

How to run an MD simulation

How to run an MD simulation

- Protocol for an MD simulation
- Initial Coordinates
 - X-ray diffraction or NMR coordinates from the Protein Data Bank
 - Coordinates constructed by modeling (homology)
- Treatment of non-bonded interactions
- Treatment of solvent
 - implicit
 - explicit
- If using explicit treatment of solvent
 - Periodic boundary conditions (PBC)
 - Solvation sphere
 - Active site dynamics

Molecular Modelling Software

- Commercial:
 - Cerius2, Insight II (from Accelrys)
- Academic:
 - MMTK
 - GROMACS
 - NAMD
 - CHARMM
 - AMBER

“If I were to rewrite MMTK today, I would use the exchange data formats accepted by the molecular simulation community”

But those formats don't exist yet.

2013 – Konrad Hinsen

Molecular Visualisation Packages

- Many!
 - RasMol
 - PyMOL
 - Chimera
 - VMD
- Select one or two, become an expert 😊

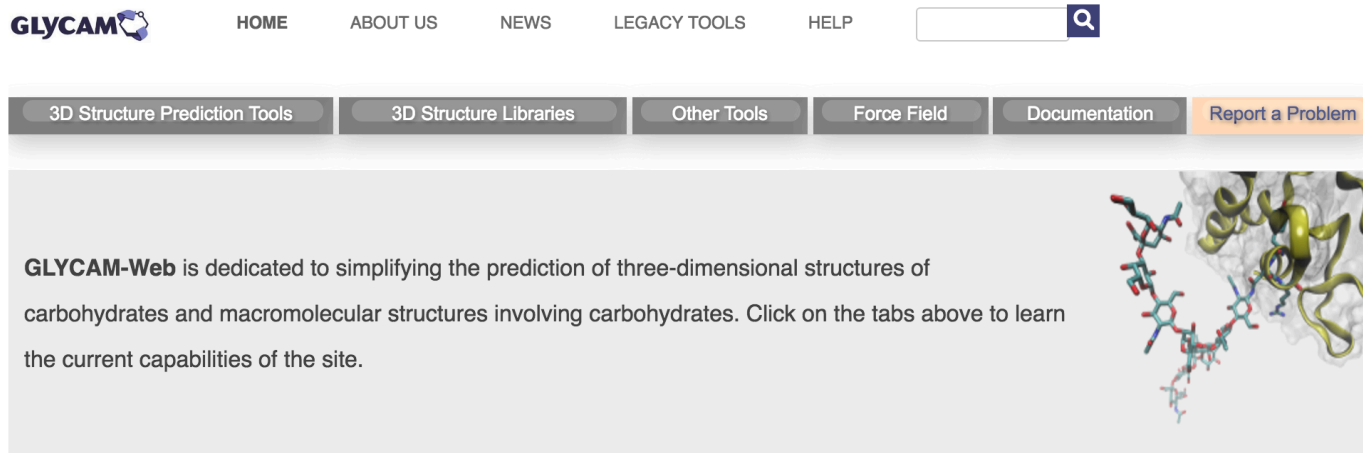
How to run an MD simulation

- Homology modelling
 - Modeller
 - Phyre2

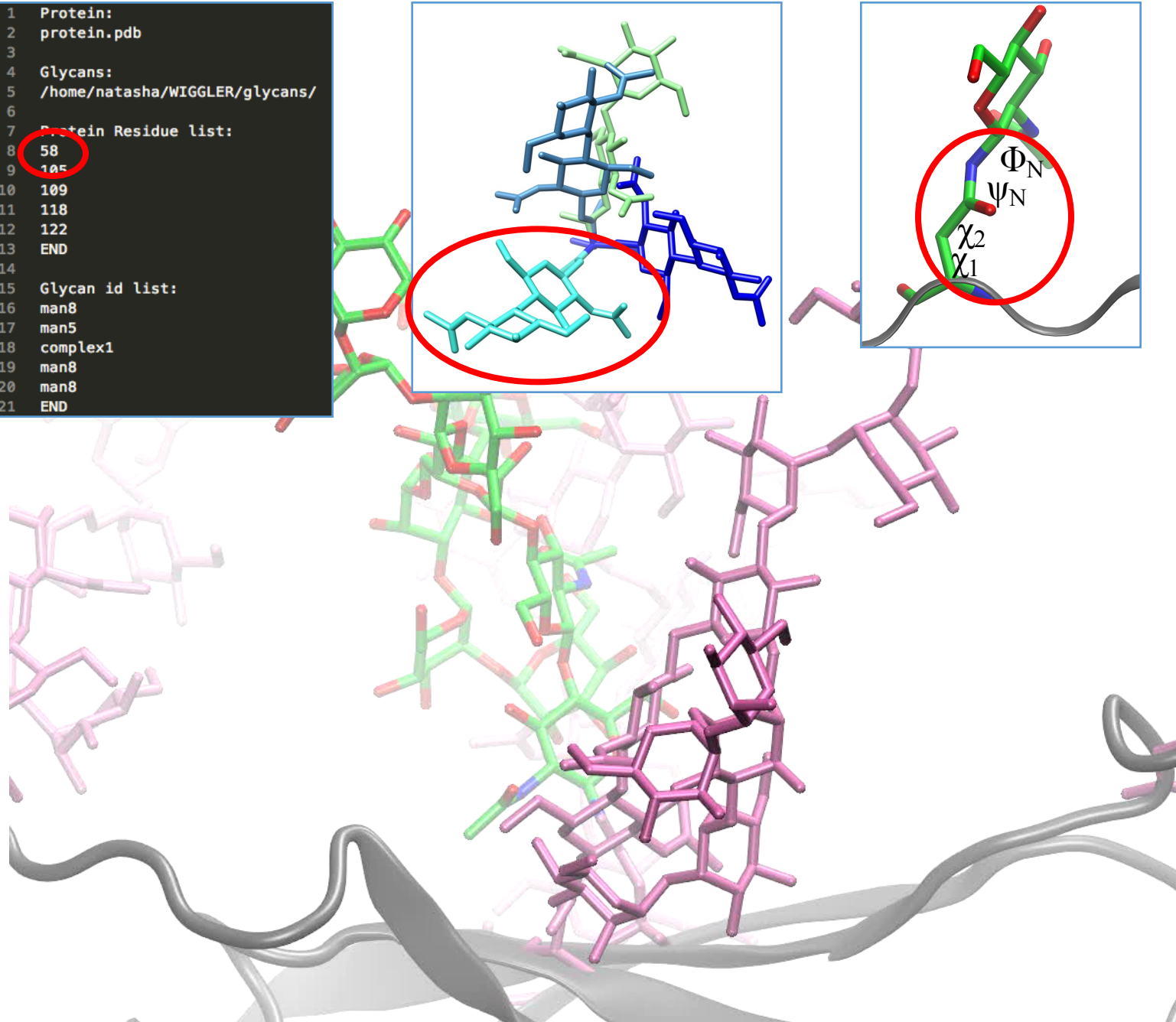


How to run an MD simulation

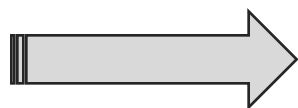
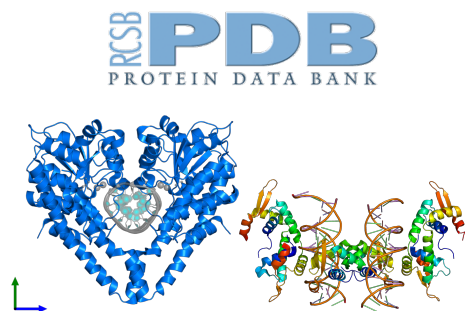
- Refine your structure
 - <http://glycam.org/>



```
1 Protein:
2 protein.pdb
3
4 Glycans:
5 /home/natasha/WIGGLER/glycans/
6
7 Protein Residue list:
8 58
9 105
10 109
11 118
12 122
13 END
14
15 Glycan id list:
16 man8
17 man5
18 complex1
19 man8
20 man8
21 END
```



How to run an MD simulation



Topology and Coordinate file

How to run an MD simulation

[HOME](#)[ABOUT US](#)[NEWS](#)[LEGACY TOOLS](#)[HELP](#)[3D Structure Prediction Tools](#)[3D Structure Libraries](#)[Other Tools](#)[Force Field](#)[Documentation](#)[Report a Problem](#)

These are other tools and services offered here.

[pdb](#)**PDB Preprocessor**

Pre-process a pdb file for use with AMBER or GLYCAM

glycam.org

<http://ambermd.org/>

AmberTools16 is now available!

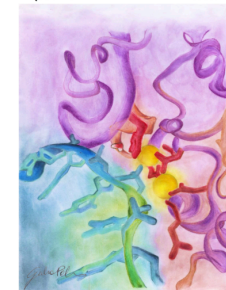
AmberTools consists of several independently developed packages that work well by themselves, and with Amber itself. The suite can also be used to carry out complete molecular dynamics simulations, with either explicit water or generalized Born solvent models.

AmberTools16 (released on April 30, 2016) consists of the following main codes:

NAB	build molecules; run MD or distance geometry, using generalized Born, Poisson-Boltzmann or 3D-RISM implicit solvent models
antechamber and MCPB	Create force fields for general organic molecules and metal centers
tleap and parmed	Basic preparation programs for Amber simulations
sqm	semiempirical and DFTB quantum chemistry program
pbsa	Performs numerical solutions to Poisson-Boltzmann models
3D-RISM	Solves integral equation models for solvation
sander	Workhorse program for molecular dynamics simulations
mdgx	Explicit solvent molecular dynamics simulations and parameter fitting
cpptraj and pytraj	Structure and dynamics analysis of trajectories
MMPBSA.py and amberlite	Energy-based analyses of MD trajectories

Amber 2016 Reference Manual

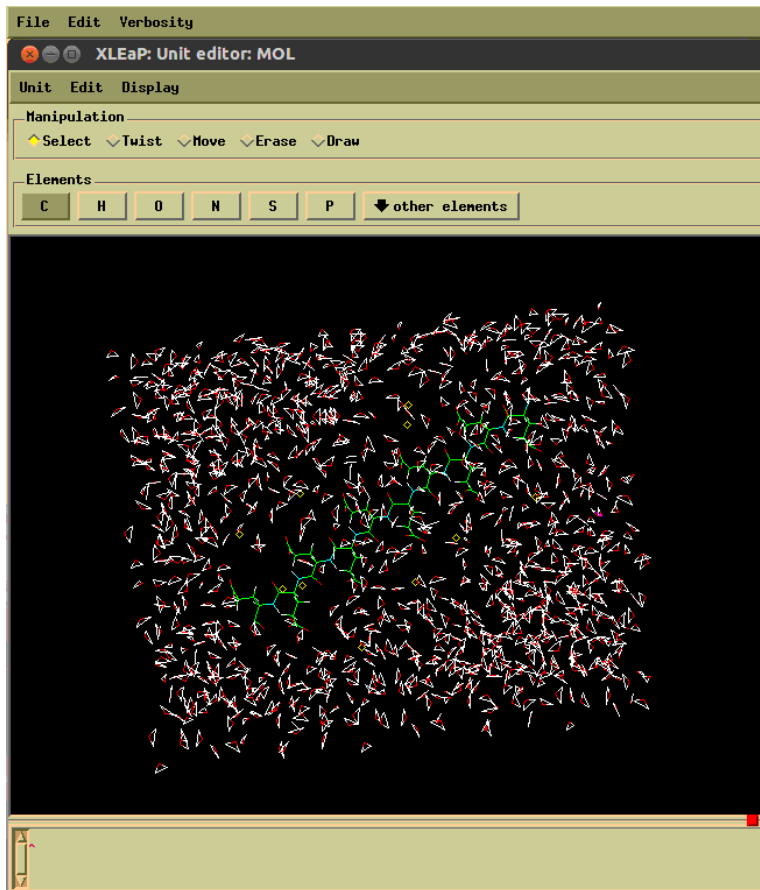
(Covers Amber16 and AmberTools16)



- The AmberTools suite is free of charge, and its components are mostly released under the GNU General Public License (GPL). A few components are included that are in the public domain or which have other, open-source, licenses. The *sander* program now has the LGPL license.

How to run an MD simulation

- AmberTools: LEaP



```
nwood$ tleap
-I: Adding /apps/chpc/chem/amber/14/dat/leap/prep to search path.
-I: Adding /apps/chpc/chem/amber/14/dat/leap/lib to search path.
-I: Adding /apps/chpc/chem/amber/14/dat/leap/parm to search path.
-I: Adding /apps/chpc/chem/amber/14/dat/leap/cmd to search path.
```

```
Welcome to LEaP!
(no leaprc in search path)
> █
```

How to run an MD simulation

```
##### Set Defaults #####  
set default PBRadii mbondi2  
#####  
##### Force Field Inputs #####  
source /apps/chpc/chem/amber/14/dat/leap/cmd/leaprc.ff14SB  
source /apps/chpc/chem/amber/14/dat/leap/cmd/leaprc.GLYCAM_06j-1  
loadAmberParams frcmod.tip5p  
#####  
  
#####load Carb#####  
mol=loadpdb structure.pdb  
  
#BONDING
```




How to run an MD simulation

- Bond information

bond mol.1798.O4 mol.1799.C1

bond mol.1809.O4 mol.1810.C1

bond mol.1820.O4 mol.1821.C1

**Bio3D**

[Home](#) [User guide](#) [Demo](#) [Tutorials](#) [Bio3D-web](#) [Documentation](#) [FAQ](#) [Download](#) [Grant Lab](#)

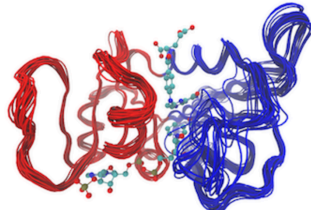
search...

Overview

Bio3D is an [R](#) package containing utilities for the analysis of protein structure, sequence and trajectory data.

It is currently distributed as platform independent source code under the [GPL version 2 license](#). Please see the [Download](#) page for installation instructions.

Features



How to run an MD simulation

```
saveamberparm mol CPLX.prmtop CPLX.rst7
savepdb mol CPLX.pdb

#####Additions#####
addIons mol Na+ 0
addIons mol Cl- 0

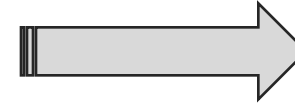
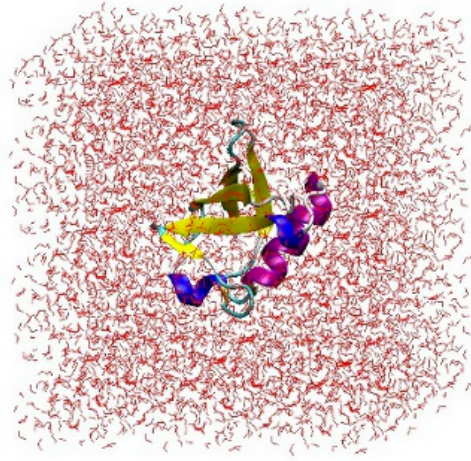
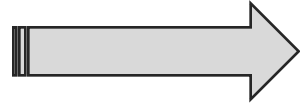
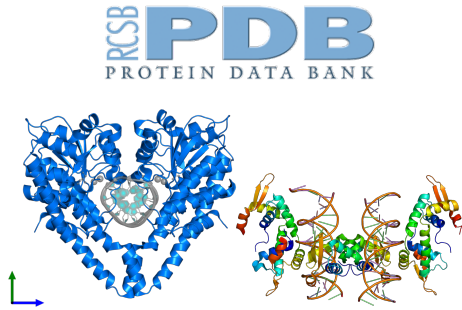
saveamberparm mol CPLX_Neut.prmtop CPLX_Neut.rst7
savepdb mol CPLX_Neut.pdb

#####Solvate#####
solvatebox mol TIP5PBOX 10.0 1.0

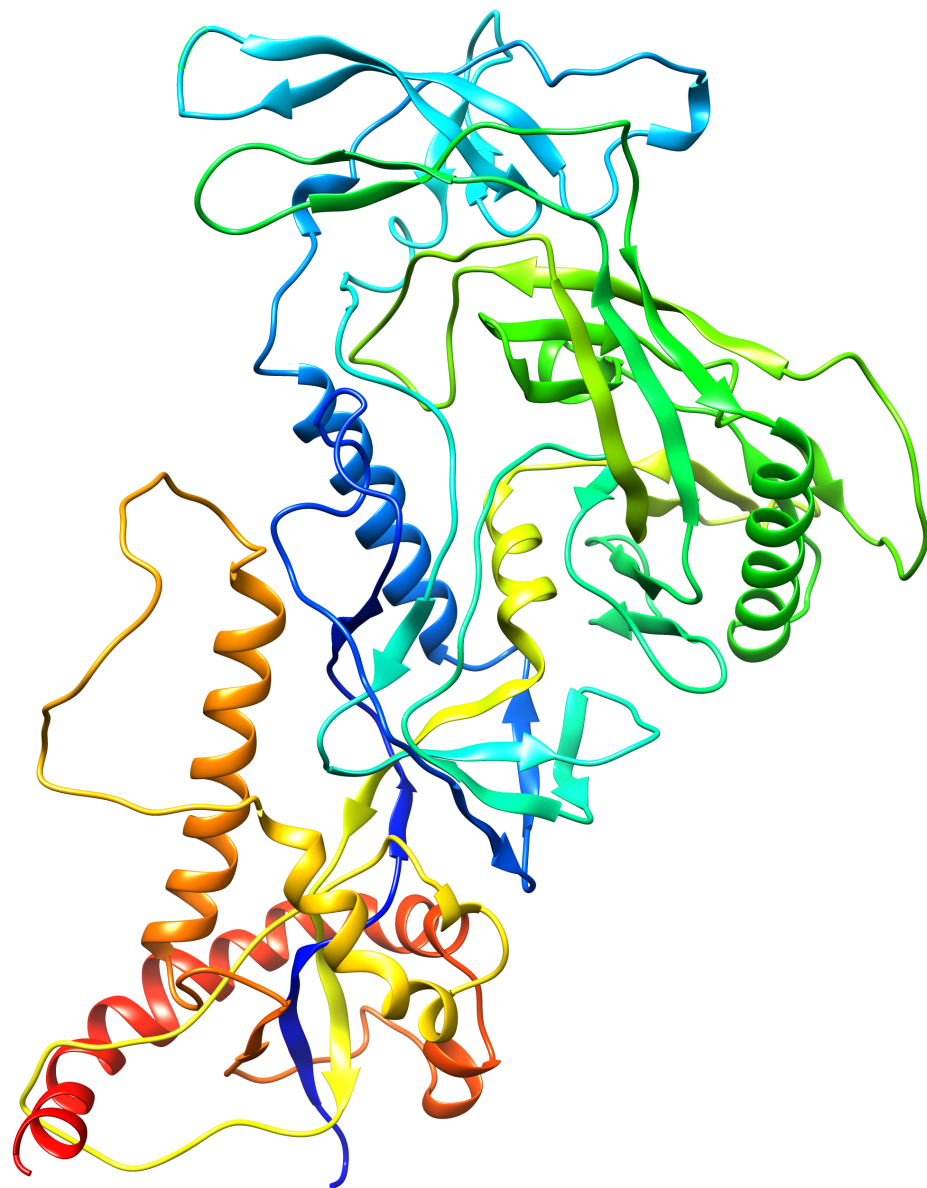
saveamberparm mol CPLX_Neut_Sol.prmtop CPLX_Neut_Sol.rst7
savepdb mol CPLX_Neut_Sol.pdb

quit
```

How to run an MD simulation



Minimisation:
*remove bad contacts
between non-bonded
neighbouring atoms*



Chimera:

find clashes/contacts

Find Clashes/Contacts

Atoms to Check

Designate currently selected atoms for checking
4965 atoms designated

Check designated atoms against:

☒ themselves
☐ all other atoms
☐ other atoms in same model
☐ second set of designated atoms

Designate selection as second set
No second set

Clash/Contact Parameters

Find atoms with VDW overlap >= 0.6 angstroms

Subtract 0.4 from overlap for potentially H-bonding pairs



Default clash / contact criteria


Ignore contacts of pairs 4 or fewer bonds apart

☐ Include intra-residue contacts
☒ Include intra-molecule contacts

Treatment of Clash/Contact Atoms

☐ Select

☐ Color  (and color all other atoms  No)

☒ Draw pseudobonds of color  and width 3.0

☐ If endpoint atom hidden, show endpoint residue

☐ Assign 'overlap' attribute

☐ Write information to file

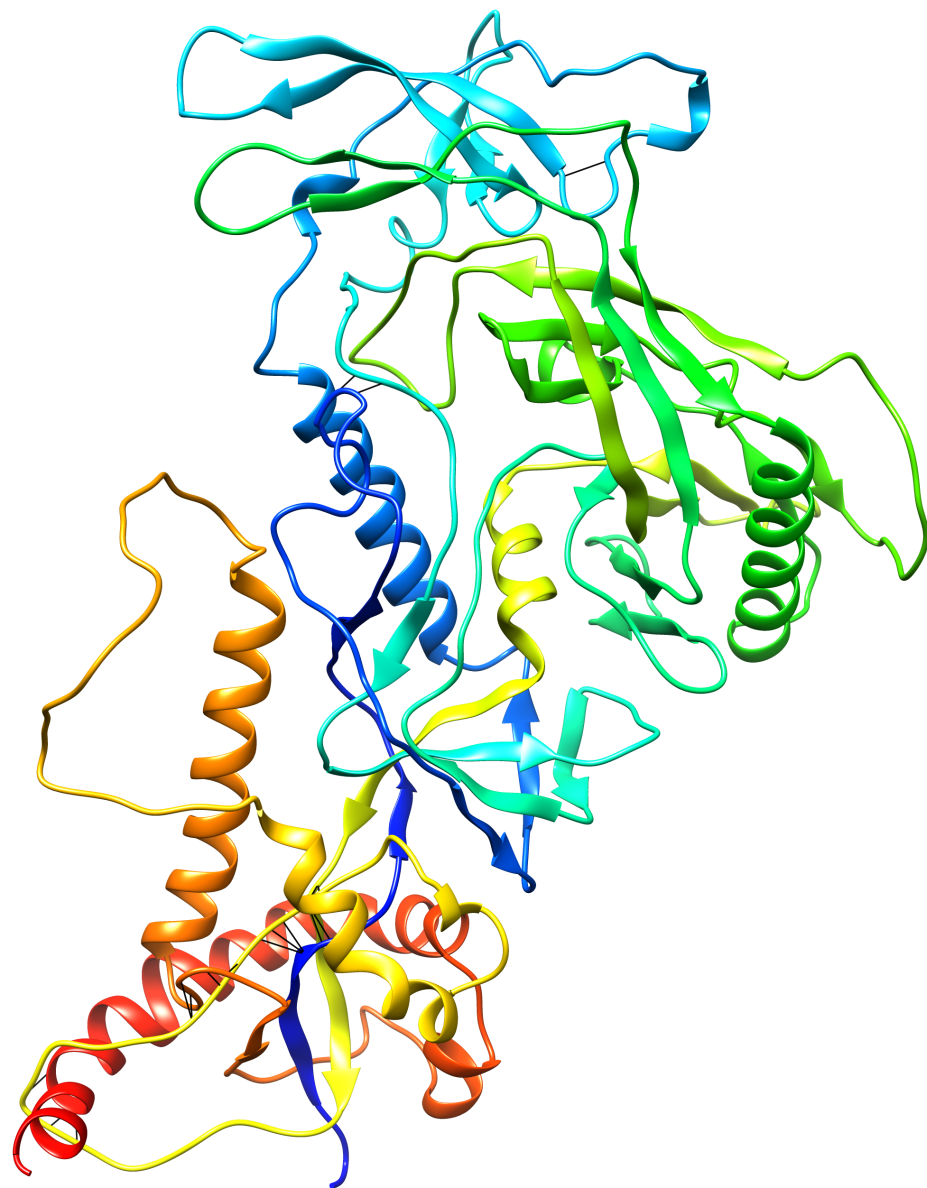
☐ Write information to reply log

Frequency of Checking

☒ when OK/Apply clicked

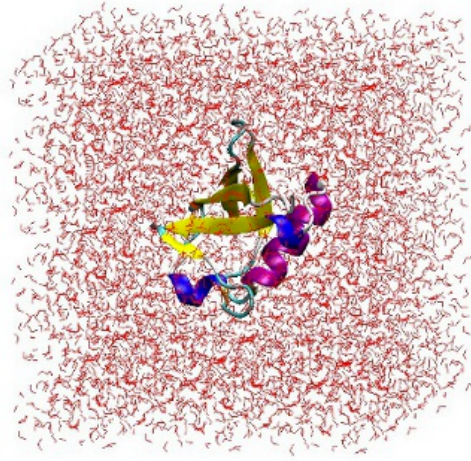
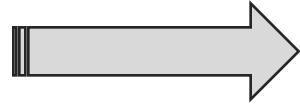
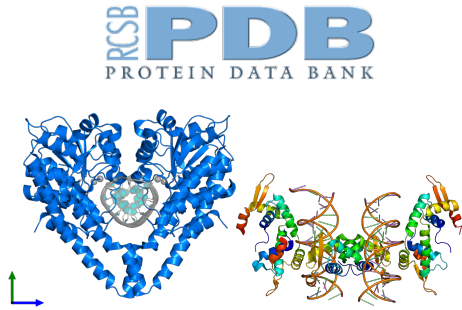
Check... ☐ after relative motions (until dialog closed)
☐ continuously (until dialog closed)

OK Apply Close Help





How to run an MD simulation



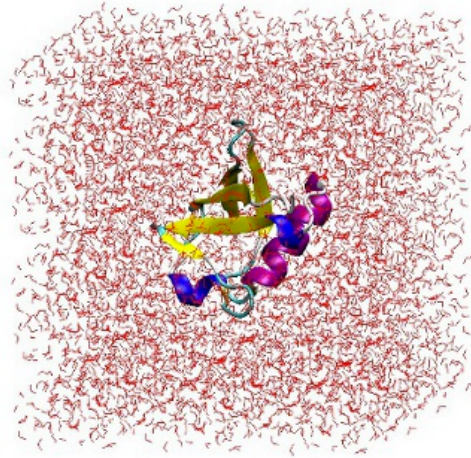
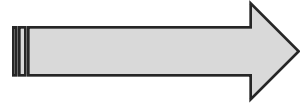
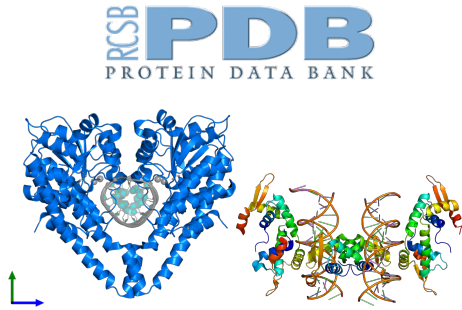
Minimisation:
*remove bad contacts
between non-bonded
neighbouring atoms*

How to run an MD simulation

```
Constant Volume Minimization
# Control section
&cntrl
  imin=1,
  dielc = 1, cut = 10.0,
  ntb = 1,
  maxcyc = 20000, dx0 = 0.01, drms = 0.0001,
  ntmin = 1, ncyc = 10000,
  ntp = 0,
  ntr = 1,
  irest = 0,
/
Restraints kcal/mol
5.0
```

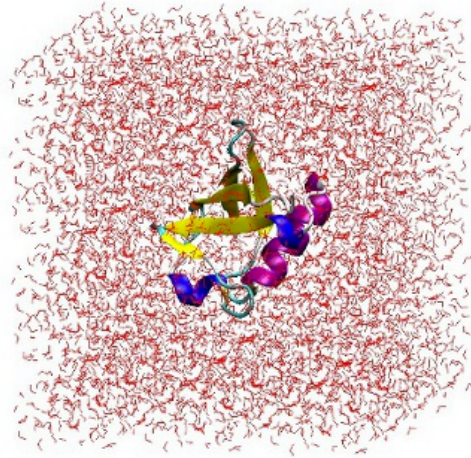
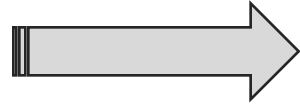
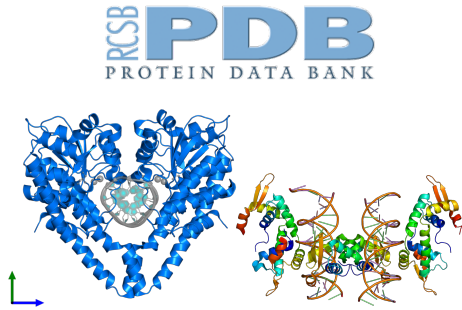
Minimisation:
Amber input file

How to run an MD simulation

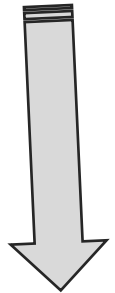


Minimisation:
*remove bad contacts
between non-bonded
neighbouring atoms*

How to run an MD simulation

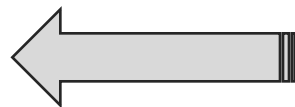


Minimisation:
*remove bad contacts
between non-bonded
neighbouring atoms*

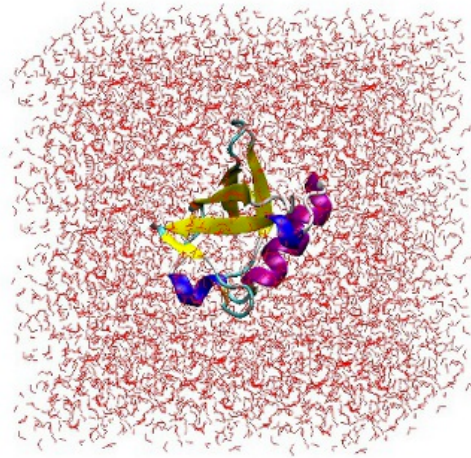
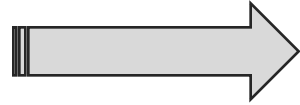
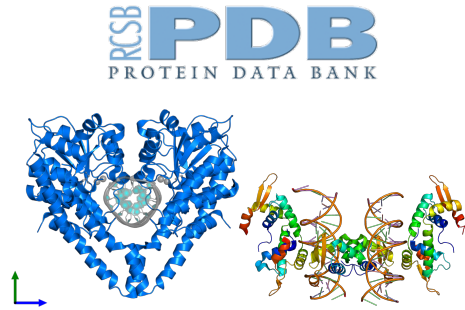


Equilibration:
*heating the system to
room temperature*

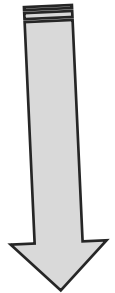
Production:
*run our simulation at
constant pressure
and temperature*



How to run an MD simulation



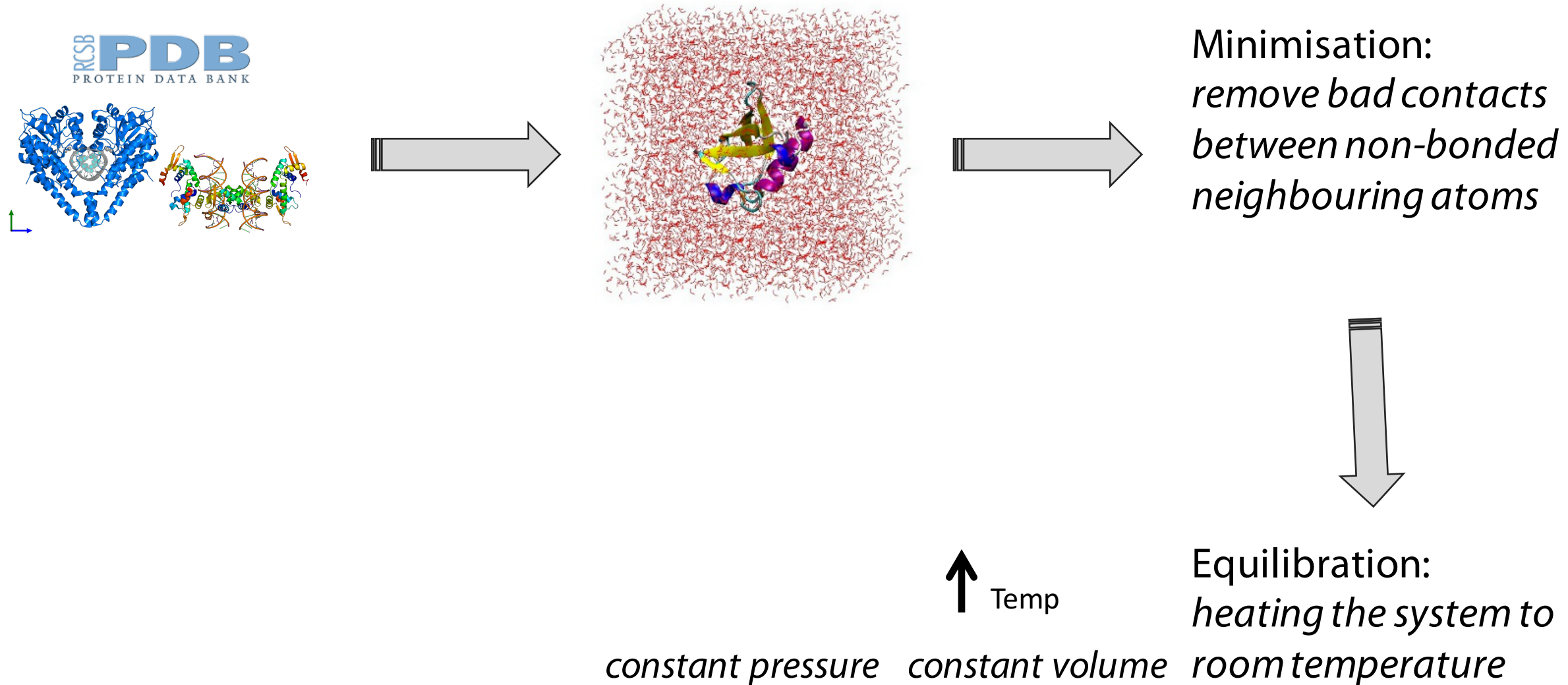
Minimisation:
*remove bad contacts
between non-bonded
neighbouring atoms*



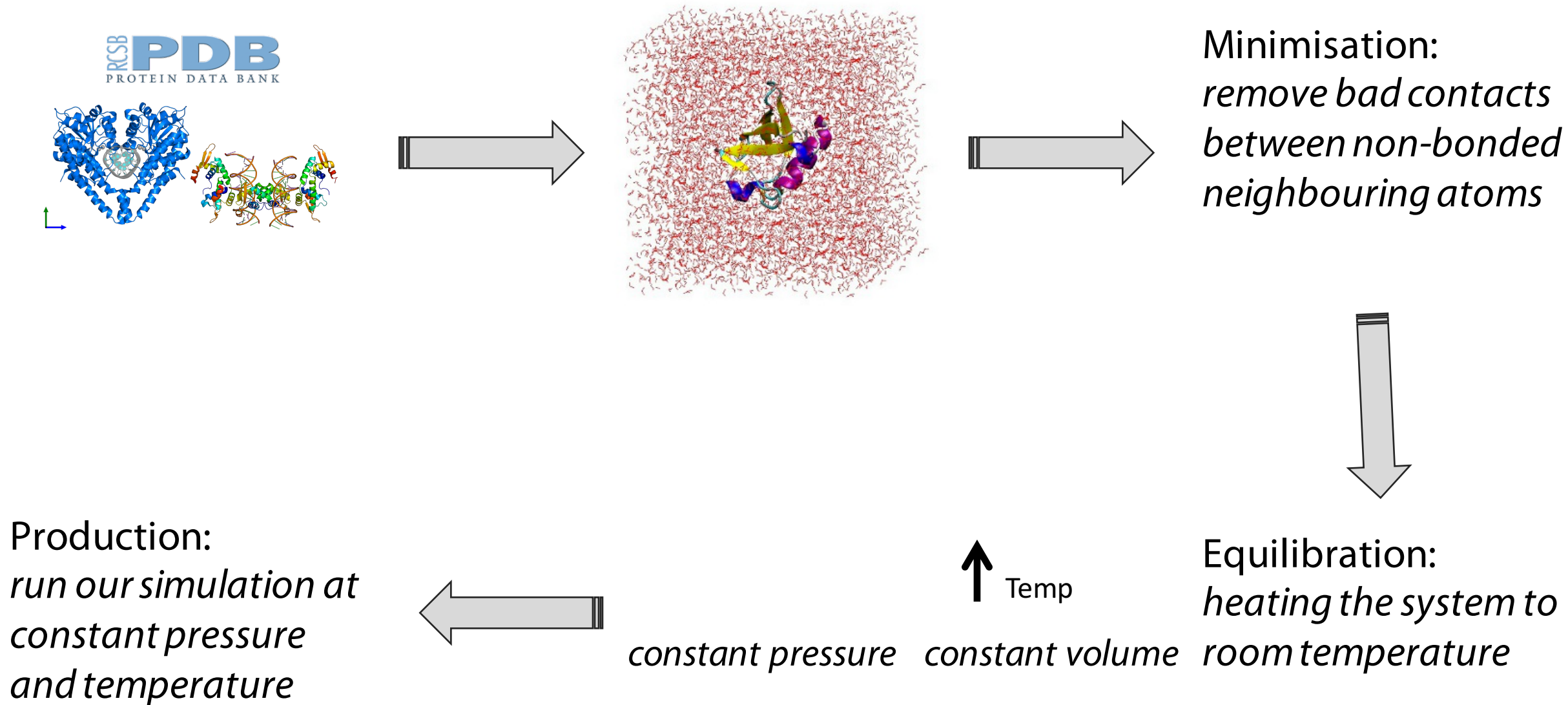
constant volume

Equilibration:
*heating the system to
room temperature*

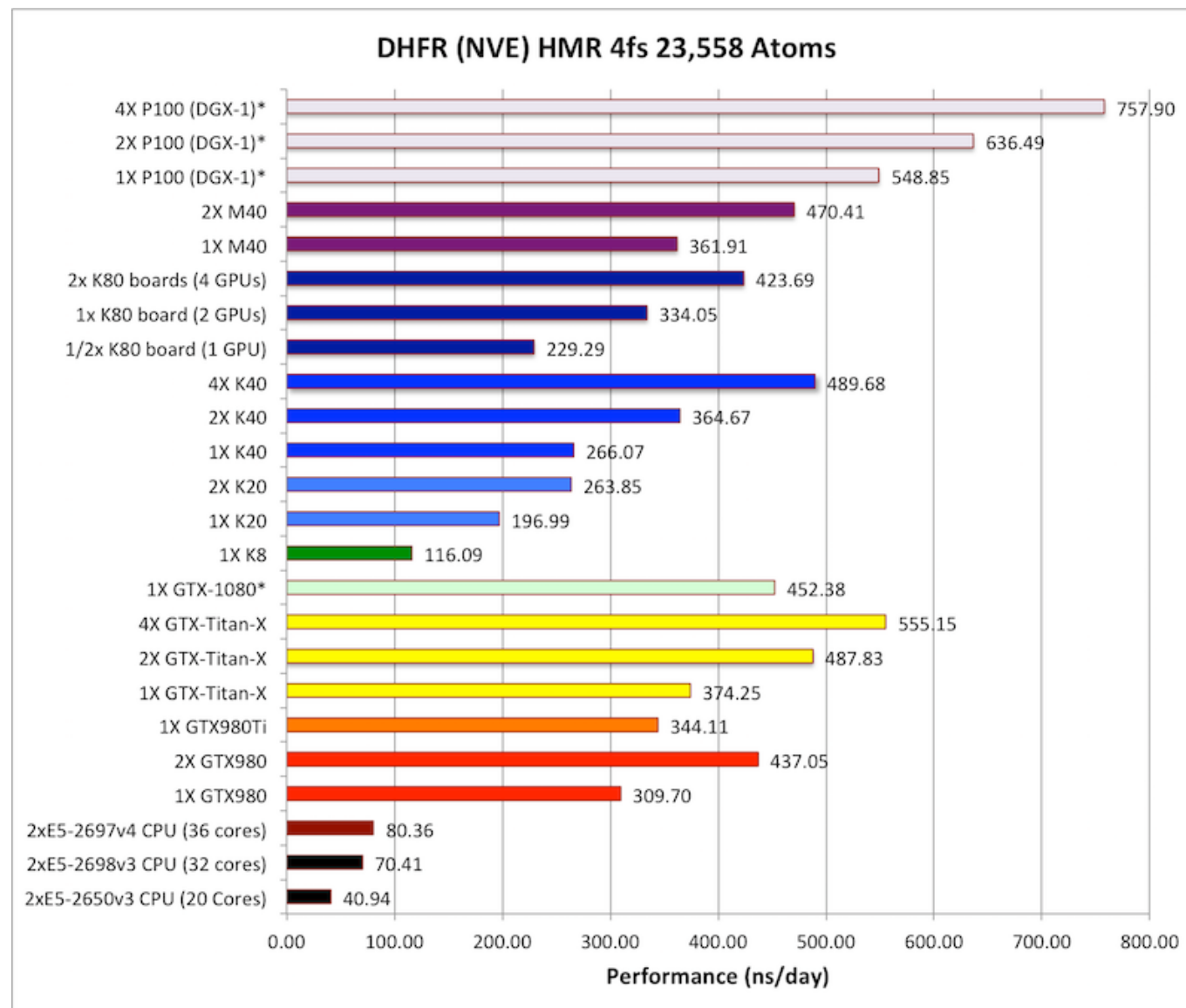
How to run an MD simulation



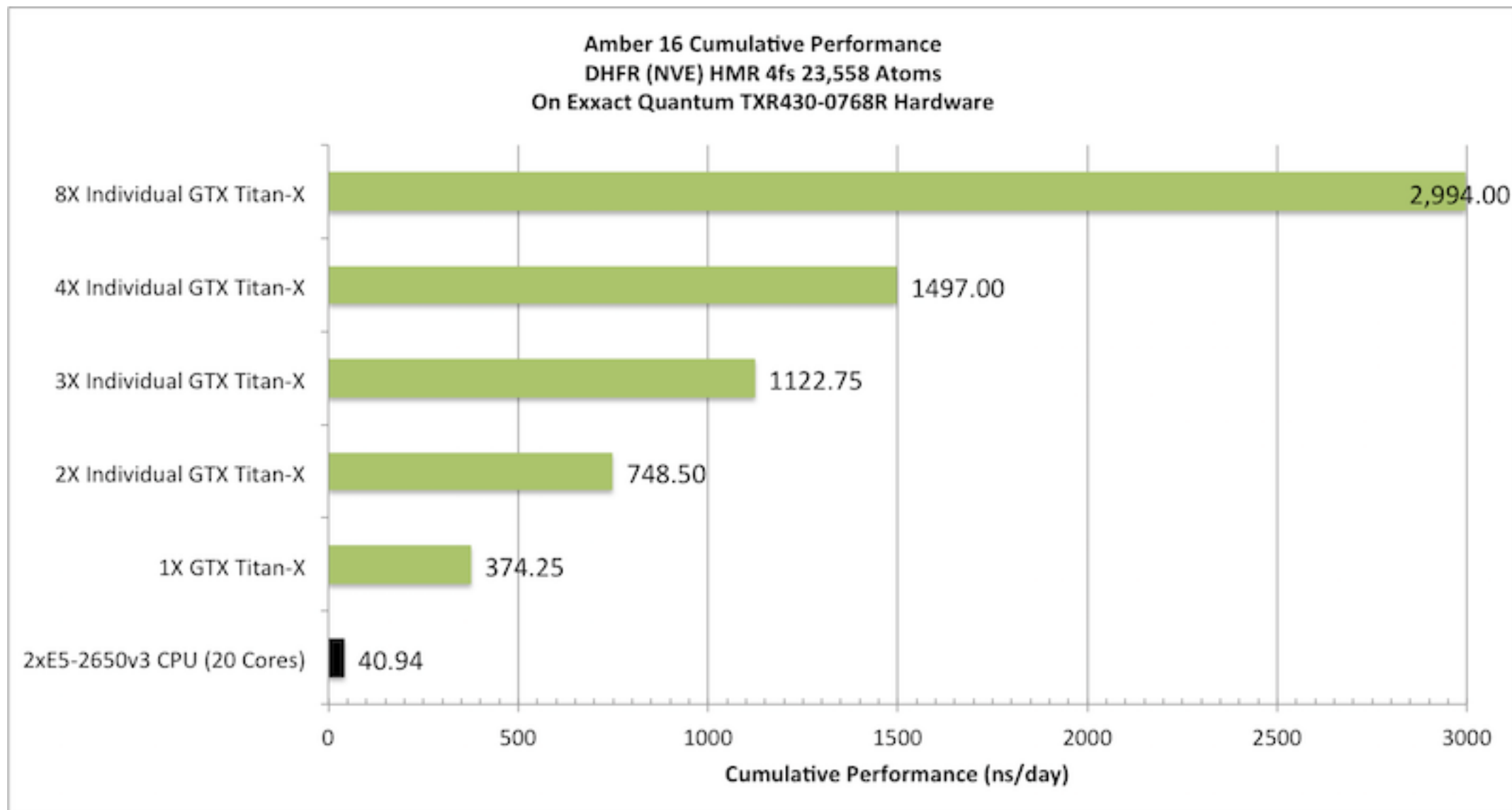
How to run an MD simulation



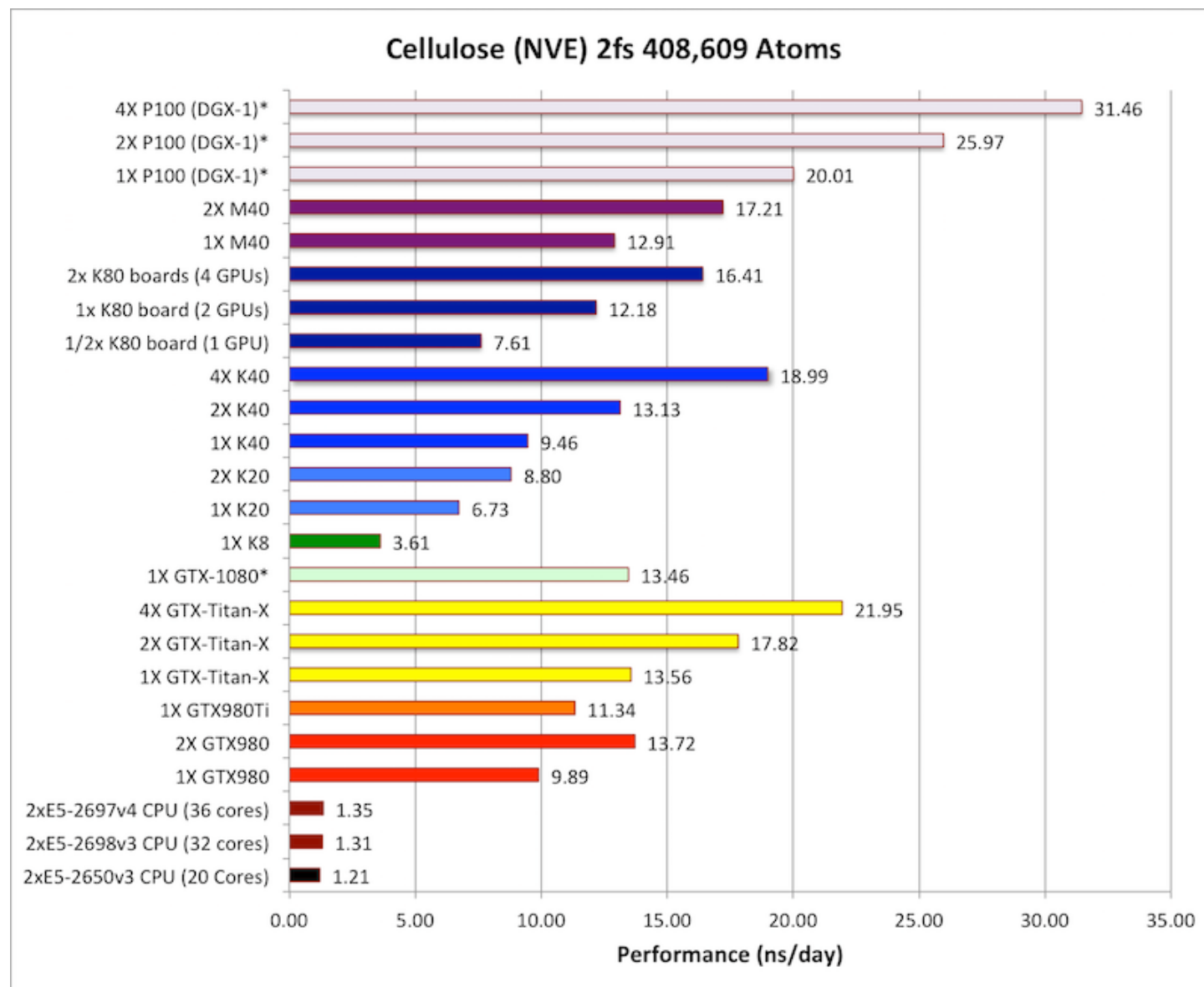
Benchmarks - Amber



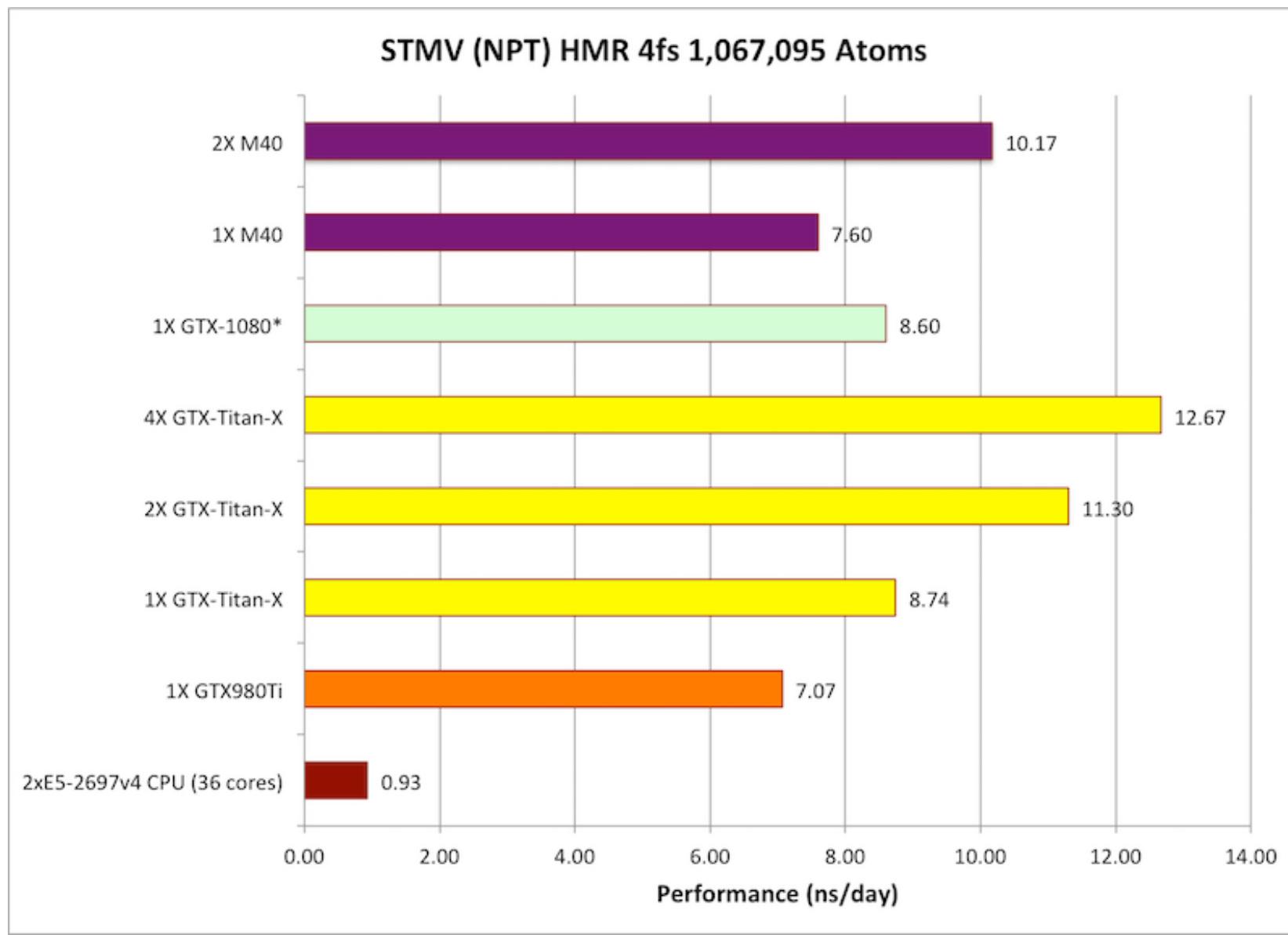
Benchmarks - Amber



Benchmarks - Amber



Benchmarks - Amber



Tutorial

Run your own MD simulation

Analyse an MD run: H-bonds over time

Manipulate your pdb file

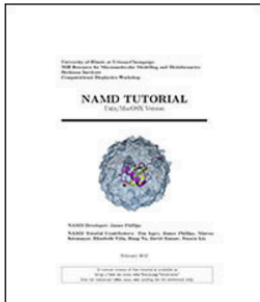
Run your own Interactive MD simulation

- VMD <http://www.ks.uiuc.edu/Research/vmd/>
- NAMD <http://www.ks.uiuc.edu/Research/namd/>
- Tutorial <http://www.ks.uiuc.edu/Research/vmd/imd/tutorial/>



NAMD Tutorials

These tutorials focus on NAMD specifically, although many others utilize it as well. Be sure you have the latest version of **NAMD**.



NAMD Tutorial:

- Participants learn how to use NAMD to set up basic molecular dynamics simulations, and to understand typical NAMD input and output files, with an emphasis on such files for protein energy minimization and equilibration in water. Tutorial versions available for Windows, or Mac and Unix/Linux platforms.
- Instructions: [[html for Unix/Mac](#)] [[pdf for Unix/Mac](#), 8.0M] [[html for Windows](#)] [[pdf for Windows](#), 6.5M]
- Required tutorial files (all platforms): [[.tar.gz](#), 148M], [[.zip](#), 148M], **individual files (all platforms)**

Run your own MD simulation

- Chimera - <https://www.cgl.ucsf.edu/chimera/docs/ContributedSoftware/md/md.html>
- File → Fetch by ID → 1zik

Chimera Animations

- `movie record ; turn y 3 120 ; wait 120 ; movie stop ; movie encode output ~/Desktop/turn.mov bitrate 10000`
- `movie record ; rock y 4 68 ; wait ; rock x 4 68 ; wait ; movie stop ; movie encode output ~/Desktop/rock.mov`

Run your own MD simulation

- Chimera - <https://www.cgl.ucsf.edu/chimera/docs/ContributedSoftware/md/md.html>
- File → Fetch by ID → 1zik
- Tools → MD/Ensemble Analysis → Molecular Dynamics Simulation

Molecular Dynamics Simulation

Select model:

1zik (#0)

Prep Structure

Solvation

Constraints Etc.

Run Parameters

Settings:

minimization

☒ Minimize before MD

Steepest descent steps:

50

Steepest descent step size (Å):

0.02

Conjugate gradient steps:

10

Conjugate gradient step size (Å):

0.02

Run

Interface designed by V. Munoz-Robles and J.-D.Marechal

The Computational Biotechnological Chemistry Team

Close

Help

1zik (#0)

Select model:

Prep Structure

Solvation

Constraints Etc.

Run Parameters

Settings: equilibration

☒ Equilibrate

2000 steps

Temperature control method:

☒ Heater

☐ Velocity scaler

☐ None

Heater Parameters

temp1 (K)0temp2 (K)298gradient (K/ps)10

start1endapply every2steps

☐ Barostat reset:

start1endapply every2steps

Time step (fs): 1

Output trajectory file: /Users/natasha/Desktop/heating.nc

Browse

Output restart-trajectory file: /Users/natasha/Desktop/heat_res.nc

Browse

Run

Interface designed by V. Munoz-Robles and J.-D.Marechal
The Computational Biotechnological Chemistry Team

Close

Help

1zik (#0)

Select model:

Prep Structure

Solvation

Constraints Etc.

Run Parameters

Settings: production

☒ Include production phase

2000

steps

Input restart-trajectory file (from previous equilibration or production):

tasha/Desktop/heat_res.nc

Browse

☐ Andersen barostat:

pressure (bars)

1.0132

relaxation time

1.5

☐ Nosé thermostat:

temperature (K)

298

relaxation time

0.2

Time step (fs):

1

Output trajectory file:

/Users/natasha/Desktop/prod.nc

Browse

☐ Output restart-trajectory file:

/Users/natasha/Desktop/prod_res.nc

Browse

Run

Interface designed by V. Munoz-Robles and J.-D.Marechal
The Computational Biotechnological Chemistry Team

Close

Help

Run your own MD simulation

- Chimera - <https://www.cgl.ucsf.edu/chimera/docs/ContributedSoftware/md/md.html>
- File → Fetch by ID → 1zik
- Tools → MD/Ensemble Analysis → Molecular Dynamics Simulation
- Use defaults!
- Run parameters → Run
 - Add hydrogens - OK
 - Assign charges for minimize - OK

Analyse an MD run: H-bonds over time

- Chimera

[Chimera Tutorials Index](#)

Trajectory and Ensemble Analysis Tutorial

This tutorial focuses on visualization and analysis of molecular dynamics (MD) trajectories and other structural ensembles with the [MD Movie](#) tool. [Part 1](#) uses an MD trajectory of a collagen peptide, and [Part 2](#) uses an NMR ensemble of Met-enkephalin.

Part 1 - Collagen Peptide

We will view an MD trajectory of the nonmutant collagen peptide described in:

[Severity of osteogenesis imperfecta and structure of a collagen-like peptide modeling a lethal mutation site](#), Radmer RJ, Klein TE. *Biochemistry*. 2004 May 11;43(18):5314-23.

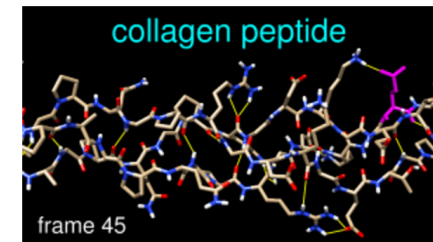
(Thanks to the authors for providing the data!) To follow along, [download](#) the data files:

- [leap.top](#) - [Amber](#) parameter/topology file
- [md01.crd](#) - [Amber](#) trajectory file
- [collagen.meta](#) - metafile specifying these input files for [MD Movie](#)

On **Windows/Mac**, click the **chimera** icon; on **UNIX**, start Chimera from the system prompt:

```
unix: chimera
```

space ^ v x



- <https://www.cgl.ucsf.edu/chimera/current/docs/UsersGuide/tutorials/ensembles2.html>

Analyse an MD run: H-bonds over time

“A better understanding of the details of collagen structure, dynamics, and hydrogen bond networks will improve our ability to predict the physicochemical properties that contribute to the stability of collagen molecules, or lack thereof, and the severity of a single-point mutation.”

5314

Biochemistry **2004**, 43, 5314–5323

Severity of Osteogenesis Imperfecta and Structure of a Collagen-like Peptide Modeling a Lethal Mutation Site[†]

Randall J. Radmer and Teri E. Klein*

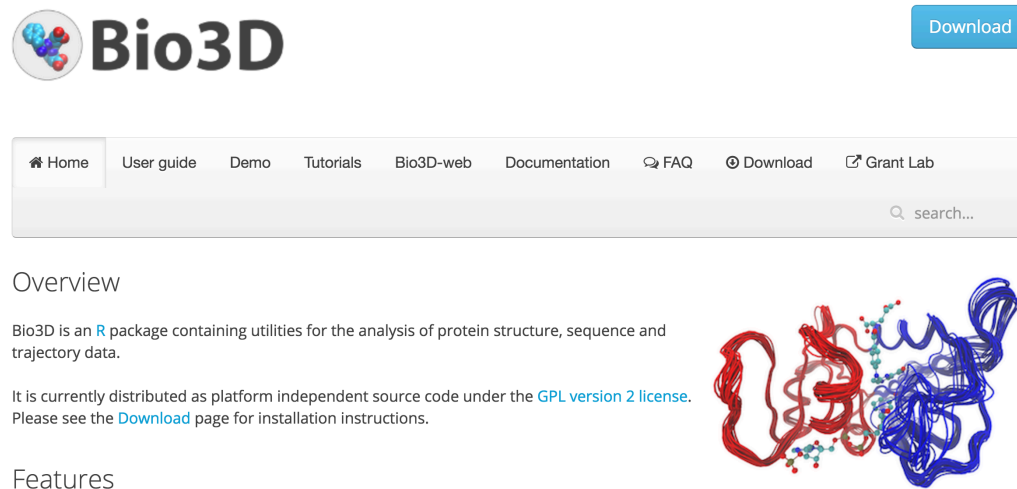
Department of Genetics, School of Medicine, Stanford University, Stanford, California 94305

Received September 17, 2003; Revised Manuscript Received March 6, 2004

ABSTRACT: We show that there are correlations between the severities of osteogenesis imperfecta (OI) phenotypes and changes in the residues near the mutation site. Our results show the correlations between the severity of various forms of the inherited disease OI and alteration of residues near the site of OI causing mutations. Among our many observed correlations are particularly striking ones between the presence of nearby proline residues and lethal mutations, and the presence of nearby alanines residues and nonlethal mutations. We investigated the possibility that these correlations have a structural basis using molecular dynamics simulations of collagen-like molecules designed to mimic the site of a lethal OI mutation in collagen type I. Our significant finding is that interchain hydrogen bonding is greatly affected by variations in residue type. We found that the strength of hydrogen bond networks between backbone atoms on different chains depends on the local residue sequence and is weaker in proline-rich regions of the molecule. We also found that an alanine at a site near an OI mutation causes less structural disruption than a proline, and that residue side chains also form interchain hydrogen bonds with frequencies that are dependent on residue type. For example, arginine side chains form strong hydrogen bonds with the backbone of the subsequent peptide chain, while lysine and glutamine less frequently form similar hydrogen bonds. This decrease in the observed hydrogen bond frequency correlates with a decrease in the experimentally determined thermal stability. We contrasted general structural properties of model collagen peptides with and without the mutation to examine the effect of the single-point mutation on the surrounding residues.

Manipulate your pdb file

- RStudio - <https://www.rstudio.com/products/rstudio/download/>
- Bio3D - <http://thegrantlab.org/bio3d/tutorials/installing-bio3d>
- Tutorial: <http://thegrantlab.org/bio3d/tutorials/structure-analysis>
- -renumbering, changing chain identifiers, identify binding site residues



köszönöm