP Presentation, March 2025, Santa Fe

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