

# MD Simulation Automatic Setup

using



*Molecular Dynamics On Web*

Macromolecular Simulation Software Workshop

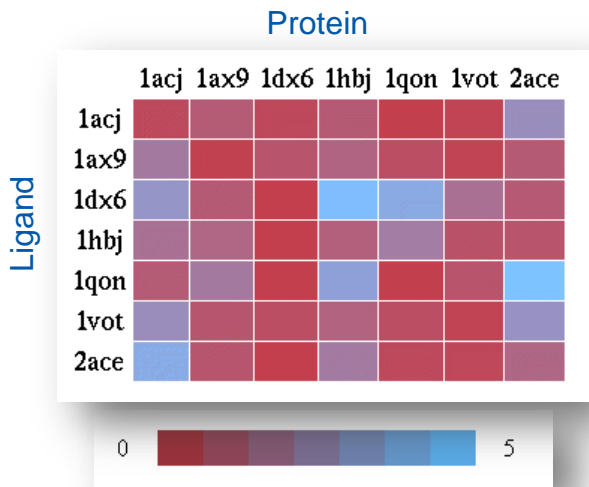
*CECAM – Jülich 2015*

Adam Hospital Gasch

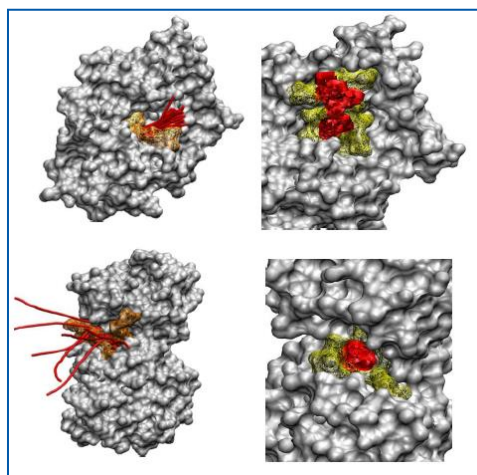
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  - *MDWeb Setup: Structure Checking, Workflows & Operations, MD Run..*
- **Simulation Setup Hands-on.**
  - *Simulation Setup (MDMoby / MDWeb).*

# Introduction: Molecular Flexibility & MD



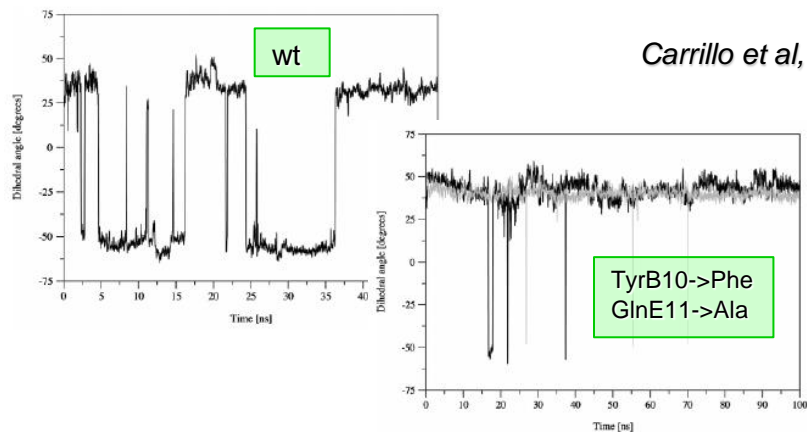
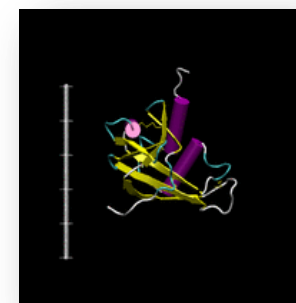
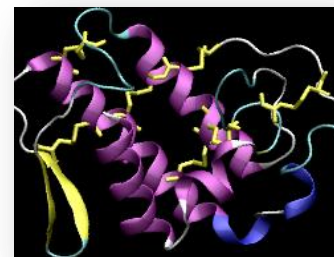
RMSd docking solutions



Protein Channels, Drug Cavities  
MDGrid

*Carrillo et al, Proteins 2008, 70, 892-899*

RCSB PDB  
PROTEIN DATA BANK



Gate Opening Molecular  
Switch.

*Bidon-Chanal et al, JACS  
2007, 129, 6782-6788*

# Introduction: MD Limitations



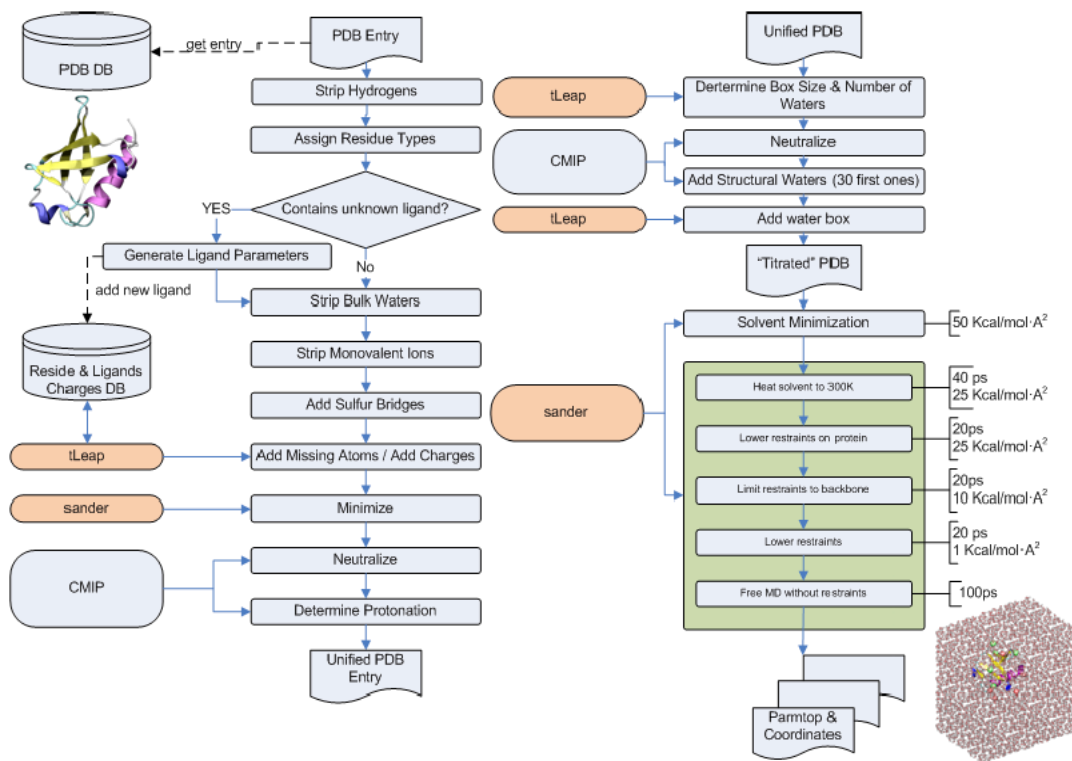
Large Computational Resources

$$V(\mathbf{r}) = \sum_{\text{bonds}} K_b (b - b_0)^2 + \sum_{\text{angles}} K_\theta (\theta - \theta_0)^2 + \sum_{\text{dihedrals}} K_\chi (1 + \cos(n\chi - \delta)) + \sum_{\text{nonbonded-pairs}, i, j} \left[ \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} - \epsilon_{ij} \left\{ \left( \frac{R_{\text{min},ij}}{r_{ij}} \right)^{12} - 2 \left( \frac{R_{\text{min},ij}}{r_{ij}} \right)^6 \right\} \right]$$

**Energy dependencies on:**

- Bond length
- Bond valence angle
- Bond dihedral angle
- Non-bonded electrostatic interactions
- Non-bonded van-der Waals interactions

Force Fields Uncertainties



High level of expertise needed

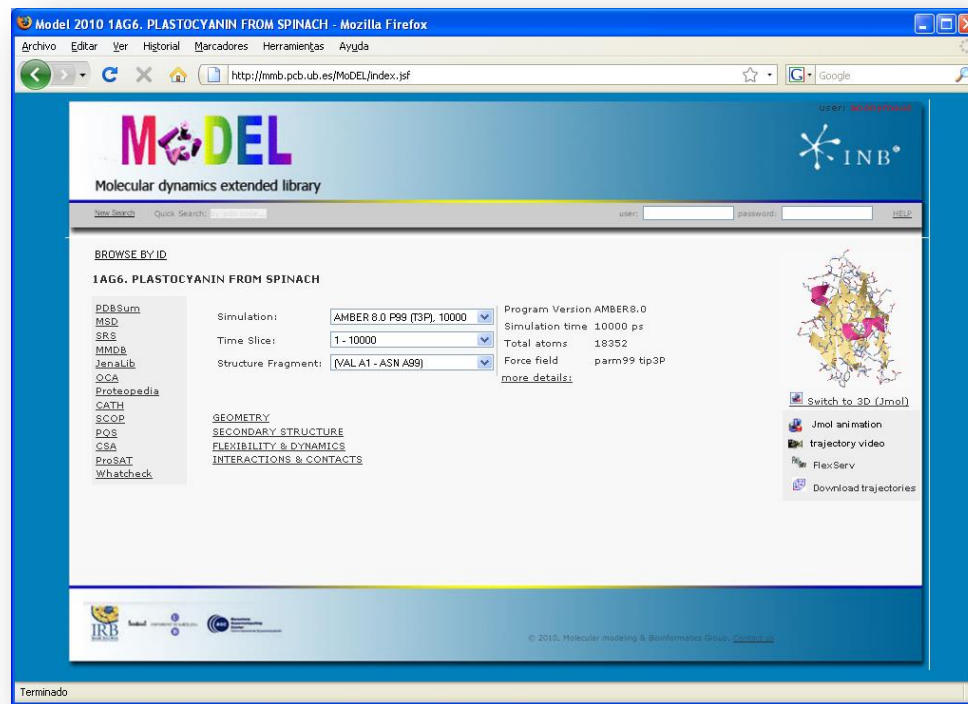
# Introduction: MoDEL



**Molecular Dynamics Extended Library.**

<http://mmb.irbbarcelona.org/MoDEL>

- **1875 Simulations (~1600 structures).**
- **Amber, Namd, Gromacs.**
- **Charmm22, Charmm27, Parm99, Parm99SB, Parm03, OPLS, etc.**
- **Automatic MD Setup, Run & Analysis.**
- **Web interface connected to a Relational Database.**



Model 2010 1AG6. PLASTOCYANIN FROM SPINACH - Mozilla Firefox

Archivo Editar Ver Historial Marcadores Herramientas Ayuda

http://mmb.pcb.ub.es/MoDEL/index.jsf

**MoDEL**  
Molecular dynamics extended library

user: [ ] password: [ ]

**BROWSE BY ID**

**1AG6. PLASTOCYANIN FROM SPINACH**

PDBSum  
 MSD  
 SRS  
 MMDL  
 JmolLib  
 OCA  
 Proteopedia  
 CATH  
 SCOP  
 PQS  
 CSA  
 ProSAT  
 Whatcheck

Simulation: AMBER 8.0 P99 (T3P), 10000  
 Time Slice: 1 - 10000  
 Structure Fragment: [VAL A1 - ASN A99]

Program Version AMBER8.0  
 Simulation time 10000 ps  
 Total atoms 18352  
 Force field parm99 tip3P

more details:

GEOMETRY  
 SECONDARY STRUCTURE  
 FLEXIBILITY & DYNAMICS  
 INTERACTIONS & CONTACTS

Switch to 3D (Jmol)  
 Jmol animation  
 trajectory video  
 FlexServ  
 Download trajectories

IRB

© 2010, Molecular modeling & Bioinformatics Group

Terminado

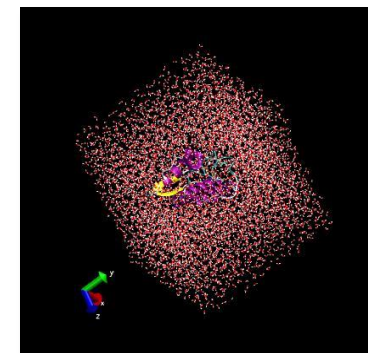
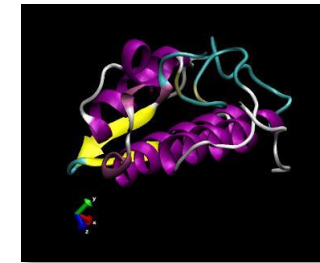
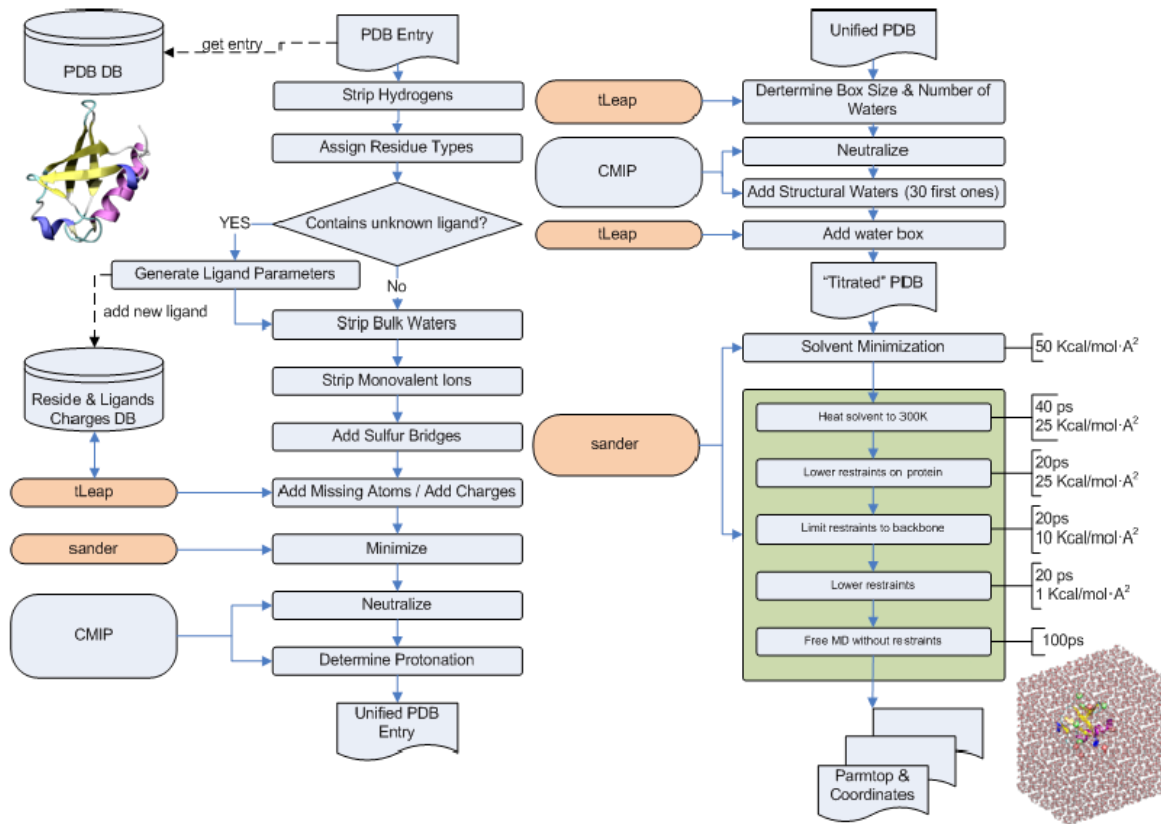
III                      II                      I  
Year 2014    (Year 2010)    (Year 2006)

- 48,896 (10,240) (4,812) IBM Processors
- 1,017.0 (94.21) (42.35) TeraFlops
- 98 (20) (9.6) TB central RAM
- 2,000 (480) (236) TB Disk
  
- Communication network: Infiniband (Myrinet, Gigabit, 10/100 Ethernet)
- OS Linux - SuSe.
- 29<sup>th</sup> (5<sup>th</sup>) (4<sup>th</sup>) in top500



## MareNostrum SuperComputer

# Introduction: Automatic Setup

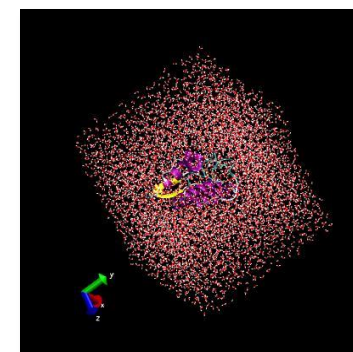
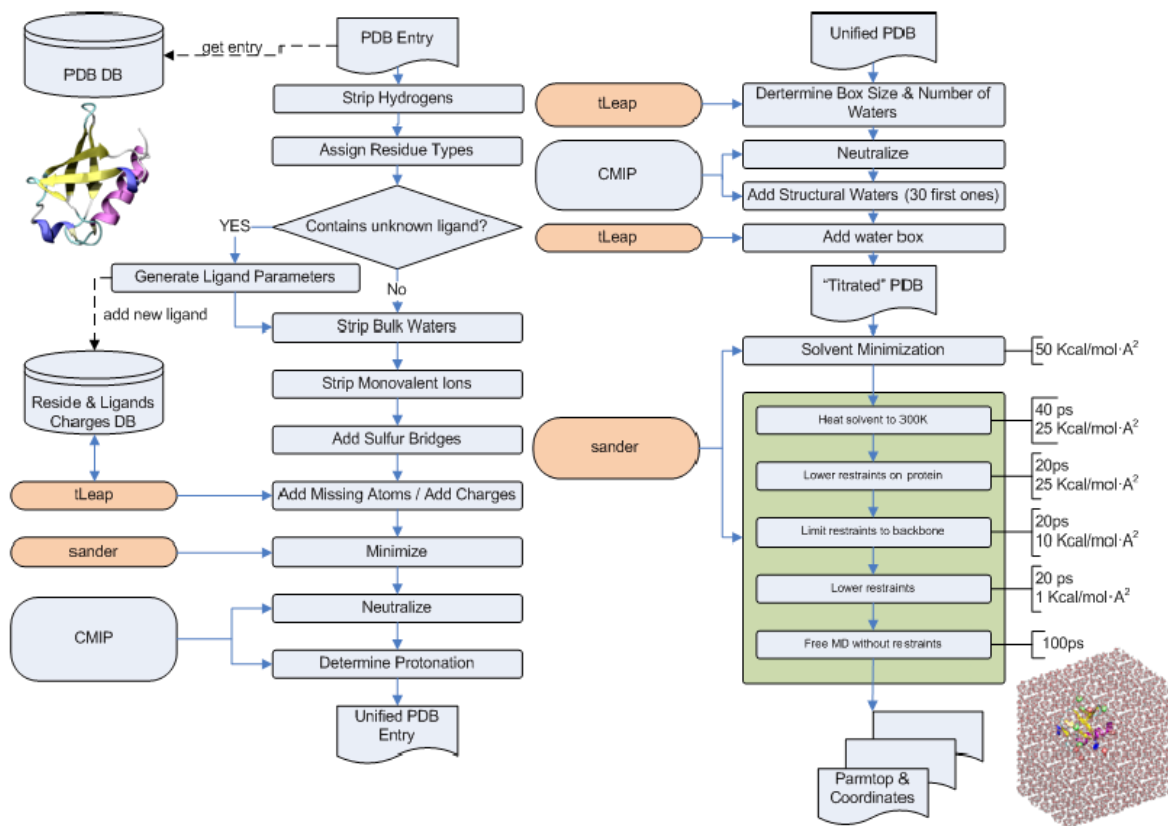


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# MDMoby Web Services



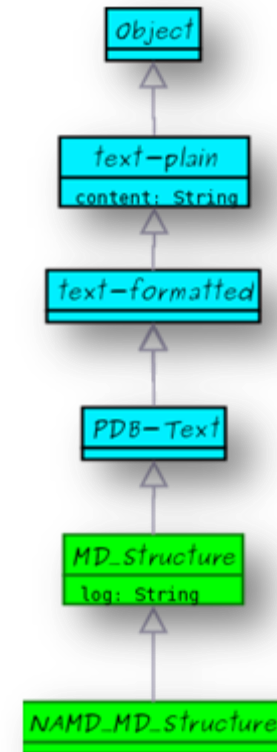
# BioMoby

### Tired of This?

*Protocol*

Create a gene list in Excel  
Go to NCBI  
Retrieve FASTA for each gene  
DragonDB Blast each sequence  
Copy/paste IDs into a spreadsheet  
Run Repeat Masker on each sequence  
copy/paste masked sequence into Excel  
Run MacVector cut each seq with EcoRI

### Try This!



**BioMOBY** defines an **ontology-based** messaging standard through which a client will be able to **automatically discover** and interact with task-appropriate **biological data** and analytical service providers, without requiring manual manipulation of data formats as data flows from one provider to the next.

# BioMoby MD Ontology

**Service  
Discovery  
based on  
Ontology**

**PDB-Text**

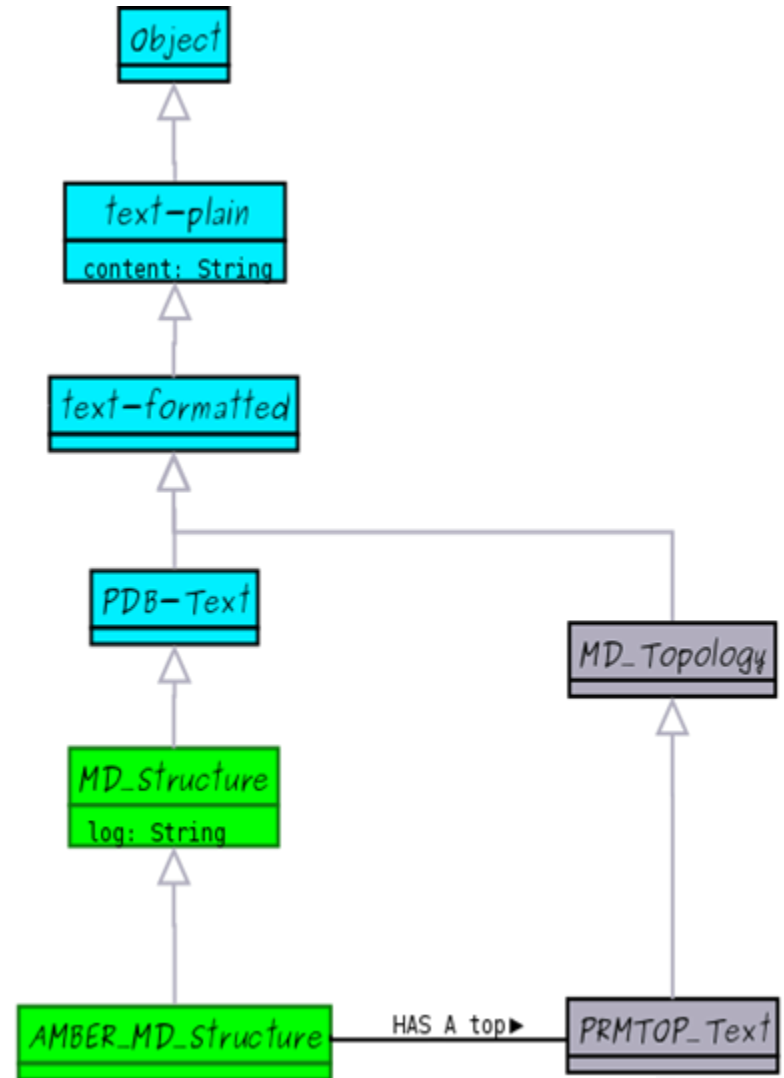
List of Operations:

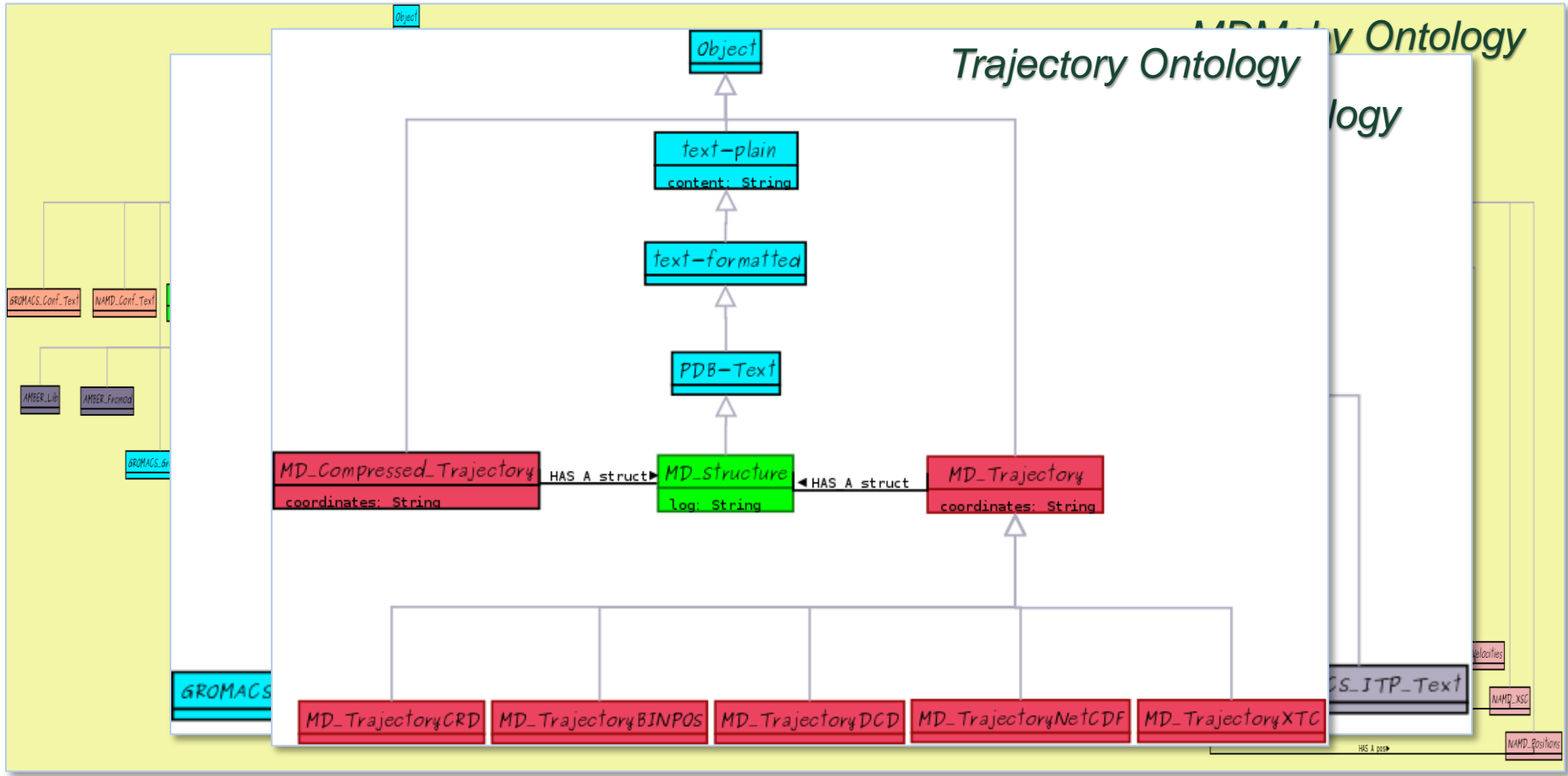
- Check for disulphide bonds
- Clean PDB
- Fix Side Chains
- Mutate residue
- Amber FULL MD Setup
- Amber MD Setup
- Amber MD Setup with Solvation
- Generate Topology for Amber
- Generate Topology for Gromacs
- Generate Topology for Namd
- Gromacs FULL MD Setup
- Gromacs MD Setup
- Gromacs MD Setup with Solvation
- Namd FULL MD Setup
- Namd MD Setup
- Namd MD Setup with Solvation

**AMBER\_MD\_Structure**

List of Operations:

- Add structural hydration waters and ions
- Hydrogen Energetic Minimization
- Properly Protonate Histidines
- Properly Protonate Ionizable Residues
- Solvate structure
- Structure Energetic Minimization





## How can you use them?

- *Web Services (Workflows) Clients. e.g. Taverna.*

- *MobyLite Perl/Java API.*

```
##### getStructurePDB Service #####
print "\n1.- Running getStructurePDB Service...\n";

my $object = Object->new($pdb,'PDB');

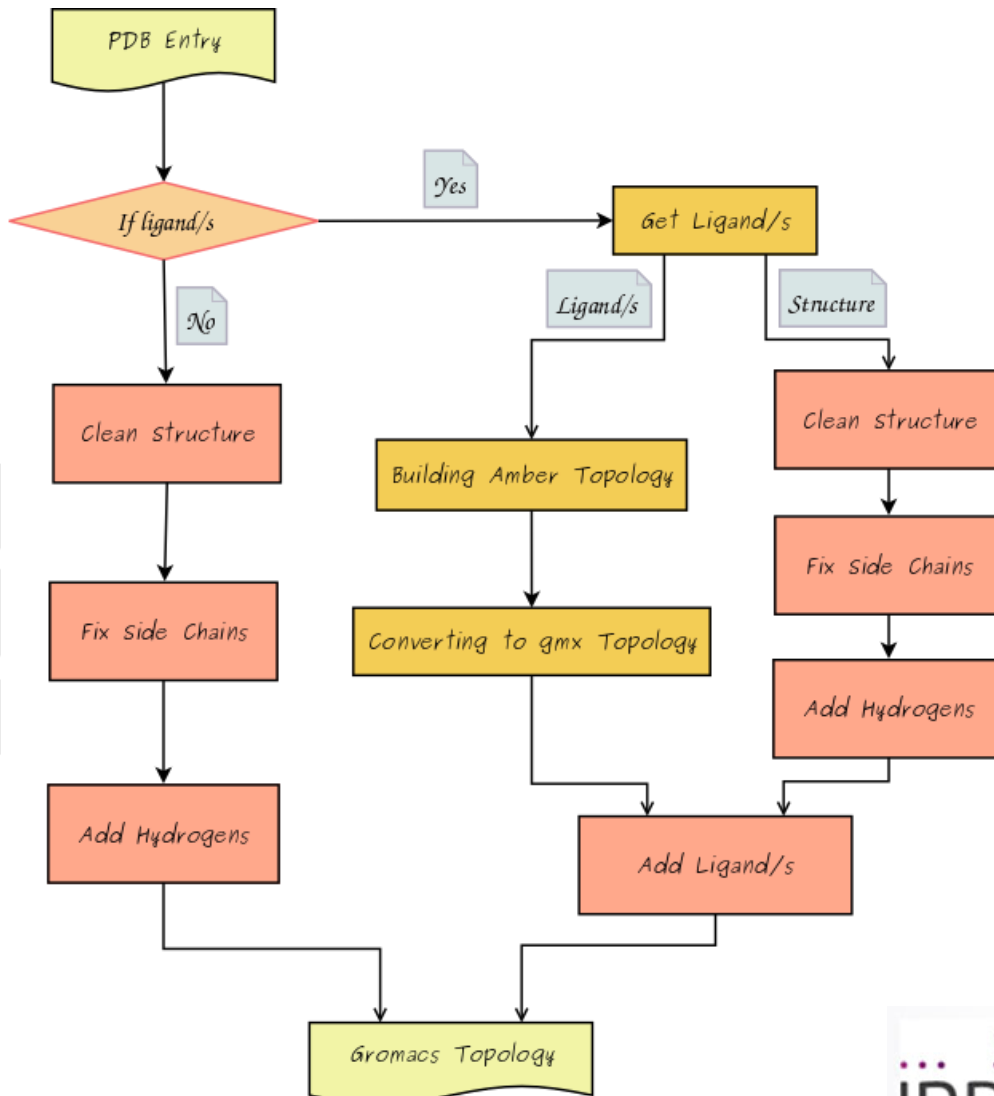
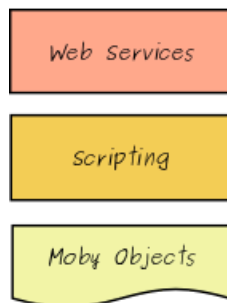
my $pdbStruct = getStructureFromPDB (
    'structure' => $object
) -> {'structure'};

if ($@) {
    print "Service execution failed:\n$@";
    exit;
}

print OUT "\#getStructureFromPDB:\n";
print OUT $pdbStruct->content;
```

# MDMoby Workflows

- Workflow Example:
- Generate Topology for Gromacs with amberff.
- Mixing web services with scripting.
- Others (Amber/Namd/Gromacs):
  - Generate Topology.
  - Setup.
  - Setup with Solvation.
  - Complete Setup (with eq).

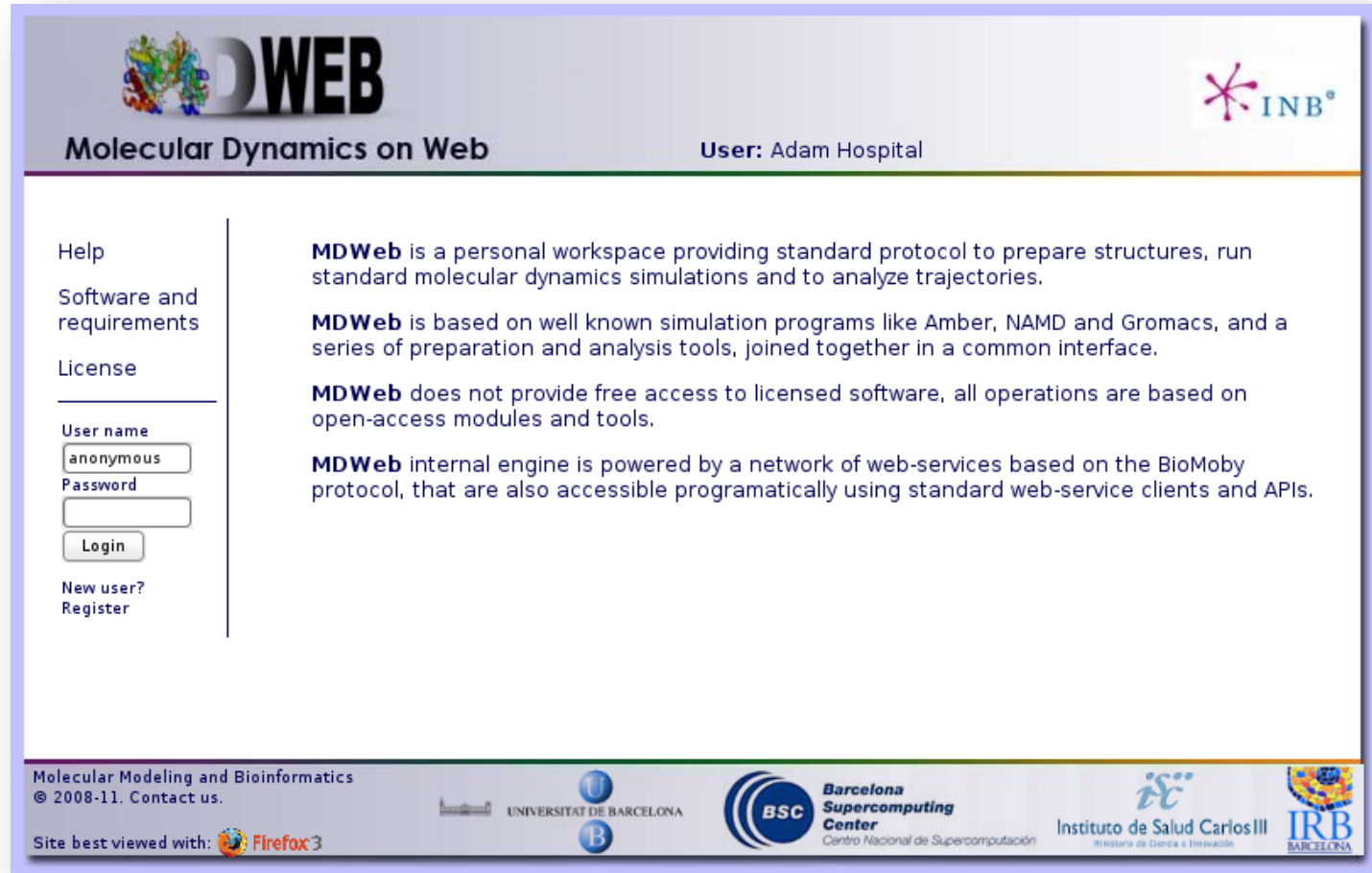


**MDWeb & MDMoby: an integrated web-based platform for molecular dynamics simulations.**

A. Hospital et al, *Bioinformatics* 2012, 28 (9), 1278-1279.

# Molecular Dynamics on Web: MDWeb

<http://mmb.irbbarcelona.org/MDWeb2>



The screenshot shows the MDWeb website interface. At the top left is the MDWeb logo, and at the top right is the INB logo. Below the logo is the text "Molecular Dynamics on Web" and "User: Adam Hospital". On the left side, there is a navigation menu with links for "Help", "Software and requirements", and "License". Below the menu is a login form with fields for "User name" (containing "anonymous") and "Password", and a "Login" button. Below the login form are links for "New user?" and "Register". The main content area contains three paragraphs of text describing MDWeb: its purpose as a personal workspace, its foundation on simulation programs like Amber, NAMD, and Gromacs, its open-access nature, and its use of a network of web-services based on the BioMoby protocol. At the bottom of the page, there is a footer with logos for "Molecular Modeling and Bioinformatics", "© 2008-11. Contact us.", "UNIVERSITAT DE BARCELONA", "BSC Barcelona Supercomputing Center", "Institut de Salut Carios III", and "IRB BARCELONA". A note at the bottom left says "Site best viewed with: Firefox 3".

# MDWeb: New project

## Start New Project:

- Base Structure.
  - *Str. checking.*
- Base Trajectory.

**MDWEB** User: Anonymous

Molecular Dynamics on Web

Home | **Start new project** | Close workspace | Analysis Tutorial | Setup Tutorial | Help

Project Title

Description (optional)

Input Type

---

**Base Structure**

Swiss-Prot or PDB Code Id (ex. 1ubq)

User provided Structure (PDB format)

*Input structure file should follow PDB File Format v.3.30 (July 13, 2011) more info...*

---

**Base Trajectory**

Tool

Trajectory format

Topology format

Trajectory File

Topology File

---

**Upload project**



# MDWeb: Structure Checking

## Initial Structure Checking:

- Models/Chains.
- Atom Alt. Location.
- Amide Assignments.
- Missing atoms/residues.
- Clashes.
- Ligands (known/unknown).

**Model:** Single one  
**Chains:** All selected [Show...](#)

**Alt. Locations:** Defaults [Select...](#)

- ✓ Amide Assignment
- ✓ Improper Chirality
- ✓ Disulphide Bonds
- ✓ Residue Insertion
- ✓ This protein doesn't contain DNA/RNA
- ✓ Unusual *cis/trans* Configuration
- ⚠ Non Consecutive Residues [Show...](#)
- ✗ Possible Sequence Gaps [Show...](#)
- ✓ Steric Clashes
- ✓ CA Steric Clashes
- ✓ Polar Donor Clashes
- ✗ Polar Acceptor Clashes [Show...](#)
- ✗ Apolar Clashes [Show...](#)
- ✗ Ionic Positive Clashes [Show...](#)
- ✓ Ionic Negative Clashes
- ✓ Heavy Metals
- ⚠ Known ligands: All ligands will be removed [Show...](#)
- ✗ Unknown ligands: All ligands will be removed [Show...](#)

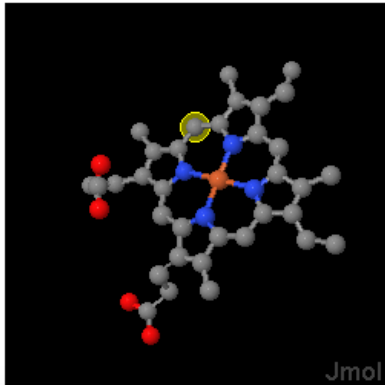
Back Next

# Ligand Atom Matching

**DWEB**  
Molecular Dynamics on Web

User: Adam Hospital

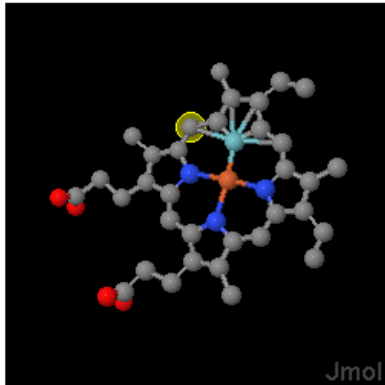
Home | Start new project | Close workspace | Help



Jmol

Reset

FE	→	FE
CHA	→	CHA
CHB	→	CHB
CHC	→	CHC
CHD	→	CHD
NA	→	NA
C1A	→	C1A
C2A	→	C2A
C3A	→	C3A
C4A	→	C4A
CMA	→	CMA
CAA	→	CAA
CBA	→	CBA
CGA	→	CGA
O1A	→	O1A
O2A	→	O2A
NR	→	NR



Jmol

Reset

Submit

**Found known ligands** [Show...](#)

Ligand: SO4 [Check](#)

**Found unknown ligands** [Show...](#)

Ligand: AC2  remove

upload

.lib file:  
 [Examinar...](#)

.fromod file:  
 [Examinar...](#)

[Check](#)

# MDWeb: Operations

The screenshot displays the MDWeb web interface. At the top, the MDWeb logo is on the left, and the INB logo is on the right. Below the logo, the text 'Molecular Dynamics on Web' and 'User: Anonymous' are visible. A navigation bar contains links for 'Home', 'Start new project', 'Close workspace', and 'Help'. The main content area shows a project titled '1a32 (MDWeb4db7444d5700b)' with a last modification date of '27/04/2011 00:16' and a disk usage of '804 kB'. A 3D protein structure is shown on the right. Below this, a section titled 'Stored structures' lists a 'PDB Base structure (86.3 kB)'. An 'Operations' dialog box is open, showing a list of operations to be performed on the selected structure. The list includes actions like 'Check for disulphide bonds', 'Clean PDB', 'Fix Side Chains', and various simulation setups for Amber, Gromacs, and Namd. The dialog also has input fields for 'Title' and 'Comment', and a 'List of Operations' dropdown menu.

**MDWEB**  
Molecular Dynamics on Web

User: Anonymous

Home | Start new project | Close workspace | Help

**1a32 (MDWeb4db7444d5700b)**

Last modification on: 27/04/2011 00:16  
Disk Usage: 804 kB

**Stored structures**

Click on structure title to deploy the toolbox.

- PDB Base structure (86.3 kB)

Select the desired operation.

Title:  Comment:

List of Operations:

- List of Operations:
- Check for disulphide bonds
- Clean PDB
- Fix Side Chains
- Mutate residue
- Amber FULL MD Setup
- Amber MD Setup
- Amber MD Setup with Solvation
- Generate Topology for Amber
- Generate Topology for Gromacs
- Generate Topology for Namd
- Gromacs FULL MD Setup
- Gromacs MD Setup
- Gromacs MD Setup with Solvation
- Namd FULL MD Setup
- Namd MD Setup
- Namd MD Setup with Solvation

**Operations**

- Perform a new setup operation on the selected structure.
- Perform a new simulation/optimization.
- Perform a new analysis.
- Visualize structure using Rasmol compatibles viewers (plug-in required).
- Visualize structure using JMol.
- View log file.
- Download results in a compressed tgz file.
- Delete item from the workspace.

Molecular M...  
© 2008-11...  
Site best vie...

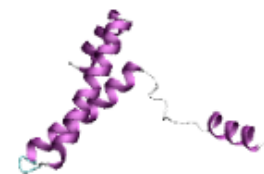
UNIVERSITAT DE BARCELONA  
BSC  
Barcelona Supercomputing Center  
Centro Nacional de Supercomputación  
Instituto de Salud Carlos III  
IRB  
BARCELONA

# MDWeb: Workflows

## 1a32 (MDWeb4d5d3df62d0da)

Last modification on: 22/04/2011 13:12

Disk Usage: 59.4 MB



### Stored structures

Click on structure title to deploy the toolbox.

PDB Base structure (86 kB)

Select the desired operation.

Title:  Comment:

Generate Topology for Gromacs



Forcefield:  
AMBER-99SB\* force field

PDB Cleaned Structure\_10 (57 kB)

GRO Structure with hydrogens added (GROMACS)\_00 (592 kB)

#### Generate top and itp Topology Files for Gromacs.

- Program: pdb2gmx from Gromacs Package.
- Crystallographic waters will be removed.
- Side chain missing atoms will be added with Leap from AmberTools package.
- Hydrogens will be added with pdb2gmx from Gromacs Package if needed.

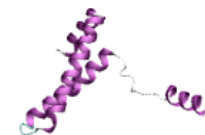
[Click for more information](#)

# MDWeb: Workflow progress report

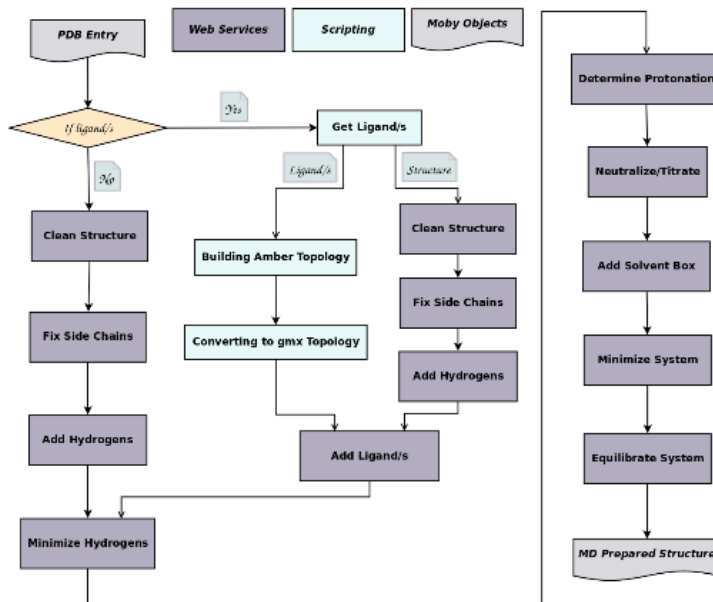
1a32 (MDWeb507e85d99bf0)

Last modification on: 17/10/2012 12:19

Disk Usage: 700 kB





Running Workflow: **GROMACS FULL Setup**



- 1.- Checking If ligand/s ... Done
- 2.- No Ligand/s found! Done
- 3.- Cleaning Structure ... Done
- 4.- Fixing Side Chains ... Done
- 5.- Adding Hydrogens ... Done
- 6.- Minimizing Hydrogens ... Done
- 7.- Determining Protonation ... Running
- 8.- Neutralizing / Titrating ... Waiting
- 9.- Adding Solvent Box ... Waiting
- 10.- Minimizing System ... Waiting
- Equilibrating system:
- 11.- Heating solvent to 300K ... Waiting
- 12.- Lowering Protein Restraints ... Waiting
- 13.- Reducing Restraints to just Protein Backbone ... Waiting
- 14.- Lowering Restraints to just 100 KJ/Mol-nm2 ... Waiting
- 15.- Free MD, without restraints ... Waiting

# MDWeb: Project tree





**Molecular Dynamics on Web**

User: Adam Hospital

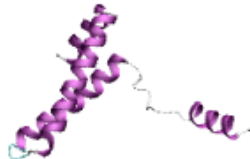
Home
Start new project
Close workspace
Help

---

**1a32 (MDWeb4d5d3df62d0da)**

Last modification on: 22/04/2011 13:12

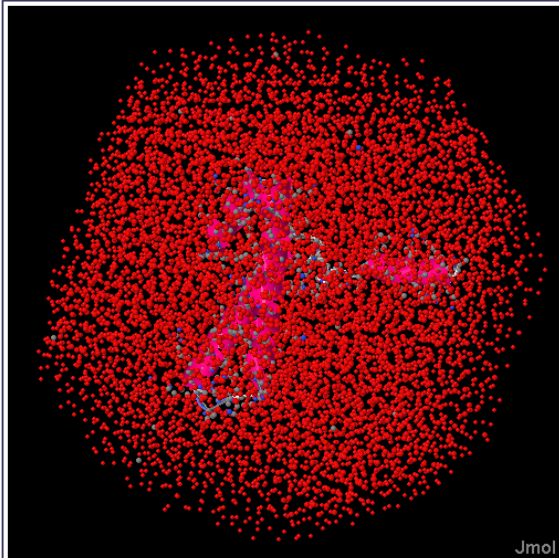
Disk Usage: 59.4 MB



**Stored structures**

Click on structure title to deploy the toolbox.

- [-] Base structure (86 kB)
- [-] Cleaned Structure\_10 (57 kB)
- [-] Structure with hydrogens added (GROMACS)\_00 (592 kB)
- [-] Energetically minimized hydrogens\_01 (636 kB)
- [-] Energetically minimized structure\_02 (520 kB)
- [-] Solvated system (GROMACS)\_03 (3.6 MB)
- [-] Energetically minimized system\_07 (3.7 MB)
- [-] Equilibrated System (NVE)\_56 (MD Config Files)
- [-] Equilibrated System (NVE)\_58 (63.1 MB)
- [-] Trajectory snapshot\_59 (17.5 kB)



**Structure**

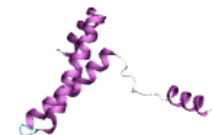
- Atoms
- Ligands
- Wireframe
- Cartoon
- Show hydrogen bonds

**Cartoon color**

Structure  Chain

Hide Hydrogens

# MDWeb: MD Run



1a32 (MDWeb50657024cc97e)

Last modification on: 28/09/2012 16:49

Disk Usage: 24.9 MB

## Stored structures

Click on structure title to deploy the toolbox.

PDB Base structure (88 kB) ✓

TRAI Prepared Amber Structure (Setup + Solvation + Equilibration) ✓

Select the desired operation.

Title:  Comment:

Simple Box Solvent Molecular Dynamics (NPT) ▾

Click for more information

**Only return Configuration Files (without running simulation) ✓**

Time step (fs)

Temperature (K)

Total Time (ps)

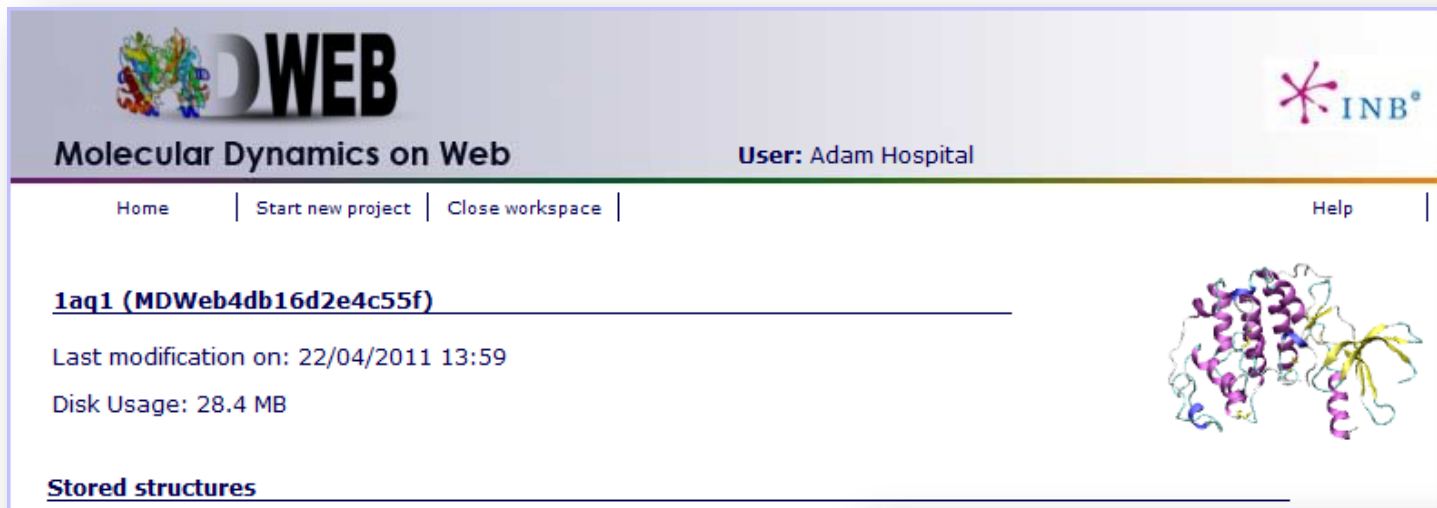
Output freq. (steps)

Total Snapshots: 10000

### System Molecular Dynamics Simulation in Water Box:

- Program: namd2 from NAMD package.
- Simulation done in NPT ensemble with Periodic Boundary Conditions.
- Particle Mesh Ewald (PME) for full-system periodic electrostatics.
- Constant temperature dynamics via Langevin Dynamics.
- Constant pressure dynamics via Nose-Hoover Langevin piston.
- SHAKE was used to maintain all bonds involving hydrogen atoms at their equilibrium values.

# MDWeb: Basic analysis & formats conversion



**MDWEB**  
Molecular Dynamics on Web

User: Adam Hospital

Home | Start new project | Close workspace | Help

**1aq1 (MDWeb4db16d2e4c55f)**

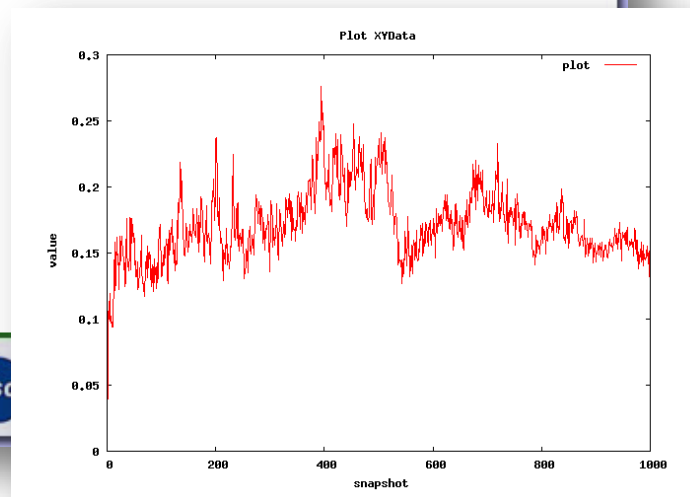
Last modification on: 22/04/2011 13:59  
Disk Usage: 28.4 MB

**Stored structures**

Click on structure title to deploy the toolbox.

- Base trajectory (23.7 MB)
- Trajectory RMSd\_00 (2.2 MB)

- List of Operations:
- List of Operations:
  - Compress trajectory to PCZ
  - Converts trajectory to a set of PDB Files
  - Converts trajectory to BINPOS Format
  - Converts trajectory to CRD Format
  - Converts trajectory to DCD Format
  - Flexibility Analysis
  - Get a trajectory fragment
  - Get a trajectory snapshot
  - Get Average Structure
  - Plot BFactor per residue
  - Plot Radius of Gyration along the trajectory
  - Plot RMSd along the trajectory
  - Plot RMSd x Residue
  - Remove Water molecules and ions from trajectory
  - Return trajectory for a set of atoms

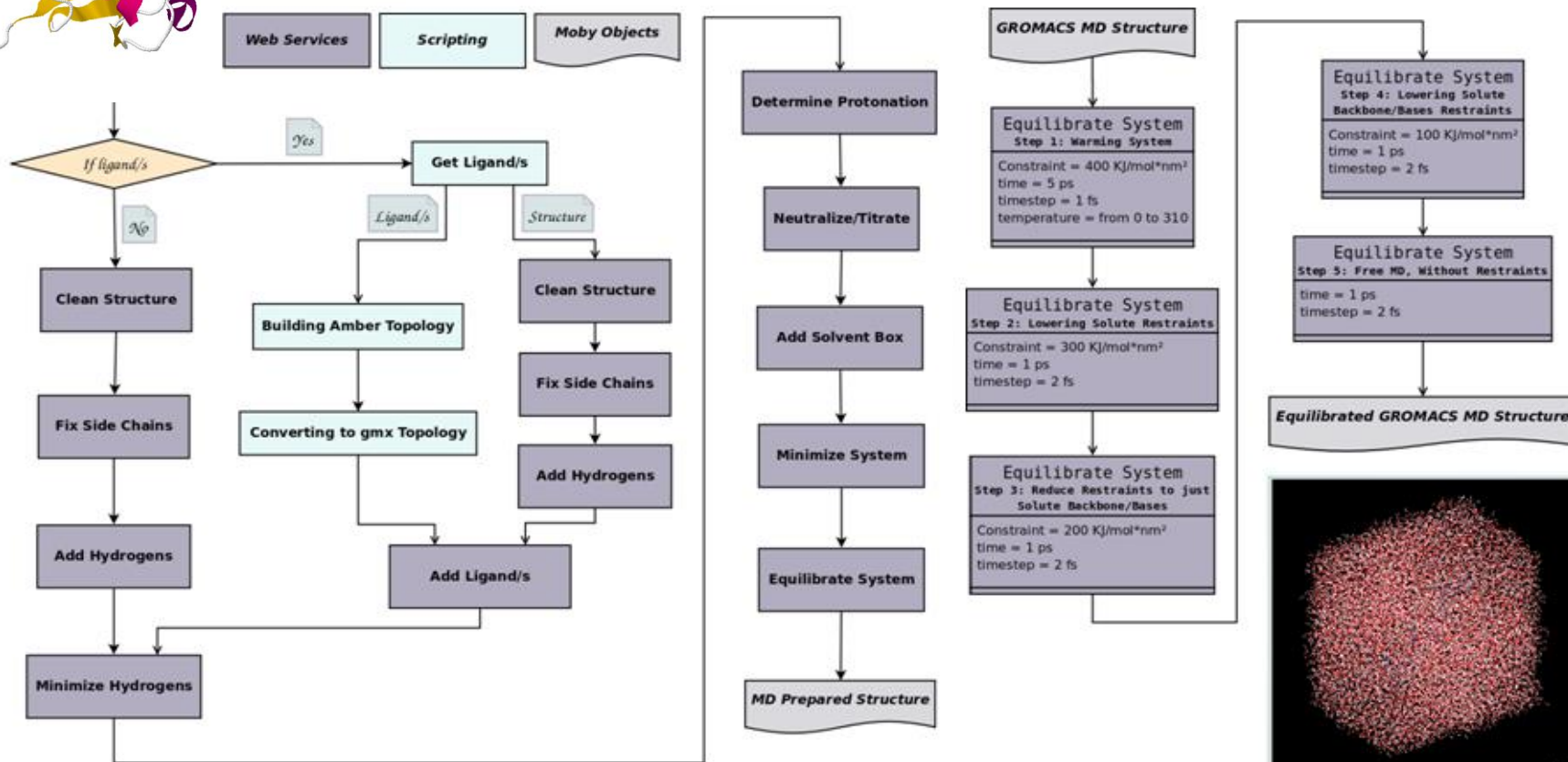
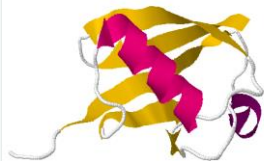




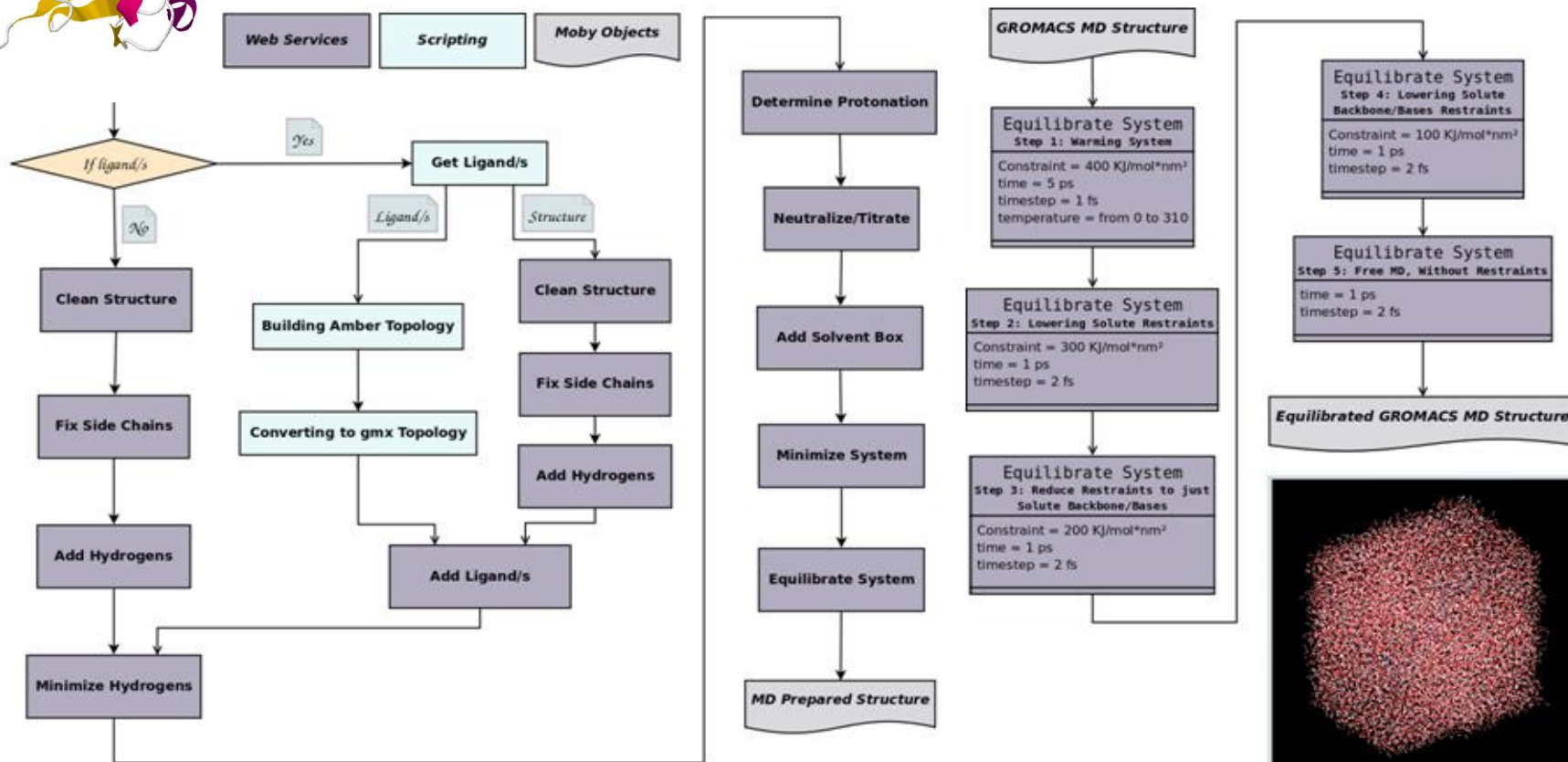
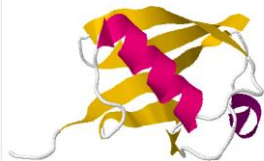
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  - *Simulation Setup (MDMoby / MDWeb).*

# Simulation Setup Hands On MDWeb



# Simulation Setup Hands On MDMoby



# Simulation Setup Hands On MDWeb - Tutorial



**MDWeb**  
Molecular Dynamics on Web

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**MDWeb Setup Tutorial**

**MDWeb** provides a friendly environment to setup new systems and run test simulations. With this short tutorial, you will be able to prepare a molecule to run a molecular dynamics simulation, following just a few steps.

1. **Registration**
2. **Starting Project**
3. **Checking the Structure**
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**Tutorial Steps**

1. **Registration**

The first thing to do is choose between working as an **anonymous** user or alternatively as a **registered** user. We **strongly** recommend working as a registered user, as it has some important advantages.

Anonymous user's projects are completely removed once the user is disconnected and also when session expires (after some minutes of inactivity), and therefore working as anonymous user is only suited for a first impression of the web server.

**Registration process** will just take a minute --> **Registration**.

Once logged in, the user **workspace** appears. In this **workspace**, all projects of the user will be shown.

Now, we are ready to start our first **MDWeb** project.

**MDWeb** Molecular Dynamics on Web User: Anonymous

Home [Start new project](#) [Close workspace](#) Help

<http://mmb.pcb.ub.es/MDWeb2/>



## Manual / Tutorial

**MDWeb** is extensively documented in this **on-line help**. Information about operations and workflows, explanations about how to use the server, tutorials for each of the main parts of it, all of that can be found in these pages.

The majority of this information can be also found in **MDWeb** Manual and Tutorial [PDF]:

- **MDWeb Manual, v1.0**
- **MDWeb Tutorial, v1.0**



Explore Help

PUBLIC REPOSITORY

adamhospital/mdmobydocker ☆

Last pushed: 2 days ago

After that, pull the prepared **MDMoby docker container**:

```
docker pull adamhospital/mdmobydocker
```

To run the **docker container**, type:

```
docker run -it adamhospital/mdmobydocker /bin/bash
```

Availability: <https://hub.docker.com/r/adamhospital/mdmobydocker/>



Perl

AmberTools



moby

```
test@6f8668b3b268:~$ perl MDMoby/Workflows/GROMACSWorkflowFull.pl  
      <inputFile> <outputFile> <workDirPATH> <forcefield> <waterType>
```

```
test@6f8668b3b268:~$ perl MDMoby/Workflows/GROMACSWorkflowFull.pl PDBs/1ubq.pdb . 6 1
```

## Simulation Setup – Tutorials:

**Amber** 

[http://sf.anu.edu.au/collaborations/amber\\_on\\_fujitsu/amber-12/tutorial/standard-setup/index.html](http://sf.anu.edu.au/collaborations/amber_on_fujitsu/amber-12/tutorial/standard-setup/index.html)

<http://ambermd.org/tutorials/>

**NAMD**  
Scalable Molecular Dynamics

<http://www.ks.uiuc.edu/Training/Tutorials/namd/namd-tutorial-win-html/index.html>

<http://www.ks.uiuc.edu/Training/Tutorials/>

**GROMACS**  
*Groningen Machine for Chemical Simulations*

<http://www.bevanlab.biochem.vt.edu/Pages/Personal/justin/gmx-tutorials/lysozyme/index.html>

<http://www.bevanlab.biochem.vt.edu/Pages/Personal/justin/gmx-tutorials/>

<http://www.gromacs.org/Documentation/Tutorials>