

AODI Molecular dynamics workshop

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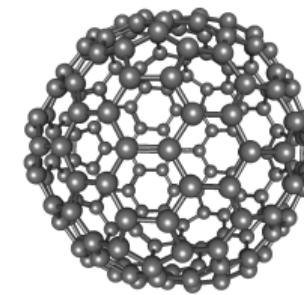
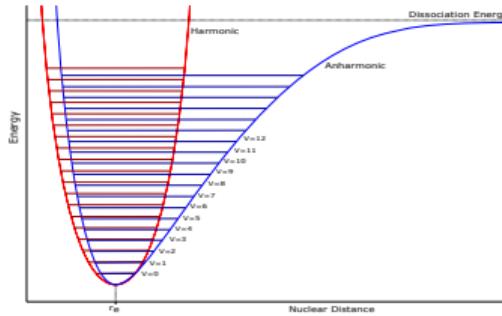
Introduction - Me

Who am I?

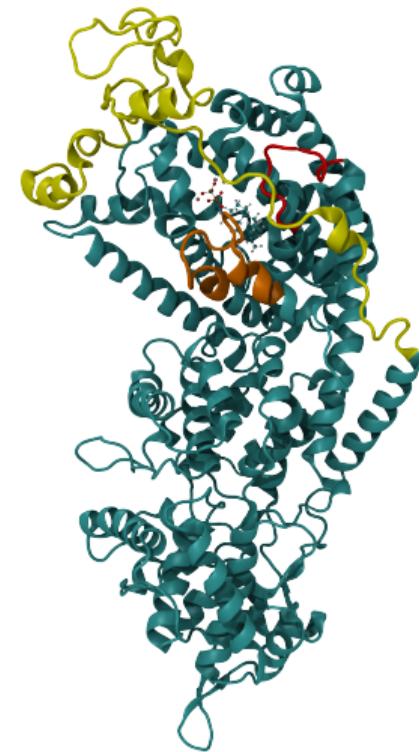
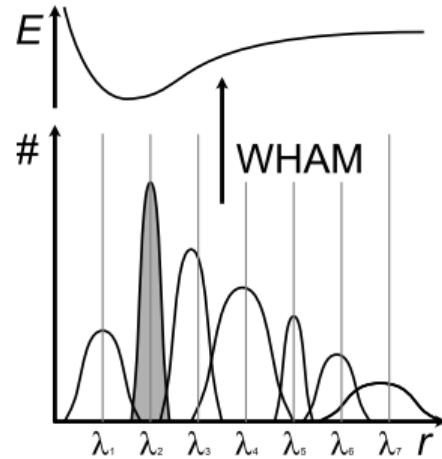
- Ross Amory
- Integrated Masters in Chemistry at the University of Nottingham
- Masters with Prof. Nicholas Besley
- PhD Student at the University of Nottingham
- Supervisors are
 - ▶ Prof. Chris Hayes,
 - ▶ Prof. Jonathan Hirst,
 - ▶ Dr. Christof Jager
 - ▶ Dr. David Rogers



Masters Project:



- Calculate an anharmonic correction for Raman Sepctroscopy
- Implement 2nd order numerical derivatives in Fortran90
- Calculate Raman Spectrum for Carbon Fullerenes using DFT methods
- Compare empirical code to DFT methodology



- Molecular dynamics simulations of Terpene Synthases
- Higher level QM/MM Umbrella sampling to obtain Potential Energy Surfaces

Introduction - Molecular Dynamics

- **Self-taught** in Molecular Dynamics
- Experience of the entire workflow:
 - ▶ Homology Modelling with AlphaFold and YASARA
 - ▶ Docking using AD4 and Gnina
 - ▶ Simulations using AMBER
 - ▶ QM/MM Simulations with AMBER and QChem
 - ▶ Analysis using GBSA, Umbrella Sampling, clustering ect.

Molecular Dynamics employs an empirical force field derived from classical physics in order to describe the system.

$$\begin{aligned} E_{Total} &= E_{Bonded} + E_{Non-Bonded} \\ E_{Bonded} &= E_{Bond} + E_{Angle} + E_{Dihedral} \\ E_{Non-Bonded} &= E_{Electrostatic} + E_{van\ der\ Waals} \end{aligned} \tag{1}$$

1. Potential energy of the system is calculated using Equation (1).

Molecular Dynamics employs an empirical force field derived from classical physics in order to describe the system.

$$F(x) = -\Delta E(x) \tag{2}$$

1. Potential energy of the system is calculated using Equation (1).
2. Forces are derived by taking the negative gradient of the potential energy with respect to the atomic coordinates.

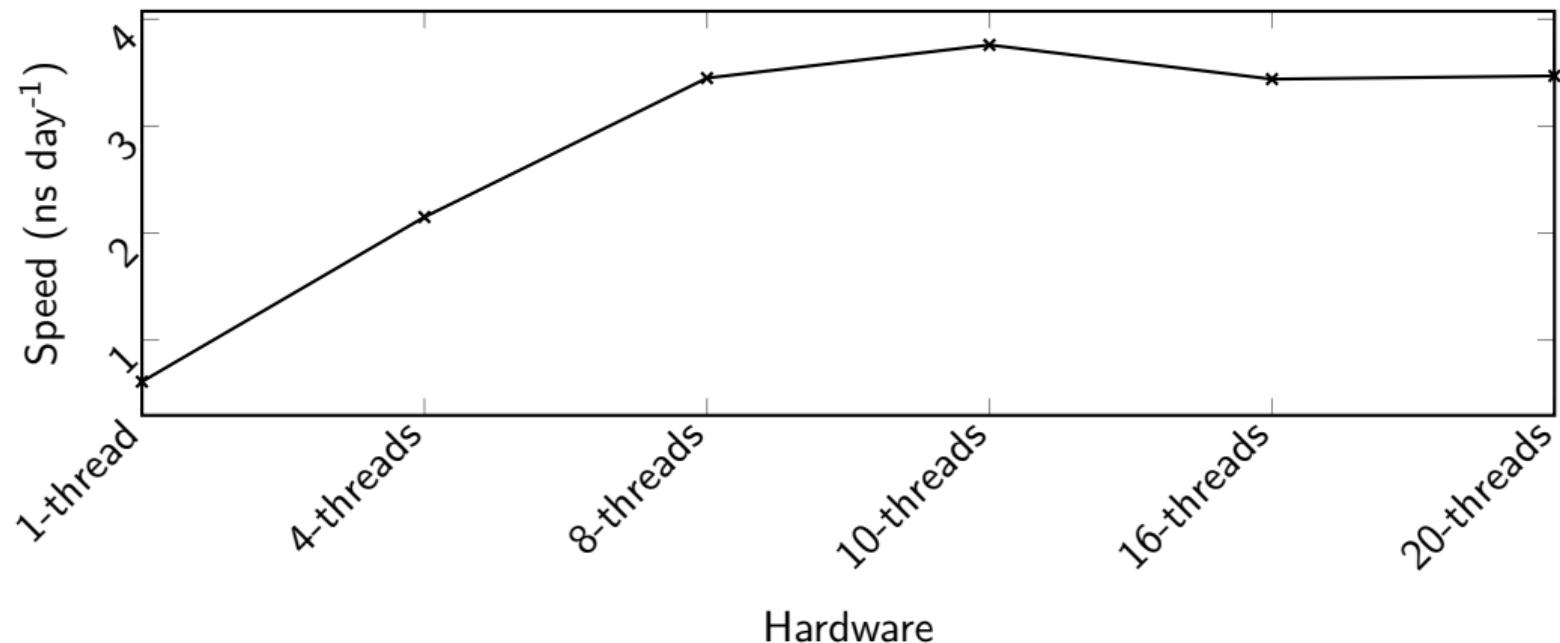
Molecular Dynamics employs an empirical force field derived from classical physics in order to describe the system.

$$\begin{aligned} F &= ma \\ x_{i+1} &= x_i + \delta_t v_i \end{aligned} \tag{3}$$

1. Potential energy of the system is calculated using Equation (1).
2. Forces are derived by taking the negative gradient of the potential energy with respect to the atomic coordinates.
3. Velocities are then calculated using Newtons Laws of motion and the positions are updated with respect to the time step.

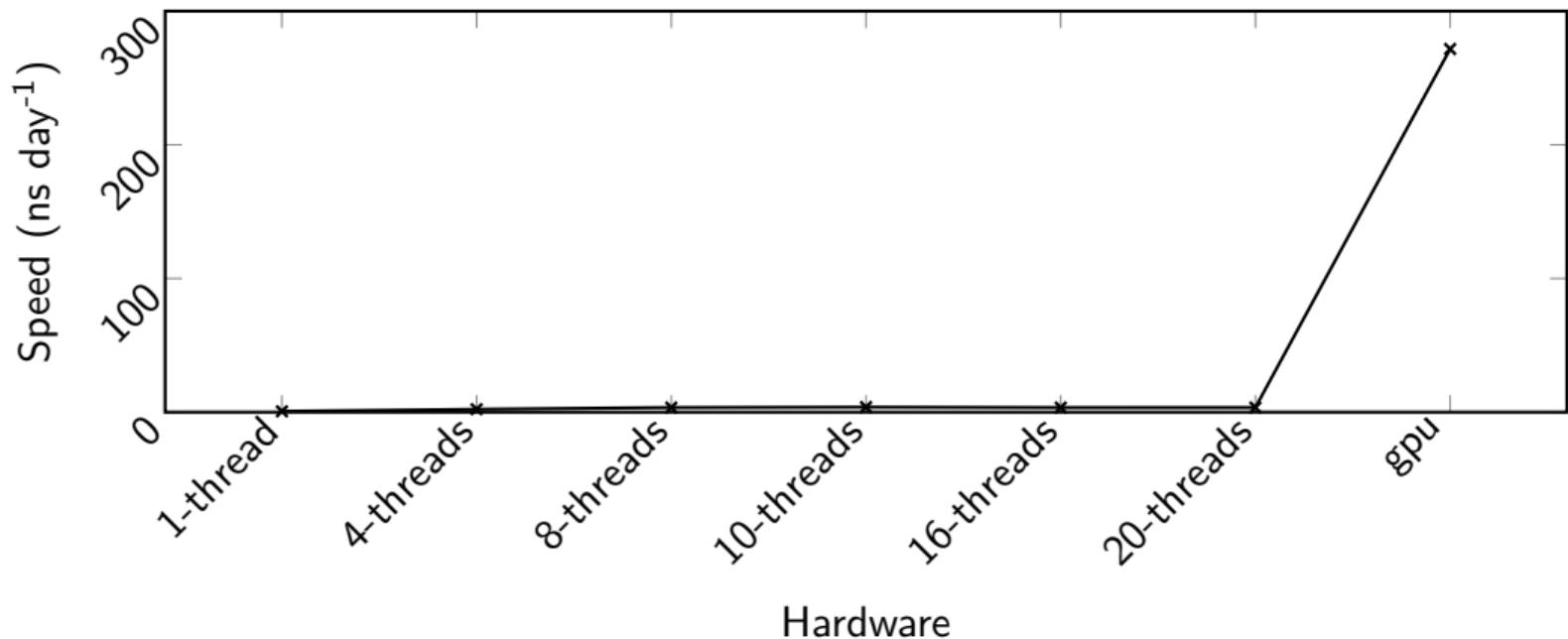
Molecular dynamics scales incredibly well with increasing computational power.

Hardware scaling of MD simulations



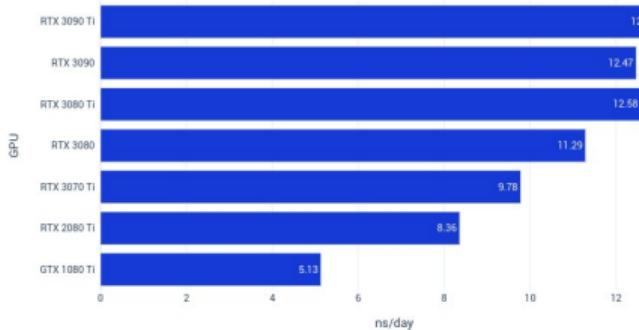
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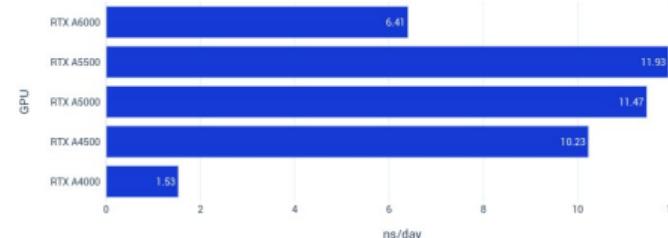
GPU Benchmark

Gromacs v2022 RIB, Ribosome in Water, 2 M atoms,
ns/day (HIGHER IS BETTER)



 Puget Systems

Gromacs v2022 RIB, Ribosome in Water, 2 M atoms,
ns/day (HIGHER IS BETTER)



 Puget Systems

Benchmark data: Puget Systems

Section	Software	Availability
Docking	gnina	Open Source
Preparation	acPype	Free
Dynamics	Amber (AmberTools)	Free*
Analysis	AmberTools	Free
Visualisation	VMD	Free for academic use

Table: Software

* AmberTools is free to use, but full Amber requires a licence. This is only used for GPU acceleration.

The system

Terpene Synthase “(+)-Bornyl Diphosphate Synthase”

- 4511 Atoms (Not including solvent or ligand)
- Dynamical system that exists at room temp.
- Protein is not in isolation (Needs solvent)
- Reactions can require nanosecond simulation lengths

Therefore DFT or ab-initio methods are too expensive!
Molecular dynamics is therefore a much more sensible option.

