Exercise Session 6

MDMC Spring 2024

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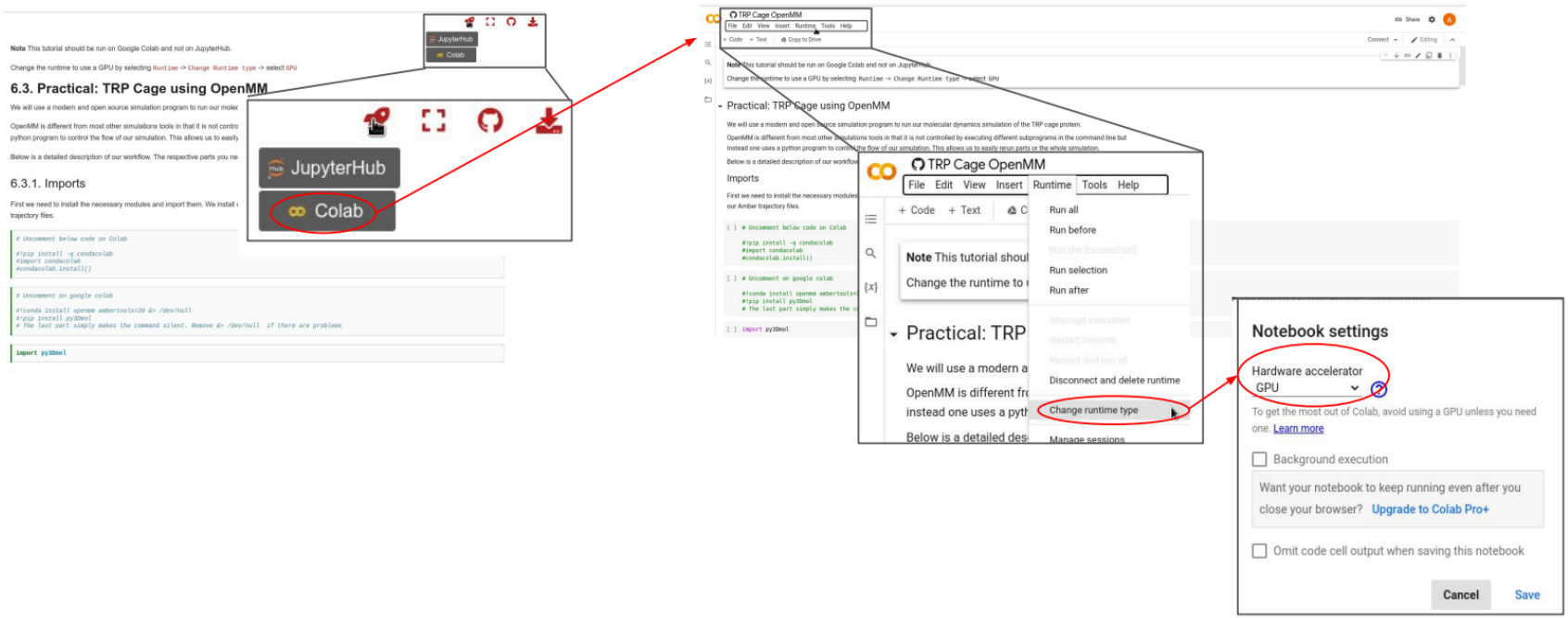
Reminders

- 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 30th 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 on Tuesday May 21st in lecture classroom – send us your questions on moodle in advance!
  - Written exam on Tuesay May 28th in lecure classroom

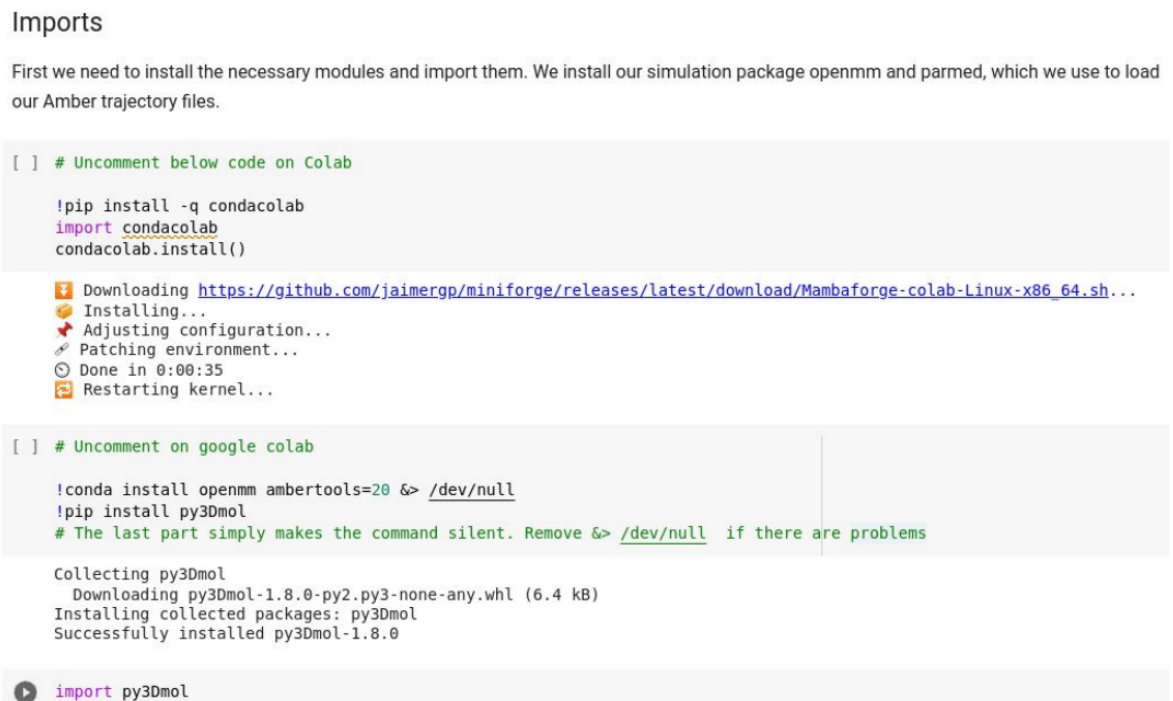
Exercise 6 - Reminders

- The first part of the exercise should be run on **GoogleColab** and not on Noto! (free access to GPUs)
- Access GoogleColab via the usual rocket button
- Change the runtime to use a GPU (Runtime > Change Runtyle type > select GPU)



Exercise 6 - Set up Google Colab

- Uncomment the necessary cells and run the `install/import` commands (the first time you may see a warning about the notebook not being authored by Google – Run anyway)
- This phase will install and import all necessary modules to run this exercise, be sure to run this at the beginning (it will take few minutes)



Imports

First we need to install the necessary modules and import them. We install our simulation package openmm and parmed, which we use to load our Amber trajectory files.

```
[ ] # Uncomment below code on Colab

    !pip install -q condacolab
    import condacolab
    condacolab.install()
```

```
⏬ Downloading https://github.com/jaimergp/miniforge/releases/latest/download/Mambaforge-colab-Linux-x86_64.sh...
📦 Installing...
📌 Adjusting configuration...
🩹 Patching environment...
⏲ Done in 0:00:35
🔁 Restarting kernel...
```

```
[ ] # Uncomment on google colab

    !conda install openmm ambertools=20 &> /dev/null
    !pip install py3Dmol
    # The last part simply makes the command silent. Remove &> /dev/null  if there are problems
```

```
Collecting py3Dmol
  Downloading py3Dmol-1.8.0-py2.py3-none-any.whl (6.4 kB)
Installing collected packages: py3Dmol
Successfully installed py3Dmol-1.8.0
```

```
    import py3Dmol
```

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

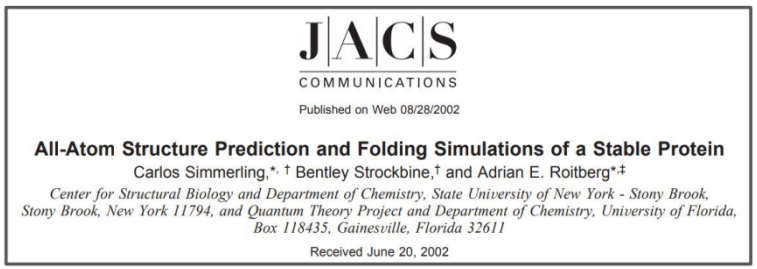
📚 Resources

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

Published on Web 08/28/2002

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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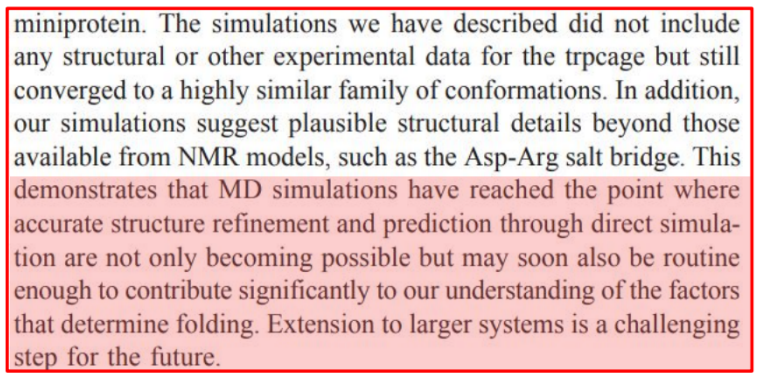

miniprotein. The simulations we have described did not include any structural or other experimental data for the trpcage but still converged to a highly similar family of conformations. In addition, our simulations suggest plausible structural details beyond those available from NMR models, such as the 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 you generate will be performed on Noto

- Upload the `archive.zip` generated on GoogleColab
- You will look at different properties during the simulation, comparing to the experimental structure (PDB 1L2Y)