Exercise Session 6

MDMC Spring 2025

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May 13, 2025

Reminders

- Today is the *final* exercise session - optional report (only best 5 out of 6 graded)
- No interview for report of Ex6
- **Extended deadline** for this report: Sunday June 29th at 23h59
- Even if you decide to not do the report, read the theory and the exercise! Important knowledge to better understand MD (possibly useful for the exam!)
- Important Dates:
  - Q&A Session and mock exam on Tuesday May 20th in lecture classroom – send us your questions on moodle in advance!
  - Written exam on Tuesay May 27th in lecure classroom

Written exam - information

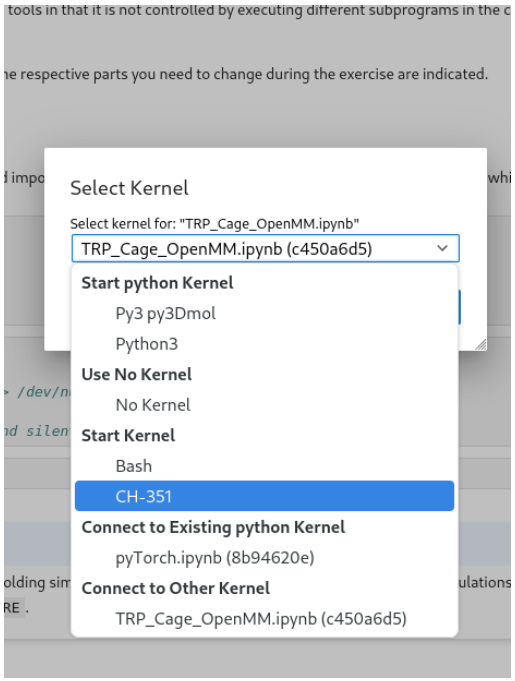
- 1 page of summary notes will be permitted during the exam (1 A4 size paper, front and back)
- Calculators will be permitted during the exam, but not necessary
- No other electronic device allowed
- We will provide paper to write your answers

Exercise 6 - Reminders

- **Note** This tutorial should be run on **gnoto** JupyterHub and not on noto JupyterHub. This is because we will use GPU-accelerated techniques to speed up the simulations.
- To this end, please use the following link instead of the usual rocket button: gnoto link
- **Select** the correct kernel for this exercise `CH-351`

Exercise 6 - Set up gnoto

- **Select** the correct kernel for this exercise `CH-351`



Exercise 6 - Learning Goals

🎯 Learning goals

Learn how to simulate solvated systems

Run a production grade simulation using a GPU

Simulate protein folding of a small peptide

Perform a basic analysis of an MD trajectory

📖 Chapter in script

Chapter 6 - Advanced Molecular Dynamics Techniques

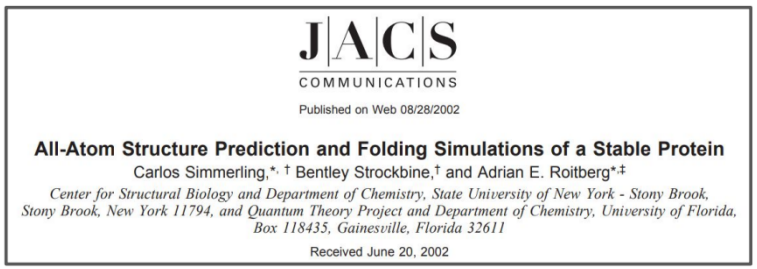
📚 Resources

Simmerling, C., Strockbine, B., and Roitberg, A.E., All-Atom Structure Prediction and Folding Simulations of a Stable Protein J. Am. Chem. Soc. 2002, 124, 38, 11258–11259 https://doi.org/10.1021/ja0273851 Braun, E., Gilmer, J., Mayes, H. B., Mobley, D. L. ., Monroe, J. I., Prasad, S., & Zuckerman, D. M. . (2018). Best Practices for Foundations in Molecular Simulations [Article v1.0]. Living Journal of Computational Molecular Science, 1(1), 5957. https://doi.org/10.33011/livecoms.1.1.5957

Exercise 6 - Context

Today you will perform a MD simulation of a Trp-cahe miniprotein

- Smallest protein to display two state folding properties, ideal candidate for computational folding simulations
- Folding dynamics of this protein with explicitly defined water molecules (see Theory section for details) is a lengthy and computationally costly process. We will use of an implicit solvent model to reduce computational cost and still include, in approximate detail, the effects of water solvation.
- You will replicate the work of Simmerling et. al. in 2002



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COMMUNICATIONS

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All-Atom Structure Prediction and Folding Simulations of a Stable Protein

Carlos Simmerling,*,† Bentley Strockbine,† and Adrian E. Roitberg*,‡

Center for Structural Biology and Department of Chemistry, State University of New York - Stony Brook, Stony Brook, New York 11794, and Quantum Theory Project and Department of Chemistry, University of Florida, Box 118435, Gainesville, Florida 32611

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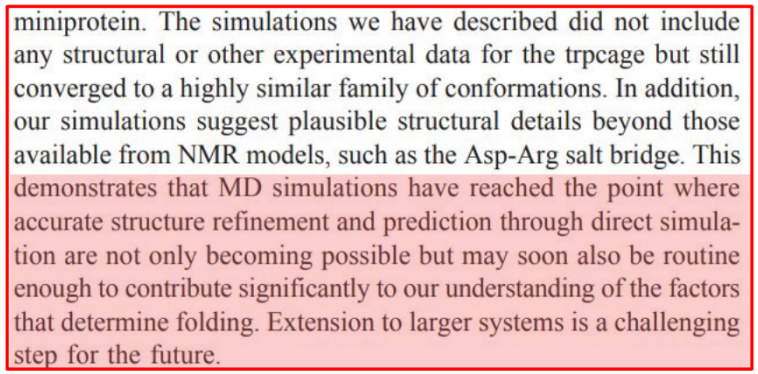

miniprotein. The simulations we have described did not include any structural or other experimental data for the trpcage but still converged to a highly similar family of conformations. In addition, our simulations suggest plausible structural details beyond those available from NMR models, such as the Asp-Arg salt bridge. This demonstrates that MD simulations have reached the point where accurate structure refinement and prediction through direct simulation are not only becoming possible but may soon also be routine enough to contribute significantly to our understanding of the factors that determine folding. Extension to larger systems is a challenging step for the future.

Exercise 6 - Analysis

The analysis of the MD trajectories:

- You will look at different properties during the simulation, comparing to the experimental structure (PDB 1L2Y)