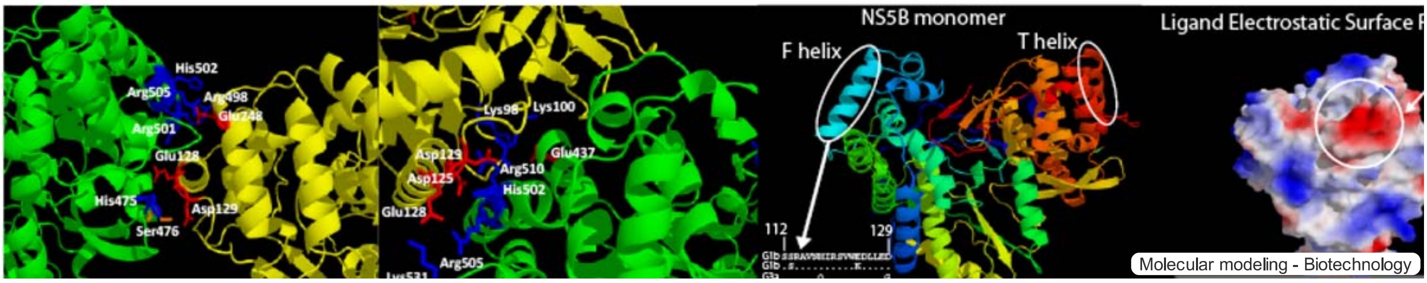
Molecular modeling



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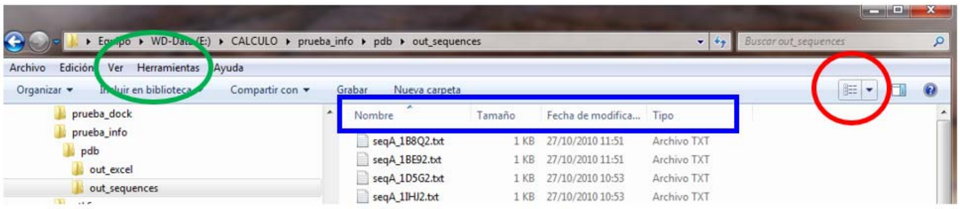
Before running the programs contained in these practices, be sure of the following: (optimized for Windows 7).

1) **NEVER** use an user account containing a written accent
- Example: User account "Andrés" in C:\Users\Andrés\
(most of the programs will not work, i.e. PyMol)

2) **NEVER** use a folder containing a written accent
- Example: C:\cálculo\
(most of the programs will not work, i.e. PyMol)

3) Put the **FILE FEATURES** under your direct control. In a fresh session of the Windows File Explorer (this is not internet explorer)
- Control the file list and file **SIZE**:



Nombre	Tamaño	Fecha de modifica...	Tipo
seqA_1B8Q2.txt	1 KB	27/10/2010 11:51	Archivo TXT
seqA_1BE92.txt	1 KB	27/10/2010 11:51	Archivo TXT
seqA_1D5G2.txt	1 KB	27/10/2010 10:53	Archivo TXT
seqA_1IHJ2.txt	1 KB	27/10/2010 10:53	Archivo TXT

Activate "Ver/Barra de estado" (green circle).
Activate "Detalles" in "Ver/Detalles" (or in the red circle).
Activate "Tamaño" (if inactive) using the contextual menu (right mouse button) in the blue square.
- Activate the file **EXTENSION**:
Open "**Herramientas**" (green circle), and press "Opciones de carpeta". Go to folder "**Ver**" and unpick "**Ocultar las extensions de archive para tipos de archivo conocidos**".
Example: The text file "seqA_1B8Q2" become "seqA_1B8Q2.txt"

4) Adjust the **REGIONAL configuration**: Most of the programs manage the dot (".") as the decimal separator. As a rule to perform the practical sessions, change **ALWAYS** this regional configuration in your PC computer.

For that, go to "**Panel de control**" and select "**Configuración regional y de idioma**". Then press "**Configuración adicional**" and under the folder "**Números**" select the dot ("**.**") as "**Símbolo decimal**", the comma ("**,**") as the "**Símbolo de separación de miles**", and press **OK**.

Practice 4: Basic training for PyMol.

PyMOL is a powerful and comprehensive molecular visualization product for rendering and animating 3D molecular structures. Explore PyMOL features by navigating the panel to the right.

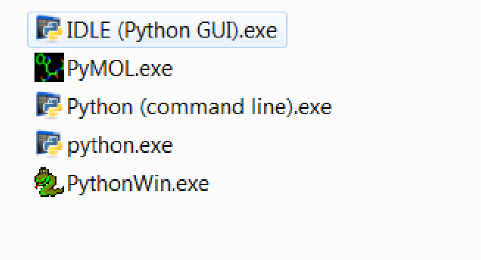
PyMOL Executable Builds for Educational Use Only

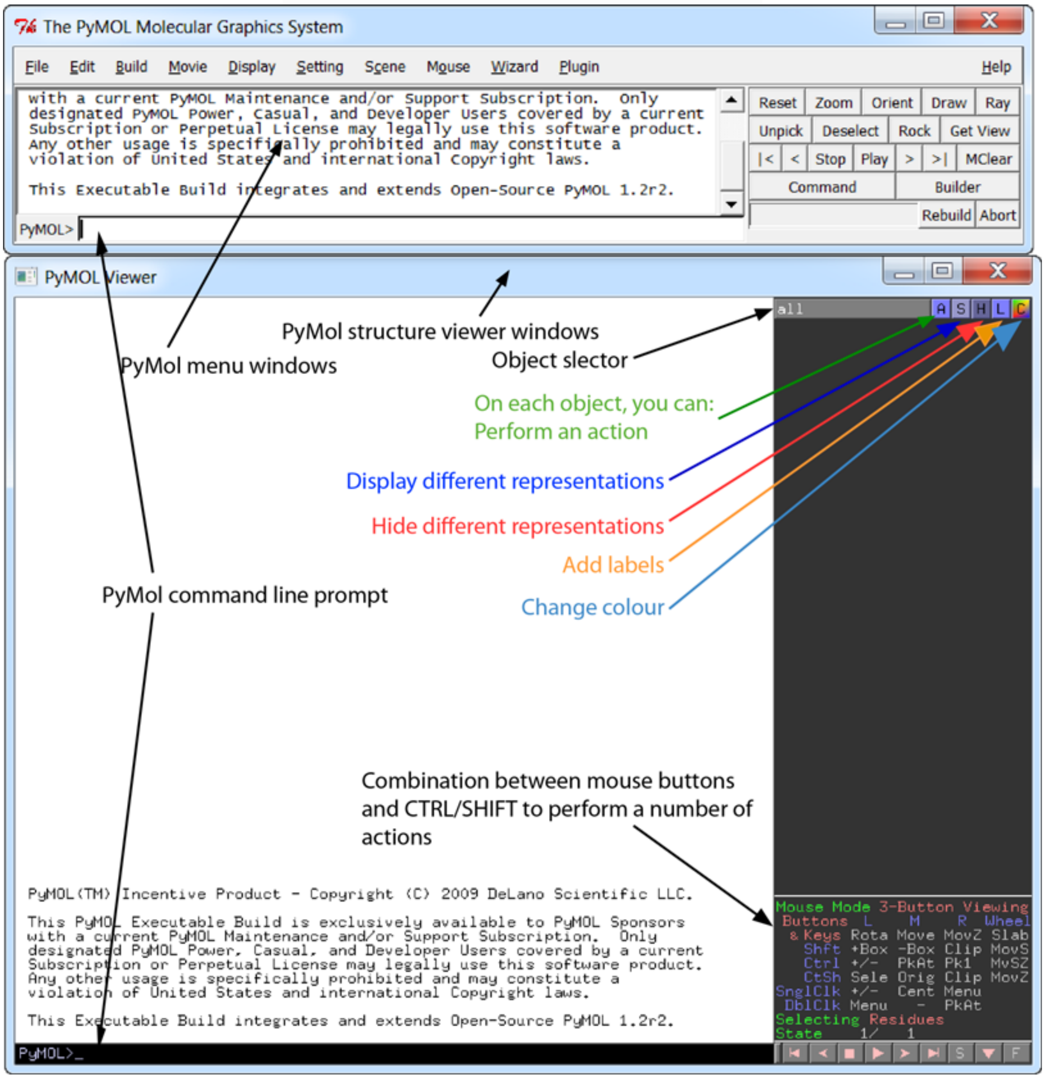
Windows:**pymol-v1.3r1-edu-Win32.msi**
MD5SUM: 265fa652aa4880304f4a59e1af653a1b

Macintosh:**MacPyMOL.app.rar**
MD5SUM: 2dfd72d120080eae69516277ee2bb284

Linux:**pymol-v1.3r1-edu-Linux-x86-TclTk8.5.tar.bz2**
MD5SUM: 96da619d58ec137bbf05769e9f59ce4b

We can also use a **portable** version of PyMol 1.5.0.3: downloading the compressed file. Run PyMol by double clicking on the file "PyMol.exe".





The PyMOL Molecular Graphics System
File Edit Build Movie Display Setting Scene Mouse Wizard Plugin Help
Reset Zoom Orient Draw Ray
Unpick Deselect Rock Get View
|< < Stop Play > >| MClear
Command Builder
Rebuild Abort
PyMOL>
PyMOL Viewer
all A S H L C
PyMol structure viewer windows
PyMol menu windows
Object slector
On each object, you can:
Perform an action
Display different representations
Hide different representations
Add labels
Change colour
PyMol command line prompt
Combination between mouse buttons
and CTRL/SHIFT to perform a number of
actions

```
with a current PyMOL Maintenance and/or Support Subscription.  Only
designated PyMOL Power, Casual, and Developer Users covered by a current
Subscription or Perpetual License may legally use this software product.
Any other usage is specifically prohibited and may constitute a
violation of United States and international copyright laws.

This Executable Build integrates and extends Open-Source PyMOL 1.2r2.
```

```
PyMOL(TM) Incentive Product - Copyright (C) 2009 DeLano Scientific LLC.

This PyMOL Executable Build is exclusively available to PyMOL Sponsors
with a current PyMOL Maintenance and/or Support Subscription.  Only
designated PyMOL Power, Casual, and Developer Users covered by a current
Subscription or Perpetual License may legally use this software product.
Any other usage is specifically prohibited and may constitute a
violation of United States and international copyright laws.

This Executable Build integrates and extends Open-Source PyMOL 1.2r2.
PyMOL>_
```

```
Mouse Mode 3-Button Viewing
Buttons  L    M    R   Wheel
& Keys Rota Move MovZ Slab
  Shft +Box -Box Clip MovS
  Ctrl +/-  PkAt Pk1  MvSZ
  CtSh Sele Orig Clip MovZ
SnglClk +/-  Cent Menu
 DblClk Menu  -   PkAt
Selecting Residues
State     1/    1
```

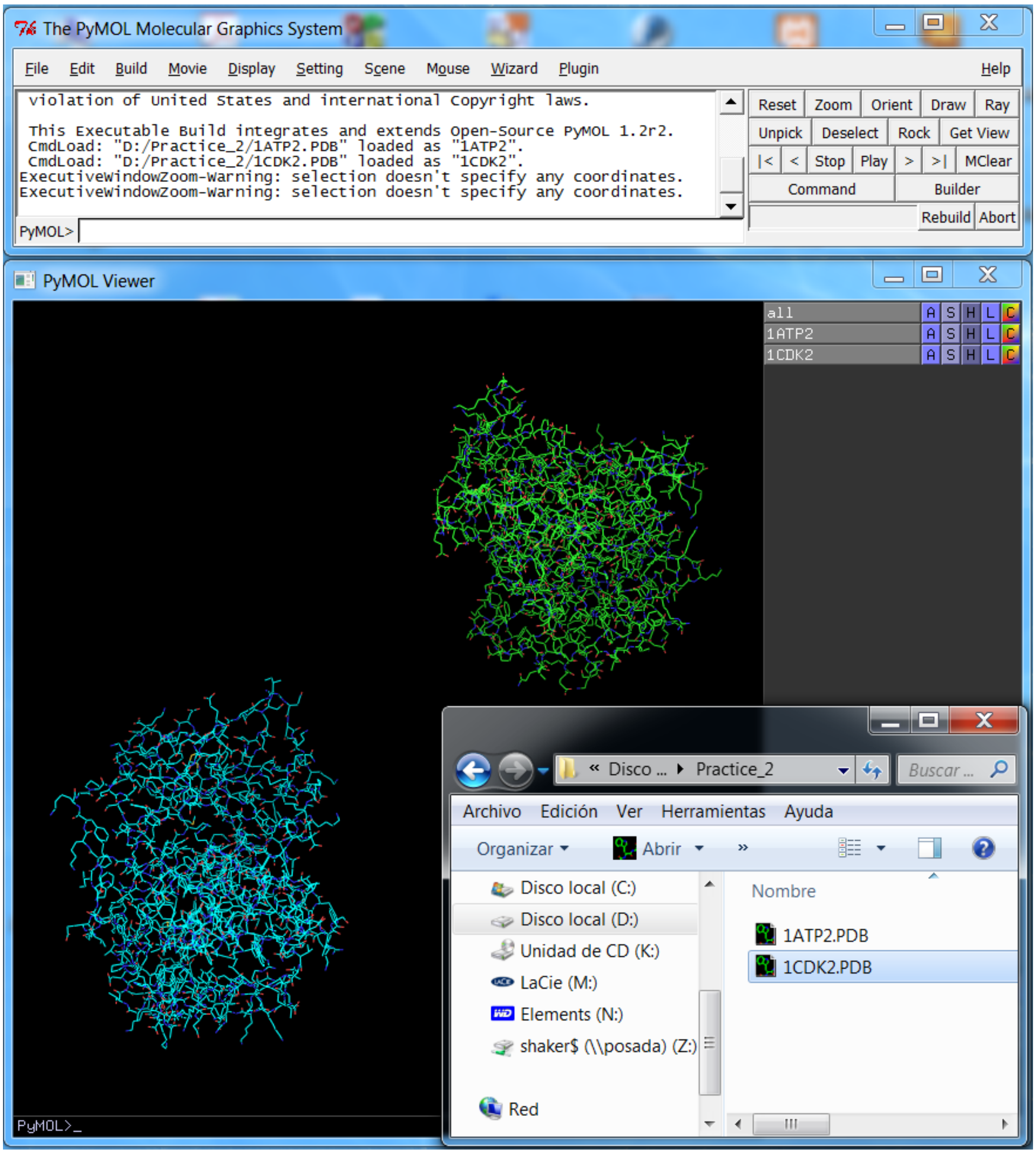
Please take some time to carefully study this scheme so you become familiar with the locations of buttons/menus that you will be using throughout this practical. Then start reading thoroughly the PyMol manual.

1.1.- Open PDB files and select aa, chain, molecule.

P04-01) Work on this task: Download from ADAN site the structure of 1ATP2.PDB and 1CDK2.PDB and open them with PyMol.

Save your files with PyMol, rename as:
P04-01&1ATP2.pdb
P04-01&1CDK2.pdb

and send them to the server (i.e. proteo.ibmc.umh.es). Open both files simultaneously with PyMol and **save a PSE scene (P04-01&1ATP2-1CDK2.pse)**, send it to the **proteo server**.



```
 violation of United States and international copyright laws.

 This Executable Build integrates and extends Open-Source PyMOL 1.2r2.
 CmdLoad: "D:/Practice_2/1ATP2.PDB" loaded as "1ATP2".
 CmdLoad: "D:/Practice_2/1CDK2.PDB" loaded as "1CDK2".
ExecutiveWindowZoom-Warning: selection doesn't specify any coordinates.
ExecutiveWindowZoom-Warning: selection doesn't specify any coordinates.
PyMOL>
```

PyMOL reads data files written in PDB, MOL/SDF, Macromodel, ChemPy Model, and Tinker XYZ formats. Some of the data fields in these formats allow PyMOL to assign properties to atoms. You can group and select atoms according to these properties using property selectors and identifiers: the selectors correspond to the fields in the data files, and the identifiers correspond to the target words to match, or the target numbers to compare.

The items in a list of identifiers are separated by plus signs (+) only. Do not add spaces within a list of identifiers. The selector **resi** takes (+)-separated lists of identifiers, as in

```
PyMOL> select nterm, resi 1+2+3
```

or, alternatively, it may take a range given with a dash

```
PyMOL> select nterm, resi 1-3
```

However, you will get an error message if you try to combine a list and a range in an identifier to a **resi** as in

```
PyMOL> select mistake, resi 1-3+6      <--This is WRONG
```

The identifier for a blank field in an input file is an empty pair of quotes

```
PyMOL> select unstruct, ss ""   # A named selection is created
                                # to contain all atoms that are not assigned
                                # a secondary structure.
```

Most property selectors select matches to their identifiers

Matching Property Selector	Short Form Selector	Identifier and Example

symbol	e.	*chemical-symbol-list* list of 1- or 2-letter chemical symbols from the periodic table `PyMOL> select polar, symbol o+n`
name	n.	*atom-name-list* list of up to 4-letter codes for atoms in proteins or nucleic acids `PyMOL> select carbons, name ca+cb+cg+cd`

resn	r.	*residue-name-list*
		list of 3-letter codes for amino acids
		`PyMOL> select aas, resn asp+glu+asn+gln`
		or list of up to 2-letter codes for nucleic acids
		`PyMOL> select bases, resn a+g`

resi	i.	*residue-identifier-list*
		list of up to 4-digit residue numbers
		`PyMOL> select mults10, resi 1+10+100+1000`
		residue-identifier-range
		`PyMOL> select nterm, resi 1-10`

alt	alt	*alternate-conformation-identifier-list* list of single letters `PyMOL> select altconf, alt a+""`
chain	c.	*chain-identifier-list* list of single letters or sometimes numbers `PyMOL> select firstch, chain a`
segi	s.	*segment-identifier-list* list of up to 4 letter identifiers `PyMOL> select ligand, segi lig`
flag	f.	*flag-number* a single integer from 0 to 31 `PyMOL> select f1, flag 0`
numeric_type	nt.	*type-number* a single integer `PyMOL> select type1, nt. 5`
text_type	tt.	*type-string* a list of up to 4 letter codes

		PyMOL> select subset, text_type HA+HC
id	id	*external-index-number* a single integer PyMOL> select idno, id 23
index	idx.	*internal-index-number* a single integer PyMOL> select intid, index 11
ss	ss	*secondary-structure-type* list of single letters PyMOL> select allstrs, ss h+s+l+""

Other *property selectors* select by comparison to numeric identifiers

Numeric Selector	Short Form	Argument and Example
b	b	*comparison-operator b-factor-value* a real number PyMOL> select fuzzy, b > 10
q	q	*comparison-operator occupancy-value* a real number PyMOL> select lowcharges, q <0.50
formal_charge	fc.	*comparison-operator formal charge-value* an integer PyMOL> select doubles, fc. = -1
partial_charge	pc.	*comparison-operator partial charge-value* a real number PyMOL> select hicharges, pc. > 1

P04-02) Work on this task: Select all the aromatic amino acids of 1ATP2 and 1CDK2 structures and change the presentation to spheres. Change it to red color, make a PSE scene (**P04-02&scene.pse**), and send it to the **proteo server**. Both structures should be observed simultaneously.

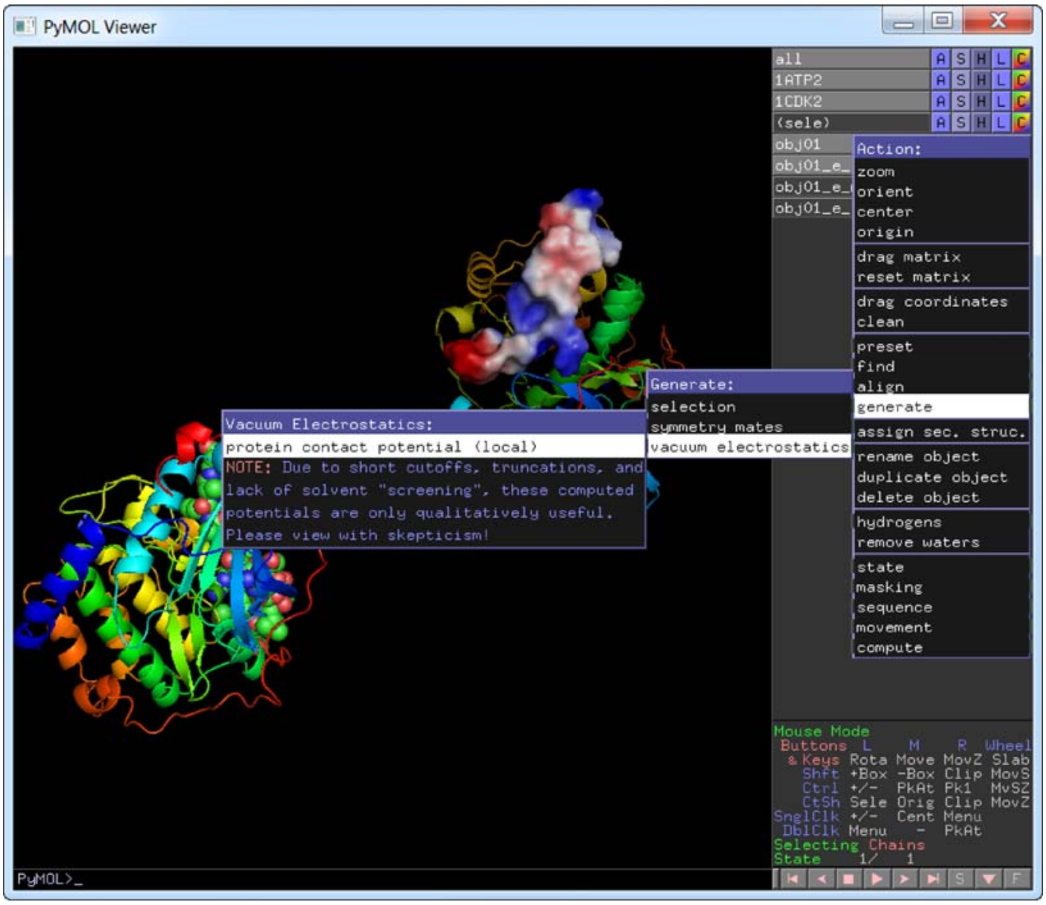
As we can observe, both structures have a kinase catalytic domain and are co-crystallized with a ligand.

Protein contact potential is an automated PyMOL representation where the false red/blue charge-smoothed surface is shown on the protein.

The rule of thumb with respect to PyMOL's internal "protein contact potential" is that if you care enough to be concerned with how it works, then you should instead be using a true Possion-Boltzman electrostatics solver such as APBS.

Regardless, what PyMOL does to generate a qualitative electrostatic representation (via action popup->generate->vacuum electrostatics->...) amounts to averaging charges over a small region of space using a quasi-Coulombic-shaped convolution function.

First you must "copy to object" the selected ligand. Next generate the protein contact potential. See next figure.



NOTE: Due to short cutoffs, truncations, and lack of solvent "screening", these computed potentials are only qualitatively useful. Please view with skepticism!

P04-03) Work on this task: Open with PyMol 1ATP2 and 1CDK2. Change the presentation to cartoon. Select the two ligands (chain B in both structures) and display as spheres. Create the "**Protein contact potential**". Make a PSE scene (**P04-03&scene.pse**), and send it to the **proteo server**.

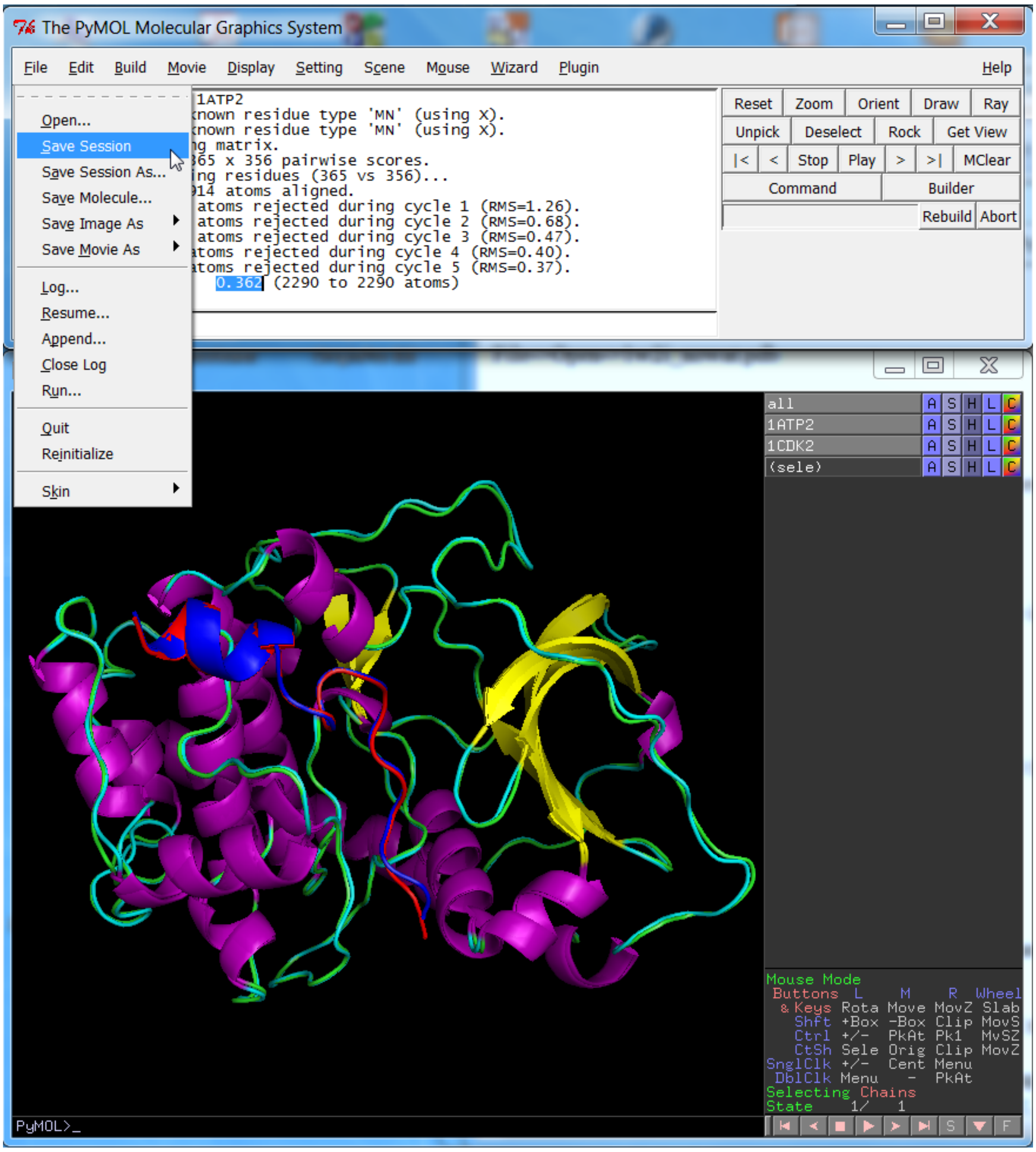
1.2.- Structural align of two homologous proteins.

Fit superimposes the model in the first selection on to the model in the second selection. Only matching atoms in both selections will be used for the fit.

With two structures (hereafter referred to as **structure1** i.e. 1CDK2, and **structure2** i.e. 1ATP2) loaded into PyMOL it is a simple matter to type the command:

```
PyMOL> align 1CDK2, 1ATP2
```

See the alignment in the next figure:



```
 1ATP2
known residue type 'MN' (using X).
known residue type 'MN' (using X).
ng matrix.
365 x 356 pairwise scores.
ing residues (365 vs 356)...
914 atoms aligned.
 atoms rejected during cycle 1 (RMS=1.26).
 atoms rejected during cycle 2 (RMS=0.68).
 atoms rejected during cycle 3 (RMS=0.47).
atoms rejected during cycle 4 (RMS=0.40).
atoms rejected during cycle 5 (RMS=0.37).
   0.362 (2290 to 2290 atoms)
```

PyMOL will first do a sequence alignment and then try to align the structures to minimize the **RMSD** (Root Mean Square Deviation) between the aligned residues. This often works very well for homologous structures, but if you have to get the RMSD for the backbone atoms of a particular set of non-homologous residues, this can be difficult.

RMSD: Root Mean Square Deviation is the square root of the mean of the square of the distances between the matched atoms.

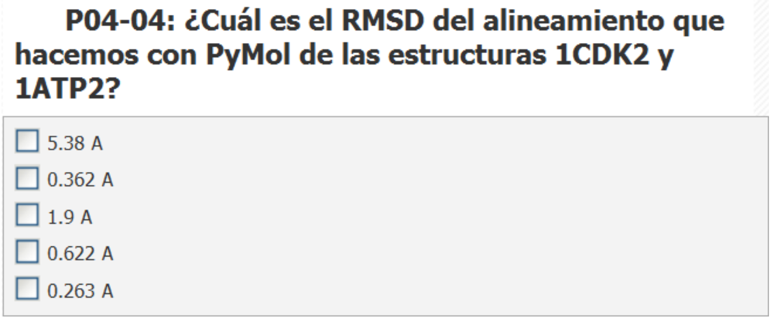
RMSD = SQRT[{SUM(d_{ii})^2}/N]

where **dii** is the distance between the ith atom of structure 1 and the **ith** atom of structure 2 and **N** is the number of atoms matched in each structure.

P04-04) Work on this task: Load **1ATP2.pdb** and **1CDK2.pdb** in a fresh session of PyMol. Superimpose both structures and save the scene as **P04-04&1ATP2-1CDK2.pse**

and send them to the server (proteo.ibmc.umh.es).

Annotate the results in your **report file** including the RMSD, and answer the question in the task web page "Cuestionarios ON-LINE":



P04-04: ¿Cuál es el RMSD del alineamiento que hacemos con PyMol de las estructuras 1CDK2 y 1ATP2?

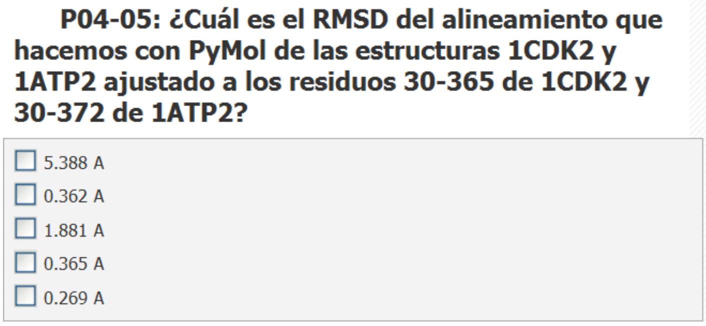
☐ 5.38 A
☐ 0.362 A
☐ 1.9 A
☐ 0.622 A
☐ 0.263 A

You may need to specify the particular residues to match. For example, you may know that only part of structure1 should match to part of structure2. In this case, you may wish to use a command like:

```
PyMOL> align 1CDK2 and resi 30-365, 1ATP2 and resi 30-372
```

P04-05) Work on this task: Based on the previous question, make the proposed alignment and save this new scene in a new file **P04-05&1ATP2-1CDK2.pse** and write down the **RMSD**. Send it to the server (proteo.ibmc.umh.es).

Annotate the results in your **report file** and answer the question in the task web page "Cuestionarios ON-LINE":



P04-05: ¿Cuál es el RMSD del alineamiento que hacemos con PyMol de las estructuras 1CDK2 y 1ATP2 ajustado a los residuos 30-365 de 1CDK2 y 30-372 de 1ATP2?

□ 5.388 A
□ 0.362 A
□ 1.881 A
□ 0.365 A
□ 0.269 A

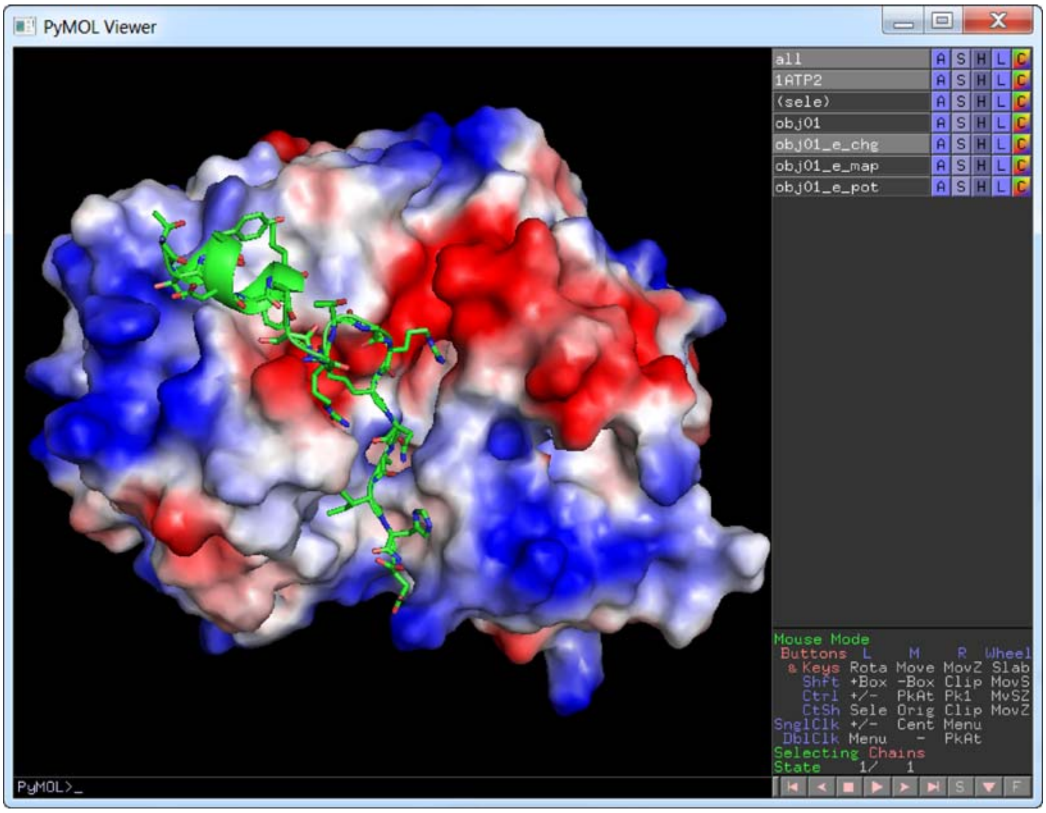
More often, people will report Calpha RMSD values, which can be determined by:

```
PyMOL> align 1CDK2 and name ca, 1ATP2 and name ca
```

1.3.- Domain and ligand presentation.

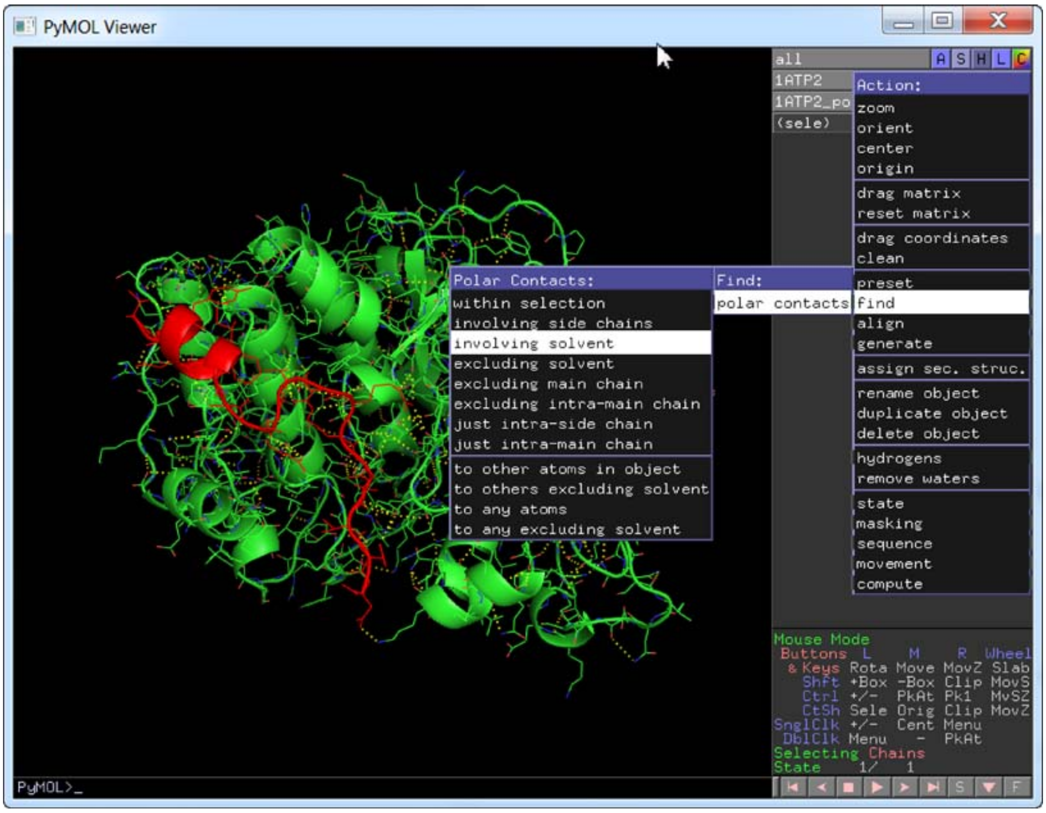
P04-06) Work on this task: Using **1ATP2** structure, create an scene similar to the scene below. Save the scene as **P04-06&1ATP2.pse** and send it to the server (proteo.ibmc.umh.es).

Annotate the results in your **report file**.



1.4.- Hydrogen bonds and Polar Contacts.

Using the actions [A] button for an object or selection you can display Hydrogen bonds and Polar Contacts. [A]->find-> polar contacts-> <select from menu>



P04-07) Work on this task: See the figure above and make a PyMol scene in *. pse format including all hydrogen bonds.

In this exercise you don't need to send any file to the server.

1.5.- Measuring distances.

To measure distances between two atoms, choose the Measurement option under the Wizard menu in the GUI window, This creates some sub-menus to the right of the view window corresponding to various measurements that can be made.

Choose Distances. A message appears in the PyMOL viewer (upper left corner) saying "Please click on the first atom..." Click on an atom using left button. A message now appears in the PyMOL viewer saying "Please click on the second atom ...".

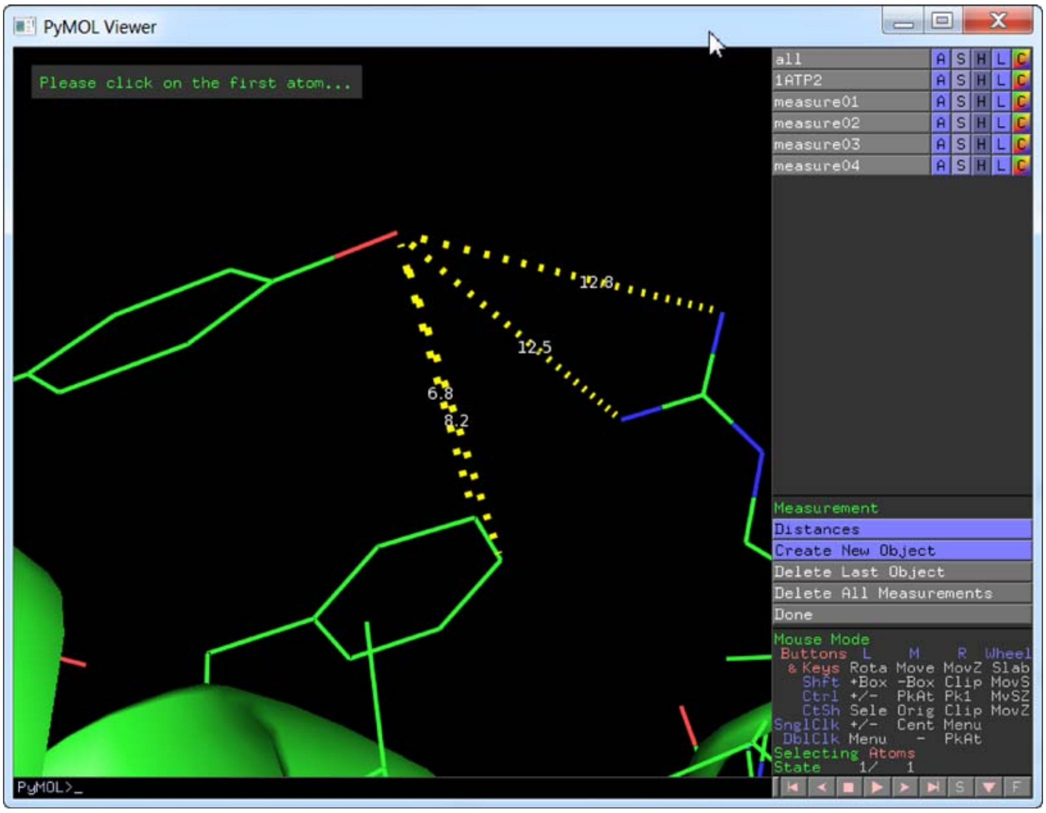
Pick a second atom and a dotted line appears between the two atoms with the distance displayed.

Get out of the Distance Wizard by clicking Done in the Measurement menu to the right of the viewer window.

P04-08) Work on this task: Display chain B of 1ATP2.pdb and present cartoon mode. Measure the distances between the following atoms: TYR`3/OH to PHE`6/CD2, PHE`6/CE2, ARG`15/NH1 and ARG`15/NH2. See next figure.

Save the scene as **P04-08&1ATP2.pse** file and send it to the server (proteo.ibmc.umh.es).

Annotate the results in your **report file**.

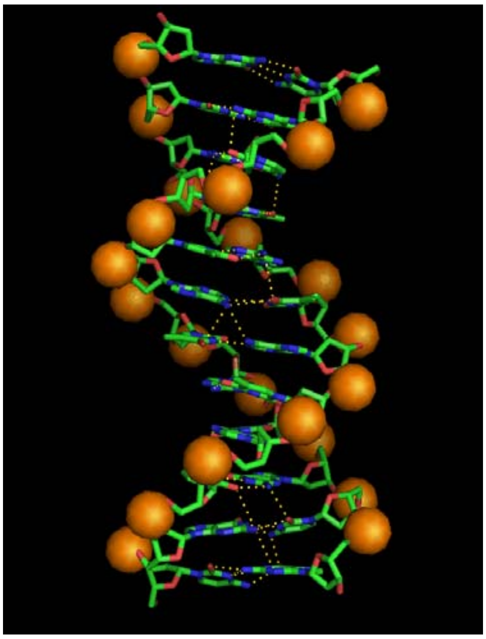


PyMOL Viewer

Please click on the first atom...

PyMOL>_

1.6.- Create a series of PNG files for animated GIF movie.



Download next PDB file for B-DNA structure. Change the presentation according to the figure on the right.

PyMOL> mset 1 x60
This command creates a movie with 60 frames
PyMOL> util.mrock 1,60,360
This command rocks the DNA molecule +/- 180 degree in 60 frames
PyMOL> mplay
This command plays the movie.

Now try this:
PyMOL> util.mroll 1,60
This command rotates the DNA molecule 360 deg in 60 frames
Type "**mstop**" to stop the animation.

Saving frames in PNG format
PyMOL> mpng frame
This will create frame0001.png frame0002.png, etc ...

You can convert these PNG files in a batch to GIF using the program ReaConverter, and then combine these GIF files to create an animated GIF using UnFREEz, in a similar way to that we can see the image on the right.

P04-09) Work on this task: Using PyMol create an animated GIF movie similar to the above figure for B-DNA.

Save as **P04-09&Z-DNA.gif**

Send it to the server (proteo.ibmc.umh.es).

Annotate the results in your **report file**.

It is strongly recommended that you have a backup copy of your results in your personal devices (hard disks, memory sticks, etc.) or in storage servers freely available (Box, DropBox, UbuntuOne, etc. 5GB for free).
Any computer is free of errors, failures or crashes!!

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