

# 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

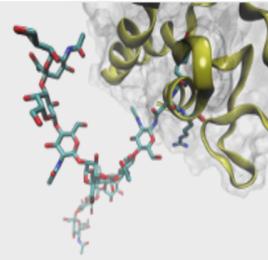
- Refine your structure
  - <http://glycam.org/>

**GLYCAM** 

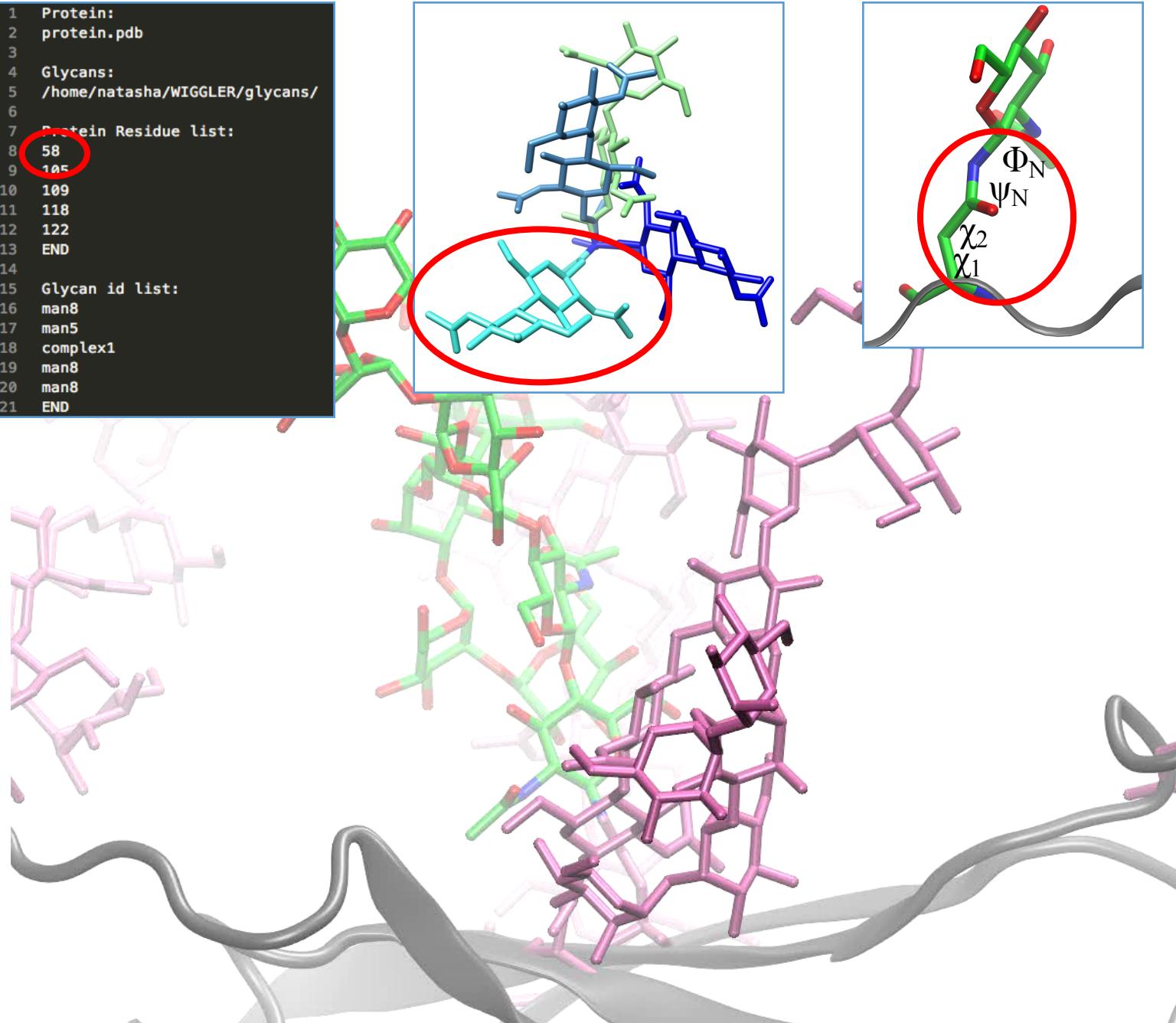
HOME ABOUT US NEWS LEGACY TOOLS HELP  

3D Structure Prediction Tools 3D Structure Libraries Other Tools Force Field Documentation Report a Problem

**GLYCAM-Web** is dedicated to simplifying the prediction of three-dimensional structures of carbohydrates and macromolecular structures involving carbohydrates. Click on the tabs above to learn the current capabilities of the site.

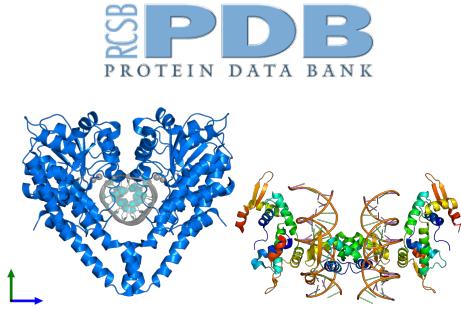


```
1 Protein:  
2 protein.pdb  
3  
4 Glycans:  
5 /home/natasha/WIGGLER/glycans/  
6  
7 Protein Residue list:  
8 58  
9 105  
10 109  
11 118  
12 122  
13 END  
14  
15 Glycan id list:  
16 man8  
17 man5  
18 complex1  
19 man8  
20 man8  
21 END
```



O Grant

# How to run an MD simulation



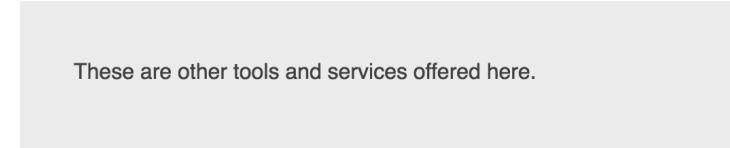
Topology and Coordinate file

# How to run an MD simulation

**GLYCAM** 

HOME    ABOUT US    NEWS    LEGACY TOOLS    HELP     

3D Structure Prediction Tools    3D Structure Libraries    Other Tools    Force Field    Documentation    Report a Problem



**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:

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

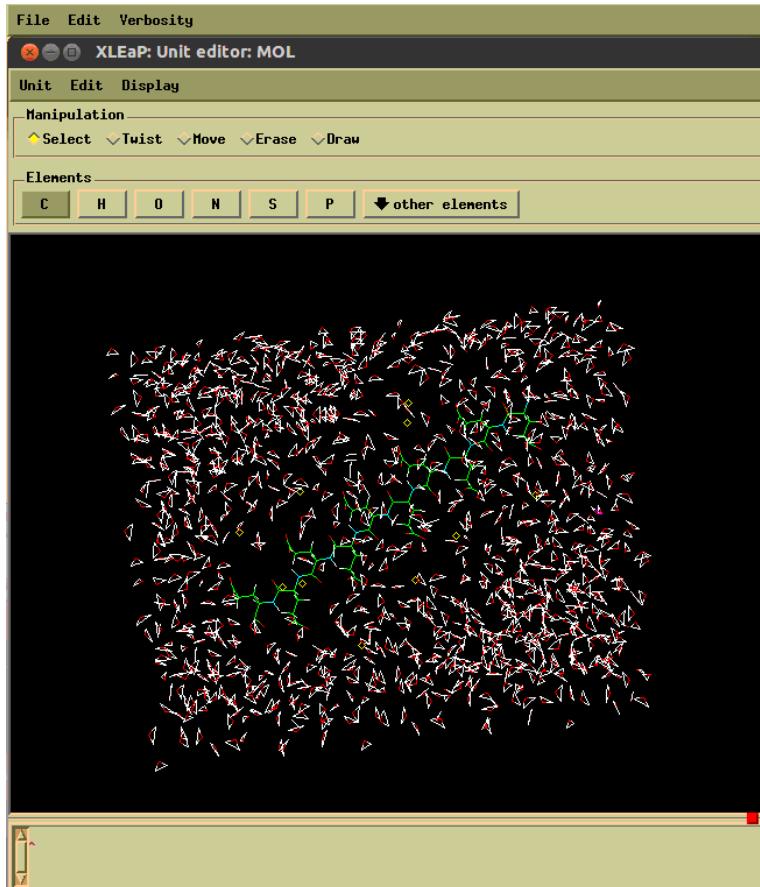
The AmberTools suite is free of charge, and its components are mostly released under the GNU General Public License (GPL). A few components are included that are in the public domain or which have other, open-source, licenses. The *sander* program now has the LGPL license.

**Amber 2016 Reference Manual**  
(Covers Amber16 and AmberTools16)



# 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.1798.04 mol.1799.C1

bond mol.1809.04 mol.1810.C1

bond mol.1820.04 mol.1821.C1

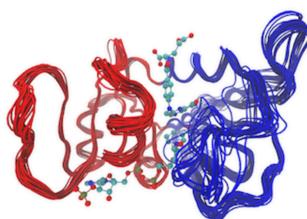
The screenshot shows the Bio3D website. At the top is the Bio3D logo, which is a circular icon containing a stylized molecular structure. To the right of the logo is a blue "Download" button. Below the logo is a navigation bar with links: Home (which is highlighted), User guide, Demo, Tutorials, Bio3D-web, Documentation, FAQ, Download, and Grant Lab. To the right of the navigation bar is a search bar with the placeholder text "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

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

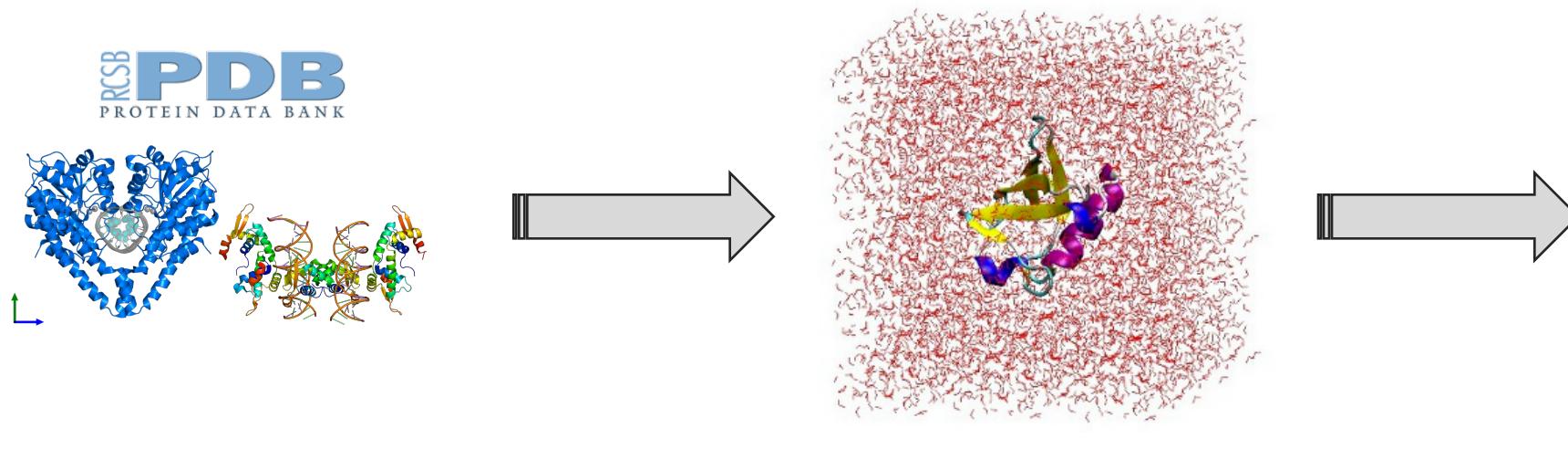
saveamberparm mol CPLX_Neut.prmtop CPLX_Neut.rst7
savepdb mol CPLX_Neut.pdb

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

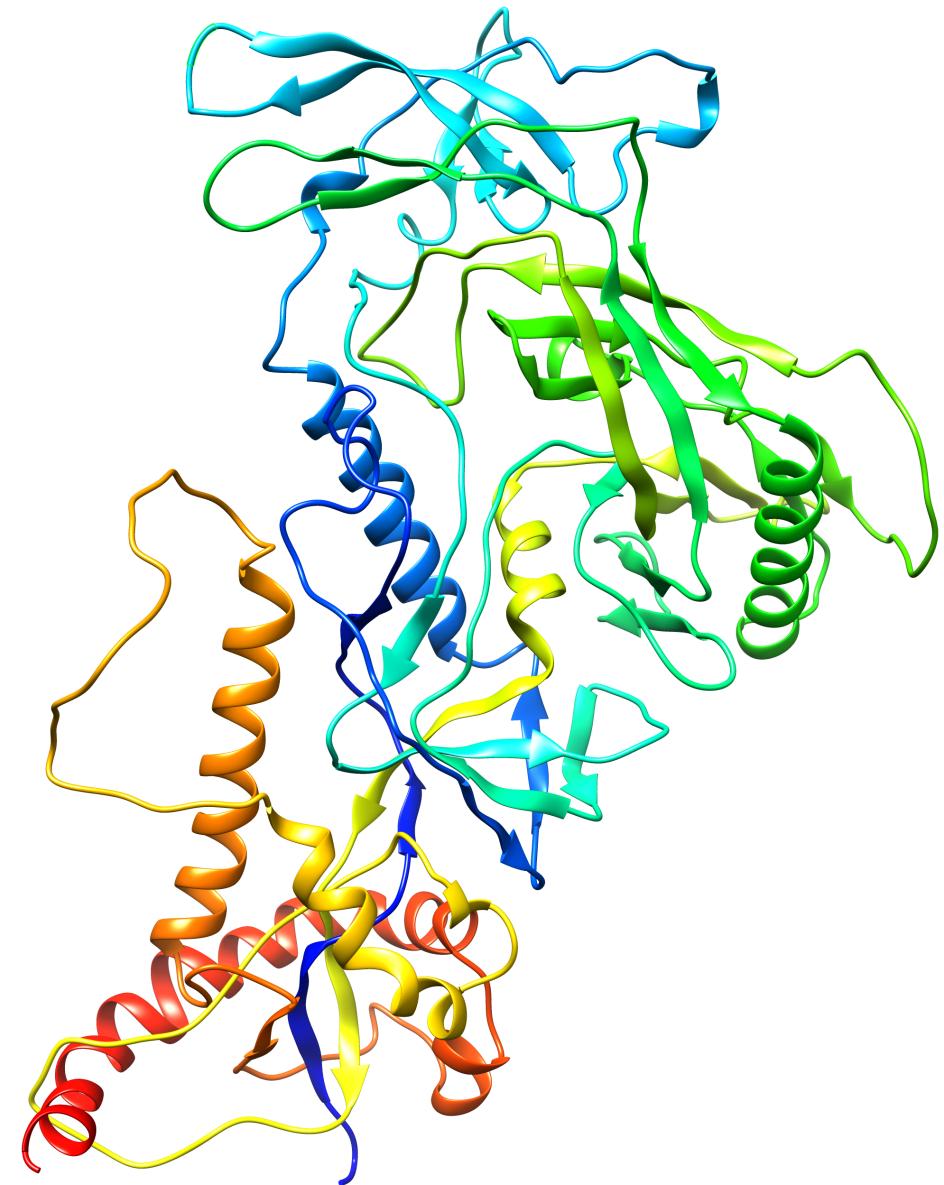
saveamberparm mol CPLX_Neut_Sol.prmtop CPLX_Neut_Sol.rst7
savepdb mol CPLX_Neut_Sol.pdb

quit
```

# How to run an MD simulation

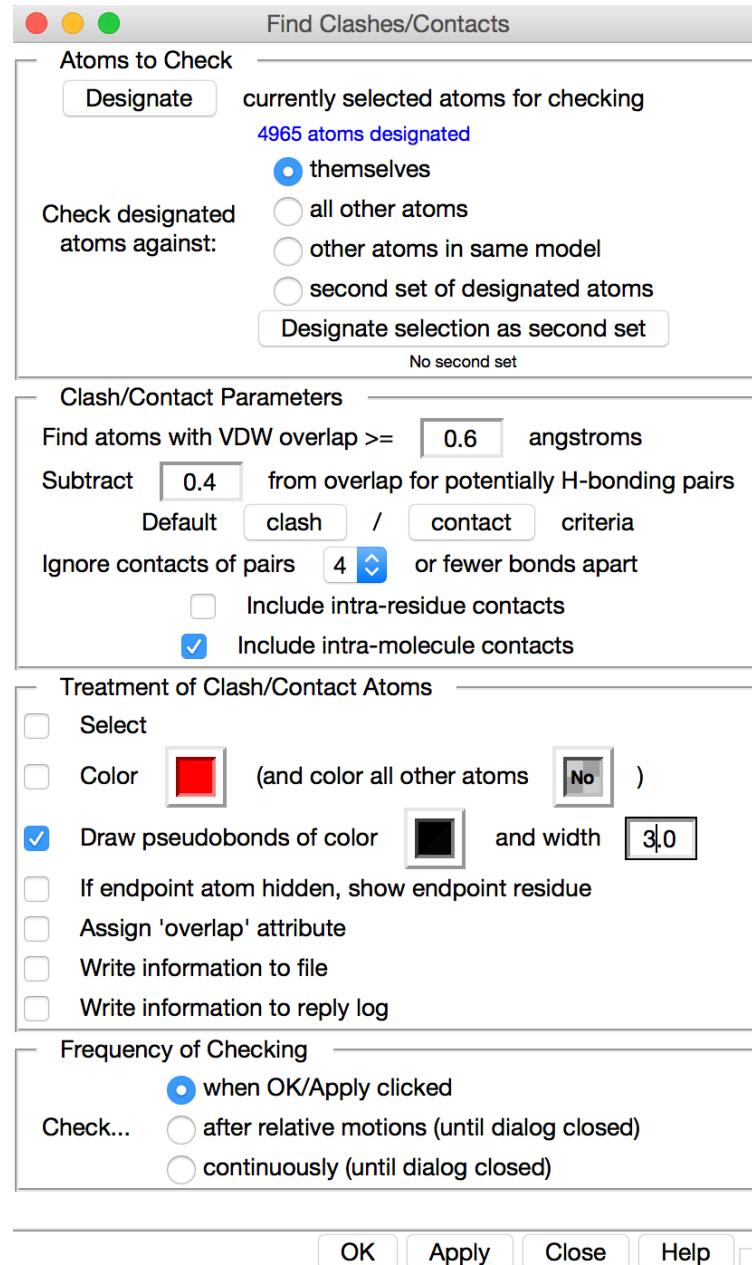


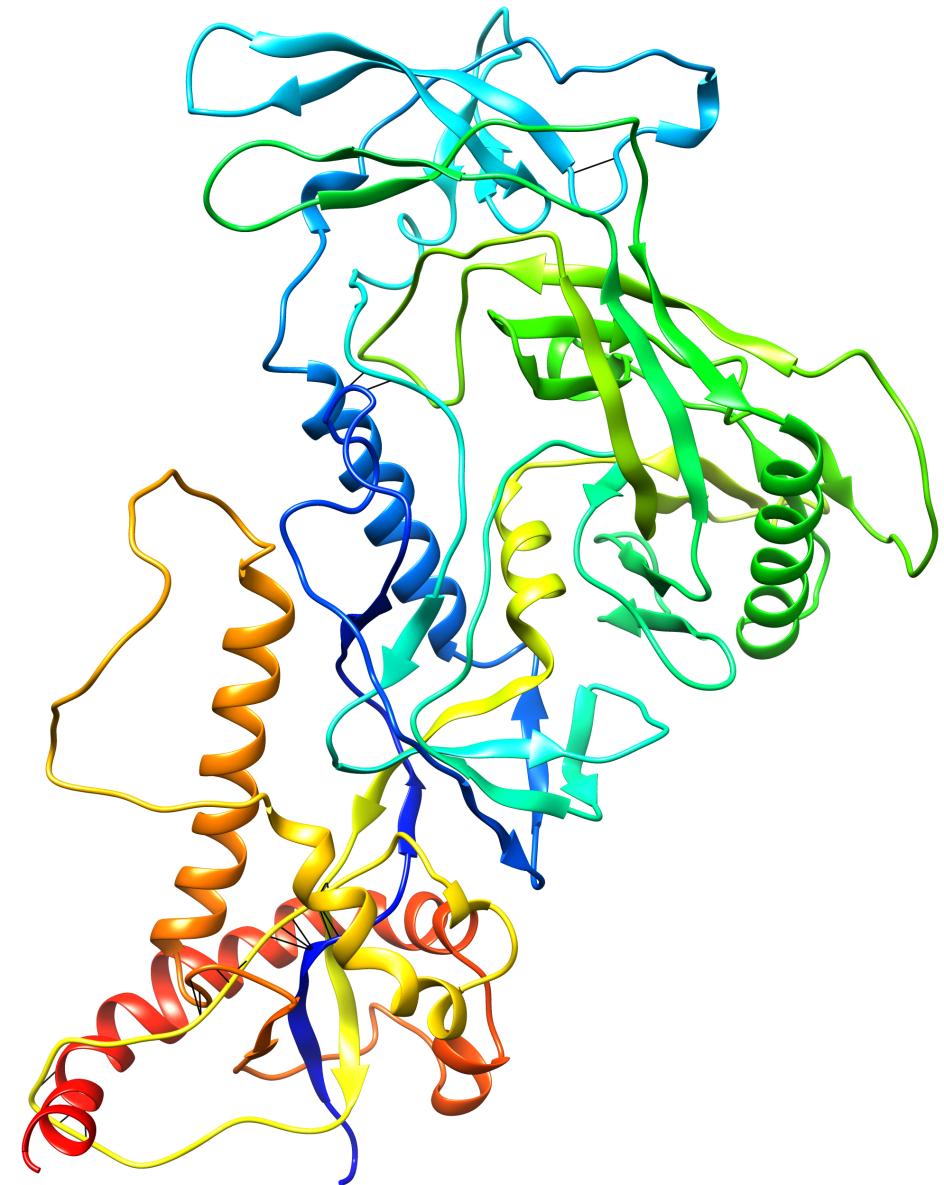
Minimisation:  
*remove bad contacts  
between non-bonded  
neighbouring atoms*



# Chimera:

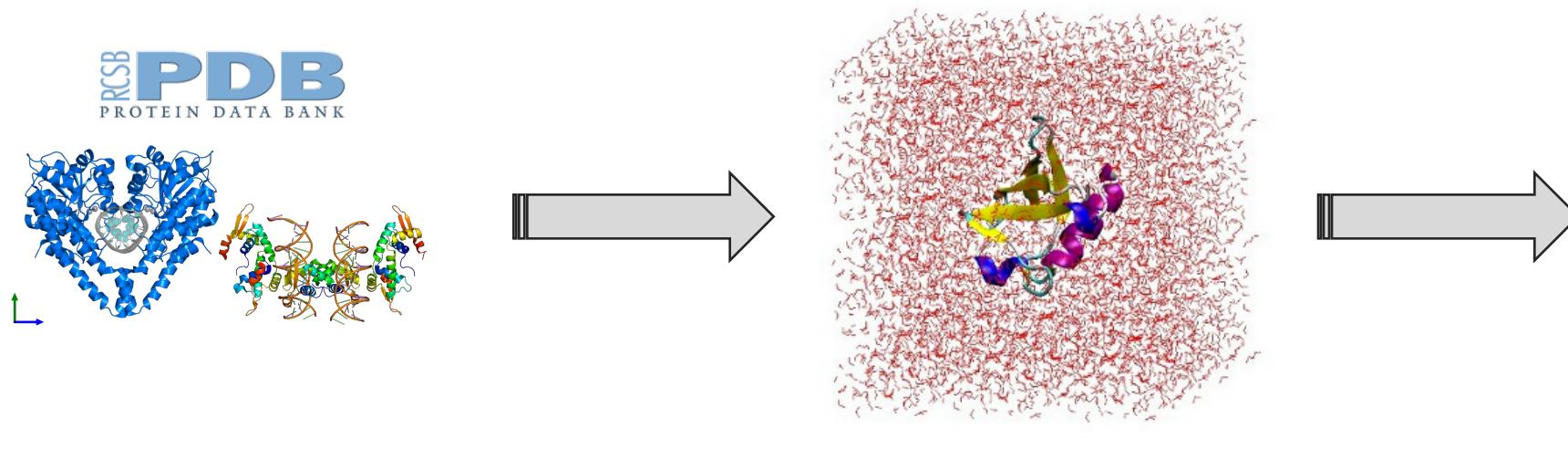
## find clashes/contacts







# How to run an MD simulation



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

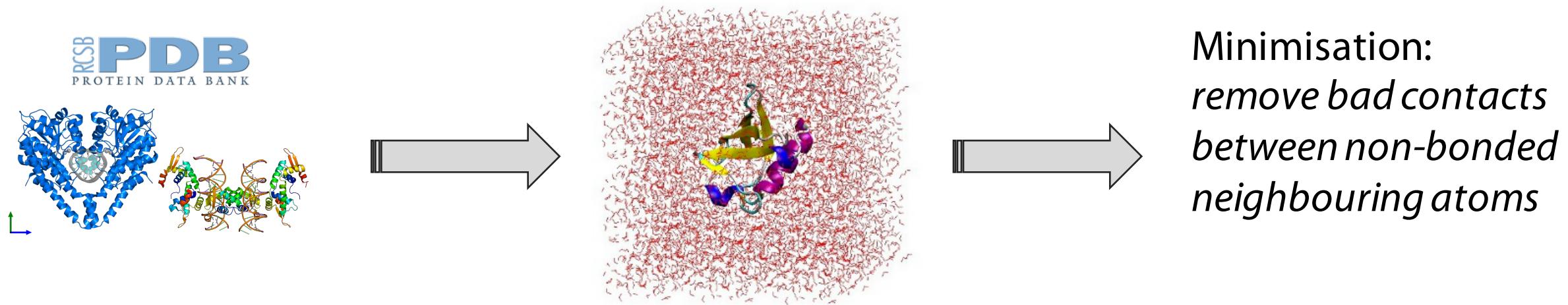
# How to run an MD simulation

## Constant Volume Minimization

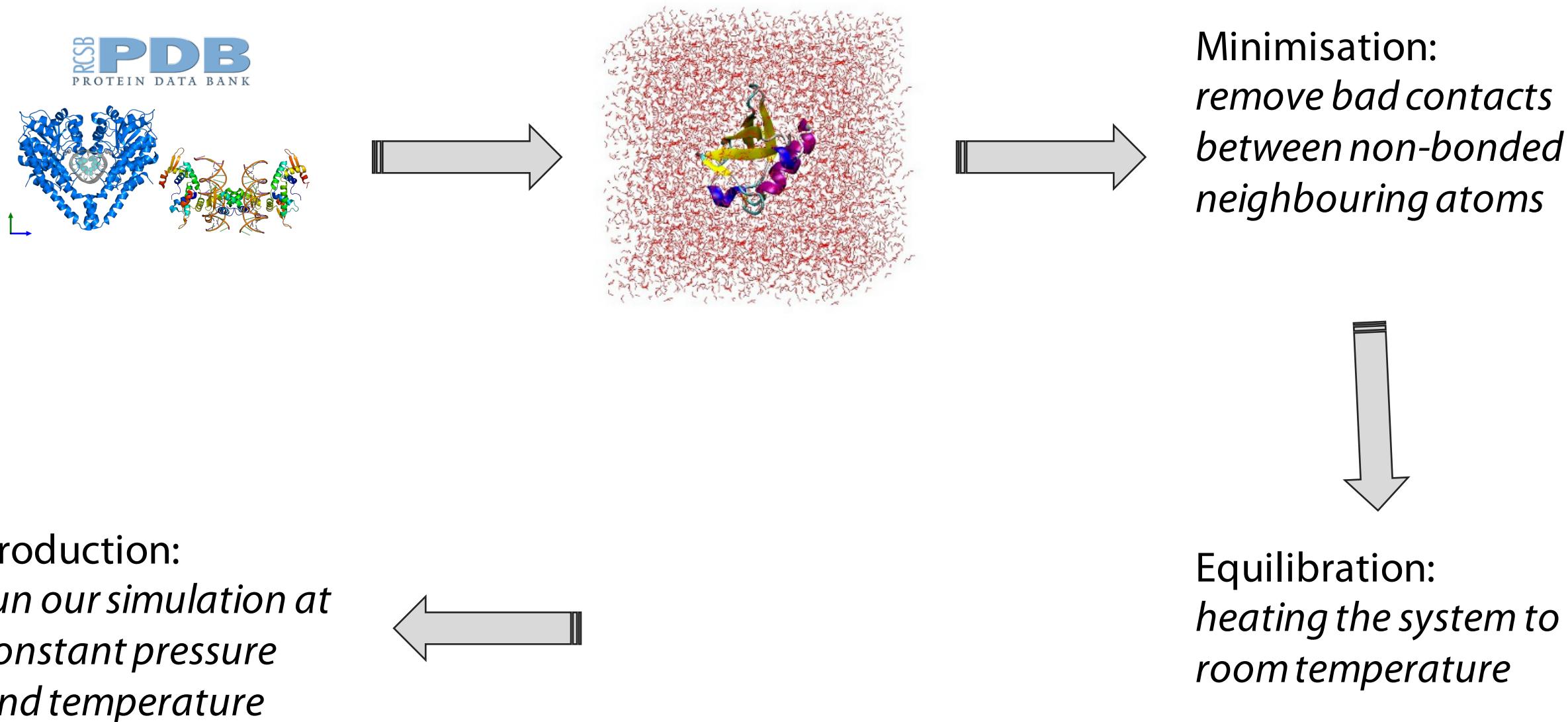
```
# Control section
&cntrl
  imin=1,
  dielc = 1, cut = 10.0,
  ntb = 1,
  maxcyc = 20000, dx0 = 0.01, drms = 0.0001,
  ntmin = 1, ncyc = 10000,
  ntp = 0,
  ntr = 1,
  irest = 0,
/
Restraints kcal/mol
```

Minimisation:  
*Amber input file*

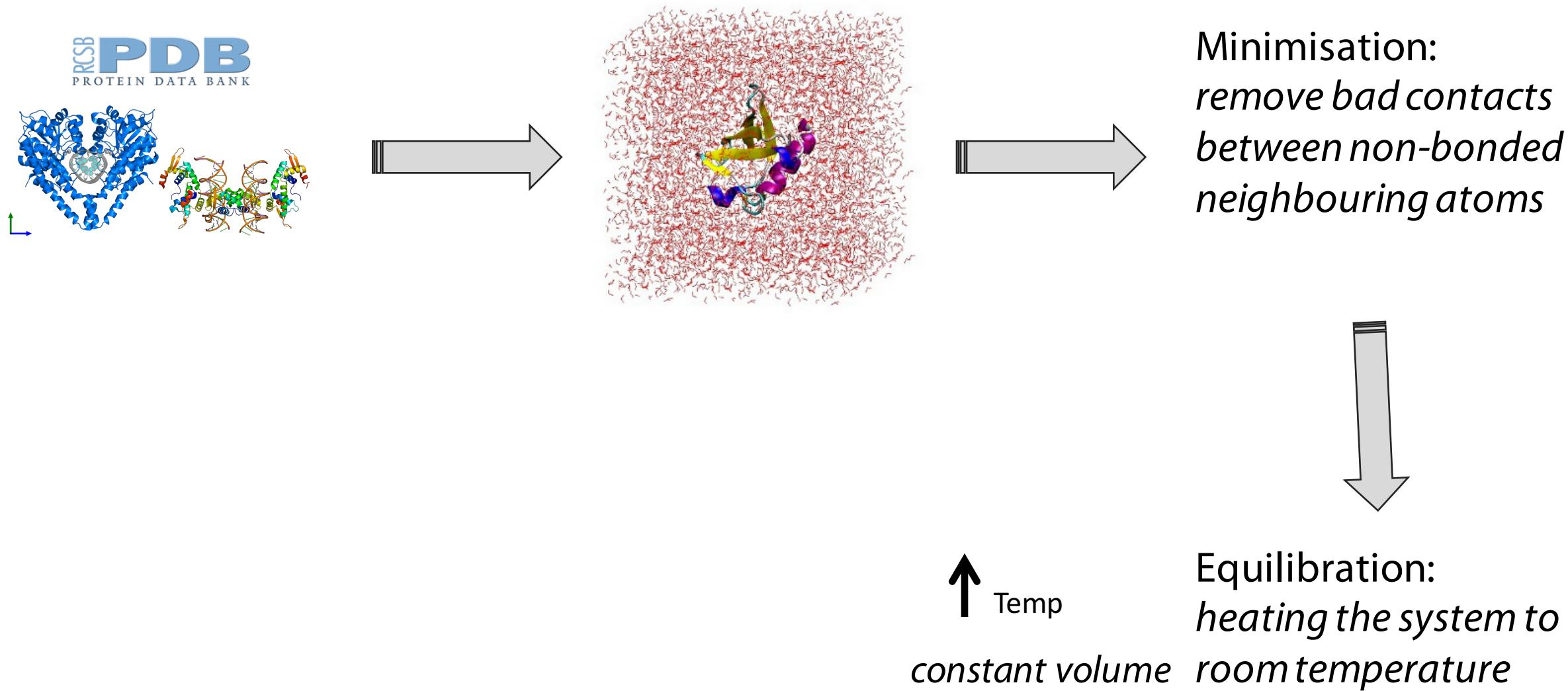
# How to run an MD simulation



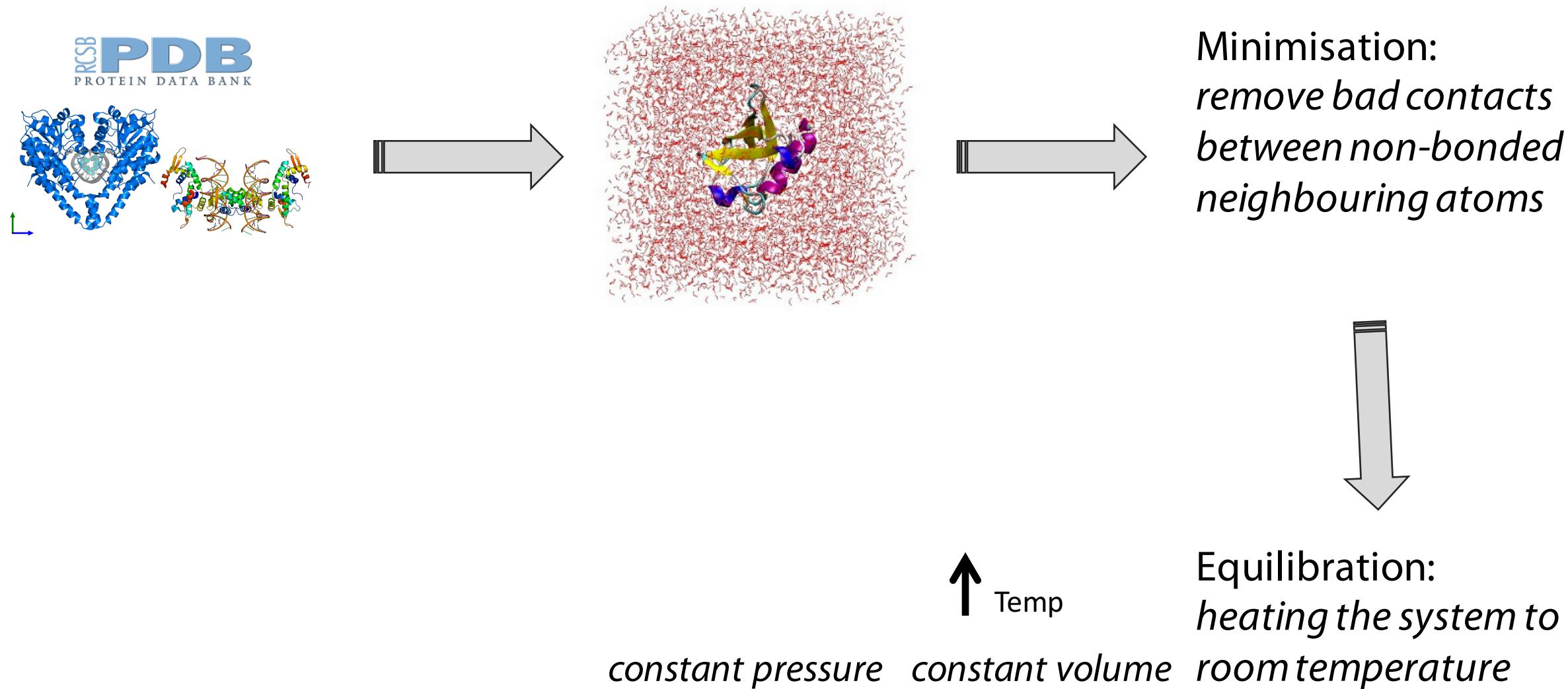
# How to run an MD simulation



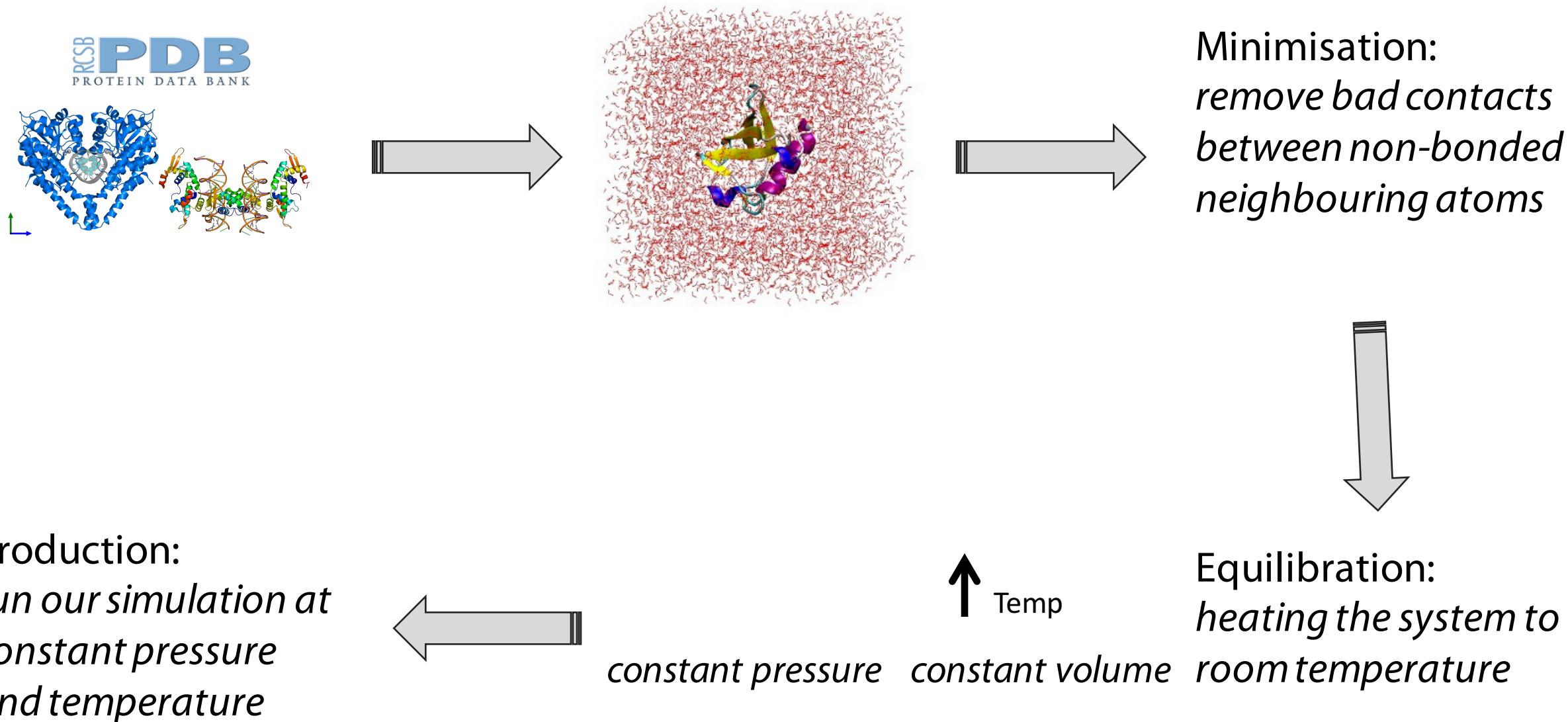
# How to run an MD simulation



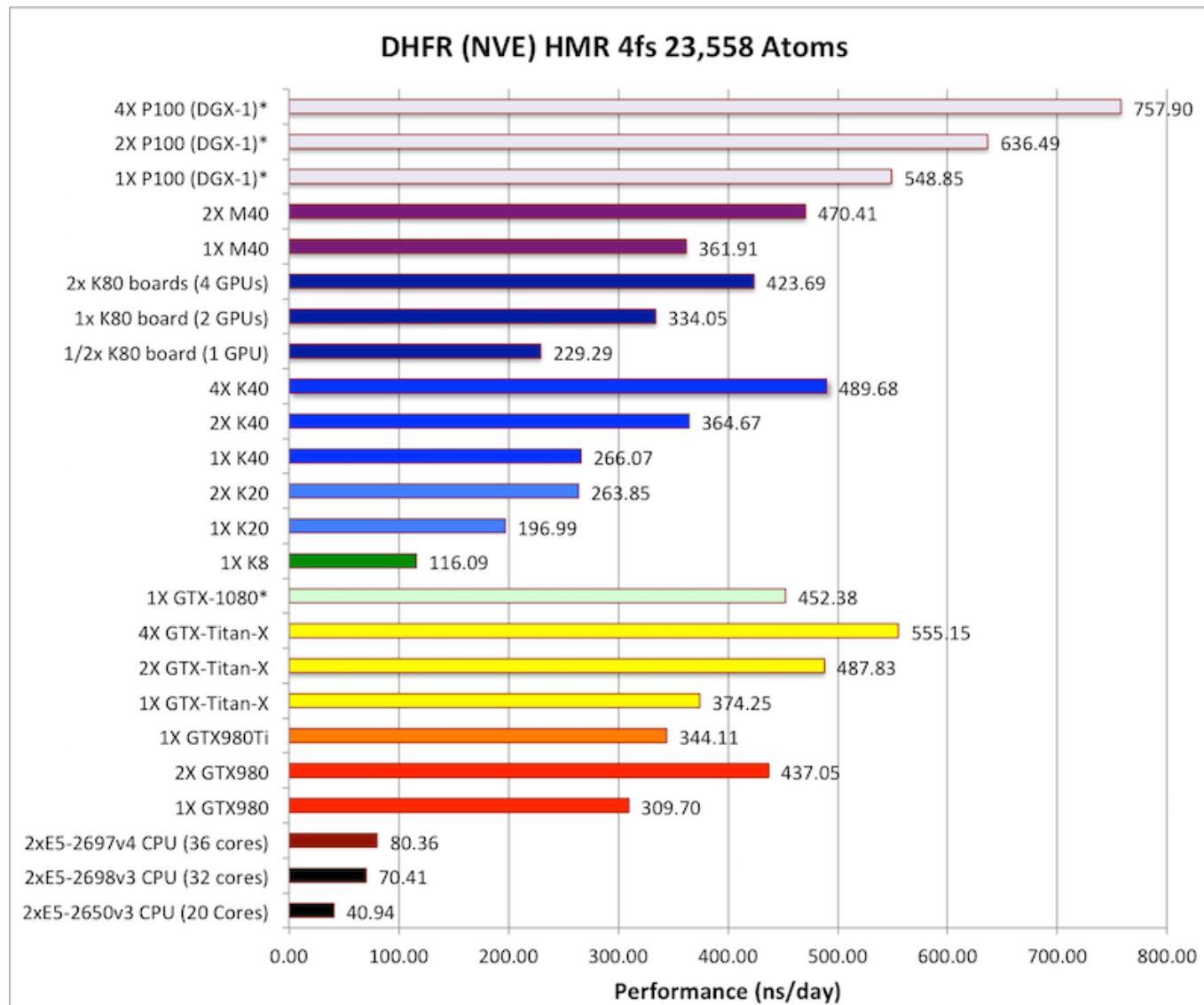
# How to run an MD simulation



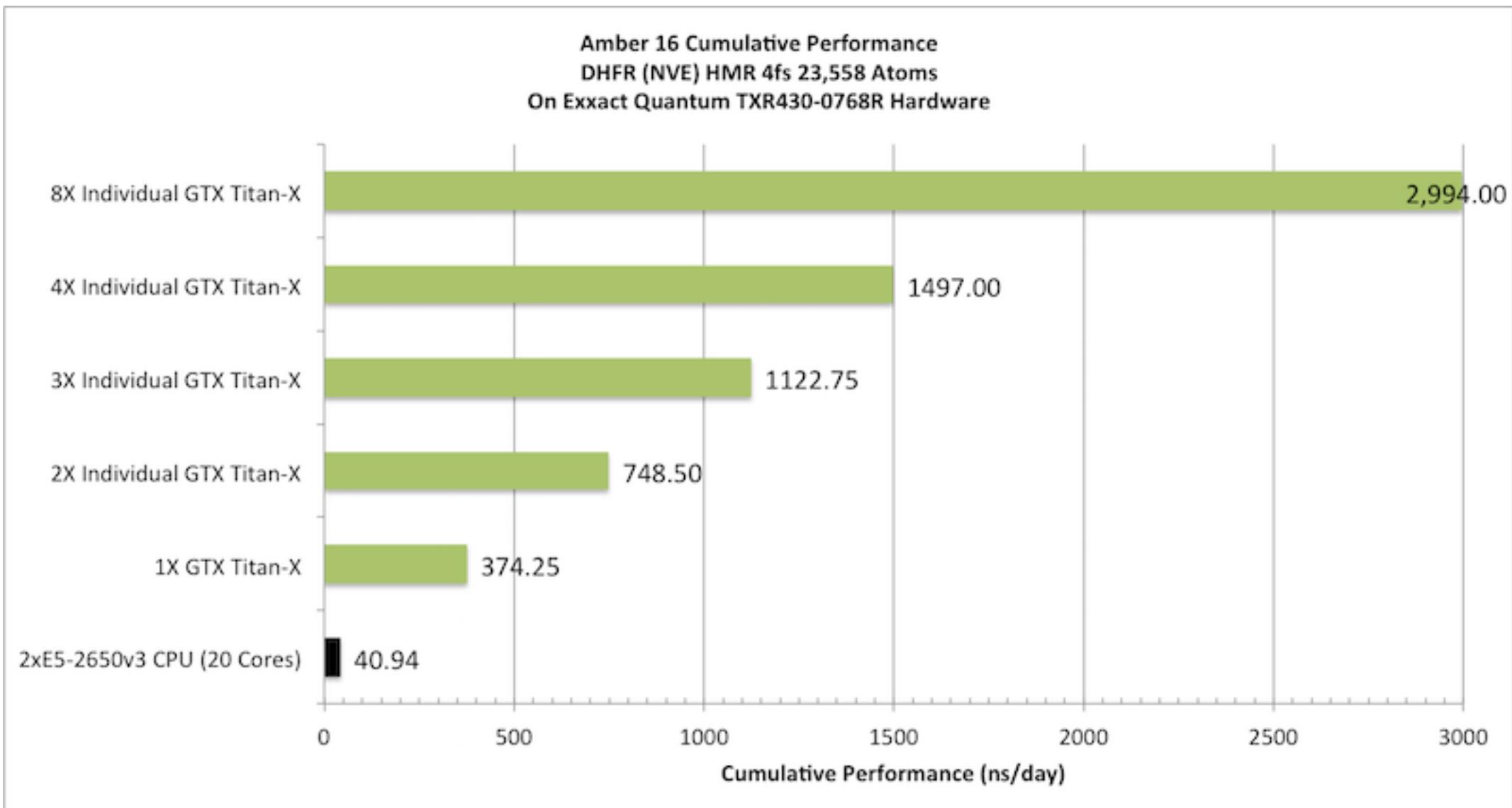
# How to run an MD simulation



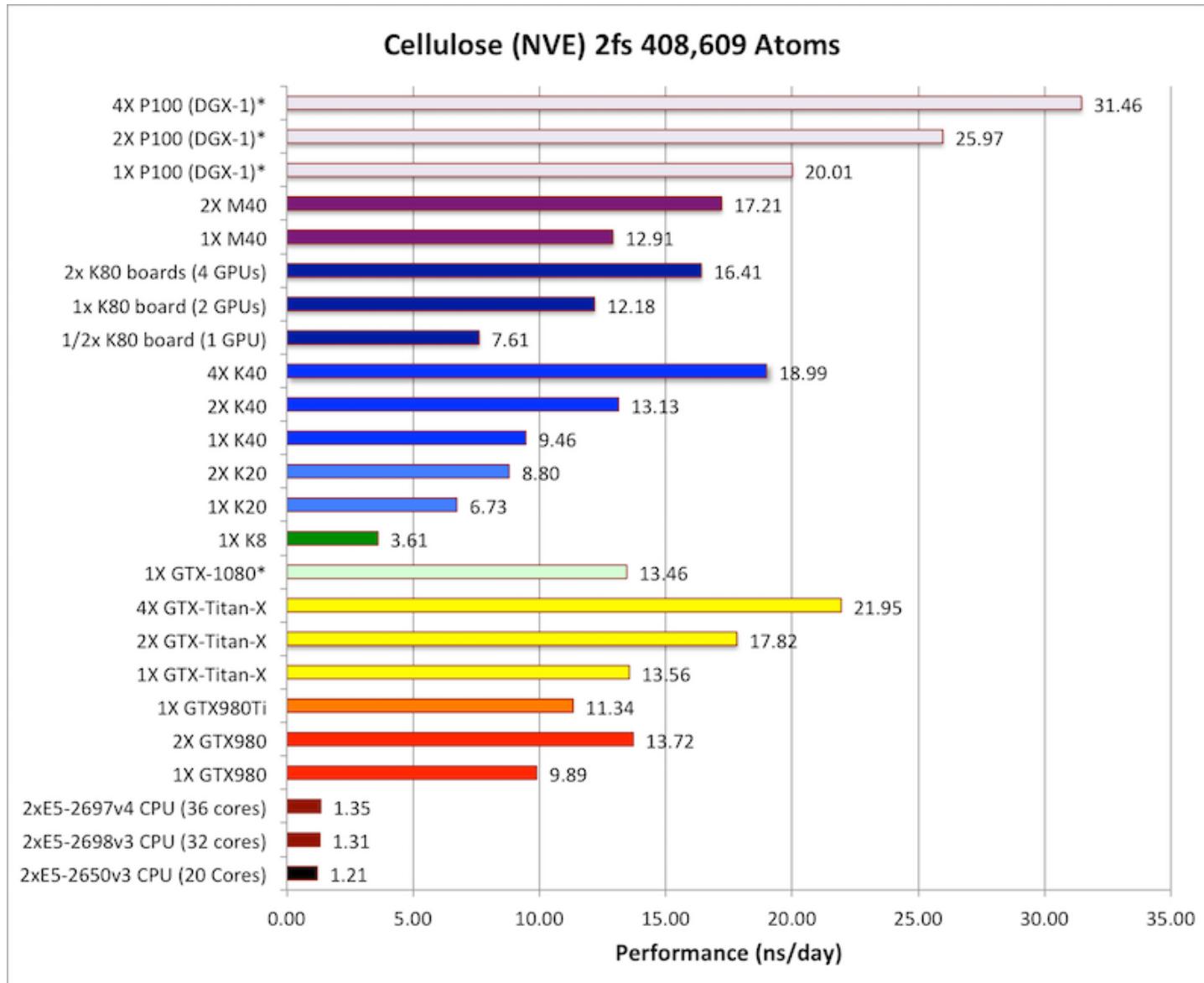
# Benchmarks - Amber



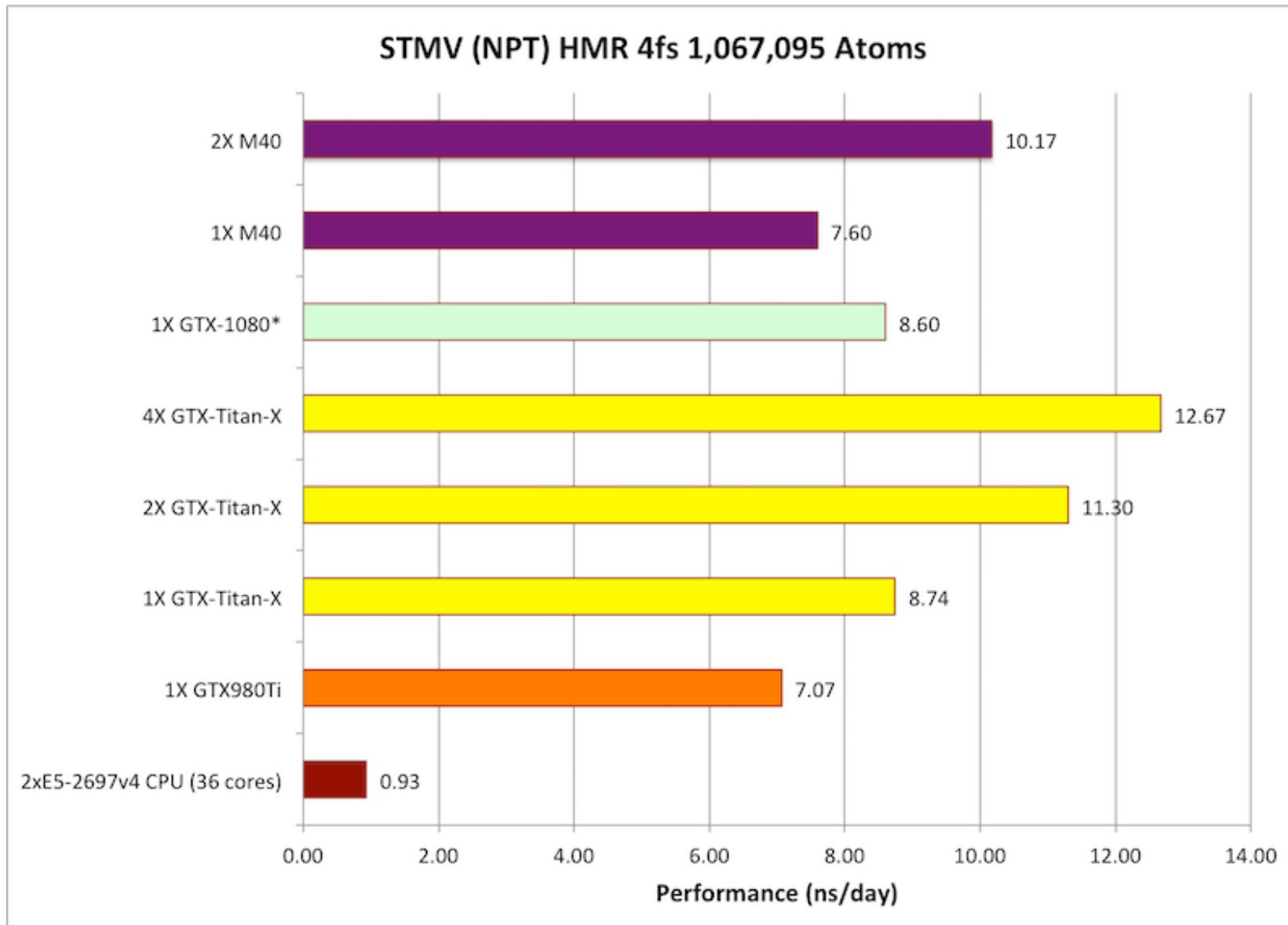
# Benchmarks - Amber



# Benchmarks - Amber



# Benchmarks - Amber



# Tutorial

Run your own MD simulation

Analyse an MD run: H-bonds over time

Manipulate your pdb file

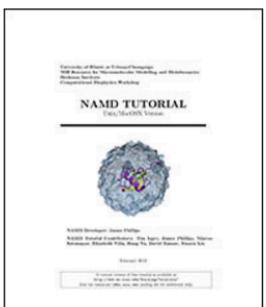
# Run your own Interactive MD simulation

- 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

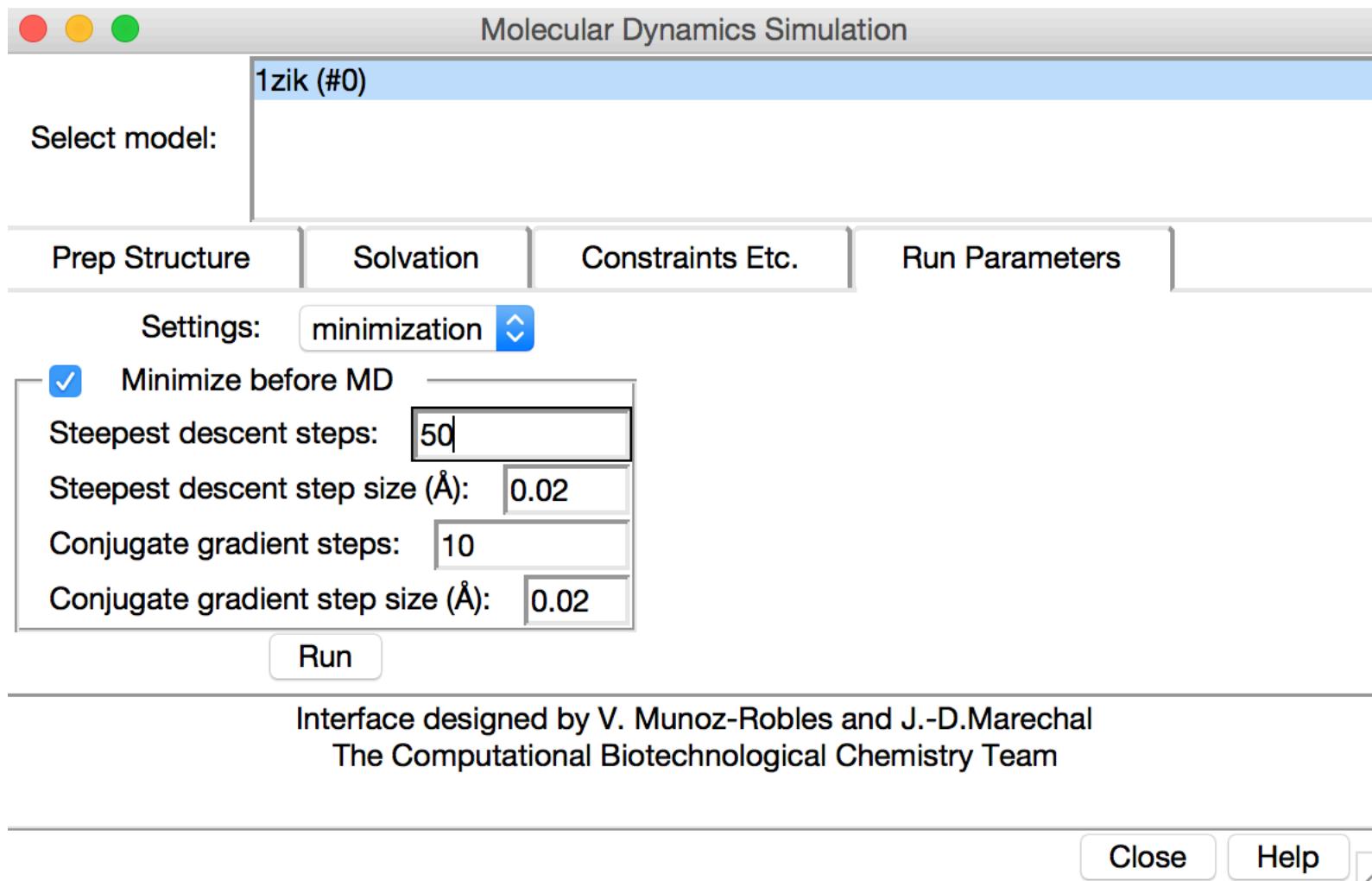
- Chimera - <https://www.cgl.ucsf.edu/chimera/docs/ContributedSoftware/md/md.html>
- File → Fetch by ID → 1zik

# 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

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)

0

temp2 (K)

298

gradient (K/ps)

10

start

1

end

apply every

2

steps

Barostat reset:

start

1

end

apply every

2

steps

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

Molecular Dynamics Simulation

1zik (#0)

Select model:

Prep Structure Solvation Constraints Etc. Run Parameters

Settings: production 

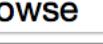
Include production phase  steps

Andersen barostat: pressure (bars)  relaxation time

Nosé thermostat: temperature (K)  relaxation time

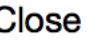
Time step (fs):

Output trajectory file:  

Output restart-trajectory file:  



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

# 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.

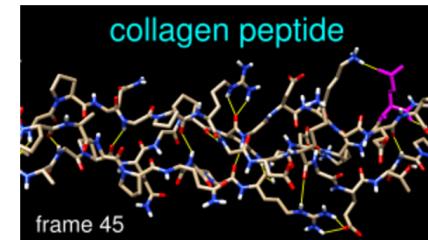
### Part 1 - Collagen Peptide

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
```

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

# Analyse an MD run: H-bonds over time

5314

*Biochemistry* 2004, 43, 5314–5323

**“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.”**

## Severity of Osteogenesis Imperfecta and Structure of a Collagen-like Peptide Modeling a Lethal Mutation Site<sup>†</sup>

Randall J. Radmer and Teri E. Klein\*

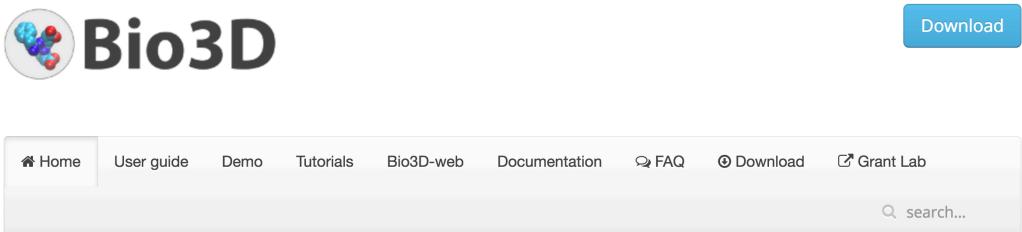
*Department of Genetics, School of Medicine, Stanford University, Stanford, California 94305*

*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



The screenshot shows the Bio3D website. At the top left is the Bio3D logo, which consists of a circular icon with a stylized protein structure and the word "Bio3D" in a bold, dark font. To the right of the logo is a blue "Download" button. Below the logo is a navigation bar with links: Home (which is highlighted), User guide, Demo, Tutorials, Bio3D-web, Documentation, FAQ, Download, and Grant Lab. A search bar with the placeholder "search..." is located below the navigation bar. The main content area has a heading "Overview" followed by a paragraph about the Bio3D package. It also includes a note about the license and a link to the download page. To the right of the text is a 3D molecular visualization showing a protein structure composed of red and blue sticks representing atoms, with some green and white spheres representing side chains or ligands.

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



köszönöm