
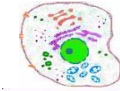








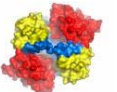







# Coarse-grained representations in biology

Natural lump sizes:

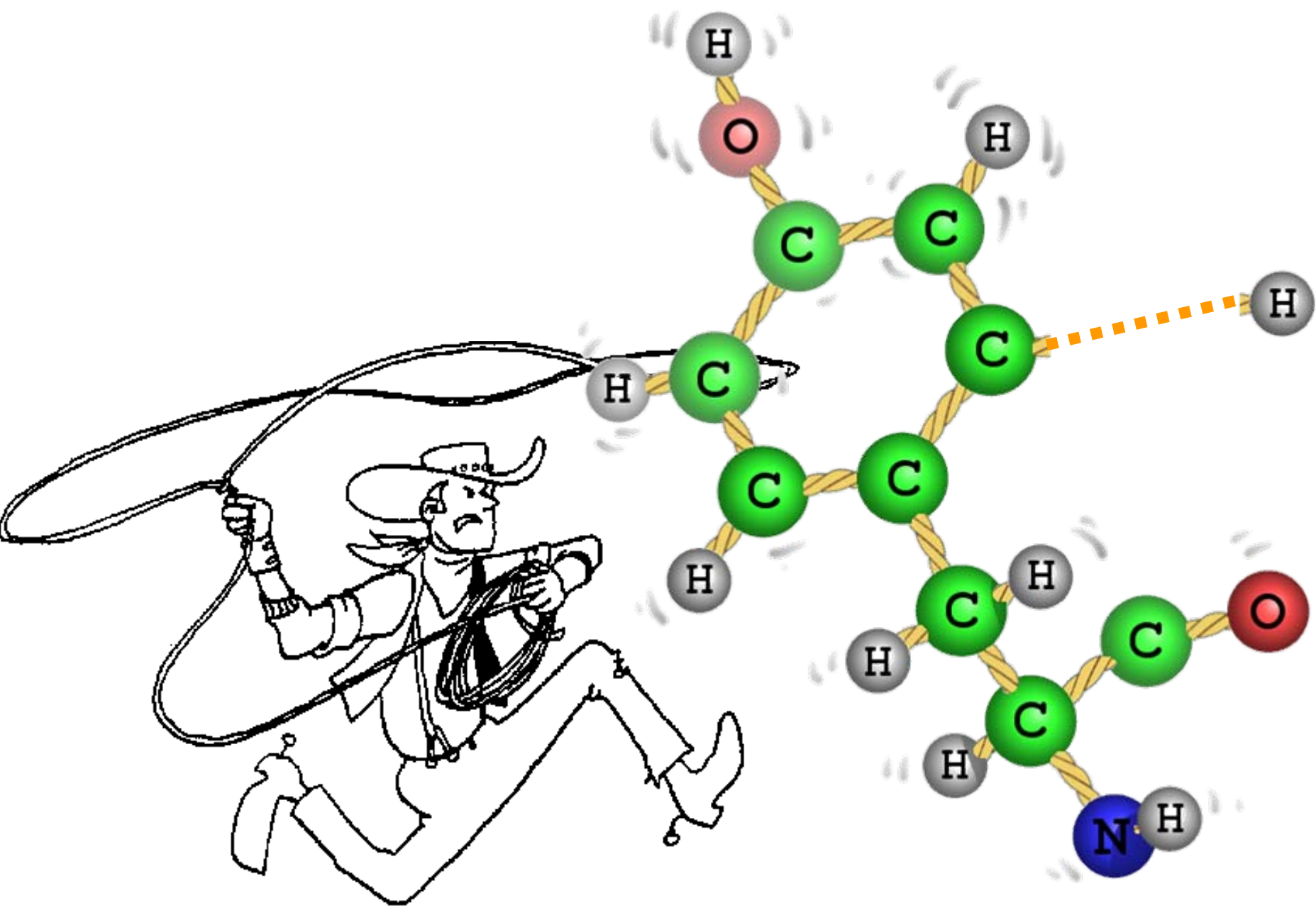
 atoms	 cells
 residues	 tissues
 base pairs	 organs
 duplexes, alpha helices, beta strands	 limbs
 macromolecules	 organisms
 molecular assemblies	 societies
 organelles	 ecosystems
	 biospheres
	 intergalactic federations

(picometer to micron scale)

(micron to mega-light-year scale)

# Coarse-grained simulation of atom-based molecular models

- Full atom force field
- coarse-grained motion permits longer integration time steps
- Increasing coarseness
  - full Cartesian
  - torsion only (internal coordinate)
  - full rigid



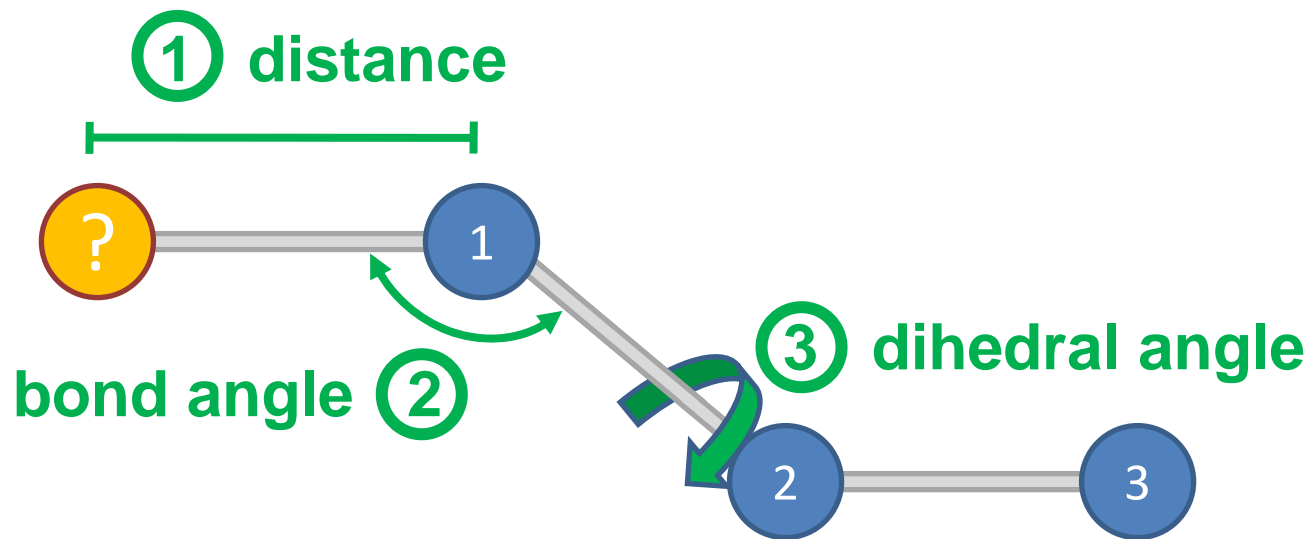


# Molecule internal coordinates

- Bond lengths, bond angles, dihedral angles
- Mandatory for Compound construction
- Optional for Compound simulation

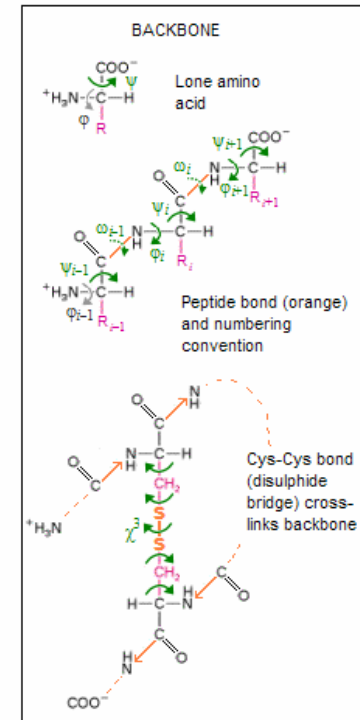
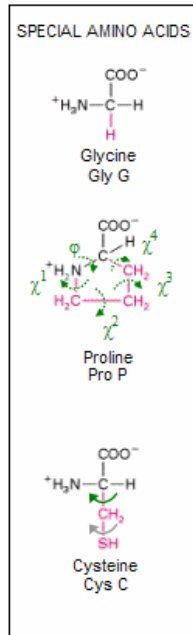
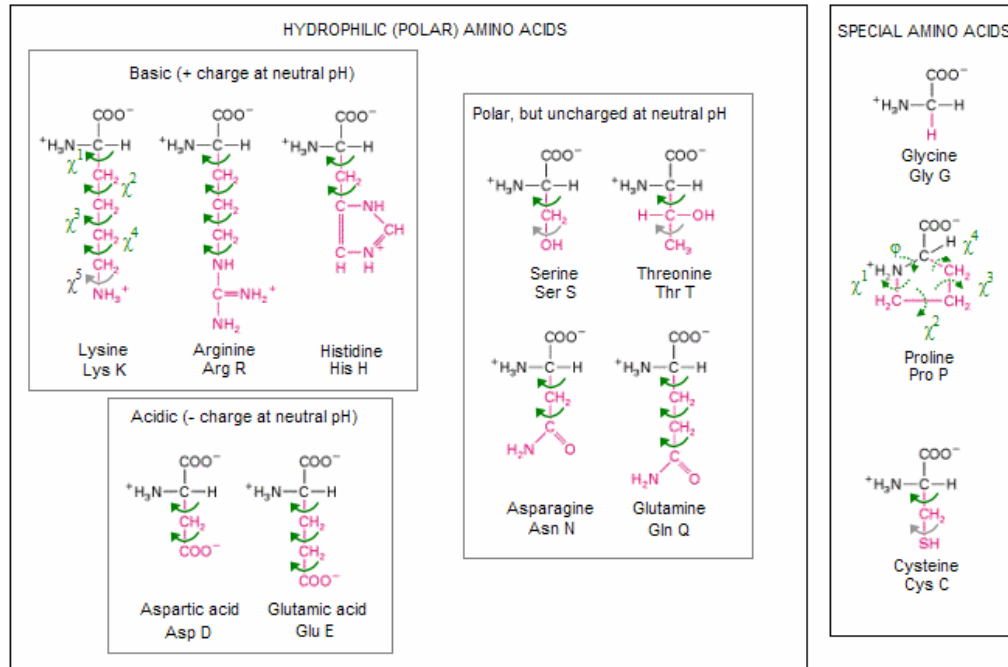
# Internal coordinates

- Instead of explicit Cartesian X, Y, Z coordinates for an atom
- Given three other atom positions, one distance, one bond angle, and one dihedral angle



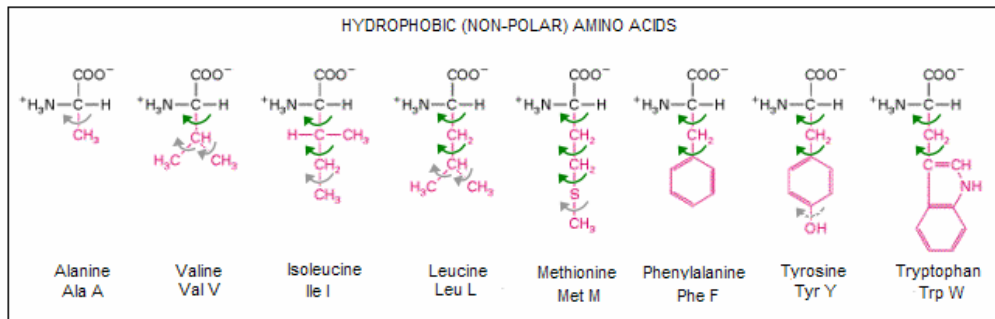
# Protein Internal Coordinates

MOBILITY OF AMINO ACID SIDECHAINS AND PROTEIN BACKBONE  
Modeling full flexibility in torsion (internal) coordinates



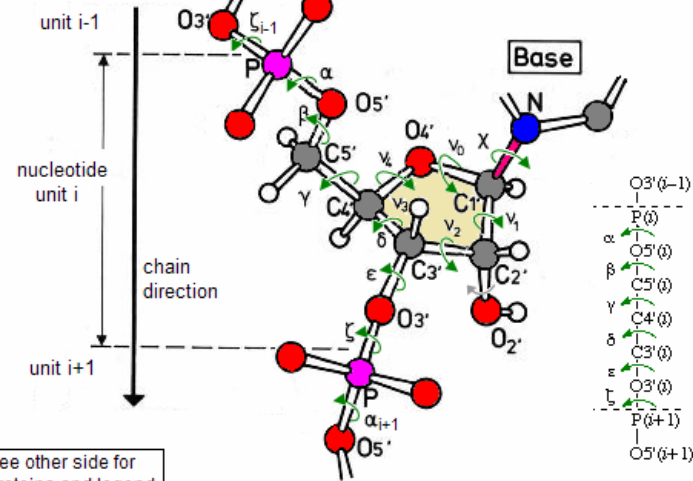
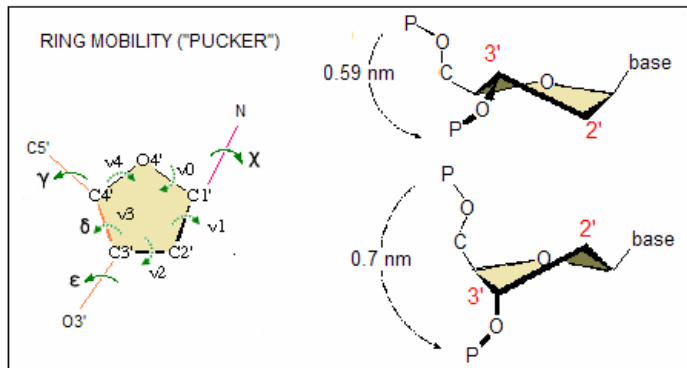
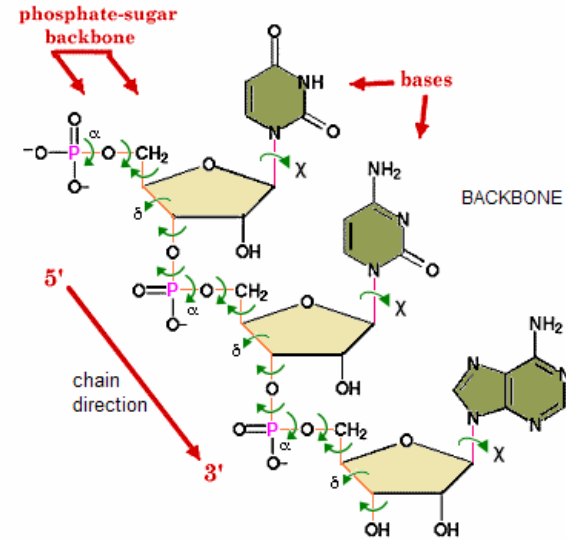
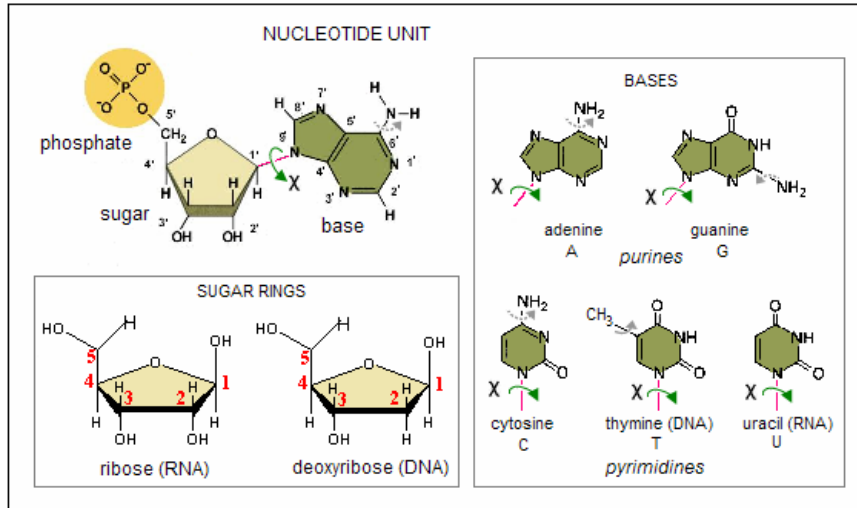
**LEGEND**

- "Heavy" degree of freedom
- "Light" DOF moves H only -- consider leaving out of model
- Limited range of motion -- consider treating as rigid
  - stiff peptide bond limits omega to about +/-10 degrees about nominal
  - proline forms near-rigid loop to backbone and locks its phi angle



# Nucleic Acid Internal Coordinates

MOBILITY OF NUCLEIC ACID BACKBONE, SUGAR RING, AND BASE  
Modeling full flexibility in torsion (internal) coordinates





# Mobility Exercises

- Simulate rigid protein
- Create second protein
- Convert to full Cartesian model
- Which way is faster?
- Simulate multi-grain Adenylate Mobilities VTK example

# VMD Molecular Graphics Viewer

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

VMD 1.8.6 OpenGL Display

VMD Main

ID	T	A	D	F	Molecule	Atoms	Frames	Vol
0	T	A	D		1L2X.pdb	919	1	0

Warning: Ribbons code encountered an unusual structure, geometry may not look as expected.  
Info: In any publication of scientific results based in part or completely on the use of the program STRIDE, please reference: Frishman, D & Argos, P. (1995) Knowledge-based secondary structure assignment. Proteins: structure, function and genetics, 23, 566-579.  
Error: reading PDB file C:\DOCUME~1\CHRIST~1\LOCALS~1\Temp\2  
ERROR) Unable to find Stride output file: C:\DOCUME~1\CHRIST~1\LOCALS~1\Temp\3  
ERROR) Stride:-read\_stride\_record: unable to read output file from Stride  
ERROR) Call to Stride program failed.

VMD - Visual Molecular Dynamics - Mozilla Firefox

THEORETICAL and COMPUTATIONAL BIOPHYSICS GROUP  
NIH RESOURCE FOR MACROMOLECULAR MODELING AND BIOINFORMATICS  
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

VMD Visual Molecular Dynamics

VMD is a molecular visualization program for displaying, animating, and analyzing large biomolecular systems using 3-D graphics and built-in scripting. VMD supports computers running MacOS-X, Unix, or Windows, is distributed free of charge, and includes source code. (more details...)

Spotlight

VMD supports user-defined material and shading properties that can be used to render molecular graphics in a more illustrative style. Future versions of VMD will expand on this capability through increased use of programmable shading technology. This will bring many molecular rendering features previously found only in batch mode software renderers into the realm of interactive molecular visualization.

Download VMD

VMD Tutorials

VMD Manuals

VMD Mailing List

Overview

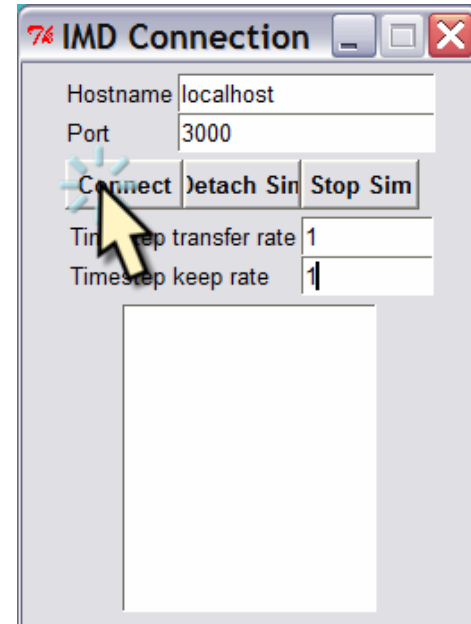
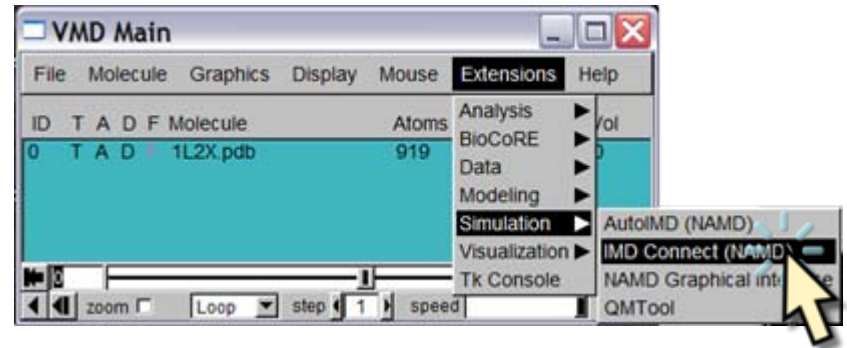
Molecular representations  
Supported molecular file formats  
GPU-accelerated computing  
Interactive molecular dynamics  
Required software  
Programs that use VMD  
VMD publications  
How to cite VMD, Papers citing VMD

News and Announcements

NVIDIA Appoints First CUDA Center of Excellence **NEW**  
Using VMD - an introductory tutorial Current Protocols - Bioinformatics, 2008. In press. **NEW**  
Membrane Structural Biology book cover made with VMD **NEW**  
GPU accelerated cutoff pair potentials paper, ACM Computing Frontiers, pp. 273-282, 2008. **NEW**  
GPU Computing paper, Proceedings of the IEEE, 96:879-899, 2008. **NEW**  
J. Comp. Chemistry cover image made with VMD GPU accelerated molecular modeling paper, J. Comp.

# Viewing SimTK simulation in VMD

1. Start SimTK simulation using PeriodicVMDReporter
2. Load molecule in VMD
  1. VMD Main->File->New Molecule...
  2. Molecule File Browser->Browse
  3. Molecule File Browser->Load
3. Connect VMD to SimTK
  1. VMD Main->Extensions->Simulation->IMD Connect (NAMD)
  2. In IMD Connection window
    1. Hostname: localhost
    2. Port: 3000 (match argument to PeriodicVMDReporter)
    3. Timestep transfer rate: 1 (to see every reported step) PRESS ENTER
    4. Timestep keep rate: 1 (to remember every step for replay value) PRESS ENTER
    5. Press "Connect" button



# RNA Mobility Exercises

- Simulate multi-grain AdenylateMobilities  
example program and connect to VMD

# 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

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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PDB ID or keyword  Author  | [Advanced Search](#)

Home Search

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- Dictionaries & File Formats
- Software Tools
- 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.

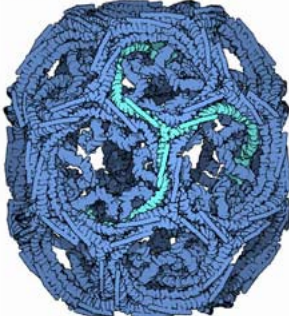
This site offers tools for browsing, searching, and reporting that utilize the data resulting from ongoing efforts to create a more consistent and comprehensive archive.

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

**News**

- Complete News
- Newsletter
- Discussion Forum

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

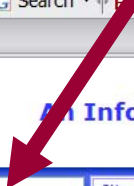
The **wwPDB** has collaborated on a project to remediate the PDB archive and create a new set of corrected files.

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

Search box



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 Site Search Advanced Search RSS Feed for the Latest Released Structures

A MEMBER OF THE PDB  
An Information Portal to Biological Macromolecular Structures  
As of Tuesday Apr 24, 2007 there are 43045 Structures | PDB Statistics

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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., Mcrec, 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	132.19	b	52.45	c	41.26
Angles [°]		alpha	90.00	beta	90.00	gamma	90.00

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

**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 <sub>4</sub> P			[View]	[View]

Images and Visualization

Asymmetric Unit



**Display Options**

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

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

4-character ID

1MRP

DOI 10.2210/pdb1mrp/pdb

Images and Visualization

Asymmetric Unit



Display Options

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

Quick Tips:

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

# PDB File format

- Text format – humans can read it too
- Most of the information is atomic coordinates
- PDB files usually contain multiple molecules, including water molecules

```
...  
ATOM 1751 N GLY C 250 32.286 1.882 43.206 1.00 22.00  
ATOM 1752 CA GLY C 250 32.365 1.086 41.969 1.00 21.39  
ATOM 1753 C GLY C 250 31.538 1.735 40.864 1.00 20.79  
ATOM 1754 O GLY C 250 30.621 2.527 41.152 1.00 21.58  
...
```



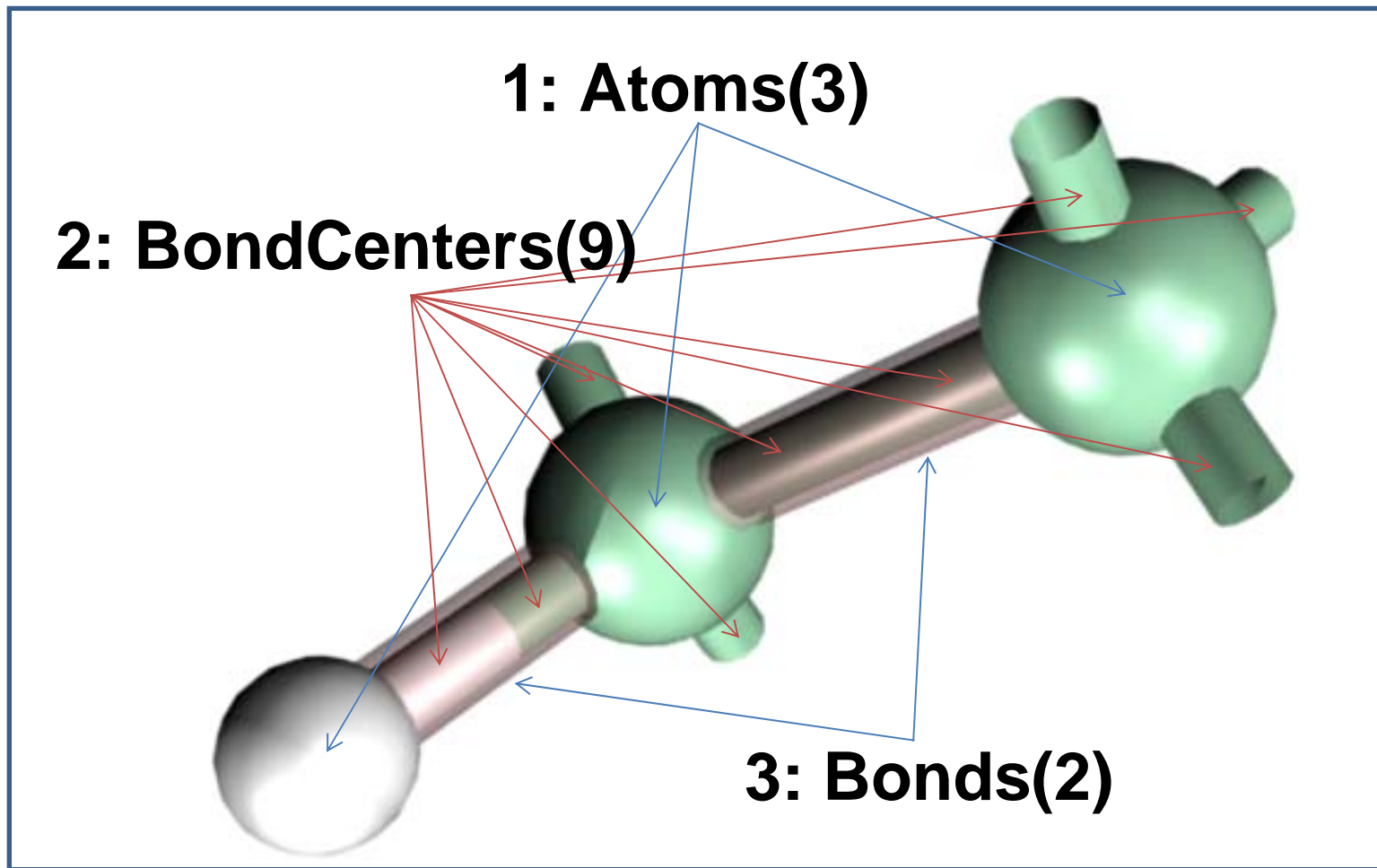
# LoadPdb Exercises

- Download 1AKG from Protein Data Bank  
<http://www.rcsb.org/pdb>
- Simulate 1AKG using Example
- Simulate 1AKG using stream constructor

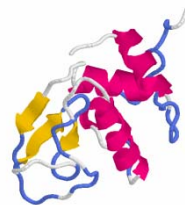
# Custom Molecule Construction

- BondCenters, Atoms, Bonds, Compounds
- Inboard bond center
- The first few atoms
- Ring closing bonds

# Molecule Construction nomenclature



**4: Compound(1)**



structure

force field

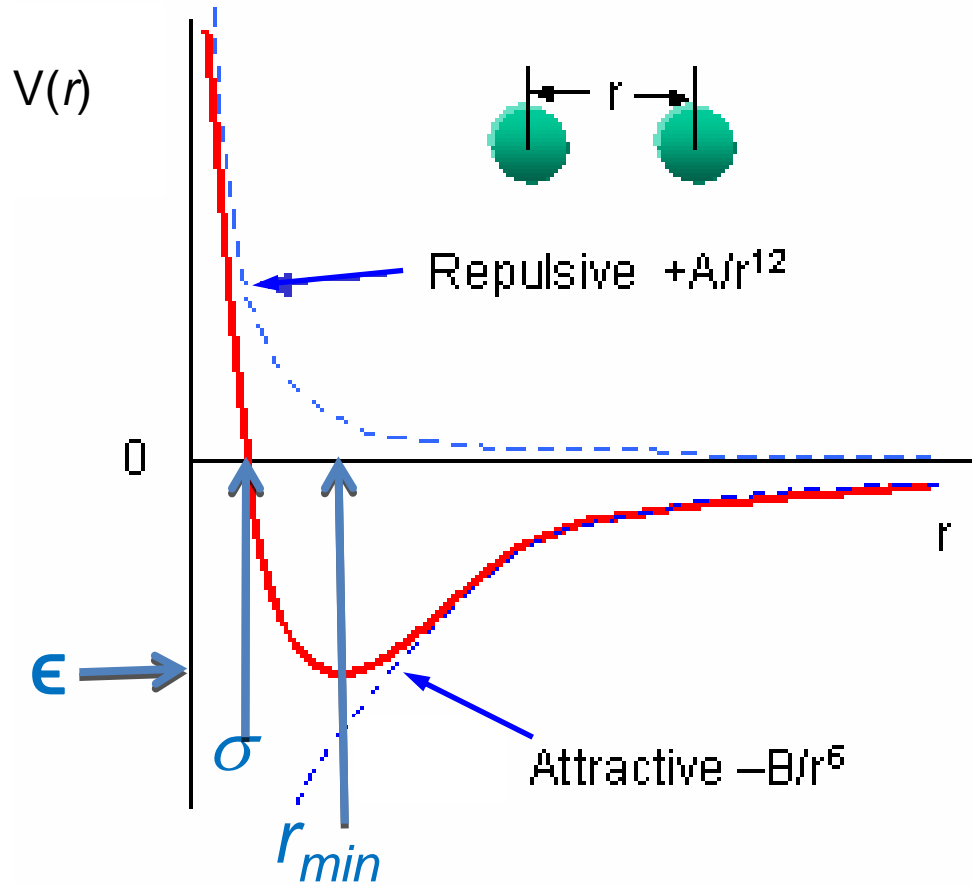
Type	Description	Protein example	RNA example	Argon example
Compound	Molecule or part of molecule	hen egg-white lysozyme	yeast phenylalanine transfer RNA	argon
Atom	one particular atom in a molecule	serine 3 nitrogen	guanosine 3, carbon C3'	argon
Biotype	links Atoms to ChargedAtom Types	serine N	guanylate C3'	argon
ChargedAtom Type	Atom type with a particular charge	serine N: charge -0.42	guanylate C3': charge +0.2022	argon: charge zero
AtomClass	Atom type	sp <sup>2</sup> amide nitrogen (N)	tetrahedral carbon (CT)	argon

# Biotype

- Bridge between structural model and force field implementation
- Concept borrowed from TINKER molecular dynamics package



# Lennard-Jones potential



$$r_{min} = 2^{1/6} \sigma$$

Four ways to express length parameter:

	$\sigma$ ( $r_0$ )	$r_{min}$
radius = diameter/2		
diameter		

$$V(r) = 4\epsilon \left[ \left( \frac{\sigma}{r} \right)^{12} - \left( \frac{\sigma}{r} \right)^6 \right]$$

$$V(r) = \epsilon \left[ \left( \frac{r_{min}}{r} \right)^{12} - 2 \left( \frac{r_{min}}{r} \right)^6 \right]$$

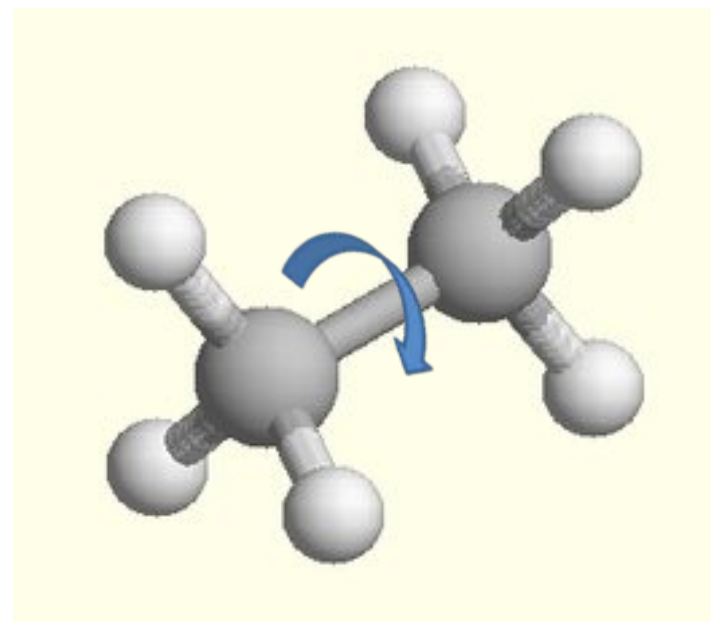
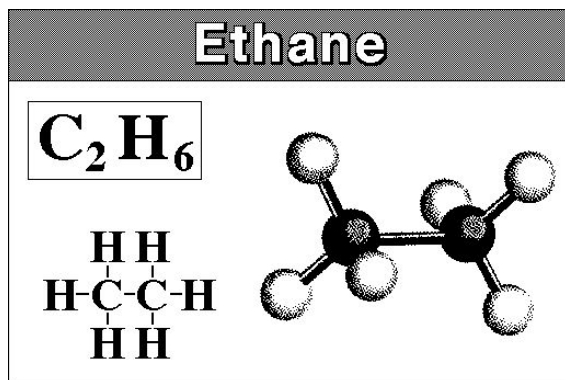
# Argon Exercises

- Compile and run TwoArgons example program
- Add a third argon atom.
- What happens when atoms start too close together? Too far apart?
- Increase the attractive force between atoms ten-fold
- Why does this example lack temperature and energy minimization stanzas?



# Ethane

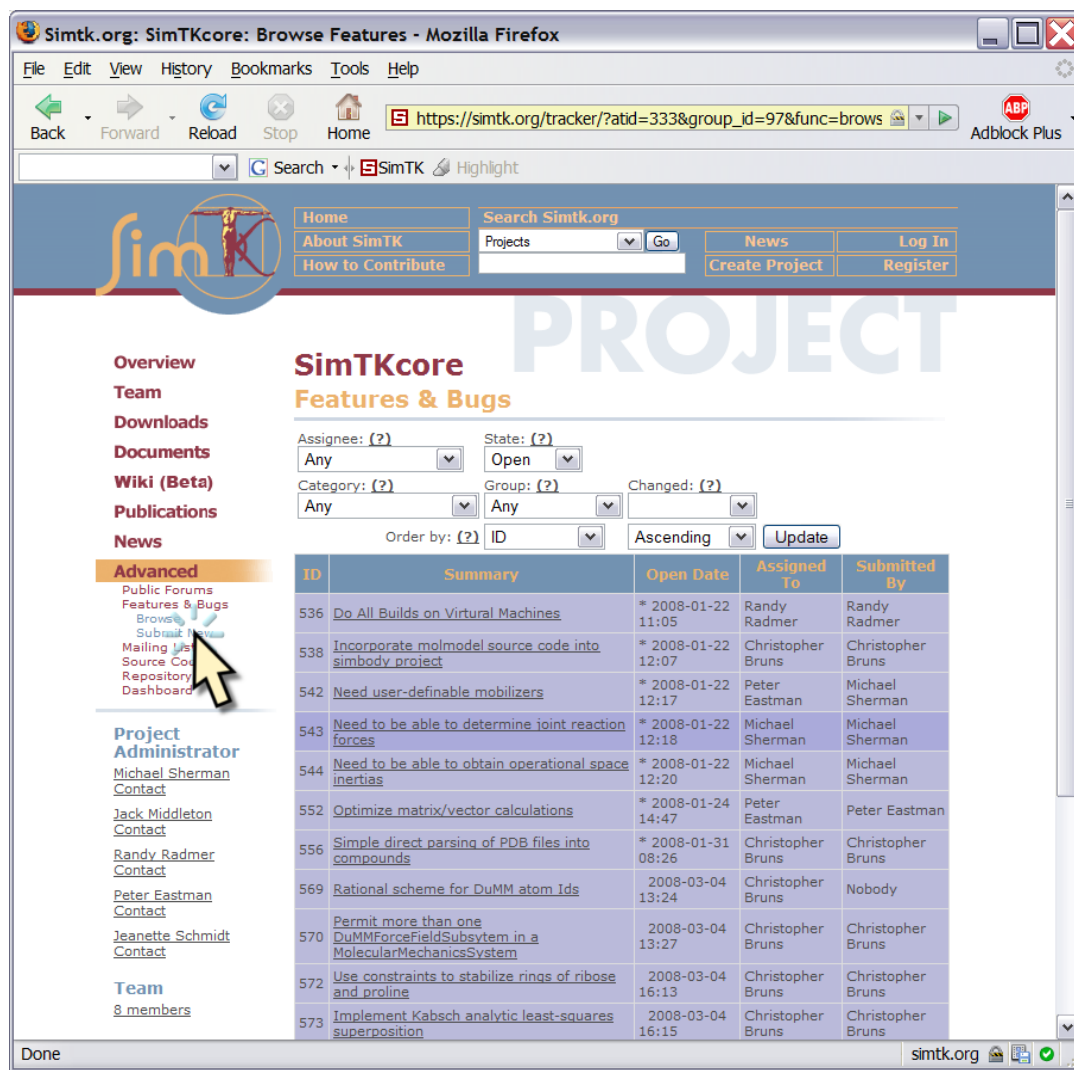
- Two carbons, six hydrogens
- One dihedral degree of freedom
- 3 kcal/mol energy barrier to rotation



# Ethane Exercises

- Compile and run TwoEthanes example program
- Add a third ethane molecule

# Submitting Bug Reports



The screenshot shows a Mozilla Firefox browser window displaying the SimTKcore website. The address bar shows the URL: [https://simtk.org/tracker/?atid=333&group\\_id=97&func=brows](https://simtk.org/tracker/?atid=333&group_id=97&func=brows). The page title is "SimTKcore: Browse Features - Mozilla Firefox".

The website header includes navigation links: Home, About SimTK, How to Contribute, Search Simtk.org, Projects, News, Log In, Create Project, and Register. The main content area is titled "SimTKcore PROJECT Features & Bugs".

On the left side, there is a sidebar menu with the following items: Overview, Team, Downloads, Documents, Wiki (Beta), Publications, News, and Advanced. The "Advanced" menu is expanded, showing sub-items: Public Forums, Features & Bugs (highlighted with a mouse cursor), Browse, Submit, Mailing Lists, Source Code, Repository, and Dashboard.

Below the sidebar, there is a "Project Administrator" section listing several team members with their contact information: Michael Sherman, Jack Middleton, Randy Radmer, Peter Eastman, and Jeanette Schmidt.

The main content area displays a table of bug reports with the following columns: ID, Summary, Open Date, Assigned To, and Submitted By. The table is filtered by Assignee: Any, State: Open, Category: Any, Group: Any, and Changed: Any. The table is sorted by ID in ascending order.

ID	Summary	Open Date	Assigned To	Submitted By
536	<a href="#">Do All Builds on Virtual Machines</a>	* 2008-01-22 11:05	Randy Radmer	Randy Radmer
538	<a href="#">Incorporate molmodel source code into simbody project</a>	* 2008-01-22 12:07	Christopher Bruns	Christopher Bruns
542	<a href="#">Need user-definable mobilizers</a>	* 2008-01-22 12:17	Peter Eastman	Michael Sherman
543	<a href="#">Need to be able to determine joint reaction forces</a>	* 2008-01-22 12:18	Michael Sherman	Michael Sherman
544	<a href="#">Need to be able to obtain operational space inertias</a>	* 2008-01-22 12:20	Michael Sherman	Michael Sherman
552	<a href="#">Optimize matrix/vector calculations</a>	* 2008-01-24 14:47	Peter Eastman	Peter Eastman
556	<a href="#">Simple direct parsing of PDB files into compounds</a>	* 2008-01-31 08:26	Christopher Bruns	Christopher Bruns
569	<a href="#">Rational scheme for DuMM atom Ids</a>	2008-03-04 13:24	Christopher Bruns	Nobody
570	<a href="#">Permit more than one DuMMForceFieldSubsystem in a MolecularMechanicsSystem</a>	2008-03-04 13:27	Christopher Bruns	Christopher Bruns
572	<a href="#">Use constraints to stabilize rings of ribose and proline</a>	2008-03-04 16:13	Christopher Bruns	Christopher Bruns
573	<a href="#">Implement Kabsch analytic least-squares superposition</a>	2008-03-04 16:15	Christopher Bruns	Christopher Bruns

The status bar at the bottom of the browser window shows "Done" and the URL "simtk.org".