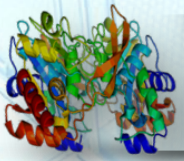
Macromolecular Simulation Software Workshop

cecam
Centre Européen de Calcul Atomique et Moléculaire

MD Simulation Automatic Setup

using



DWEB

*Molecular **D**ynamics On **Web***

Macromolecular Simulation Software Workshop

***CECAM – Jülich* 2015**

Adam Hospital Gasch

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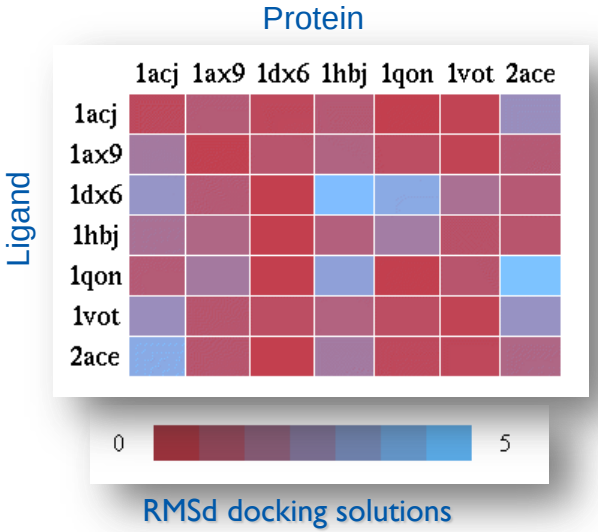
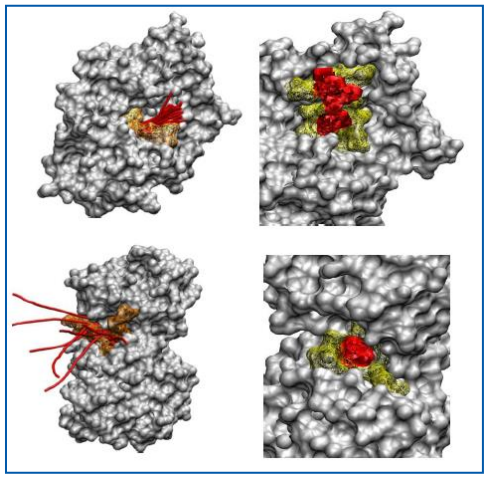
Introduction: Molecular Flexibility & MD



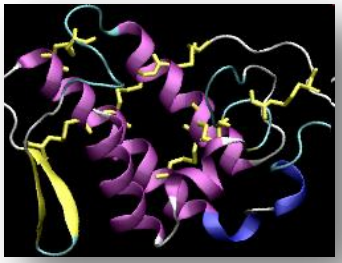
RMSd docking solutions

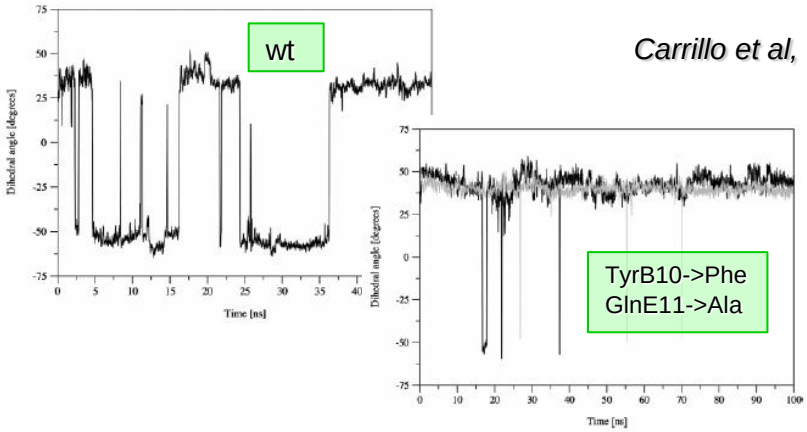


Protein Channels, Drug Cavities
MDGrid

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

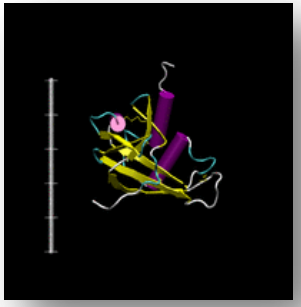
RCSB PDB PROTEIN DATA BANK





Gate Opening Molecular Switch.

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



Introduction: MD Limitations

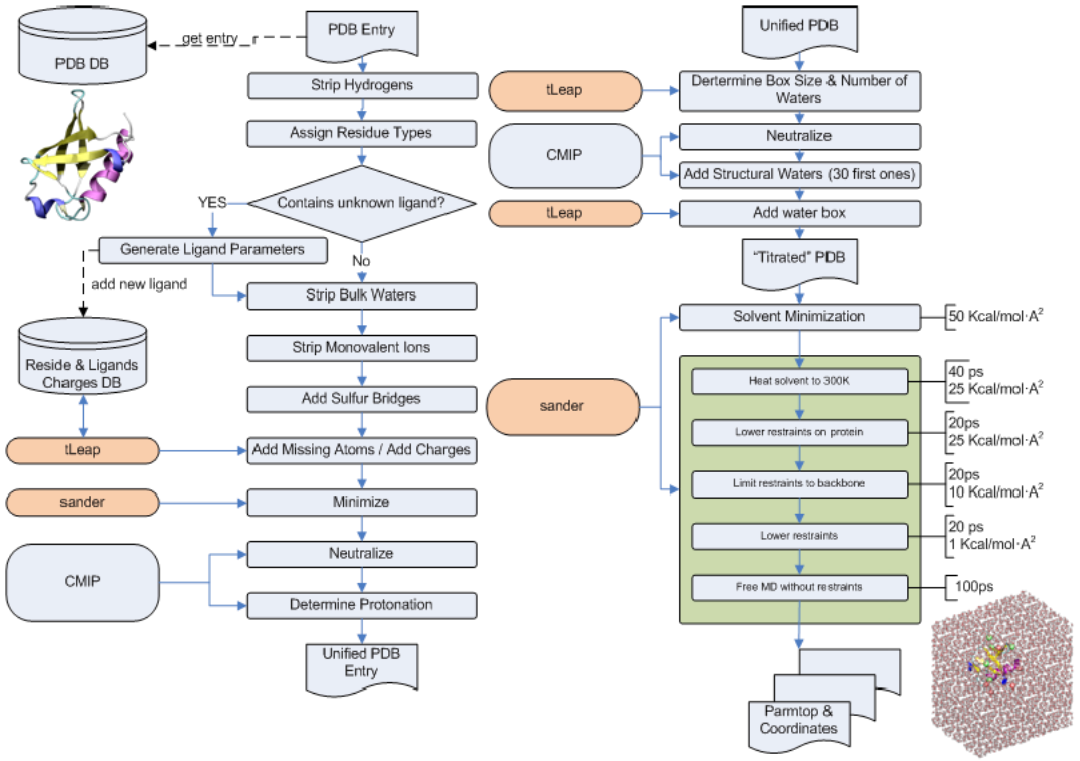
Large Computational Resources

$$V(\vec{r}) = \sum_{\text{bonds}} {}^{(1)}K_b(b-b_0)^2 + \sum_{\text{angles}} {}^{(2)}K_\theta(\theta-\theta_0)^2 + \sum_{\text{dihedrals}} {}^{(3)}K_\chi(1+\cos(n\chi-\delta)) + \sum_{\text{nonbonded-pairs},i,j} {}^{(4)}\left[\frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} - \varepsilon_{ij}\left\{\left(\frac{R_{\min ij}}{r_{ij}}\right)^{12} - {}^{(5)}2\left(\frac{R_{\min ij}}{r_{ij}}\right)^{6}\right\}\right]$$

Energy dependencies on:

1. Bond length
2. Bond valence angle
3. Bond dihedral angle
4. Non-bonded electrostatic interactions
5. Non-bonded van-der Waals interactions

Force Fields Uncertainties



High level of expertise needed

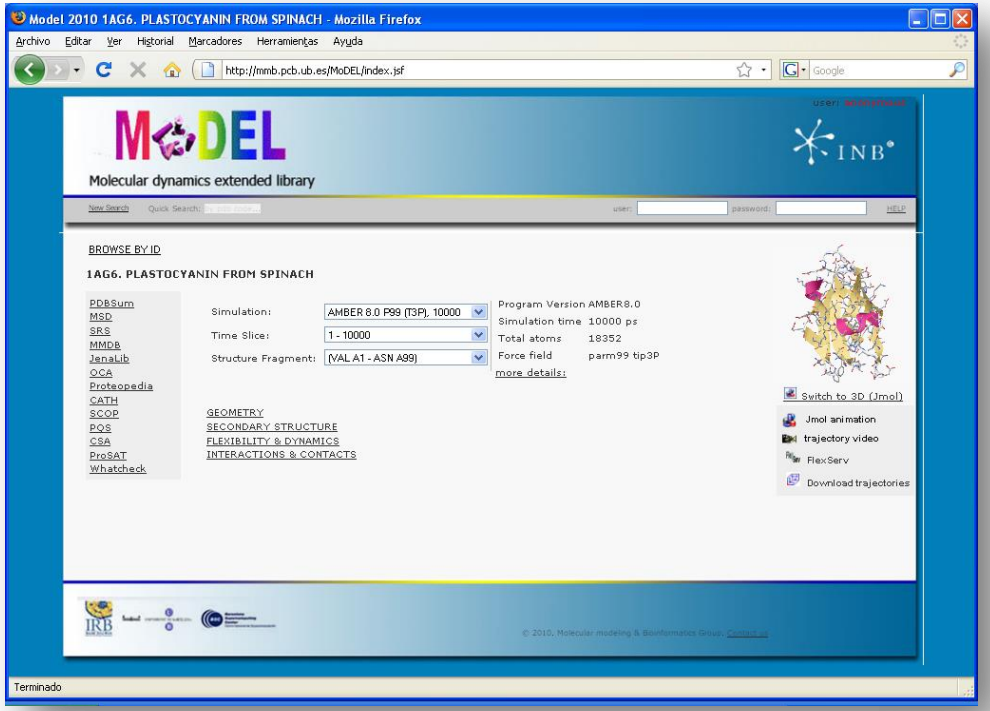
ParmBSC0: *A. Pérez et al. Biophys J. (2007) 92 (11), 3817-3829.*
ParmBSC1: *I. Ivani et al. Nature Methods (2015) In press.*

Introduction: MoDEL

Molecular **D**ynamics **E**xtended **L**ibrary.

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.**



Meyer et al, Structure 2010, 18 (11), 1399-1409.
Rueda et al, PNAS 2007, 104, 796-801.

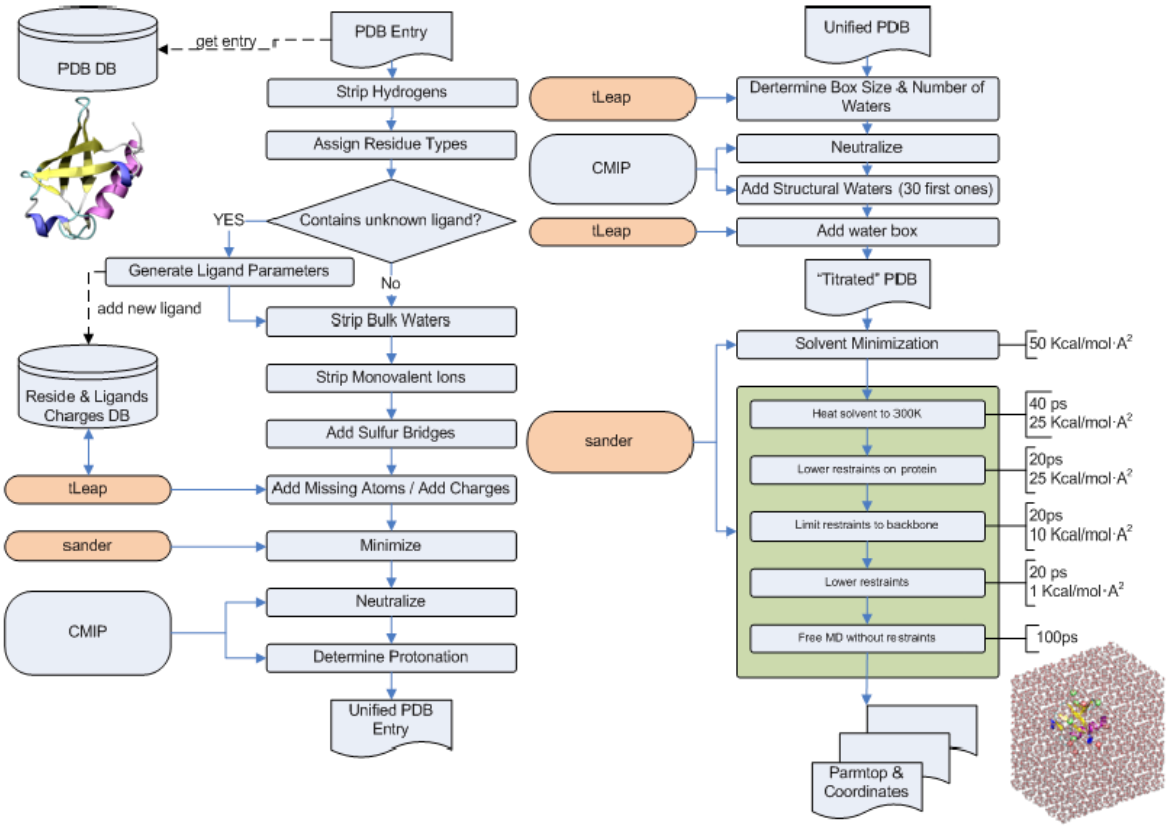
III II I
Year 2014 (Year 2010) (Year 2006)

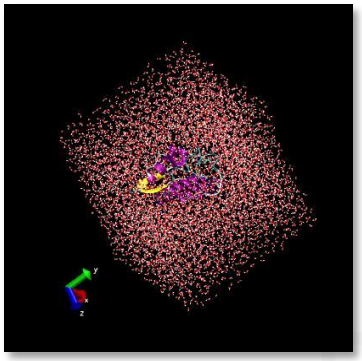
- 48,896 (10,240) (4,812) IBM Processors
- 1,017.0 (94.21) (42.35) TeraFlops
- 98 (20) (9.6) TB central RAM
- 2,000 (480) (236) TB Disk

- Communication network: Infiniband (Myrinet, Gigabit, 10/100 Ethernet)
- OS Linux - SuSe.
- 29th (5th) (4th) in top500

MareNostrum SuperComputer

Introduction: Automatic Setup





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

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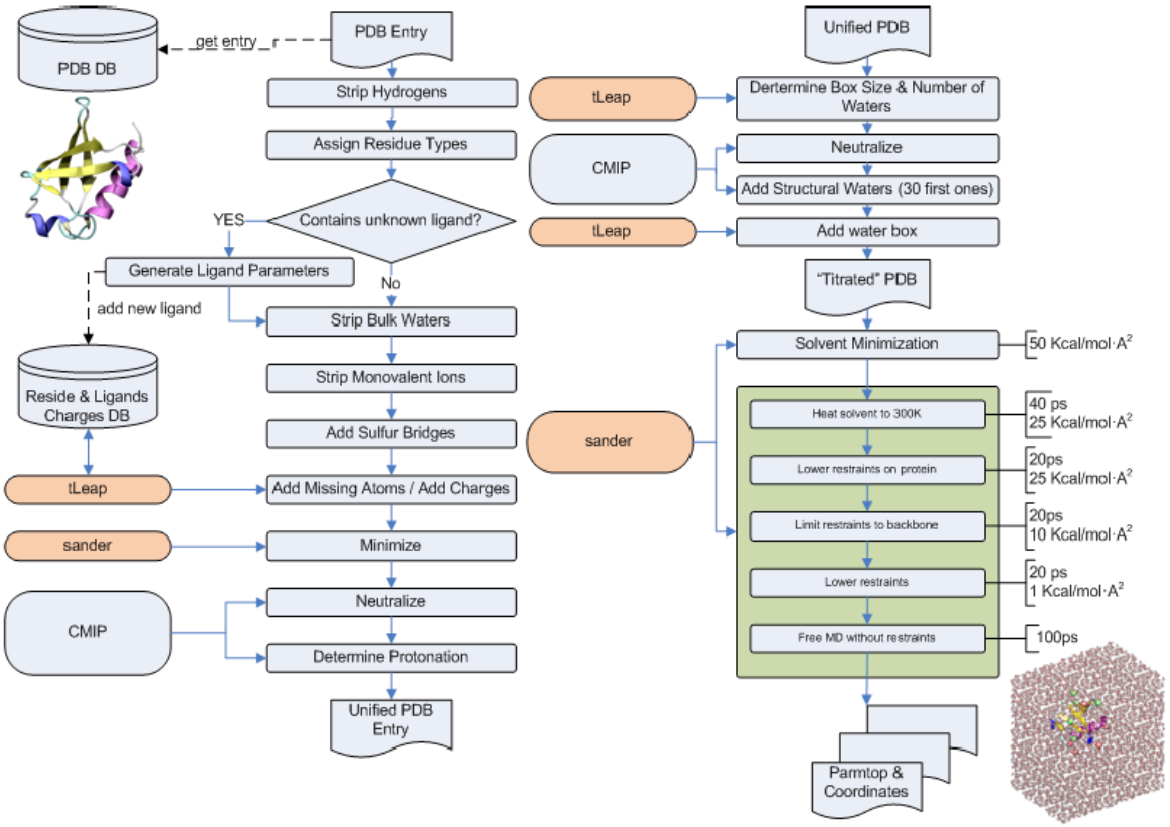
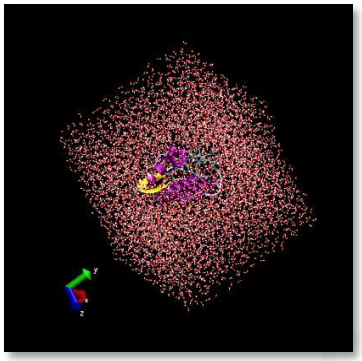
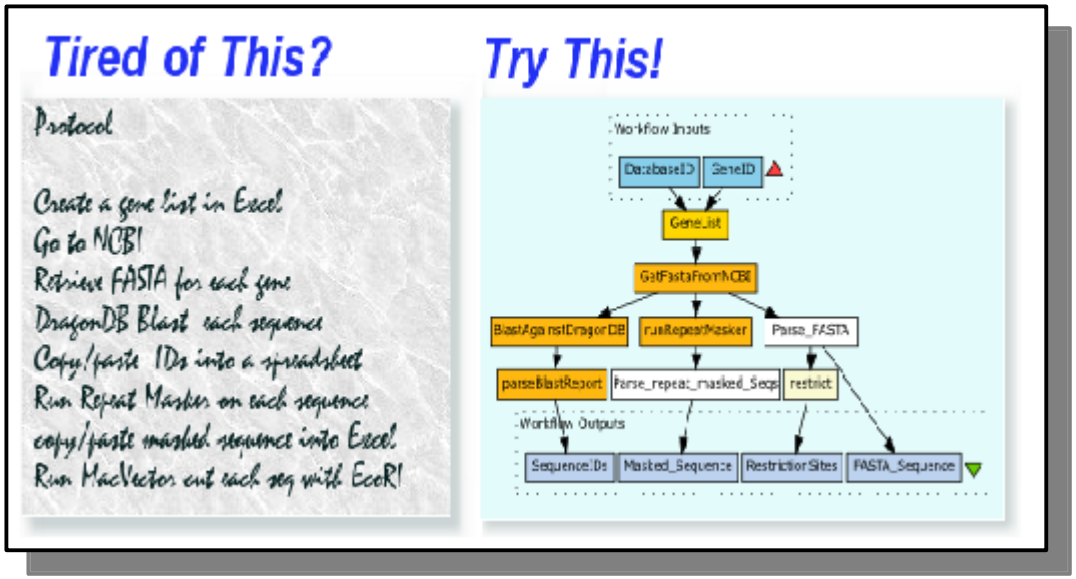
MDMoby Web Services

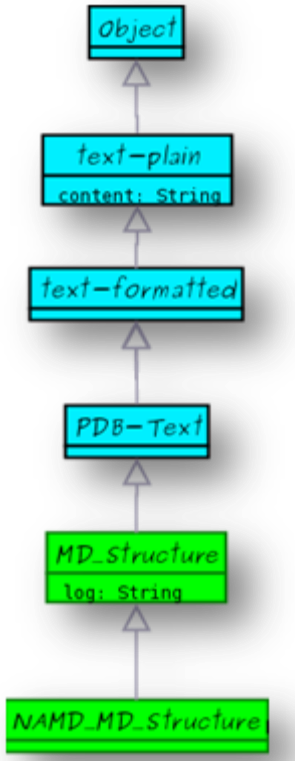




A. Hospital et al, Bioinformatics 2012, 28 (9), 1278-1279.

BioMoby





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

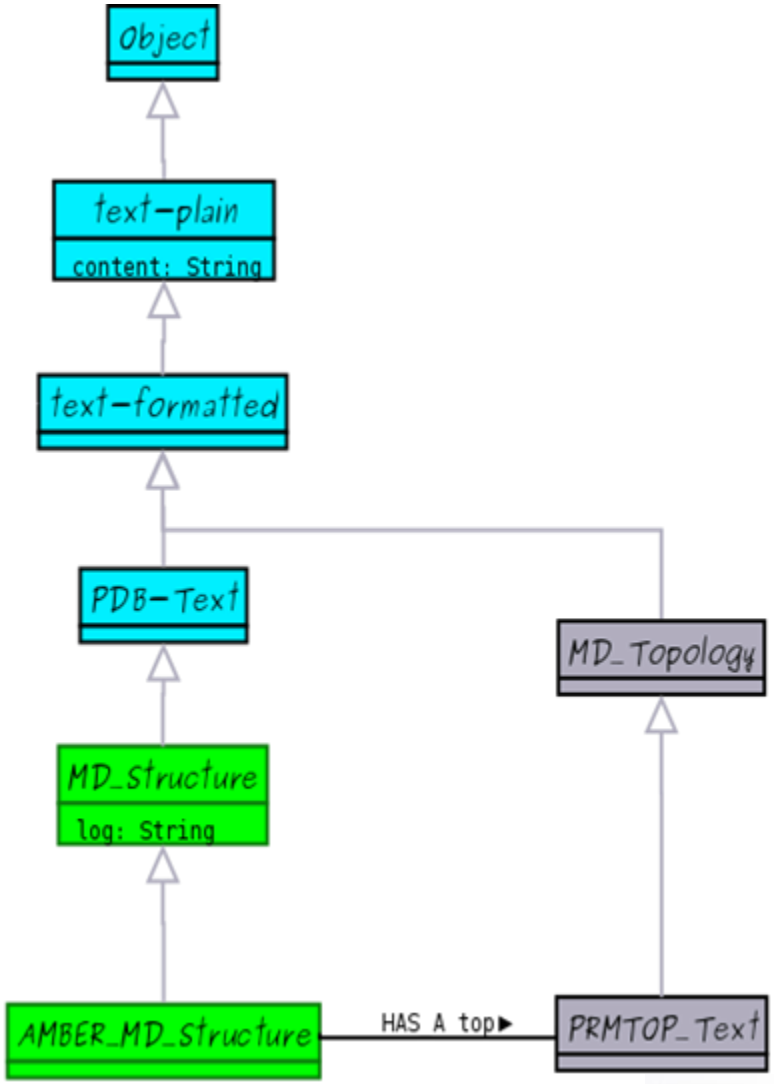
List of Operations:

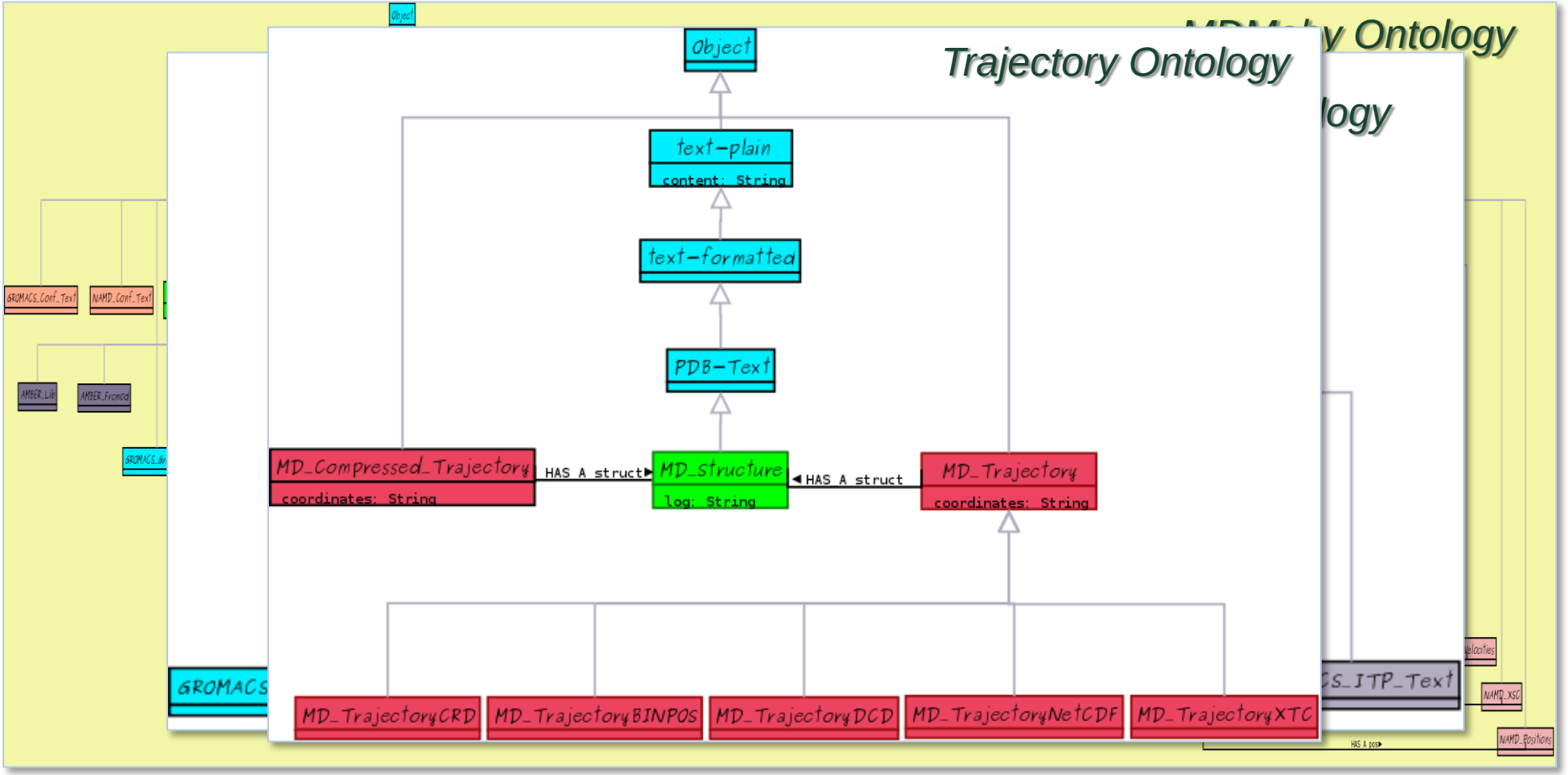
- List of Operations:
- Check for disulphide bonds
- Clean PDB
- Fix Side Chains
- Mutate residue
- Amber FULL MD Setup
- Amber MD Setup
- Amber MD Setup with Solvation
- Generate Topology for Amber
- Generate Topology for Gromacs
- Generate Topology for Namd
- Gromacs FULL MD Setup
- Gromacs MD Setup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

AMBER_MD_Structure

List of Operations:

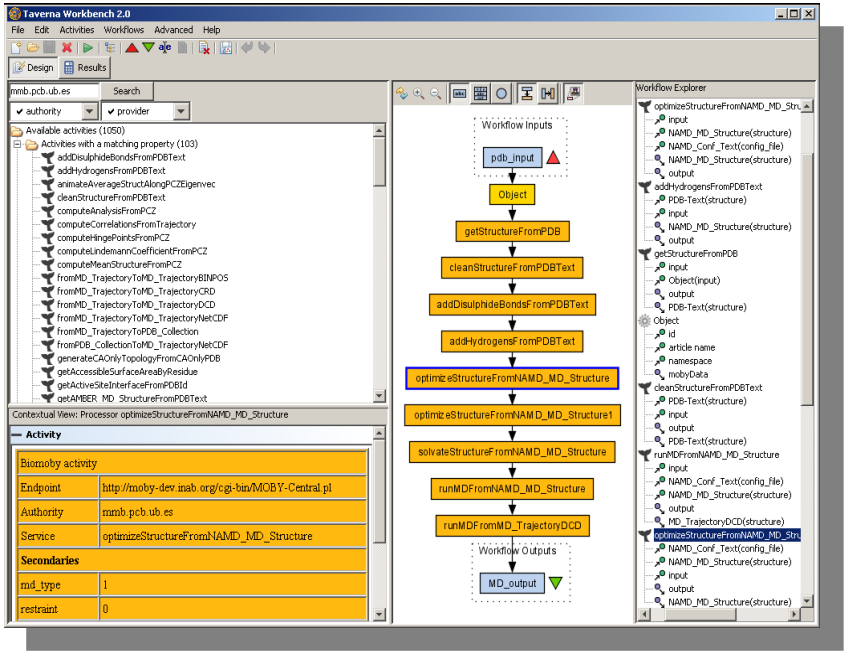
- List of Operations:
- Add structural hydration waters and ions
- Hydrogen Energetic Minimization
- Properly Protonate Histidines
- Properly Protonate Ionizable Residues
- Solvate structure
- Structure Energetic Minimization




Trajectory Ontology
Object
text-plain
content: String
text-formatted
PDB-Text
MD_Compressed_Trajectory
coordinates: String
HAS A struct
MD_Structure
log: String
HAS A struct
MD_Trajectory
coordinates: String
MD_TrajectoryCRD
MD_TrajectoryBINPOS
MD_TrajectoryDCD
MD_TrajectoryNetCDF
MD_TrajectoryXTC
GROMACS_Conf_Text
NAMD_Conf_Text
AMBER_Lib
AMBER_Frcmod
GROMACS_Itp
GROMACS
CS_ITP_Text
NAMD_XSC
NAMD_Positions
HAS A pos

How can you use them?

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

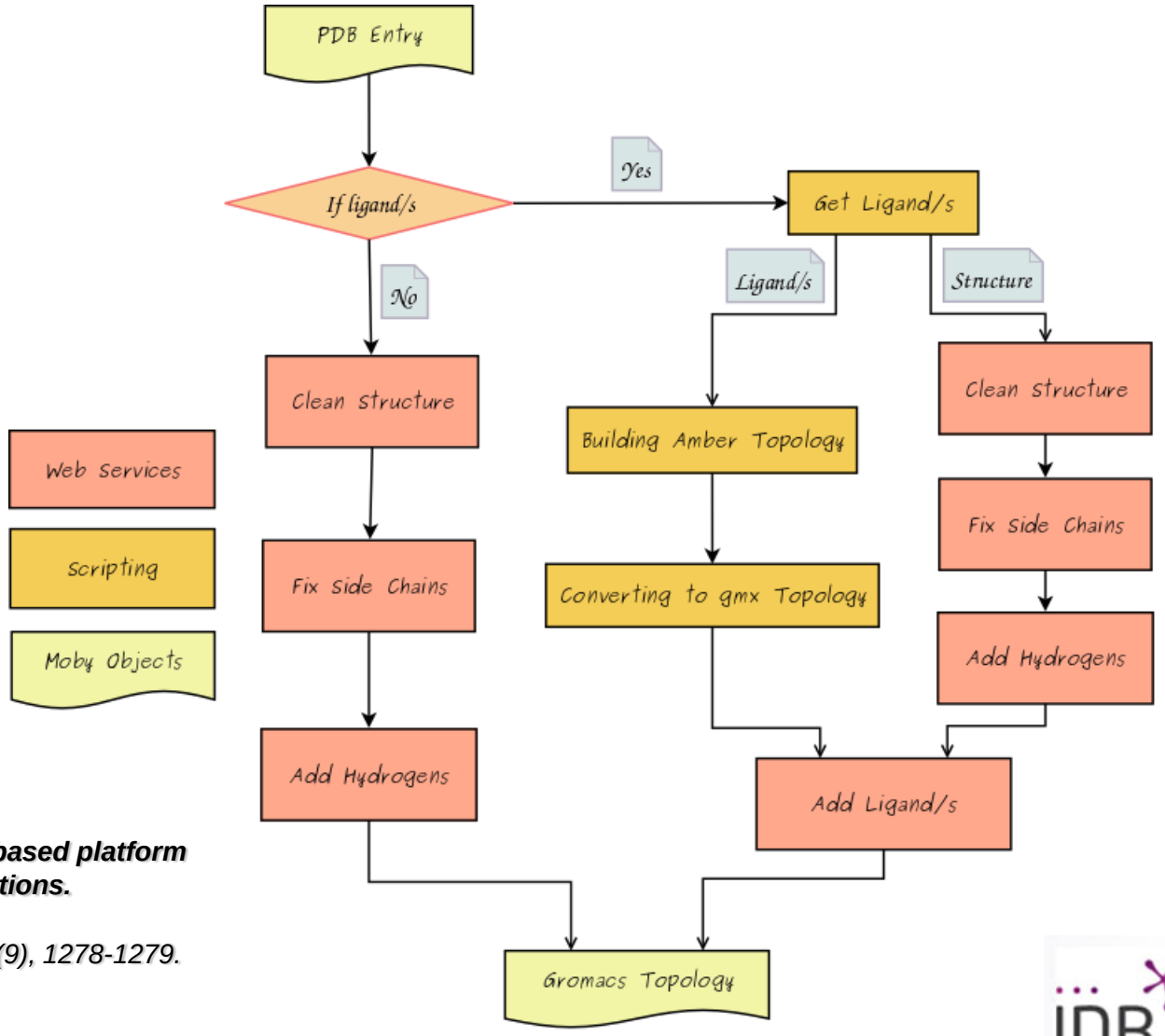


- *MobyLite Perl/Java API.*

```
########## 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).

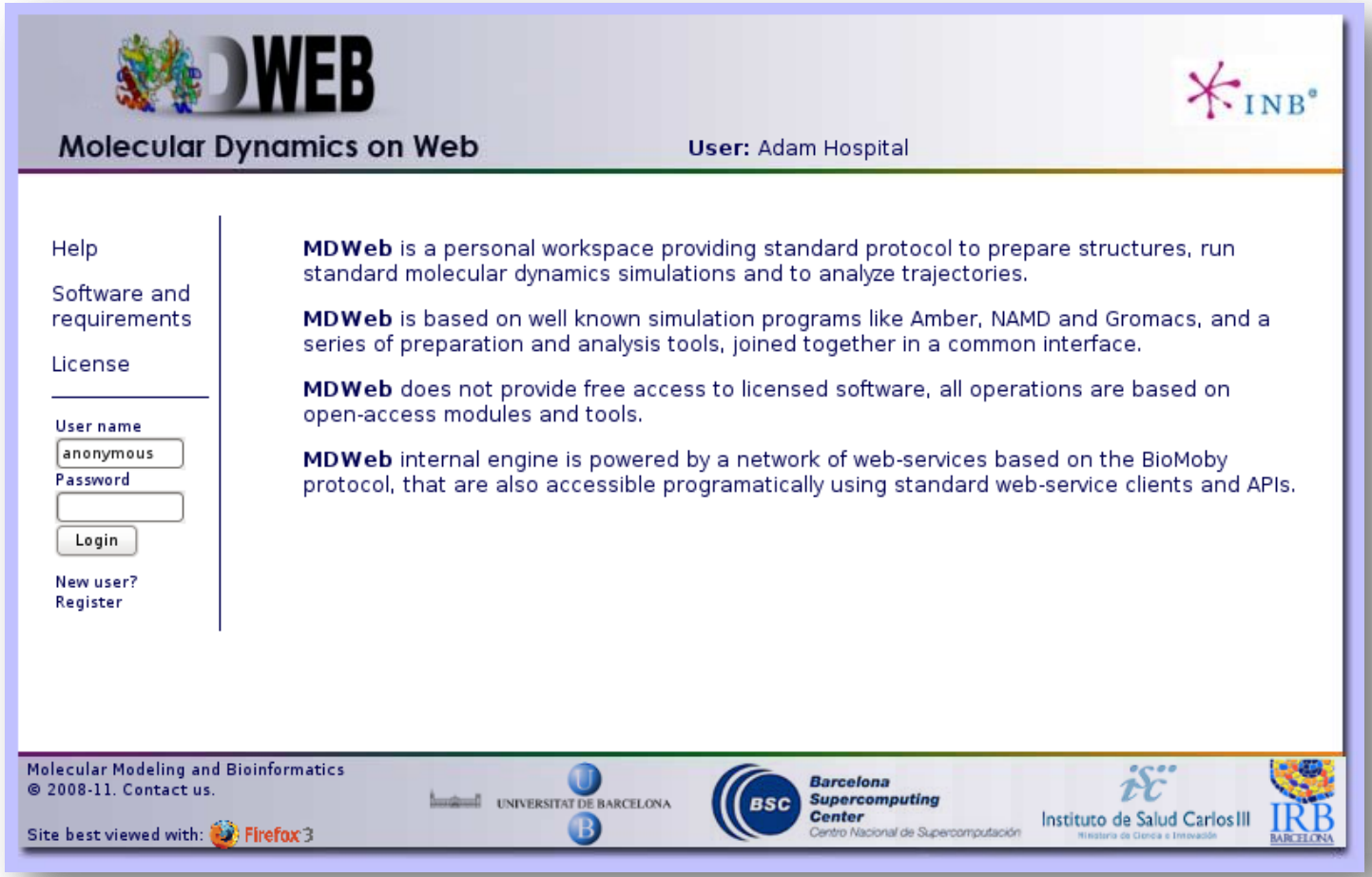


MDWeb & MDMoby: an integrated web-based platform for molecular dynamics simulations.

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

Molecular Dynamics on Web: MDWeb

http://mmb.irbbarcelona.org/MDWeb2

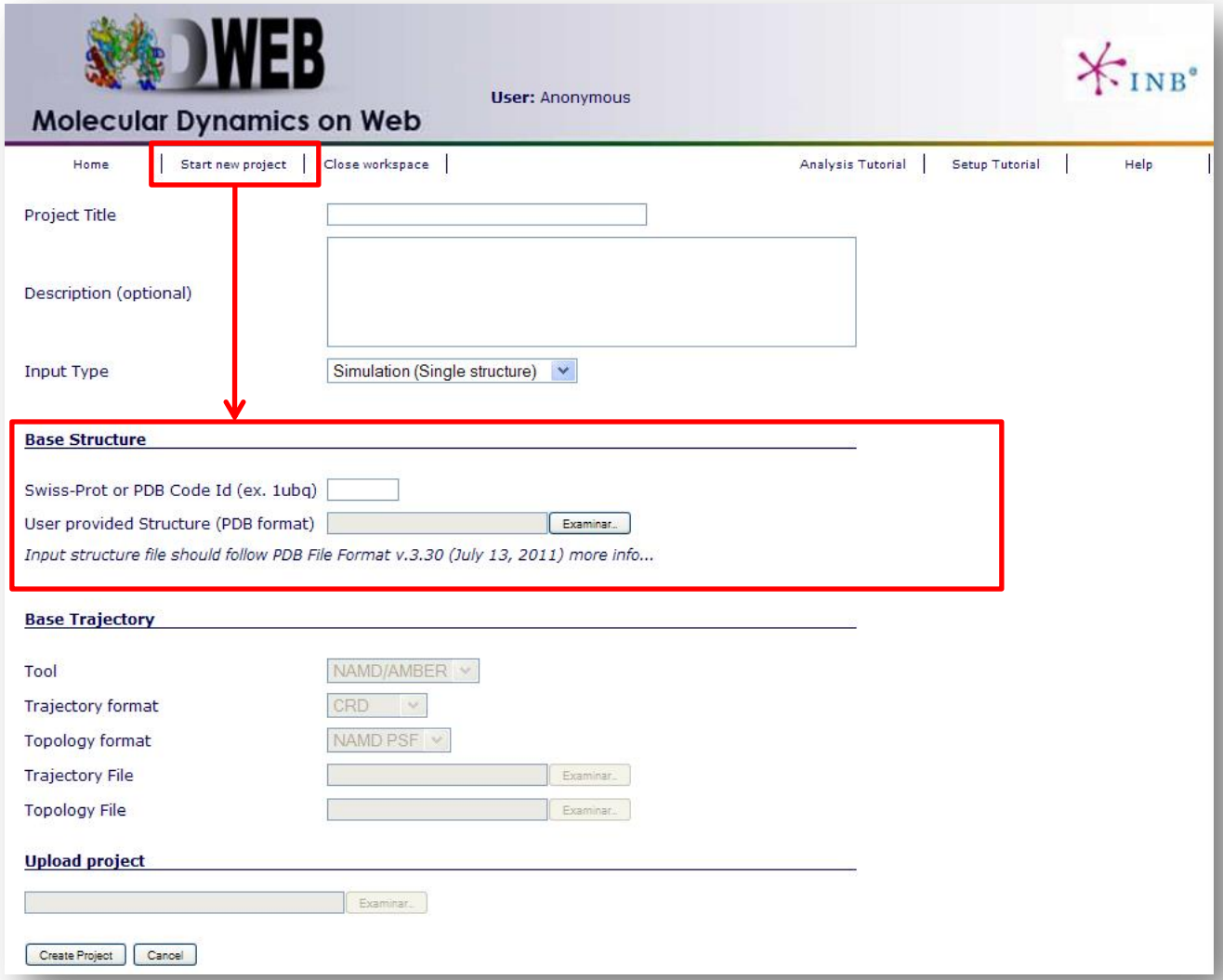


A. Hospital et al, Bioinformatics 2012, 28 (9), 1278-1279.

MDWeb: New project

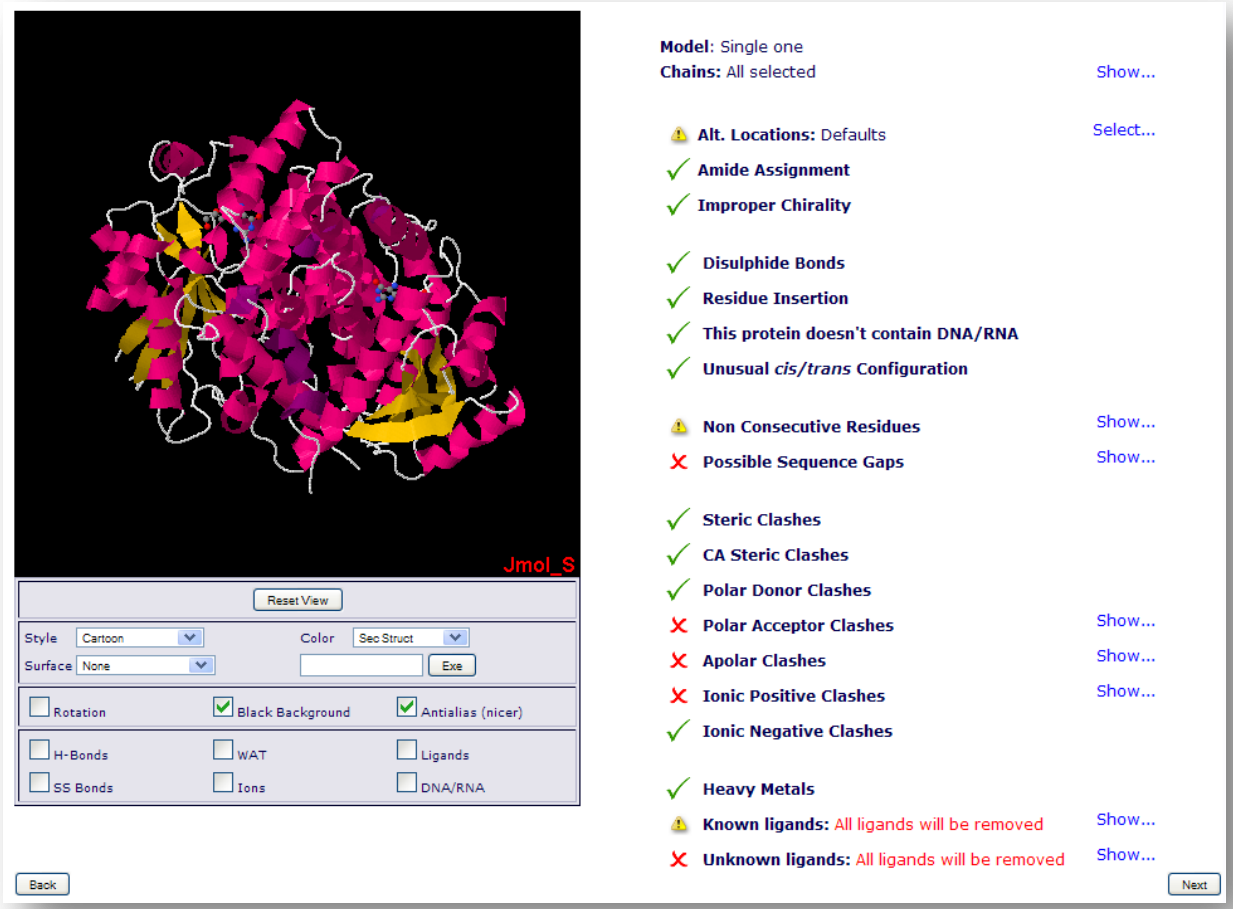
Start New Project:

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

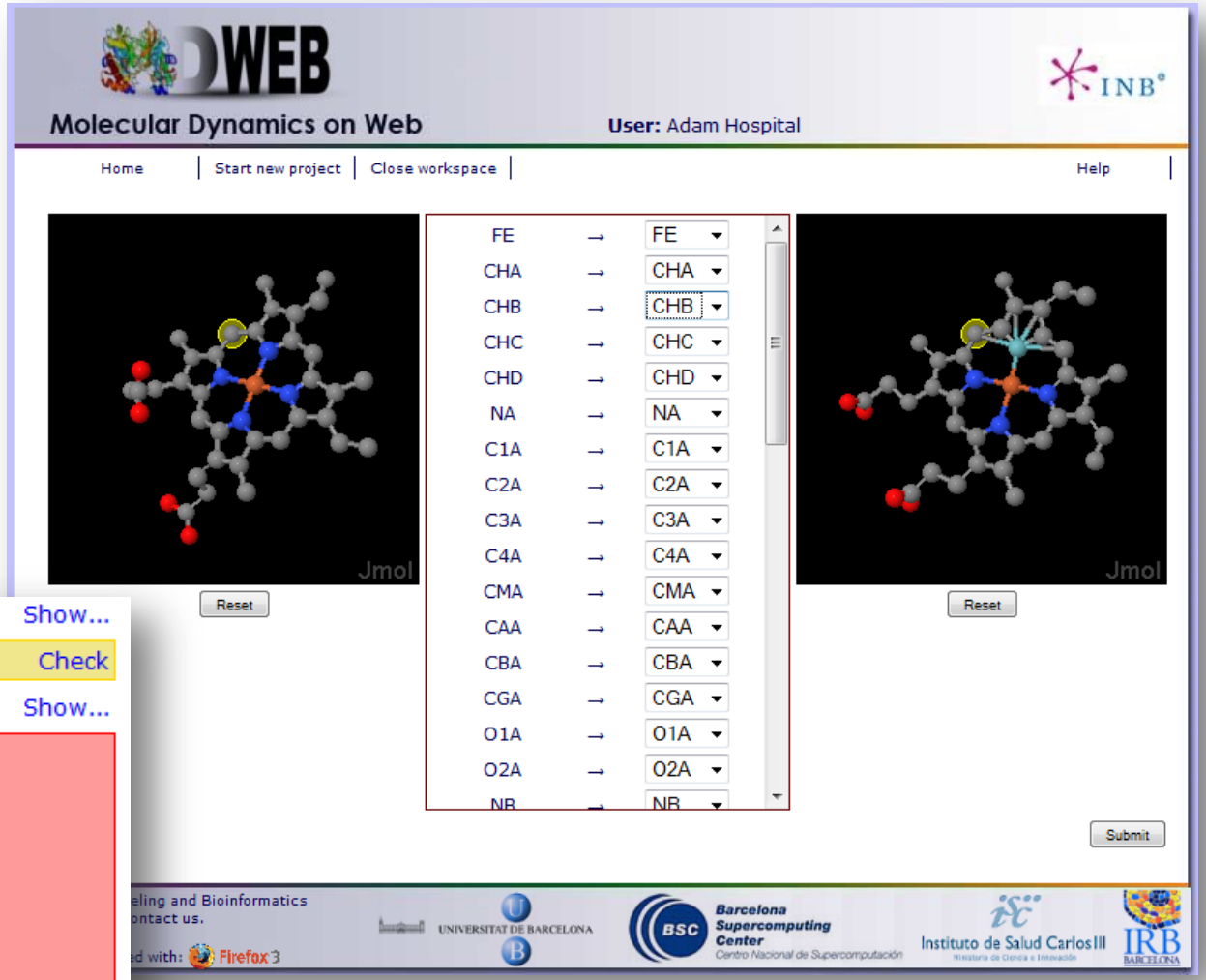


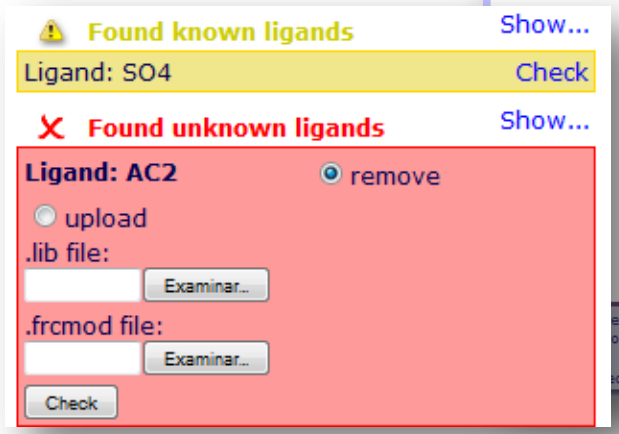
MDWeb: Structure Checking

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

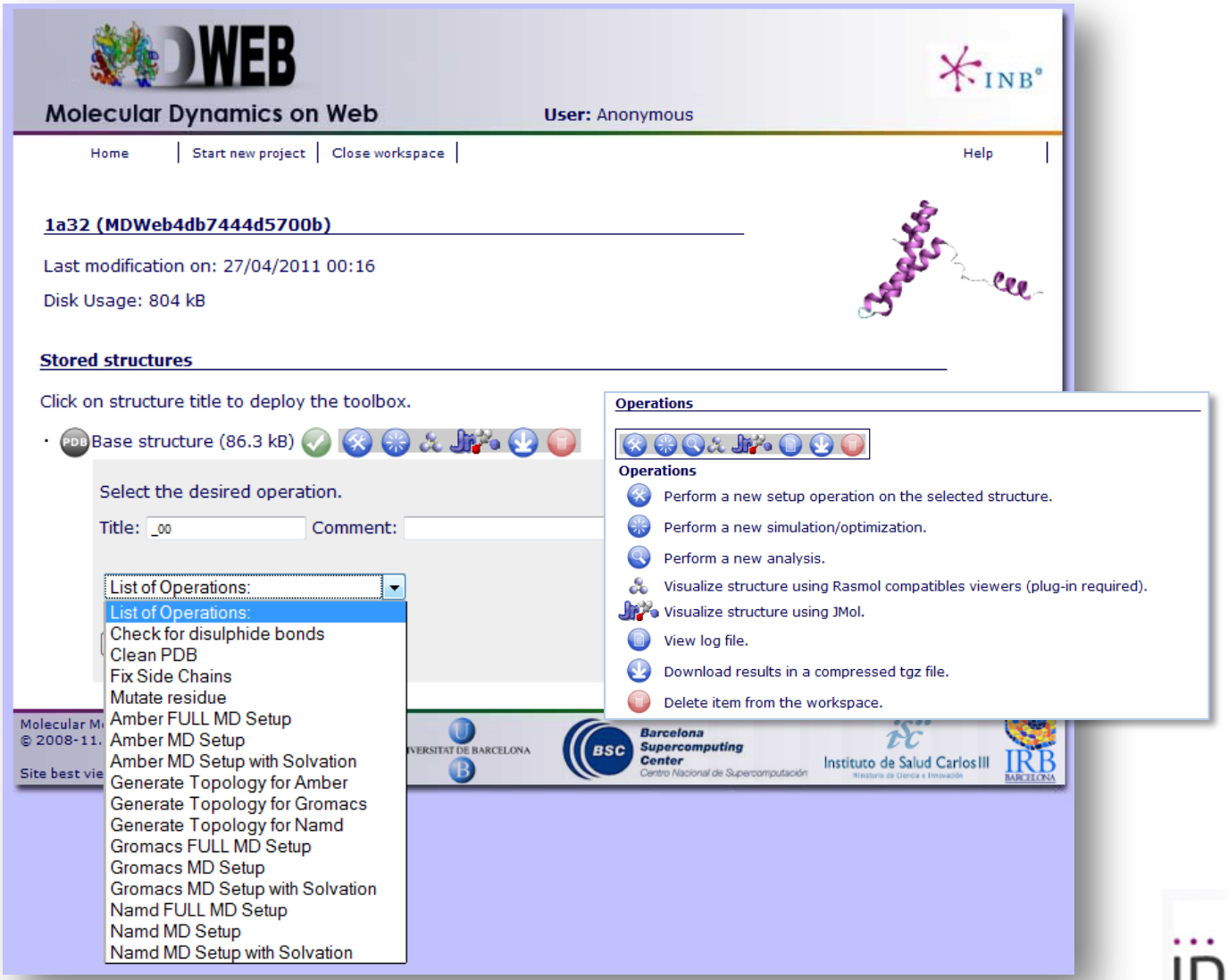


Ligand Atom Matching

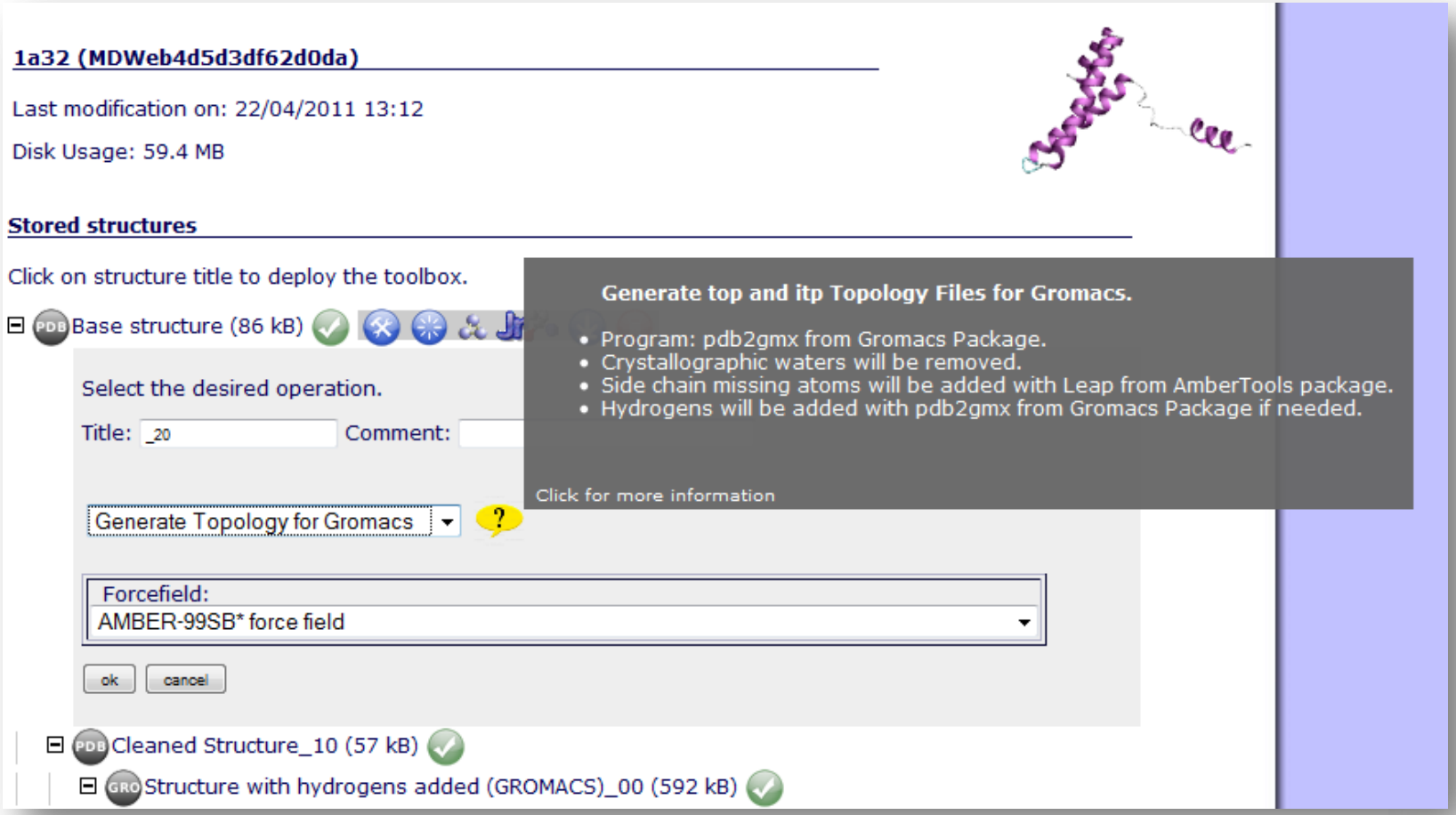




MDWeb: Operations



MDWeb: Workflows

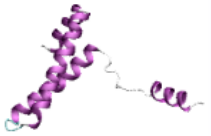


MDWeb: Workflow progress report

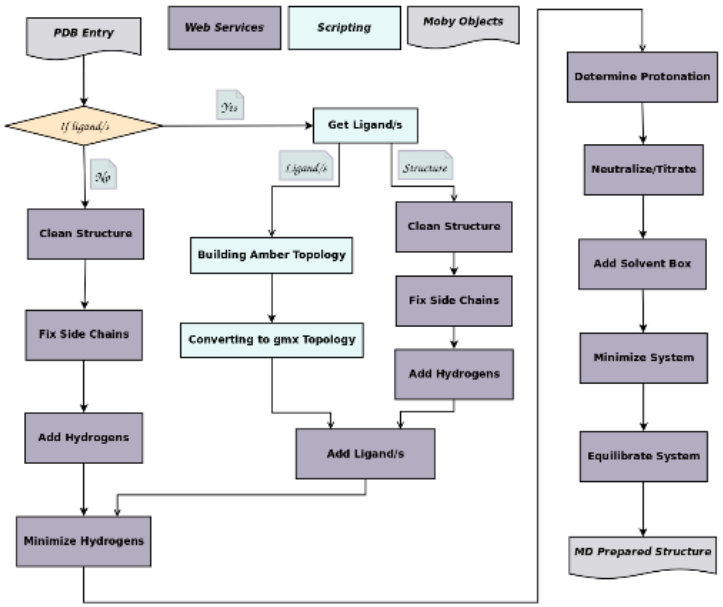
1a32 (MDWeb507e85d99fbf0)

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

Disk Usage: 700 kB

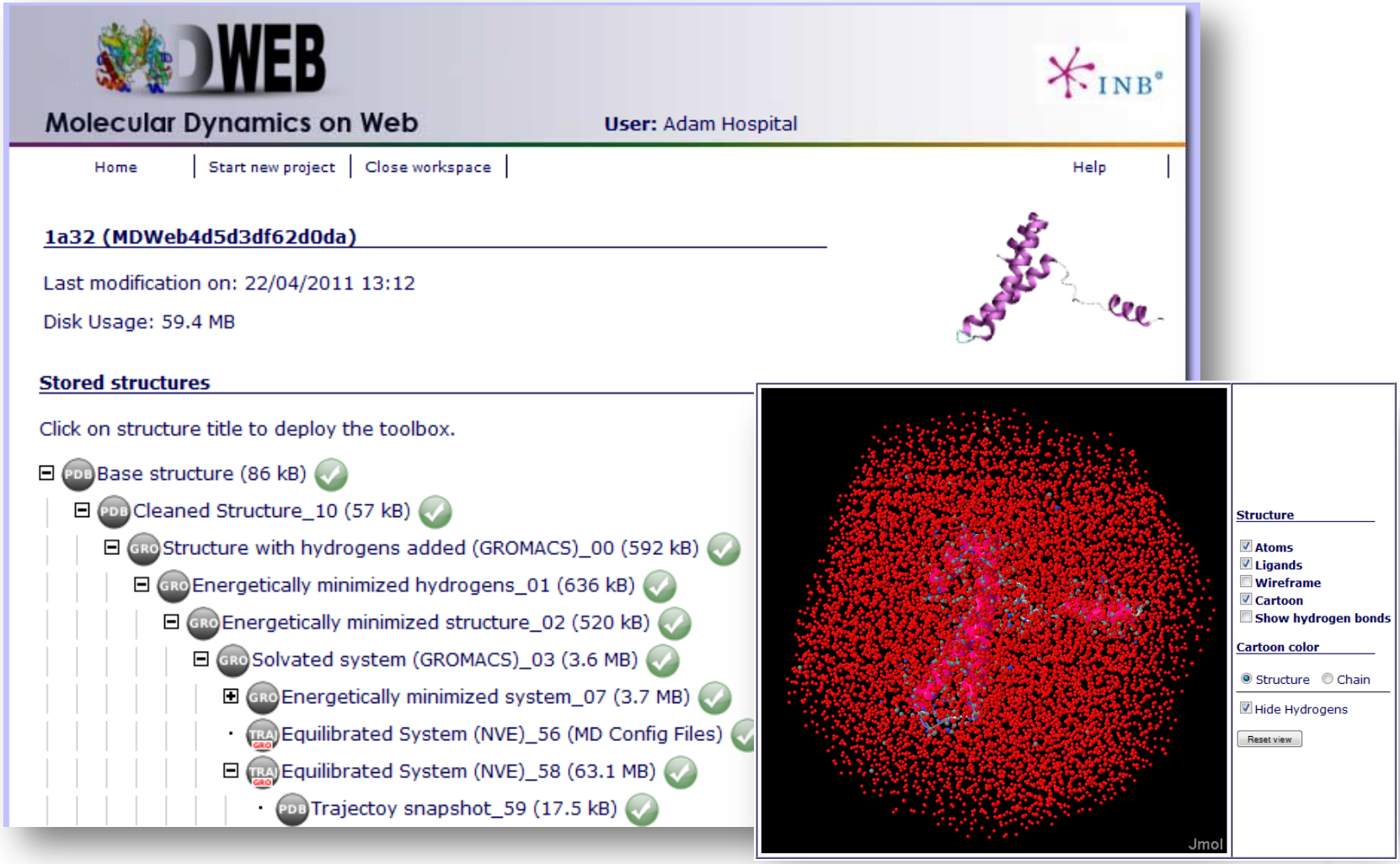


Running Workflow: *GROMACS FULL Setup*

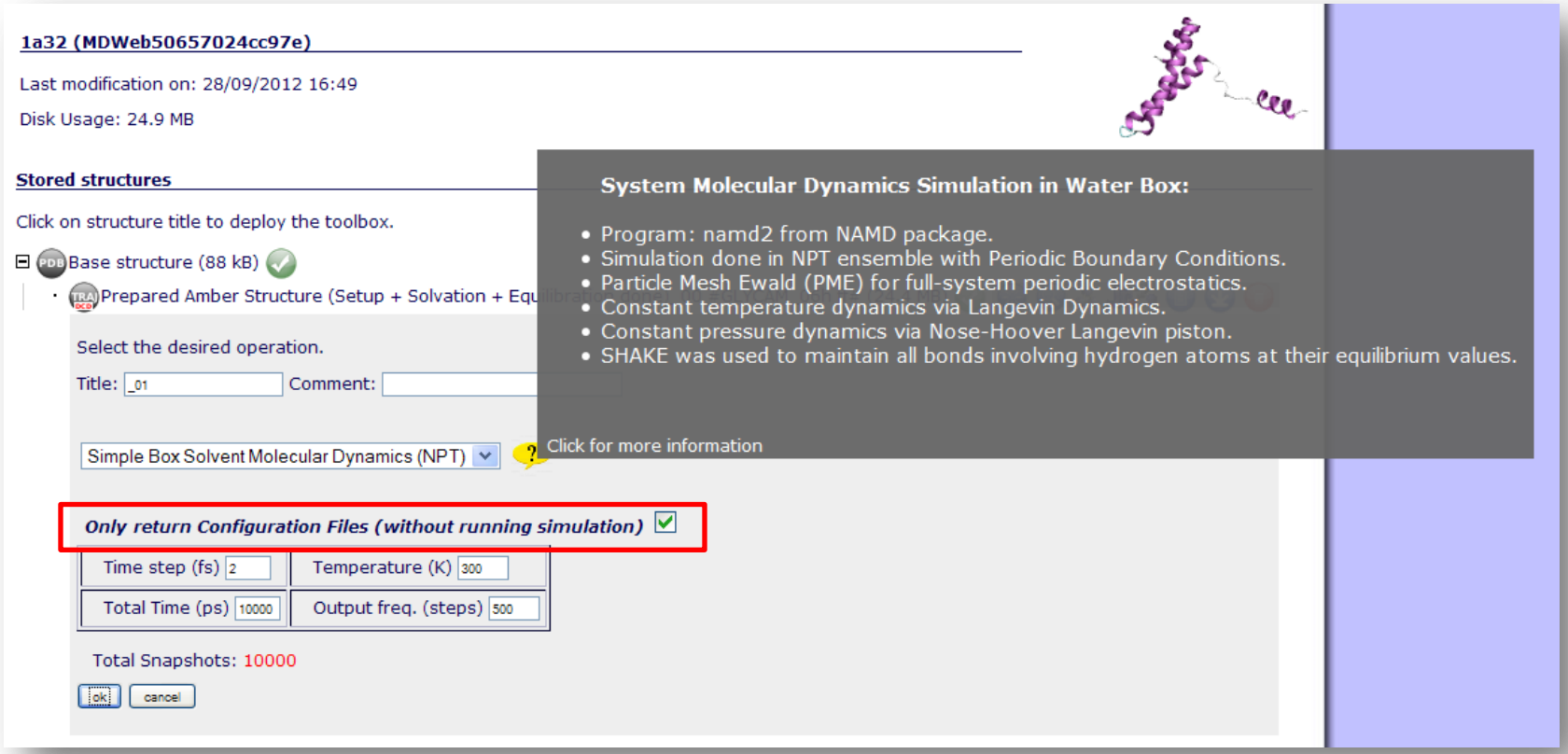


1 .- Checking If ligand/s ...	Done
2 .- No Ligand/s found!	Done
3 .- Cleaning Structure ...	Done
4 .- Fixing Side Chains ...	Done
5 .- Adding Hydrogens ...	Done
6 .- Minimizing Hydrogens ...	Done
7 .- Determining Protonation ...	Running
8 .- Neutralizing / Titrating ...	Waiting
9 .- Adding Solvent Box ...	Waiting
10 .- Minimizing System ...	Waiting
Equilibrating system:	Waiting
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

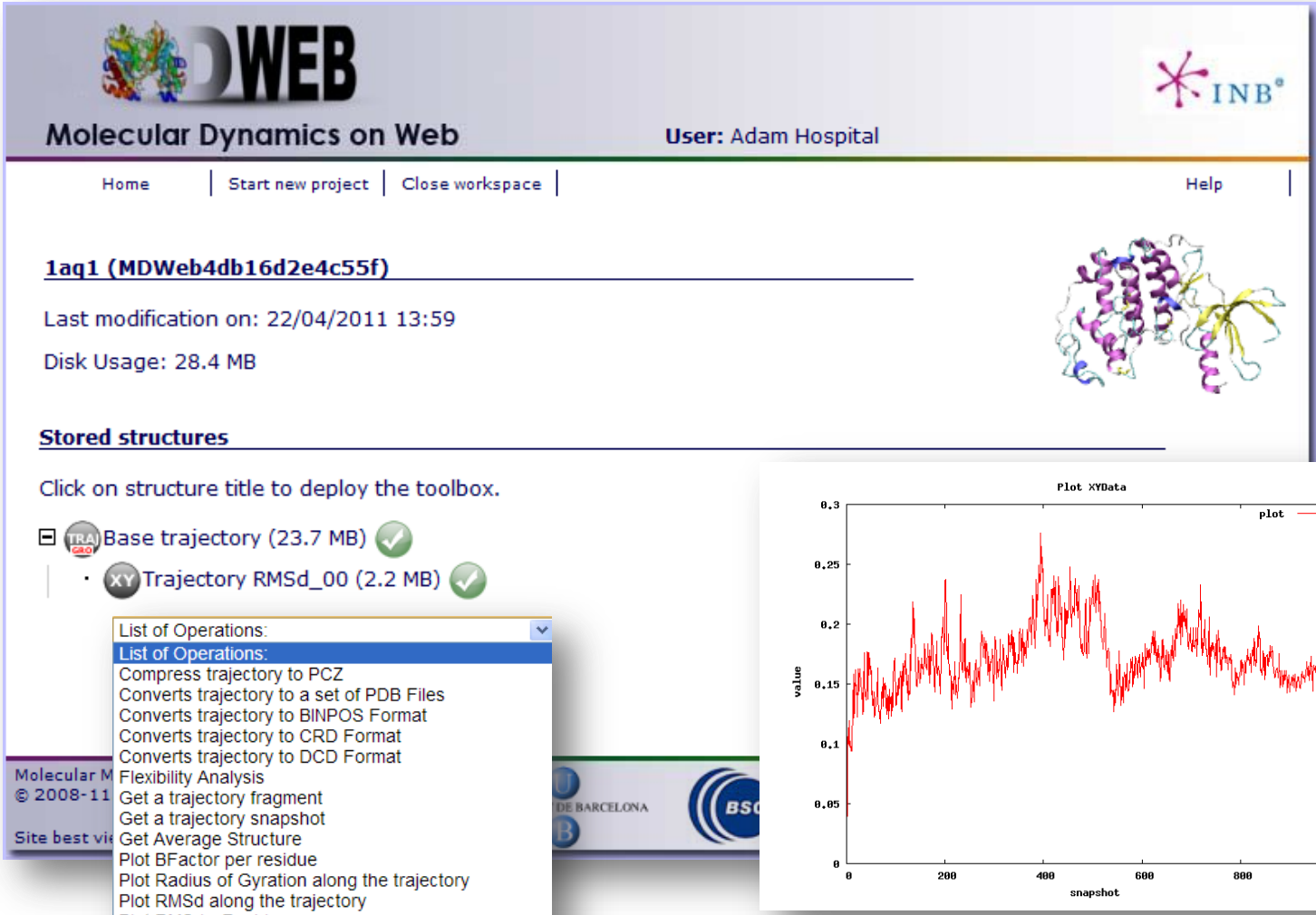
MDWeb: Project tree



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.
Base structure (88 kB)
Prepared Amber Structure (Setup + Solvation + Equ
Select the desired operation.
Title: _01
Comment:
Simple Box Solvent Molecular Dynamics (NPT)
Click for more information
Only return Configuration Files (without running simulation)
Time step (fs) 2
Temperature (K) 300
Total Time (ps) 10000
Output freq. (steps) 500
Total Snapshots: 10000
ok
cancel
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



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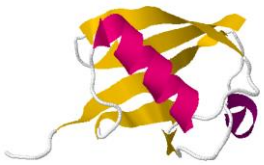
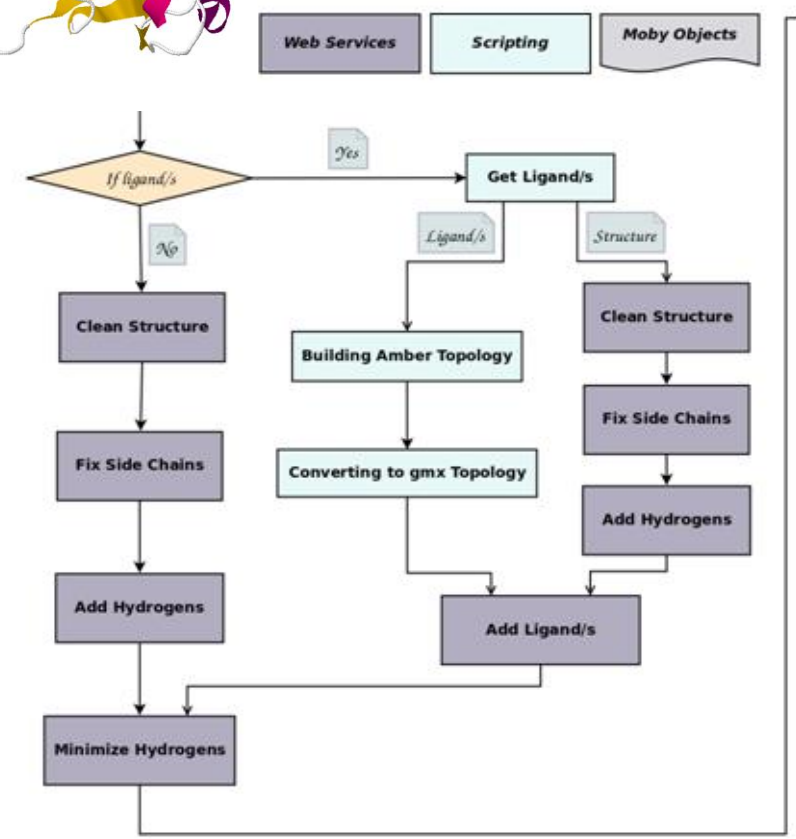
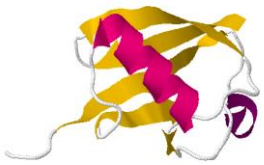
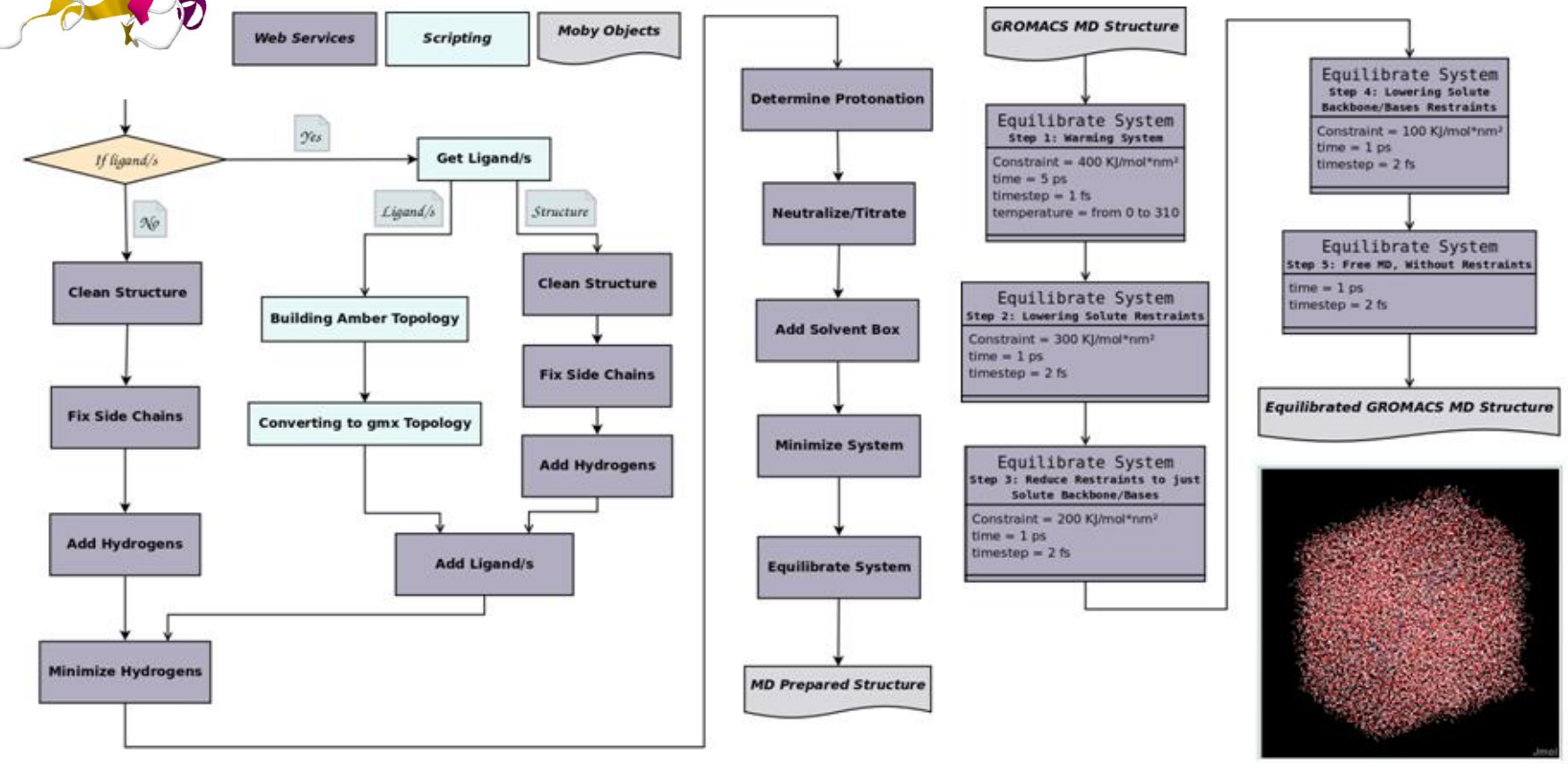
Simulation Setup Hands On MDWeb





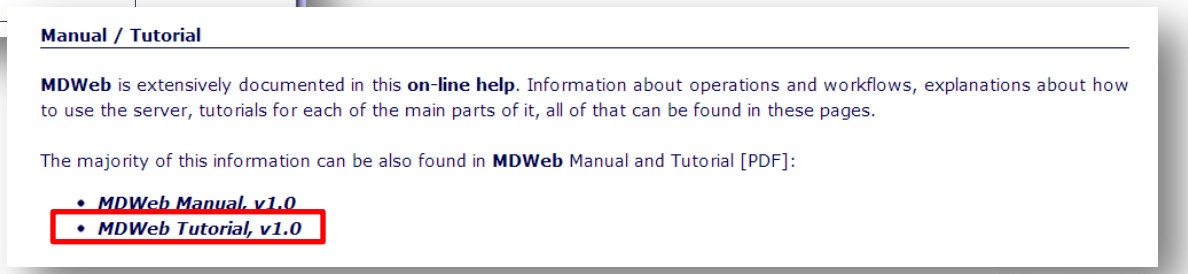
Simulation Setup Hands On MDMoby





Simulation Setup Hands On MDWeb - Tutorial

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



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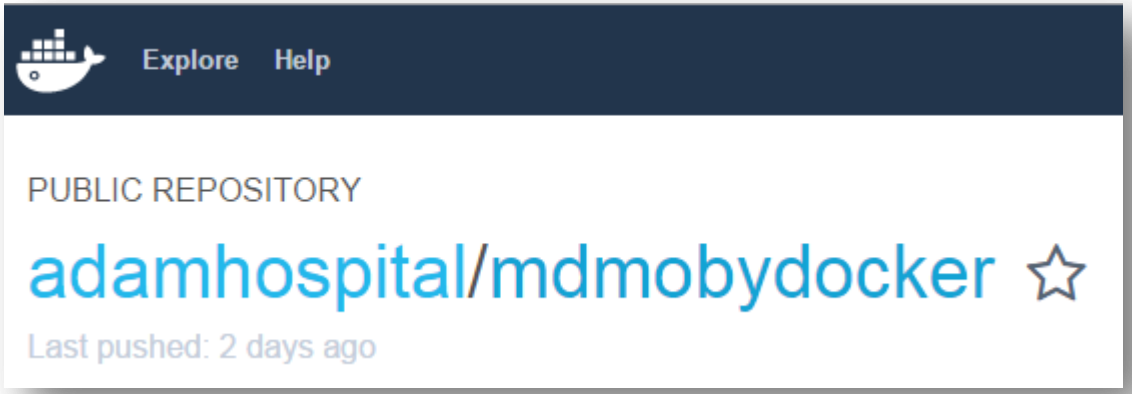

After that, pull the prepared **MDMoby docker container**:

```
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/

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

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

1) MDMoby/Workflows/ -- MDMoby/Scripts
2) MOBY **3) PDBs** **4) AmberTools**

INB

Simulation Setup – Tutorials:

Amber

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