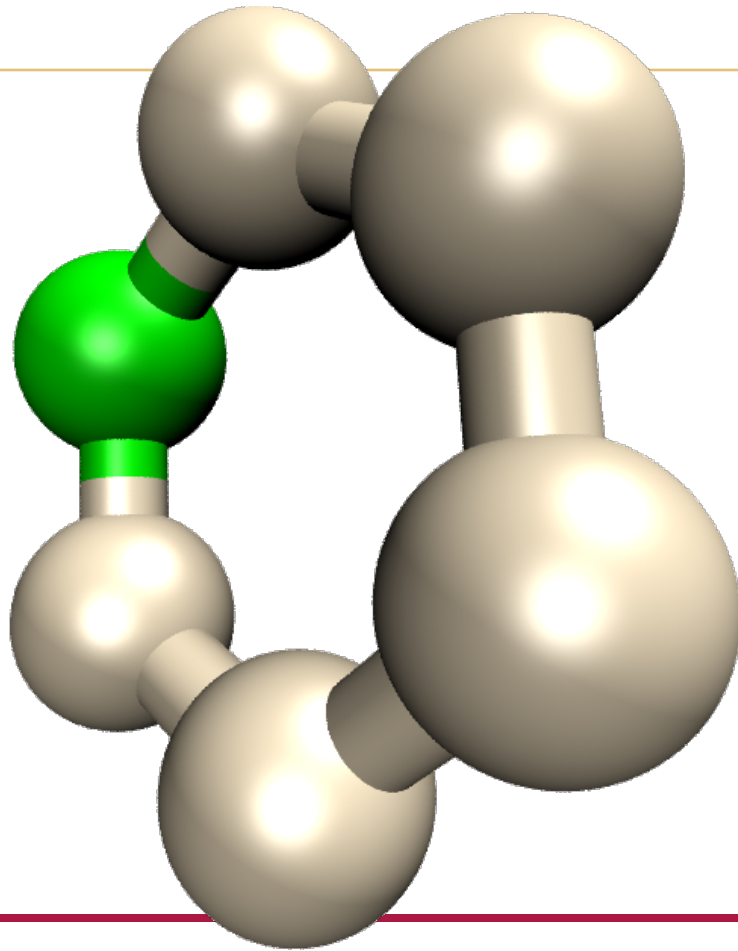


# Molecular Simulation with OpenMM Zephyr



*February 2010*  
*Christopher Bruns*

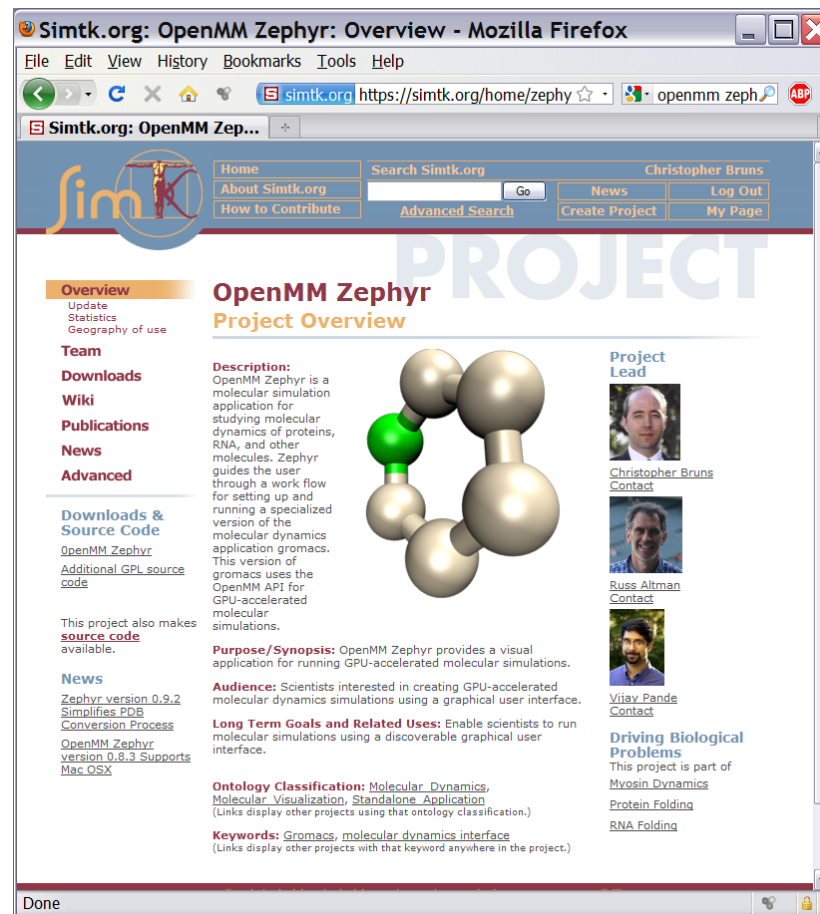
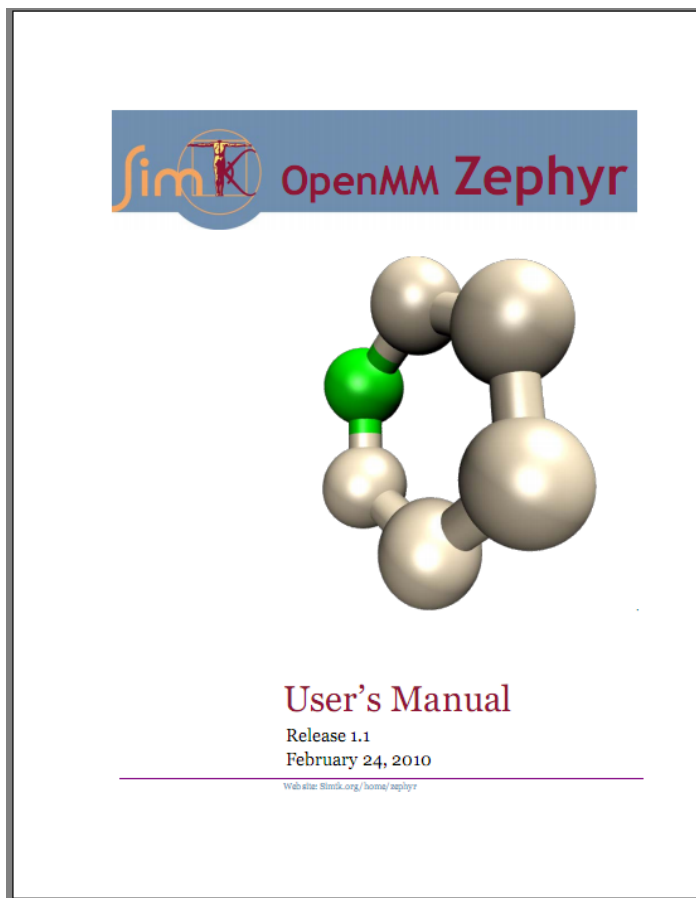


# What is OpenMM Zephyr?

---

- Graphical user interface for running GPU accelerated molecular dynamics simulations
- Automates running of gromacs programs
  - <http://www.gromacs.org/>
- Discoverable interface
- Showcases OpenMM library

# Zephyr Resources

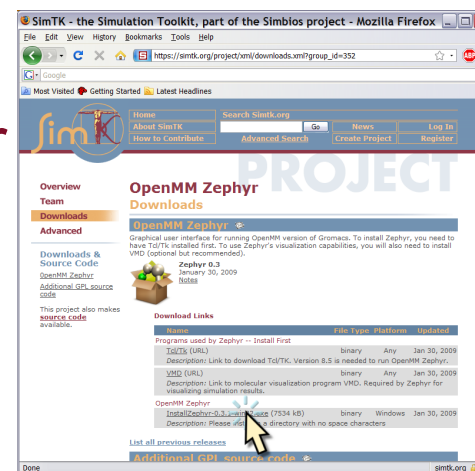


<https://simtk.org/home/zephyr>

# Getting Zephyr and VMD

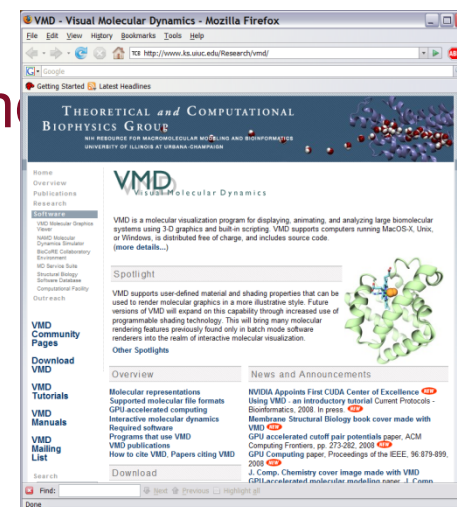
## Zephyr

<https://simtk.org/home/zephyr>  
Downloads => (installer)  
Get User Guide also



## VMD

<http://www.ks.uiuc.edu/Research/vmd/>





# Install in a Folder with no space characters (Windows)

---

- Install in “C:\Zephyr”
- NOT “Program Files”
- NOT “My Documents”
- Issue with this version of gromacs
- No spaces in the entire path



# Overview of exercises

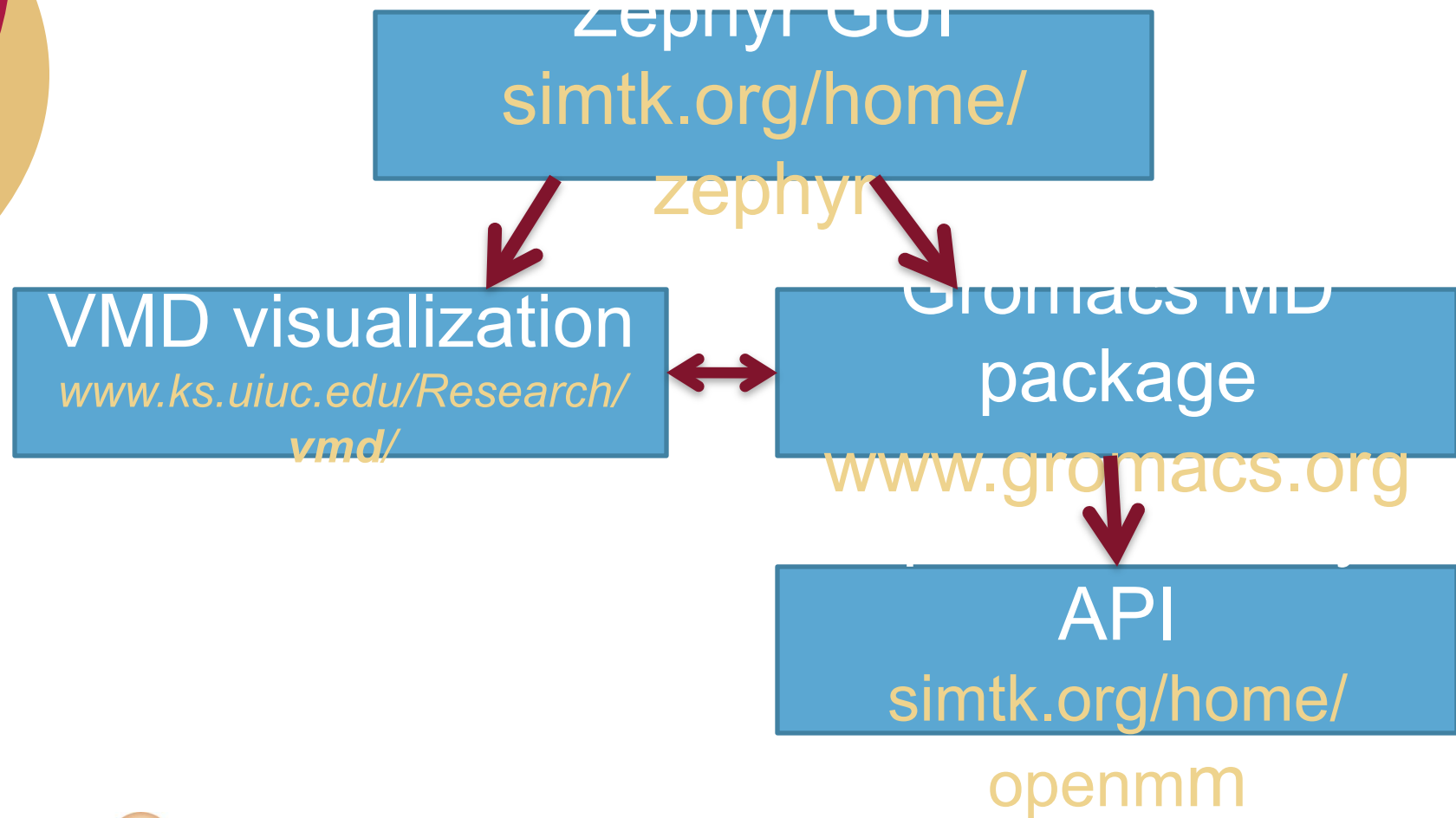
---

○ Be sure to get handout with just the exercise, to help you work at your own pace.

- Dinucleotide (adenylyladenylate) 2 residues
  - change viscosity
  - replay simulation in VMD
- Tetraloop (GCAA) 12 residues
  - attempt GPU acceleration
  - write trajectory in PDB format using VMD
- Unfold an alpha helix
  - modify temperature
- double helix (255d)
  - From PDB web site

# Zephyr is a GUI layer on OpenMM, Gromacs, and VMD

---



# Introductory Demonstration

Running OpenMM Zephyr : alanylalanine\_capped.pdb

OpenMM Zephyr

Molecules Parameters Status: Running VMD console About

Simulation running...

0.100 picoseconds simulated (of 100.000 total)  
Elapsed lab time 2.8s  
Calculating time remaining...

gromacs output :

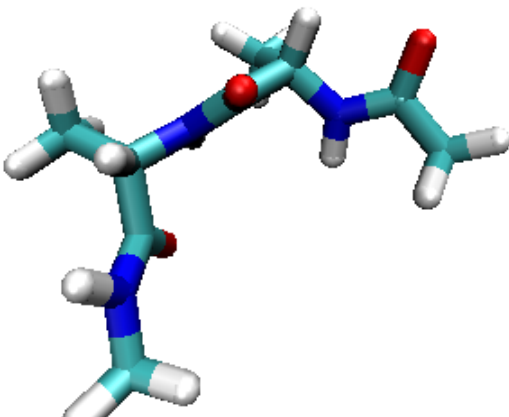
```
Started mdrun on node 0 Mon Feb 02 21:19:58 2009
```

Step	Time	Lambda
1	0.00200	0.00000
50	0.10000	0.00000

Waiting for IMD socket connection to VMD on port 3000...  
Waiting for IMD socket connection to VMD on port 3000...  
Waiting for IMD socket connection to VMD on port 3000...

< Parameters Cancel

VMD 1.8.6 OpenGL Display



VMD Main

File Molecule Graphics Display Mouse Extensions Help

ID	T	A	D	F	Molecule	Atoms	Frames	Vol
0	T	A	D	F	alanylalanine_capped_p	32	757	0

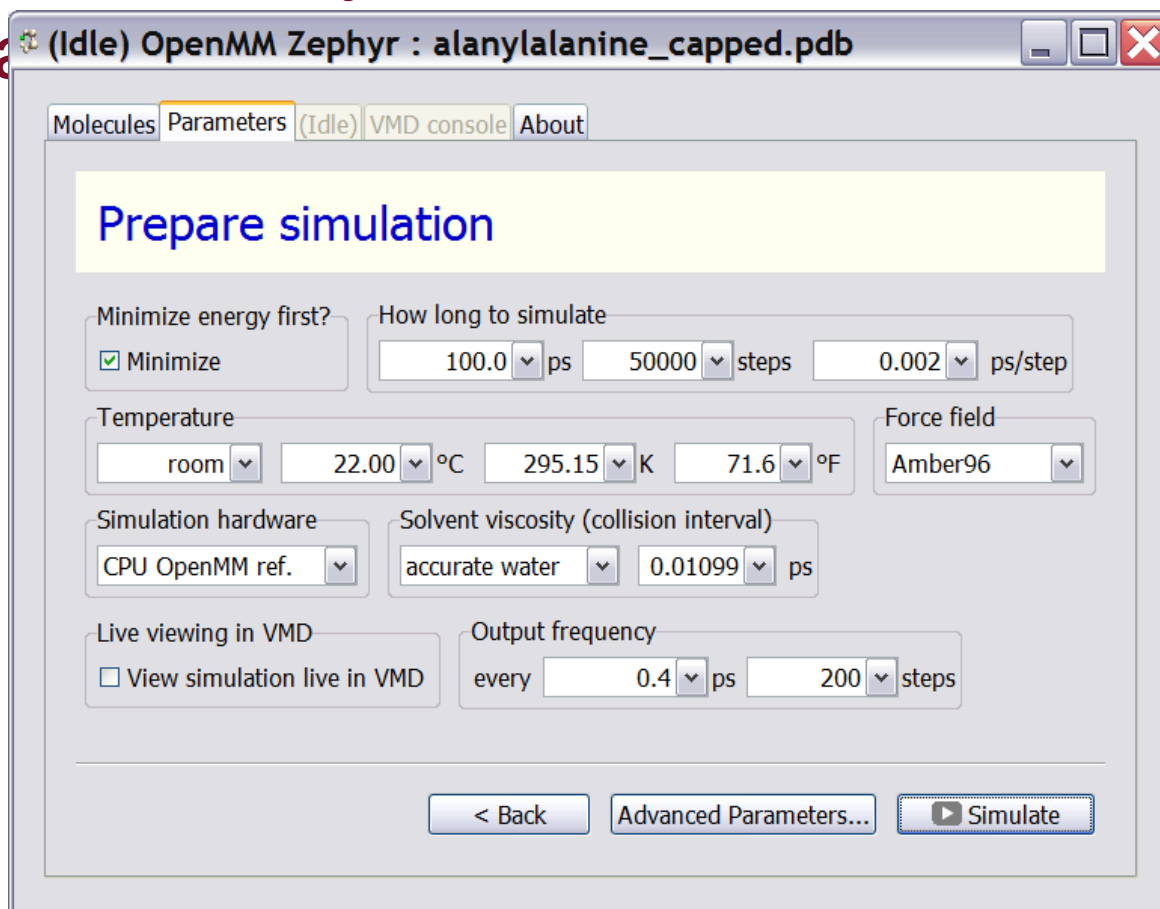
756

zoom Loop step 1 speed



# Simulation parameters

Implicit solvent only – unlike standard  
gromacs



The screenshot shows the 'Prepare simulation' window of the OpenMM Zephyr application. The window title is '(Idle) OpenMM Zephyr : alanylalanine\_capped.pdb'. It has tabs for 'Molecules', 'Parameters' (selected), '(Idle)', 'VMD console', and 'About'. The 'Prepare simulation' section contains the following settings:

- Minimize energy first?**: ☒ Minimize
- How long to simulate**: 100.0 ps, 50000 steps, 0.002 ps/step
- Temperature**: room (dropdown), 22.00 °C, 295.15 K, 71.6 °F
- Force field**: Amber96 (dropdown)
- Simulation hardware**: CPU OpenMM ref. (dropdown)
- Solvent viscosity (collision interval)**: accurate water (dropdown), 0.01099 ps
- Live viewing in VMD**: ☐ View simulation live in VMD
- Output frequency**: every 0.4 ps, 200 steps

At the bottom, there are three buttons: '< Back', 'Advanced Parameters...', and '▶ Simulate'.



## Exercises: RNA Dinucleotide

---

1. Launch Zephyr and simulate adenylyladenylate.pdb for 40 picoseconds. Does it run to completion?
2. Raise solvent collision interval from 0.01099 to 1.0 ps. Simulate again. Does the simulation look any different?
3. Replay the trajectory in VMD. Vary the speed of the playback.
4. Restore the solvent collision interval to 0.01099 ps.



## RNA Dinucleotide

---

- Increased collision interval means lower viscosity.
- Lower viscosity permits faster exploration of conformational space.
- VMD provides a rich environment for exploring molecular simulations.

# Exercises - VMD

---

○ Load a Zephyr trajectory from your simulations directory into VMD

- VMDMain->File->New Molecule

---

1. select Determine file type: Gromacs GRO
2. click Browse-><whatever>.em.gro
3. click Load
4. select Determine file type: Gromacs TRR trajectory
5. click Browse-><whatever>.md.trr
6. click Load (again)

○ Save trajectory in PDB format from VMD

- Select trajectory in VMD Main window
- File->Save Coordinates->pdb, all->Save  
“my\_trajectory.pdb”



# Zephyr Design Principles

---

## 1. Discoverability

- Not a black box
- Learn molecular dynamics by investigating simulation interface

## 2. Convention

- Harvest best practices of experts for default work flow

## 3. Feedback

- Reveal when things go wrong
- Reveal when things go right

# Either:

A: Run these gromacs programs

OR B: Click “Simulate” button in Zephyr

INPUT:

PDB structure file

force field parameters

pdb2gm

.pdb

.top

.gro

editconf

.top

gromp

minimize energy

.tpr

mdrun

simulation parameters

.gro

.mdp

gromp

molecular dynamics

.tpr

GBSA parameters

.agb

mdrun

.pdb

.trr

OUTPUT: structure and trajectory

INPUT:

PDB structure file

.pdb

Simulate

.pdb

.trr

OUTPUT: structure and trajectory

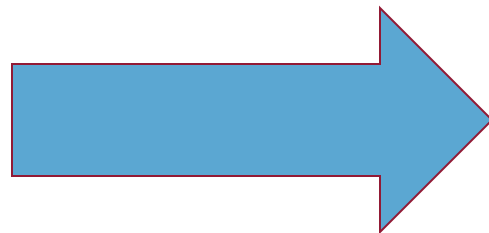


## Exercises: Tetraloop hairpin

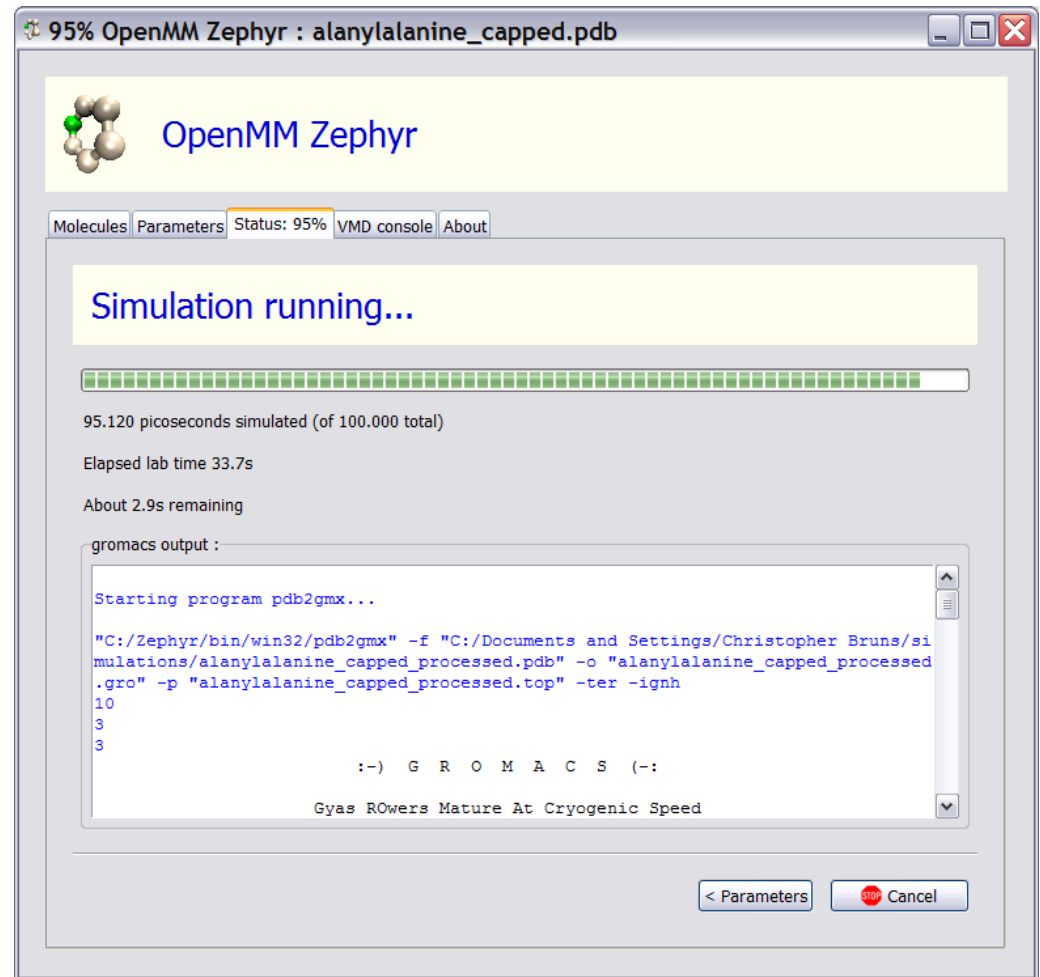
---

1. Begin simulating gcaa.pdb using default parameters. How long would it take to complete? Press “Cancel” to halt the simulation. (On Mac you may need to close VMD and/or Zephyr to halt)
2. Set “Simulation Hardware” to “GPU Nvidia”. Simulate again. What happens?
3. If GPU acceleration is unavailable:
  1. Restore hardware to “CPU OpenMM ref.”
  2. Reload adenylyladenylate.pdb

# Read the blue lines to learn to run Gromacs-OpenMM on the command line



see also zephyr.log file







# Zephyr Capabilities

---

- OS: Windows (XP or Vista), Mac, Linux
- 32 bit
- Implicit solvent only
- Amber96 force field only
- Standard protein/RNA/DNA molecules only
  - No ATP, heme, flavins, etc.
- For GPU accelerated dynamics:
  - you must have supported GPU and drivers



# Time Scales in Molecular Mechanics

---

femtosecond	$10^{-15}$ second	bond vibration
picosecond	$10^{-12}$ second	side chain motion
nanosecond	$10^{-9}$ second	protein/RNA tumbling
microsecond	$10^{-6}$ second	helix/coil transition
	$10^{-4}$ second	RNA duplex formation
millisecond	$10^{-3}$ second	protein/RNA folding
second	$10^0$ second	protein synthesis



## Exercise: Unfolding an alpha helix

---

1. Simulate polyala10helix.pdb for 40 ps at 1000C.
2. Select in VMD Main window. Then Set VMD->Graphics->Representation to “NewCartoon”
3. Simulate same structure again for 60 ps at 300K. View as New Cartoon again. What is different?



## Unfolding an alpha helix

---

- You will be unable to fold a protein in the lab time available, but you might be able to unfold something.



# Pushing the envelope: Temperature

---

1. Increase temperature to 6000 kelvin, the temperature of the sun. Simulate. What happens; and why?
2. Cancel and restart with simulation step size set to 0.0005 ps. Is this what would really happen on the sun? (On Mac you may need to close VMD and/or Zephyr to halt)
3. Restore temperature and step size to 300K and 0.002ps



# Temperature

---

- Temperature of 6000 degrees requires a smaller step size for stable integration. “Blowing up” reveals numerical sensitivity of the integration algorithm, not physics.
- Molecular dynamics does not handle breaking or forming covalent bonds. i.e. no chemistry. Chemistry might really happen at sun temperature.



## Tips for fast simulation

---

- Increase step interval for VMD and trajectory output. (Is it slower or faster?)
- Use GPU acceleration
- Increase solvent collision interval to 1 (lower viscosity)



# PDB: The Protein Data Bank

---

- <http://www.rcsb.org/pdb/>
- Repository of DNA, RNA, and protein atomic structures
- Contains experimental results, not perfect models
- Entries identified by 4 character ID, e.g. “1MRP”, “1GRZ”
- Use “advanced search” at PDB web site to find structures.



RCSB Protein Data Bank - Mozilla Firefox

File Edit View History Bookmarks Tools Help

http://www.rcsb.org/pdb/home/home.do

Search

pd

Gmail - Inbox (460) RCSB Protein Data Bank

**RCSB PDB**  
PROTEIN DATA BANK

A MEMBER OF THE **wwPDB**

An Information Portal to Biological Macromolecular Structures

As of Tuesday Apr 24, 2007 there are 43045 Structures | PDB Statistics

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  - Dictionaries & File Formats
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  - General Education
  - Site Tutorials
- BioSync
- General Information
  - Acknowledgements
  - Frequently Asked Questions
  - Report Bugs/Comments

**Welcome to the RCSB PDB**

The **RCSB** PDB provides a variety of tools and resources for studying the structures of biological macromolecules and their relationships to sequence, function, and disease.

The RCSB is a member of the **wwPDB** whose mission is to ensure that the PDB archive remains an international resource with uniform data.

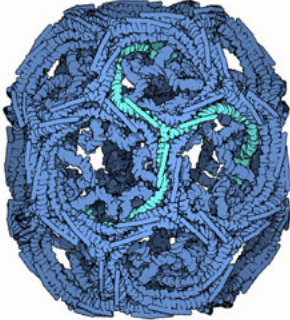
This site offers tools for browsing, searching, and reporting that utilize the data resulting from ongoing efforts to create a more consistent and comprehensive archive.

Information about compatible browsers can be found [here](#).

A **narrated tutorial** illustrates how to search, navigate, browse, generate reports and visualize structures using this new site. [This requires the Macromedia [Flash player](#) download.]

Comments? [info@rcsb.org](mailto:info@rcsb.org)

**Molecule of the Month: Clathrin**



With its intricate meshwork of protein braids and alluring symmetry, clathrin is sure to seize your attention. It was named in the 1960s for its clathrate (lattice of bars) appearance in electron micrographs, and to this day, this beautiful molecule invokes intensive study. Like many proteins, clathrin represents a perfect case of form following function; it performs critical roles in shaping rounded vesicles for intracellular trafficking.

- More ...
- Previous Features

**Quick Tips:**

Retrieve structures of sequence variants for any PDB ID using Advanced Search? Click [here](#).

**News**

- Complete News
- Newsletter
- Discussion Forum

24-April-2007  
**Announcement: Release of Remediated PDB Data**

The **wwPDB** has collaborated on a project to remediate the PDB archive and create a new set of corrected files.

A new FTP server containing the remediated data has been set up for testing. The access details for this site are provided at <http://www.wwpdb.org/remediation-downloads.html>. The new ftp site will be updated weekly in concert with the current production site at <ftp://ftp.rcsb.org>. Both sites share the same organizational structure.

The entire archive has been reviewed and remediated with the objectives of improving the detailed chemical description of non-polymer and monomer chemical components; standardizing atom nomenclature; updating

Done

RCSB PDB : Structure Explorer - Mozilla Firefox

File Edit View History Bookmarks Tools Help

http://www.rcsb.org/pdb/explore/explore.do?structureId=1MRP

pdb Search Search

Gmail - Inbox (461) RCSB PDB : Structure Expl...

**RCSB PDB**  
PROTEIN DATA BANK

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Home Search Structure Queries Help Structure Summary Biology & Chemistry Materials & Methods Sequence Details Geometry

1MRP DOI 10.2210/pdb1mrp/pdb

Red - Derived Information

**Title** FERRIC-BINDING PROTEIN FROM HAEMOPHILUS INFLUENZAE

**Authors** Bruns, C.M., Nowalk, A.J., Arvai, A.S., Mctigue, M.A., Vaughan, K.G., Mietzner, T.A., Mcree, D.E.

**Primary Citation** Bruns, C.M., Nowalk, A.J., Arvai, A.S., McTigue, M.A., Vaughan, K.G., Mietzner, T.A., McRee, D.E. Structure of Haemophilus influenzae Fe(+3)-binding protein reveals convergent evolution within a superfamily. *Nat.Struct.Biol.* v4 pp.919-924, 1997 [Abstract]

**History** Deposition 1997-05-14 Release 1998-01-28

**Experimental Method** Type X-RAY DIFFRACTION Data [EDS]

**Parameters**

Resolution[Å]	R-Value	R-Free	Space Group
1.60	0.179 (obs.)	0.240	P 2 <sub>1</sub> 2 <sub>1</sub> 2

**Unit Cell**

Length [Å]	a	b	c
132.19	52.45	41.26	
Angles [°]	alpha	beta	gamma
90.00	90.00	90.00	

**Molecular Description** Polymer: 1 Molecule: FERRIC IRON BINDING PROTEIN Chains: \_

**Classification** Iron Transport


**Source** Polymer: 1 Scientific Name: *Haemophilus influenzae* Expression system: *Escherichia coli*

**Chemical Component**

Identifier	Name	Formula	Drug Similarity	Hapten Similarity	Ligand Structure	Ligand Interaction
PO4	PHOSPHATE ION	O=P(=O)([O-])[O-]	[X]	[X]	[View]	[View]

**Images and Visualization**

Asymmetric Unit



**Display Options**

- KiNG
- Jmol
- WebMol
- MBT SimpleViewer
- MBT Protein Workshop
- QuickPDB
- All Images

**Download Files**

- PDB File
- PDB gz
- PDB File (Header)
- mmCIF File
- mmCIF gz
- mmCIF File (Header)
- PDBML/XML File
- PDBML/XML gz
- PDBML/XML File (Header)
- Structure Factors File
- Structure Factors gz
- Biological Unit Coordinates
- FASTA Sequence

**Display Files**

- Display Molecule
- Structural Reports
- External Links
- Structure Analysis
- Help

**Quick Tips:**

To view sequence details of this structure click on the Sequence Details tab above the summary page.

http://www.rcsb.org/pdb/rss/LastLoad



# Exercises

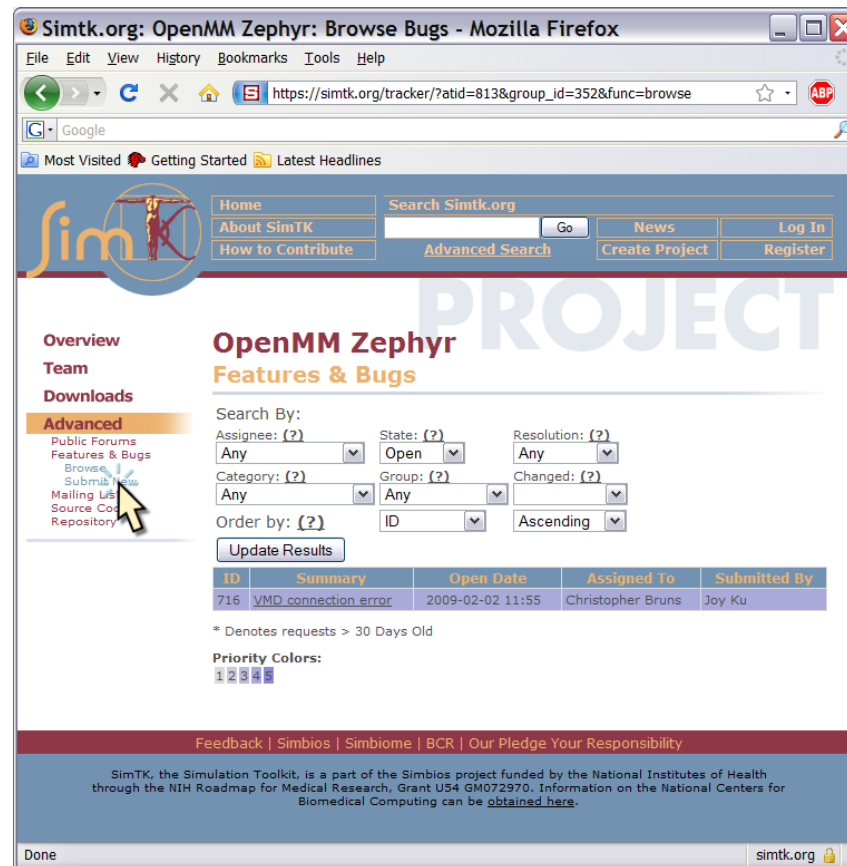
---

○ Download structure 255d from the Protein Data Bank. Try simulating in Zephyr.

---

- Be aware that most other PDB structures won't work without modification.

# Submit feature requests and bug reports



The screenshot shows the Simtk.org OpenMM Zephyr bug tracker interface. The browser window title is "Simtk.org: OpenMM Zephyr: Browse Bugs - Mozilla Firefox". The address bar shows the URL "https://simtk.org/tracker/?atid=813&group\_id=352&func=browse". The page features a navigation menu with links like Home, About SimTK, How to Contribute, Search Simtk.org, News, Log In, Create Project, and Register. The main content area is titled "OpenMM Zephyr Features & Bugs" and includes a search form with filters for Assignee, State, Resolution, Category, Group, and Changed. Below the search form is a table of bugs, with one bug listed: ID 716, Summary "VMD connection error", Open Date "2009-02-02 11:55", Assigned To "Christopher Bruns", and Submitted By "Joy Ku". The footer contains a "Feedback" link and a statement about the Simtk project's funding by the National Institutes of Health.

Simtk.org: OpenMM Zephyr: Browse Bugs - Mozilla Firefox

File Edit View History Bookmarks Tools Help

https://simtk.org/tracker/?atid=813&group\_id=352&func=browse

Google

Most Visited Getting Started Latest Headlines

simtk.org

Home About SimTK How to Contribute Search Simtk.org Go News Log In Create Project Register

Advanced Search

PROJECT

Overview Team Downloads

Advanced

Public Forums Features & Bugs Browse Submit News Mailing List Source Code Repository

OpenMM Zephyr Features & Bugs

Search By:

Assignee: (?) Any State: (?) Open Resolution: (?) Any

Category: (?) Any Group: (?) Any Changed: (?) Any

Order by: (?) ID Ascending

Update Results

ID	Summary	Open Date	Assigned To	Submitted By
716	VMD connection error	2009-02-02 11:55	Christopher Bruns	Joy Ku

\* Denotes requests > 30 Days Old

Priority Colors: 1 2 3 4 5

Feedback | Simbios | Simbiome | BCR | Our Pledge Your Responsibility

SimTK, the Simulation Toolkit, is a part of the Simbios project funded by the National Institutes of Health through the NIH Roadmap for Medical Research, Grant U54 GM072970. Information on the National Centers for Biomedical Computing can be [obtained here](#).

Done simtk.org



## Where to go from here

---

- Running OpenMM gromacs from the command line
  - see chapter 5 of the Zephyr Users Guide
- Pyopenmm: Python bindings for the OpenMM API
  - <https://simtk.org/home/pyopenmm>



# Zephyr Community Resources

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○ Sign up for “OpenMM Zephyr News” mailing list

- [https://simtk.org/mail/?group\\_id=352](https://simtk.org/mail/?group_id=352)

○ OpenMM Zephyr forums

- [https://simtk.org/forum/?group\\_id=352](https://simtk.org/forum/?group_id=352)