

Enhanced Sampling Method for Ligand Unbinding

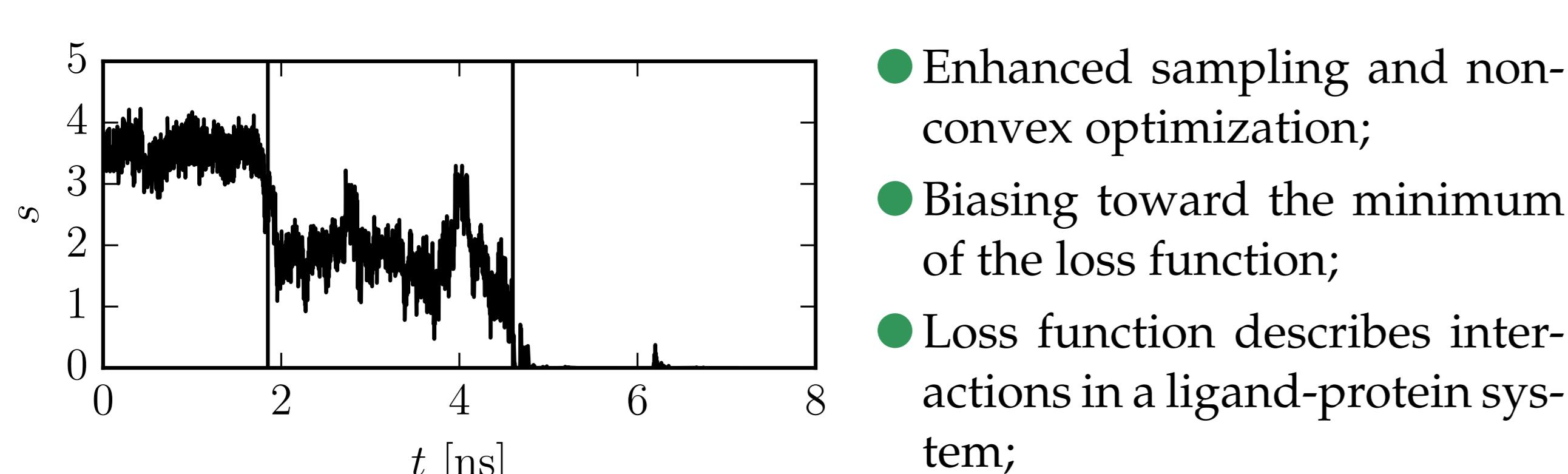
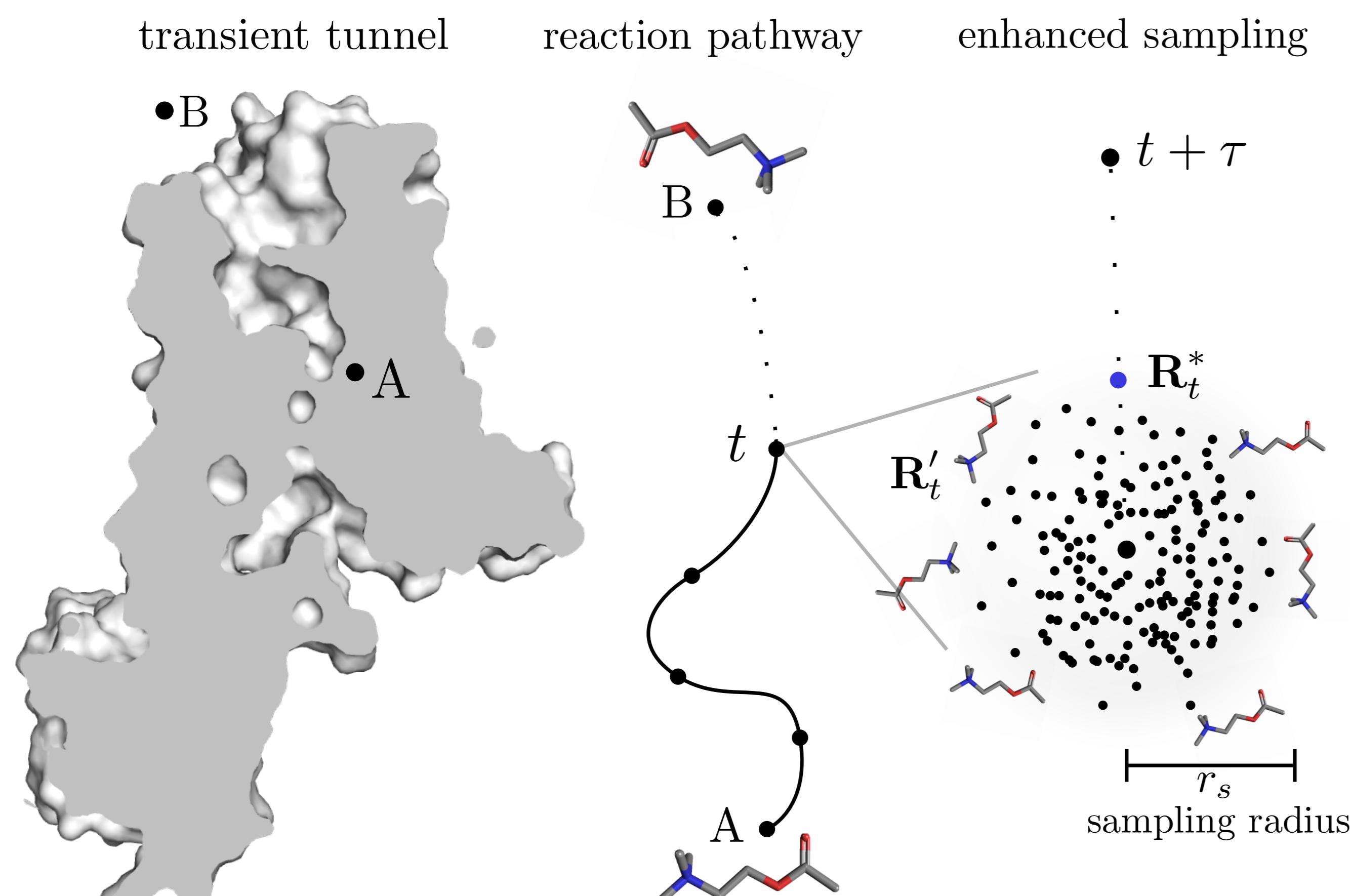
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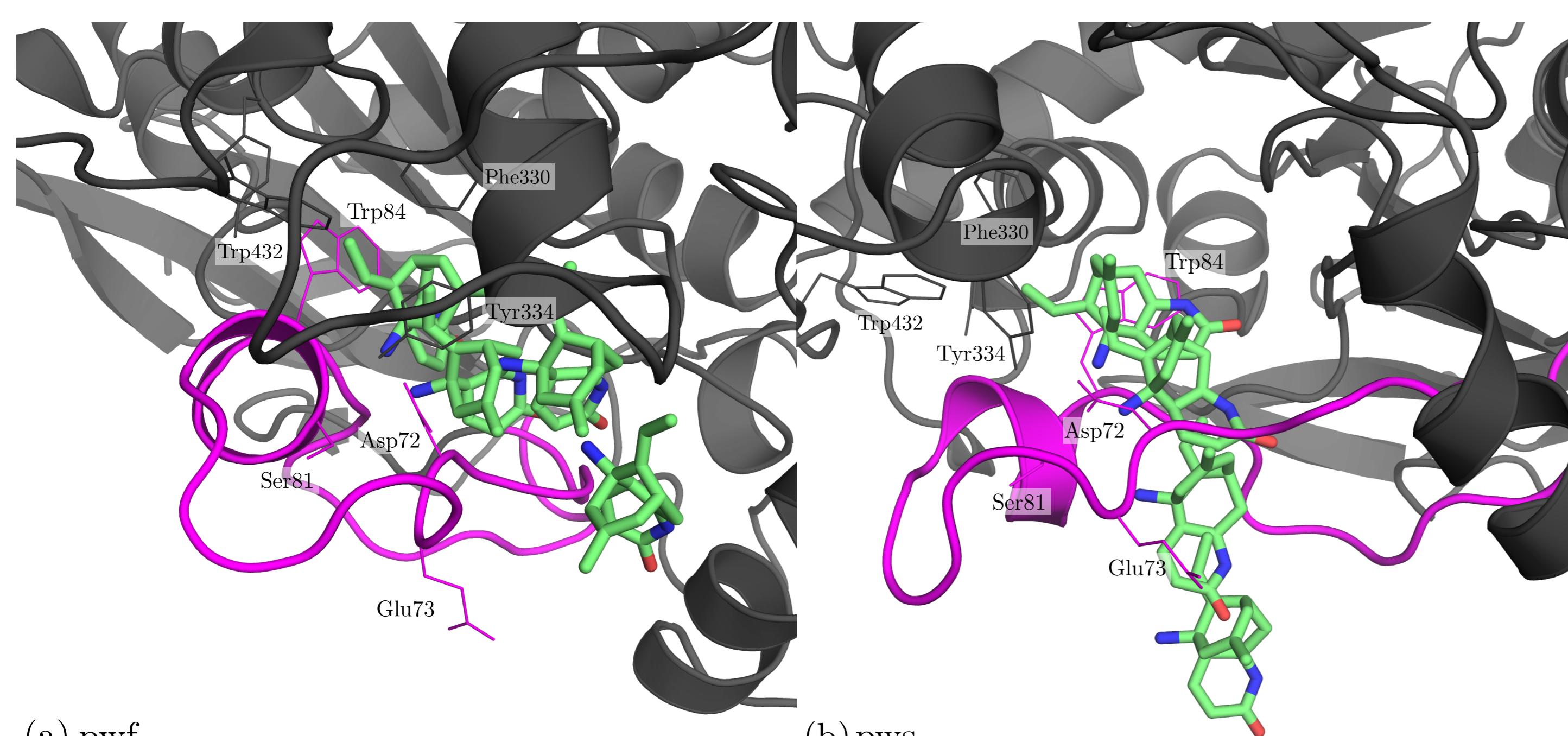
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How to Find an Exit Tunnel?



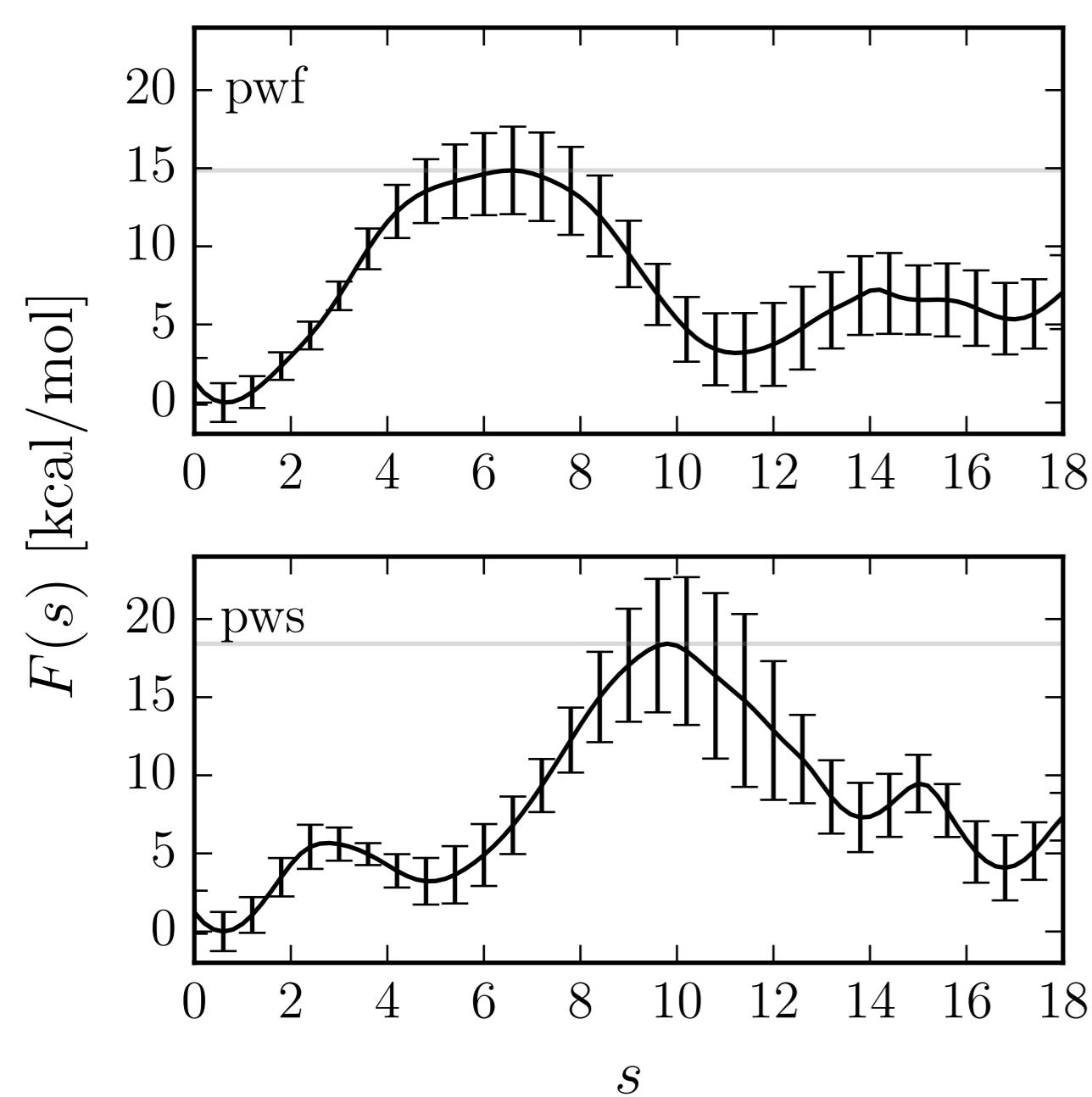
Slow-Onset Inhibitor Unbinding



(a) pwf

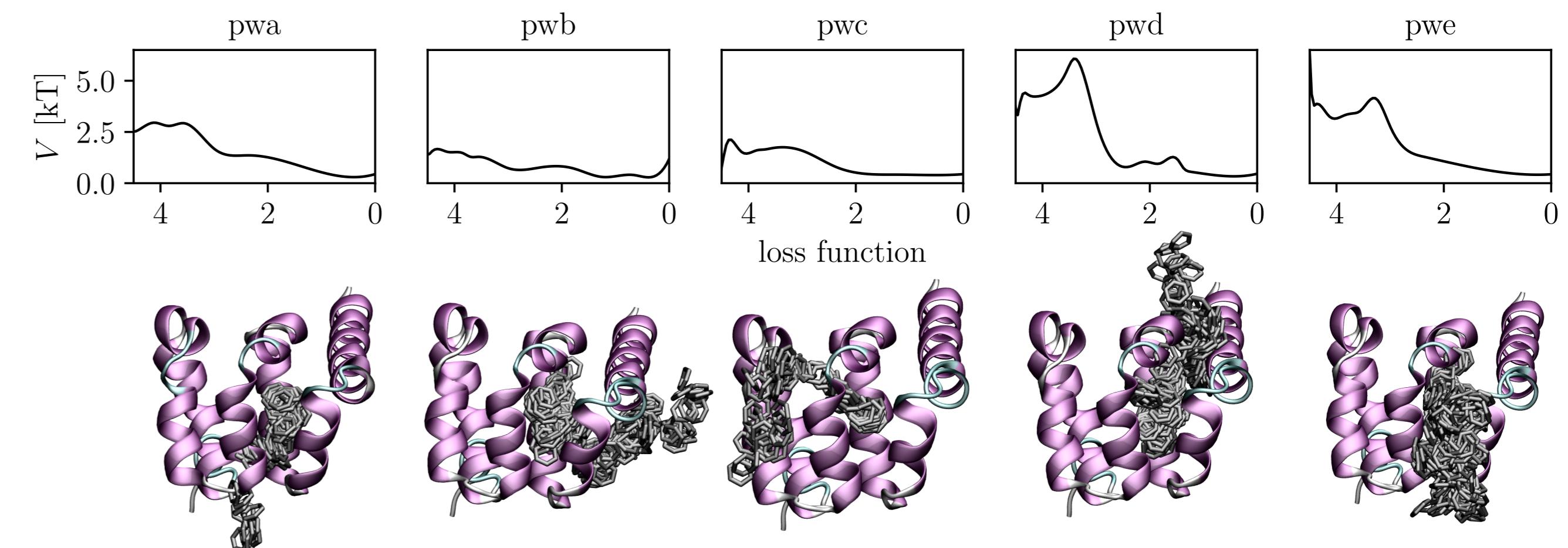
(b) pws

Structural representation of intermediate unbinding configurations along the RPs which atomistically characterize the dissociation of hupA (shown as sticks) along (a) pwf and (b) pws. (pwf) or through the partially disordered-loop



- Free-energy profiles along hupA dissociation pathways pwf and pws;
- The error bars are calculated as standard errors from the well-tempered metadynamics simulations.

Are Transient Pathways Heterogeneous?



Reaction pathways of the benzene unbinding from the lysozyme L99A mutant classified in five clusters. In the upper panel the bias potential is shown as a function of the minimized loss function. The bottom panel depicts atomistically the reaction pathways.

maze: A Module for Plumed 2



maze is a code that implements enhanced sampling methods for simulating the reaction pathways of ligand unbinding. It is made as a module for Plumed 2, an engine for free energy calculations of atomistic systems.



Fork maze from Github.



Ask us on Gitter.

References

- [1] J. Rydzewski, ..., H. Grubmüller. *J. Chem. Theory Comput.* 14, 2843 (2018).
- [2] J. Rydzewski, O. Valsson, *J. Chem. Phys.* 150 (2019).
- [3] J. Rydzewski, *Submitted* (2019).

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Acknowledgments

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All the data and PLUMED input files required to reproduce the results reported in this study will be available on PLUMED-NEST (www.plumed-nest.org), the public repository of the PLUMED consortium.