Homology modelling workshop

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https://ub.cbm.uam.es/downloads/Homol-Mod-workshop-2026.pdf

(https://tinyurl.com/HMWS26)

Create Linux VM

- Download image: https://tinyurl.com/LU22BIO
- Uncompress it
- Launch Virtual Box
  - Click on “Nueva”
    - Nombre: “Bioinfo-Lubuntu22”
    - Tipo: “Linux”
    - Version: “Lubuntu (64-bit)”
  - Click on “Siguiente”
    - Memoria base: 3072
    - Procesadores: 4
  - Click on “Siguiente”
    - “Usar un archivo de disco virtual existente”
    - Path to uncompressed file
  - Click on “Siguiente”
  - Click on “Terminar”
  - Select the new virtual machine and click on “Configuración”
  - Click on “Pantalla” and increase “Memoria de vídeo” up to 128MB

Homology modelling

- Open terminal:
- Set variables:

workdir=$HOME/cdk2

exampdir=$HOME/cdk2-examp

export PATH=/opt/jalview/bin/:$PATH

export LANG=en_US.UTF-8

- Make working directory:

  mkdir $workdir

- Make example files directory:

  mkdir $exampdir

- Go to example files directory:

  cd $exampdir

- Get files and uncompress:

  wget https://saco.csic.es/index.php/s/cgfst9Ccg97aQcj/download/cdk2-mod.tgz

  tar -xzf cdk2-mod.tgz

- Change directory

  cd ..

Homology modelling

CDK2, CELL DIVISION PROTEIN KINASE 2

- Go to working directory:
  cd $workdir
- copy fasta file:
  cp $exampdir/cdk2.fasta .
- View fasta file:
  cat cdk2.fasta

>cdk2
GPLGSPEFMENFQKVEKIGEGTYGVVYKARNKLTGEVVALKKIRLDTETEGVPSTAIREISLLKELNHPNIVKLLDVIHT
ENKLYLVFEFLHQDLKKFMDASALTGIPLPLIKSYLFQLLQGLAFCHSHRVLHRDLKPQNLLINTEGAIKLADFGLARAF
GVPVRTYTHEVVTLWYRAPEILLGCKYYSTAVDIWSLGCIFAEMVTRRALFPGDSEIDQLFRIFRTLGTPDEVVWPGVTS
MPDYKPSFPKWARQDFSKVVPPLDEDGRSLLSQMLHYDPNKRISAKAALAHPFFQDVTKPVPHLRL

Search for templates

- Make blast:

  blastp -db $exampdir/pdball-nr0.5 -query cdk2.fasta > cdk2.blast

- View blast results:

  less cdk2.blast

  >1tvo_A Chain A

  Length=351

  Score = 190 bits (482), Expect = 2e-58, Method: Compositional matrix adjust.

  Identities = 112/302 (37%), Positives = 167/302 (55%), Gaps = 19/302 (6%)

- Get 1tvo.pdb (MITOGEN-ACTIVATED PROTEIN KINASE 1) :

  cp $exampdir/1tvo.pdb .

View template with pymol

View 1tvo structure

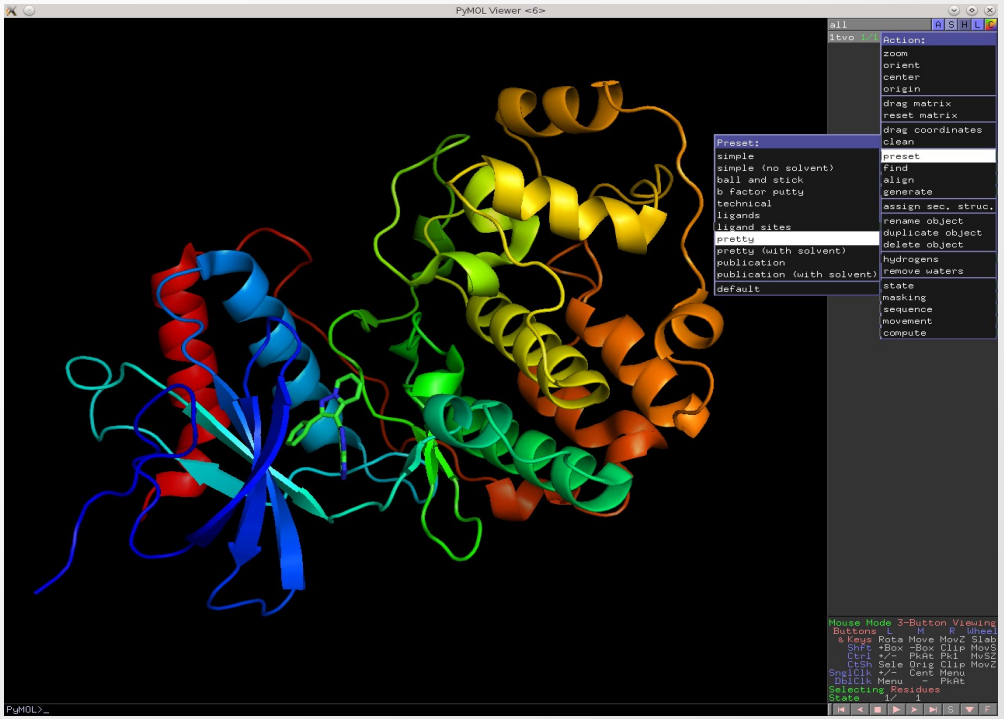
pymol 1tvo.pdb

Go to “Setting→Rendering”:

Uncheck “OpenGL 2.0 shaders”

Show “cartoons”:

A->preset->pretty



Make target – template alignment

- Copy 1tvo sequence:

  cp $exampdir/1tvo.fasta .
- Copy Modeller alignment script:

  cp $exampdir/cdk2-1tvo.aln.py .
- View script:

  cat cdk2-1tvo.aln.py

  ```
  from modeller import *


  env = environ()
  aln = alignment(env)
  m = model(env, file='1tvo', model_segment=('FIRST:A', 'LAST:A'))
  aln.append_model(m, atom_files='1tvo', align_codes='1tvo_x')


  aln.append( file='cdk2.fasta',  alignment_format='FASTA', align_codes='cdk2')
  aln.salign()
  aln.write(file='cdk2-1tvo.pir')
  ```
- Run Modeller (ignore errors):

  mod10.5 cdk2-1tvo.aln.py

View alignment

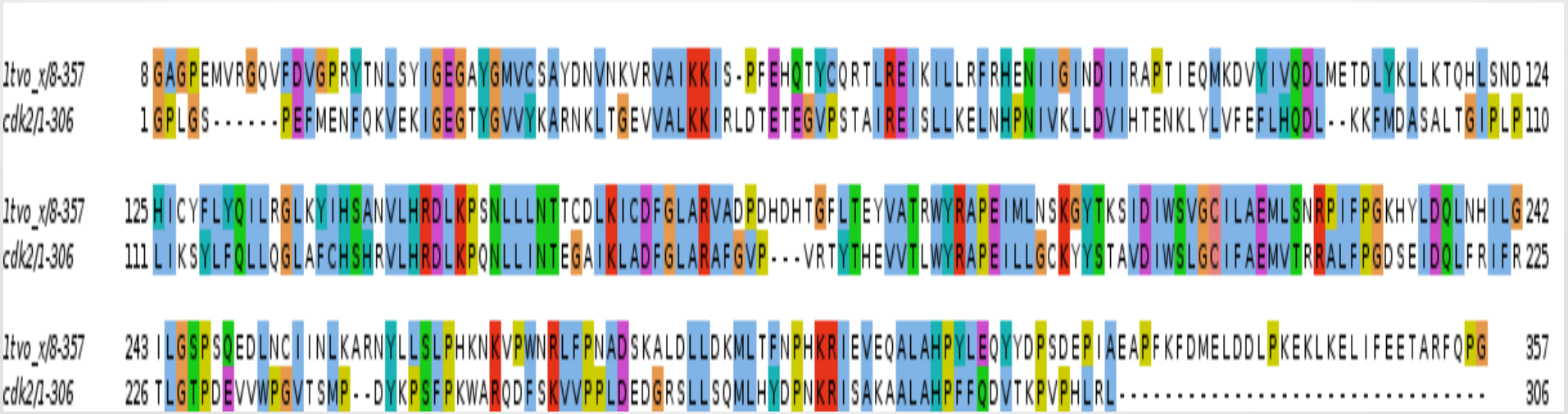
- Launch Jalview (and close all windows inside Jalview)

  jalview

- Load alignment in Jalview:
  - File -> Input Alignment -> From file:
  - Filtro: PIR(.pir)

    /home/usuario/cdk2

    cdk2-1tvo.pir
  - Format: Wrap
  - Annotations: Show Annotations
  - Colour: ClustalX



Make model

- Use another alignment:

  cp $exampdir/cdk2-1tvo-cl.pir .

- Copy modeller script:

  cp $exampdir/cdk2-1tvo.mod.py .

- View modeller script:

  cat cdk2-1tvo.mod.py

- Run modeller:

  mod10.5 cdk2-1tvo.mod.py

```
from modeller import *
from modeller.automodel import *

log.verbose()
env = environ()

env.io.hydrogen = env.io.hetatm = env.io.water = True

a = dope_loopmodel(env, alnfile = 'cdk2-1tvo-cl.pir',
            knowns = ('1tvo_x'),sequence = 'cdk2')
a.starting_model= 1
a.ending_model  = 5

a.make()
```

Modeller output

- List modeller generated files:

  ls -lrt cdk2.* *.log

- View modeller log:

  less cdk2-1tvo.mod.log

- Go to the end of file:

```
>> Summary of successfully produced loop
models:
Filename                       molpdf
------------------------------------
cdk2.BL00010001.pdb
-648.46350
cdk2.BL00010002.pdb
-602.38818
cdk2.BL00010003.pdb          144.40594
cdk2.BL00010004.pdb
-635.31982
cdk2.BL00010005.pdb
```

View models

- Show models in pymol:

  pymol cdk2.BL*.pdb
- Show “cartoons”:

  A->preset->pretty
- Align all structures (from pymol):

  alignto cdk2.BL00010001
- Compare with template:

  load 1tvo.pdb

  alignto cdk2.BL00010001

Evaluate models with DOPE

- Copy script:

  cp $exampdir/pdb.ls-dope.py .
- View script:

  cat pdb.ls-dope.py
- Run evaluation:

  mod10.5 pdb.ls-dope.py
- View results:

  cp $exampdir/pdb.ls-dope.gnuplot .

  gnuplot -persistent pdb.ls-dope.gnuplot
- Map profile to pdb

  ./prof2bfact.pl -v cdk2.BL00010003.pdb.profile -p cdk2.BL00010003.pdb > cdk2.BL00010003.bfact.pdb

Compare models with real

- Copy CDK2 structure:

  cp $exampdir/3qqg.pdb .

- From pymol:

  load 3qqg.pdb

  alignto cdk2.BL00010001