Investigation on non-ergodicity of protein dynamics. Supplementary Materials

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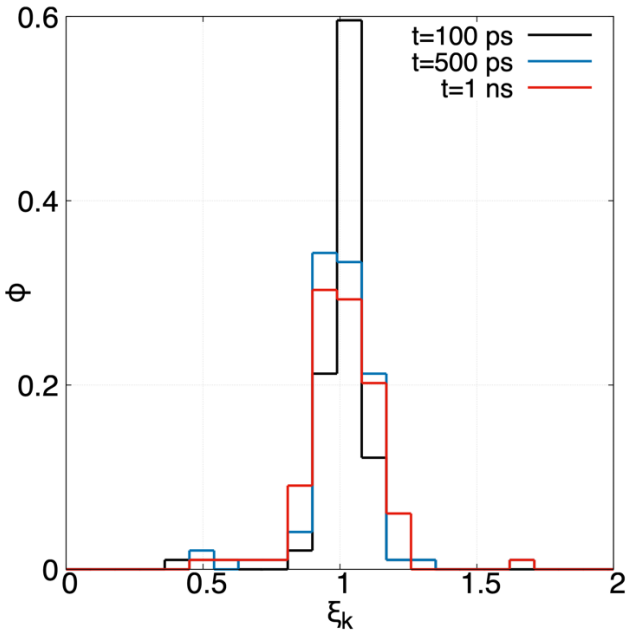

Figure S1: ϕ distribution varying the lag time t for CAP including the three trajectories outlined in the main text

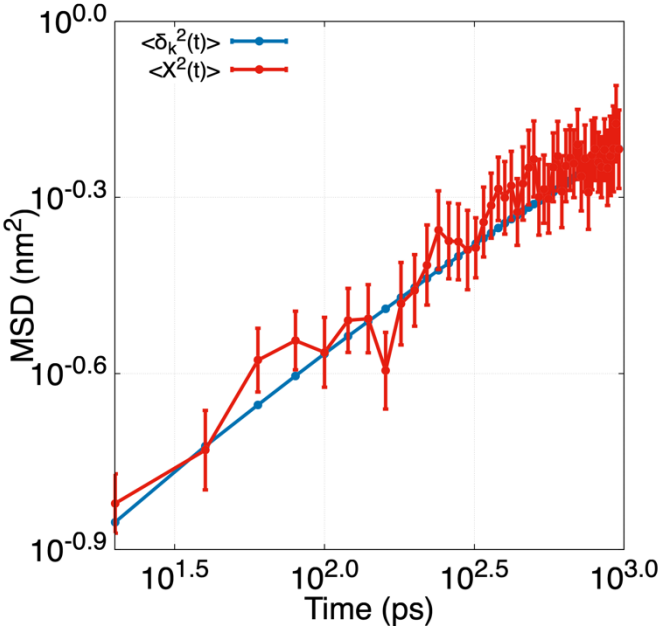

Figure S2: Ensemble averaged MSD $\langle \Delta \boldsymbol{X}^2(t) \rangle$ (red line) and ensembled averaged TA-MSD $\langle \overline{\delta^2(T,t)} \rangle$ (botted blu line) for CAP including the three trajectories outlined in the main text.

Supplemental Methods:

Metadynamics protocol:

After the equilibration steps in NVT and NPT ensembles as described in the main text a 600-ns long metadynamics has been carried out employing the well-tempered protocols[1] employing GROMACS 2022 package[2] patched with PLUMED software[3]. The chosen collective variable was the center of mass between the two arginines mentioned in the text. The potential hills were deposited each 500 steps with a height of $0.7\ KJ/mol$ and a width of $0.2\ nm$. The bias factor was set at 30. Two potential barriers were placed at 0.5 and $3.0\ nm$ to hinder the exploration of undesired portions of the conformational space. These where a lower and upper barriers modeled as described in PLUMED manual. These barriers were featured by an elastic constat of $250\ KJ/mol$ and exponential of 2.

Supplemental Reference

1. Barducci, A., Bussi, G. & Parrinello, M. Well-Tempered Metadynamics: A Smoothly Converging and Tunable Free-Energy Method. *Phys. Rev. Lett.* **100**, 020603 (2008).

2. Abraham, M. J. *et al.* Gromacs: High performance molecular simulations through multi-level parallelism from laptops to supercomputers. *SoftwareX* **1–2**, (2015).

3. Bonomi, M. *et al.* Promoting transparency and reproducibility in enhanced molecular simulations. *Nature Methods* vol. 16 Preprint at https://doi.org/10.1038/s41592-019-0506-8 (2019).