iMODS

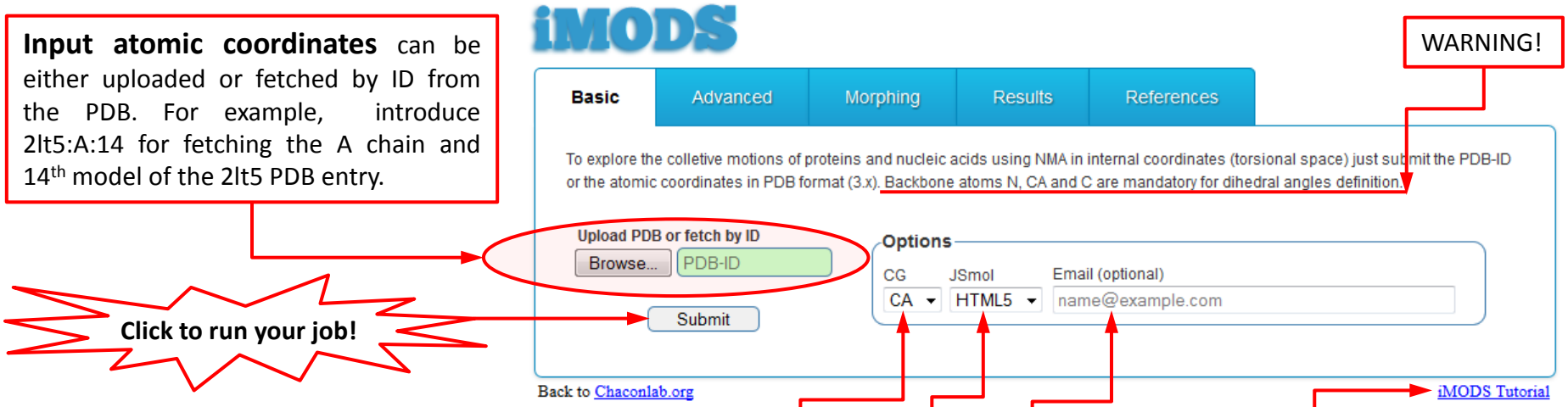
http://imods.chaconlab.org/

Internal coordinates normal mode analysis server

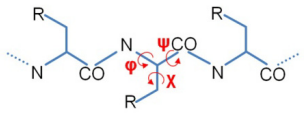
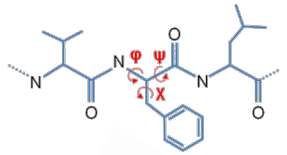
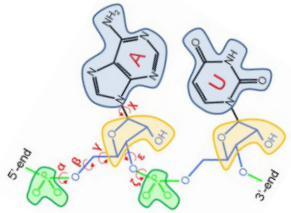
- **QUICK REFERENCE**
  - Basic NMA
  - Advanced NMA
  - Morphing
- **TUTORIALS**
  - Basic NMA
  - Advanced NMA
  - Morphing

iMODS quick reference – Basic NMA interface

Input atomic coordinates can be either uploaded or fetched by ID from the PDB. For example, introduce 2lt5:A:14 for fetching the A chain and 14th model of the 2lt5 PDB entry.



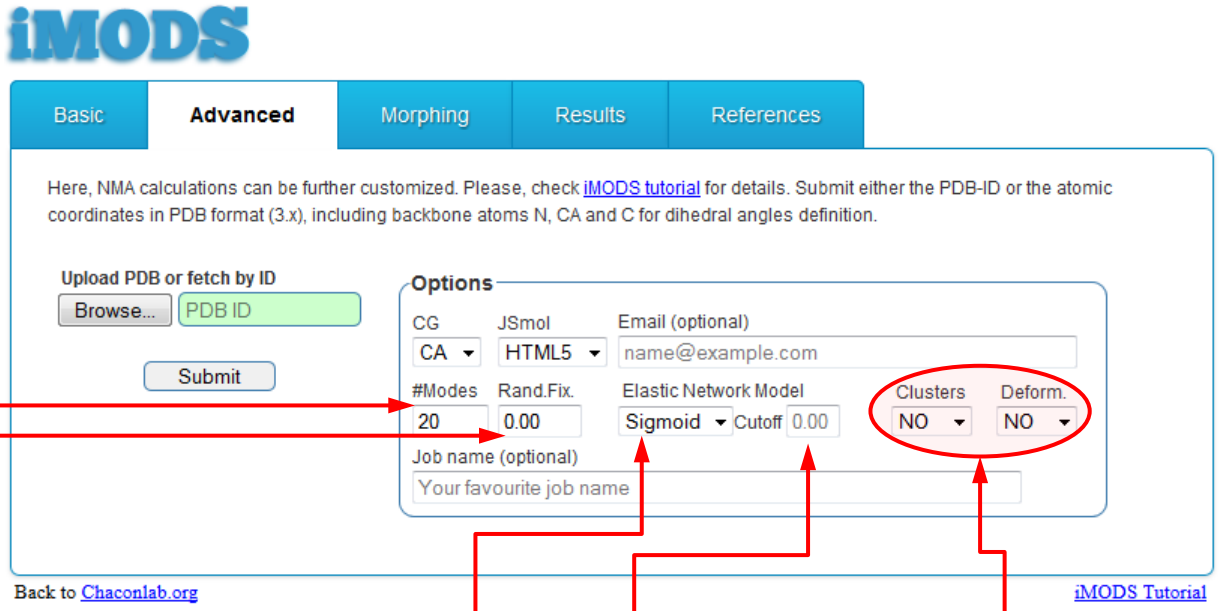
Atomic model selection: for proteins it can be selected at three Coarse Graining (CG) model representations:

CG	Description	Sketch
CA	Cα atoms accounting for whole residue mass.	
C5	5 atoms per residue, 3 for backbone (N, Cα and C) and 2 for side chain (Cβ and a pseudo-atom (R) for the remaining side chain)	
HA *For nucleic acids this HA is automatically selected.	All heavy atoms, each one accounting for its own mass.	 

JSmol plugin: The JSmol implementation offers three display modes:

JSmol	Description
HTML5	JavaScript based Jmol, compatible with new handheld devices and major browsers. However, slow visualization is expected for large macromolecules.
JAVA	Standard Jmol Java applet. It is the fastest and memory efficient mode.
WebGL	JavaScript & OpenGL mode. Despite very developmental, it will be likely the new standard for on-line 3D graphics.

iMODS quick reference – Advanced NMA interface



Number of modes

You can compute from 1 to 100 modes with this interface. The default value is 20.

Fixed angles ratio

Ratio (between 0 and 1) of the backbone dihedral angles (ϕ,ψ) to be randomly fixed. The removal of up to 50% does not affect much and speeds up a lot the calculations.

Elastic network model (ENM)

The ENM defines the potential energy of the system. Select one of the following:

ENM	Comments	Formula
Sigmoid	Smooth distance dependence (*Cutoff* = x0)	x < c → f(x) = k/(1+(x/x0)^p) x ≥ c → f(x) = 0 (k=1, x0=3.8Å, c = x0+5Å, p=6)
Tirion	Simple distance cutoff (*Cutoff* = c)	x < c → f(x) = k x ≥ c → f(x) = 0 (k=1, c(CA)=10Å, c(C5)=7Å, c(HA)=5Å)
Hinsen	Derived from Amber94 force field. (only for CA model)	K. Hinsen et al., Chem. Phys. 261, 25 (2000)
edNMA	MD based (only for CA model)	Orellana et al., J. Chem. Theory Comput. 6 (9):2910–2923 (2010)

ENM cutoff

In Tirion´s ENM only those pairs of atoms at distances closer than the *Cutoff* will be linked by springs. In case of Sigmoid ENM, the *Cutoff* defines the inflexion point (x0) of the function.

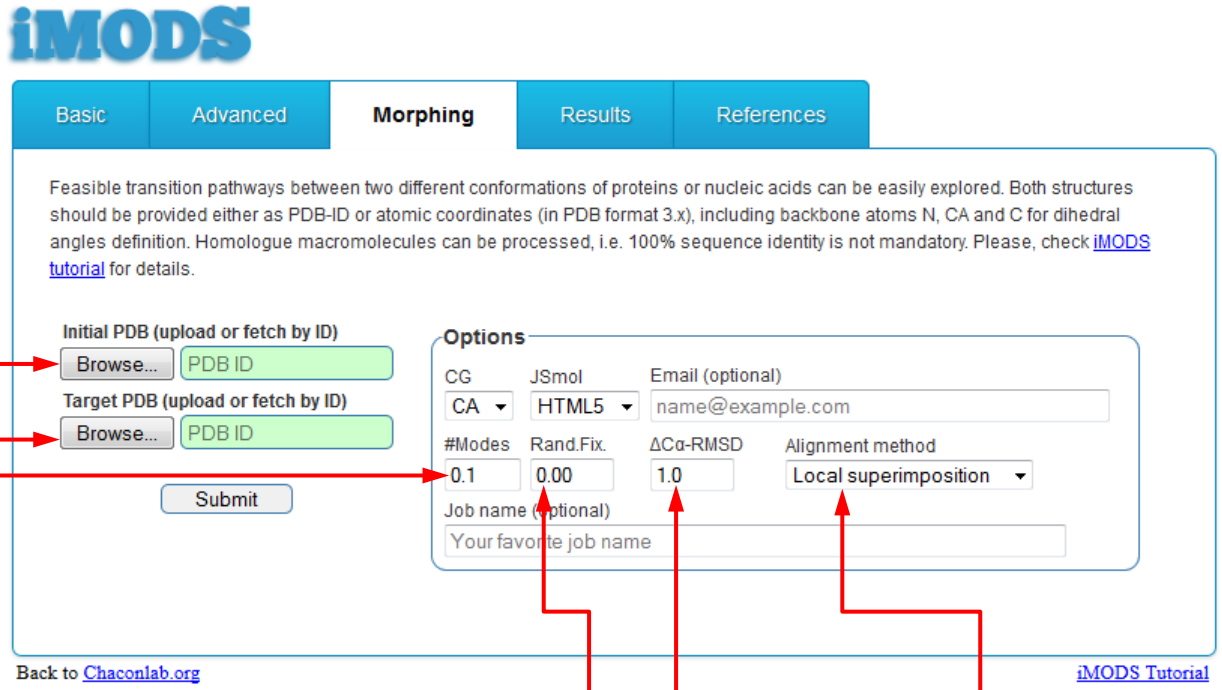
Clusters & Deformability

The most time consuming tasks are the calculation of the affine models (*Clusters*) and deformability (*Deform.*), which may be very slow for large systems. You may disable them to obtain the collective motions faster by choosing NO in the corresponding pull-down selectors.

***THOSE PARAMETERS NON EXPLAINED HERE ARE DETAILED IN BASIC INTERFACE.**

iMODS quick reference – Morphing interface

Input atomic coordinates of the initial and target structures can be either uploaded or fetched by ID from the PDB. The input format is **ID:Chain(s):Model#**
For example, introduce 2lt5:A:14 for fetching the A chain and 14th model of the 2lt5 PDB entry.



Introduce number of modes
Besides specifying some integer number of modes between 1 and 100, a fraction of the total available can be selected as well. By default the 10% are considered (**0.1**).

Fixed angles ratio
Ratio (between 0 and 1) of the backbone dihedral angles (ϕ,ψ) to be randomly fixed. The removal of up to 50% does not affect much and speeds up a lot the calculations.

7. ΔCα-RMSD between frames
It controls RMSD distance between consecutive models (frames) in the saved trajectory.

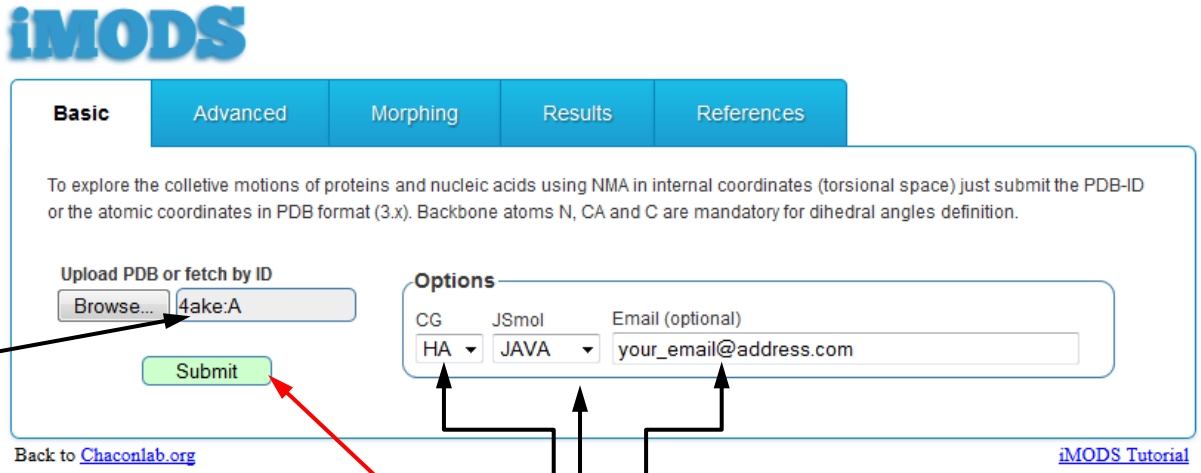
8. Alignment method
Besides *User defined* initial alignment, you can choose between *Local* or *Global superimposition* methods. The *Global* method minimizes de RMSD of all corresponding pairs of atoms while the *Local* one minimizes the RMSD of the most similar regions.

***THOSE PARAMETERS NON EXPLAINED HERE ARE DETAILED IN BASIC INTERFACE.**

iMODS tutorial – Basic NMA interface: Input

Basic NMA interface:

In this brief tutorial we are going to compute some of the lowest frequency normal modes of the A chain of the adenylate kinase from Escherichia coli (4ake), a small protein with 214 aminoacids.



1. Introduce atomic coordinates.

You can direcly fetch the file from the PDB using: **4ake:A**

The input format is **ID:Chain(s):Model#**

For multiple chains selection type their ids together, for example: **1sx4:ABCDEFH**

To select all chains use an asterisk: **1sx4:***

For PDB entries containing multiple models, the first one will be used if not specified. To select the, for example, 18th model type: **2lt5:A:18**

Alternatively, your can upload your coordinates in PDB format (3.x) by clicking the *Browse* button and selecting the corresponding file.

2. Select atomic model

Here you select the coarse grained atomic representation. Please check the *Basic NMA quick reference* for details. In this tutorial we are going to use the simplest CA model.

3. Select JSmol plugin mode

For small systems like 4ake use the **HTML5** mode. It will provide satisfactory visualization while maximizing compatibility. However, for a faster 3D experience use the JAVA mode. In this case, be sure that Java is enabled in your browser.

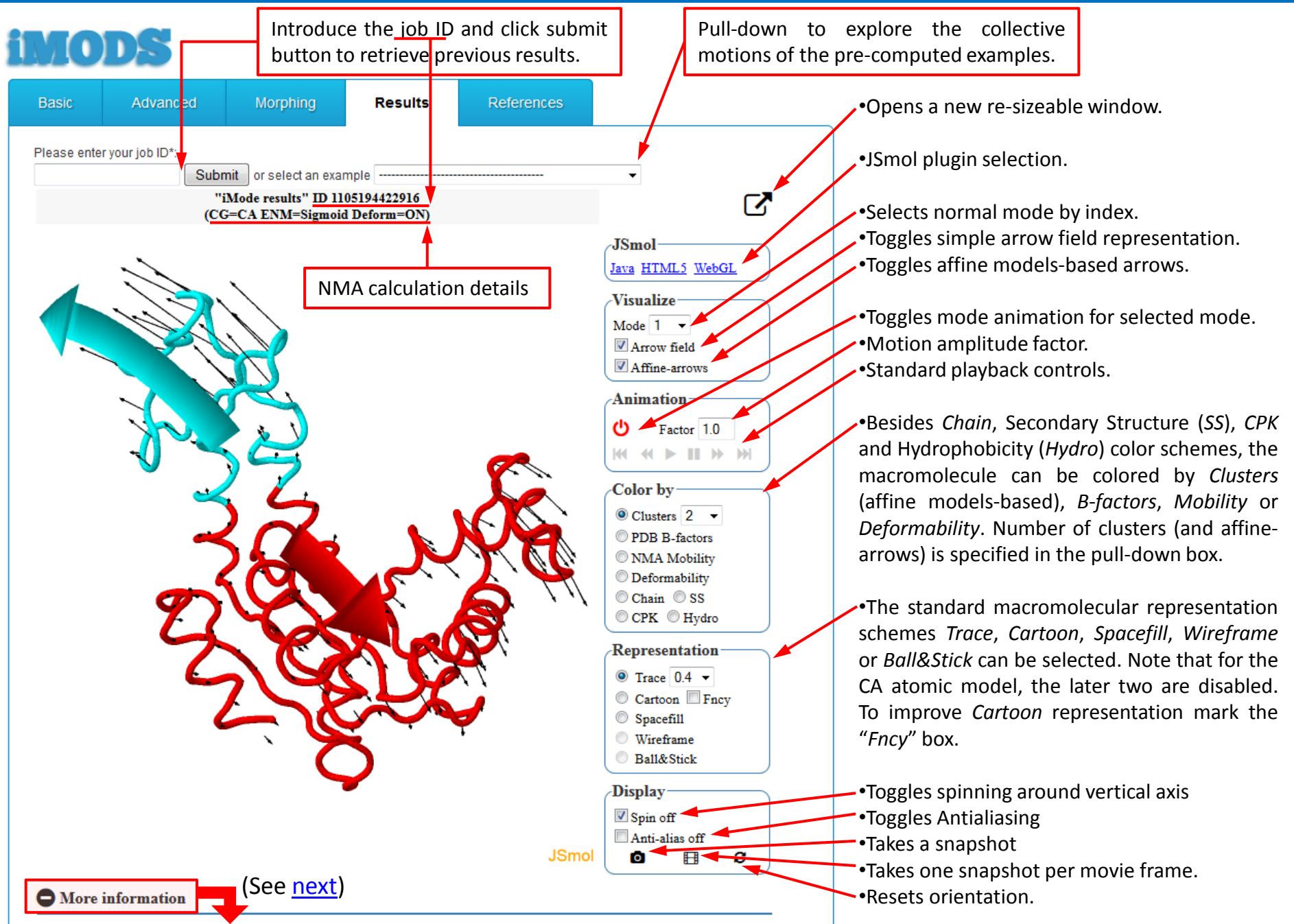
4. Introduce your email (optional)

The link to your results will be sent to this address after completion.

Submit the job!

You will be redirected automatically to the results tab in a few seconds.

iMODS tutorial – Basic NMA interface: Results

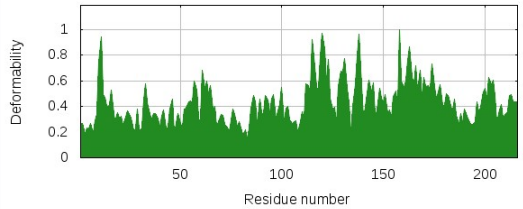


- Opens a new re-sizeable window.
- JSmol plugin selection.
- Selects normal mode by index.
- Toggles simple arrow field representation.
- Toggles affine models-based arrows.
- Toggles mode animation for selected mode.
- Motion amplitude factor.
- Standard playback controls.
- Besides *Chain*, Secondary Structure (*SS*), *CPK* and Hydrophobicity (*Hydro*) color schemes, the macromolecule can be colored by *Clusters* (affine models-based), *B-factors*, *Mobility* or *Deformability*. Number of clusters (and affine-arrows) is specified in the pull-down box.
- The standard macromolecular representation schemes *Trace*, *Cartoon*, *Spacefill*, *Wireframe* or *Ball&Stick* can be selected. Note that for the CA atomic model, the later two are disabled. To improve *Cartoon* representation mark the "*Fncy*" box.
- Toggles spinning around vertical axis
- Toggles Antialiasing
- Takes a snapshot
- Takes one snapshot per movie frame.
- Resets orientation.

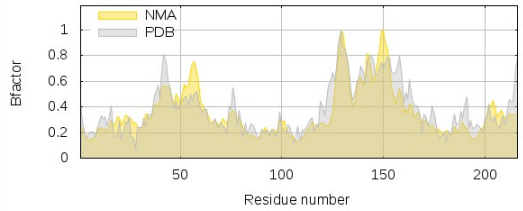
iMODS tutorial – Basic NMA interface: “More information”

B-factor/Mobility

The main-chain deformability is a measure of the capability of a given molecule to deform at each of its residues. The location of the chain 'hinges' can be derived from high deformability regions.



The experimental B-factor is taken from the corresponding PDB field and the calculated from NMA is obtained by multiplying the NMA mobility by (8pi^2). Be aware that many PDB files of averaged NMR models contain no B-factors (actually, the B-factor column gives an averaged RMS).

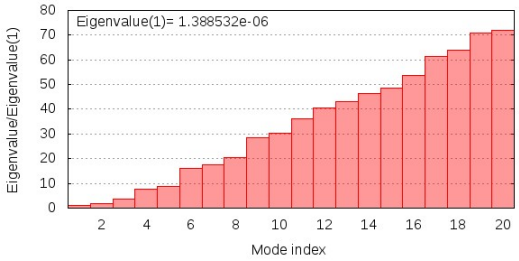


Residues with high deformability values may be part of “hinges”.

In general, experimental B-factors and NMA predicted mobilities are very similar.

Eigenvalues

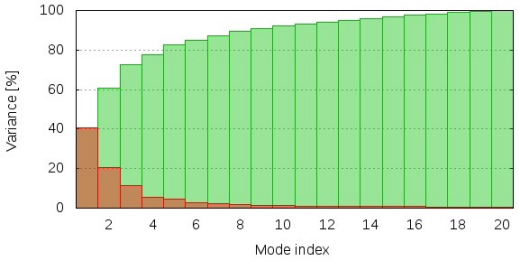
The eigenvalue associated to each normal mode represents the motion stiffness. Its value is directly related to the energy required to deform the structure. The lower the eigenvalue, the easier the deformation.



Eigenvalues plot evidences the relative modal stiffness.

Variance

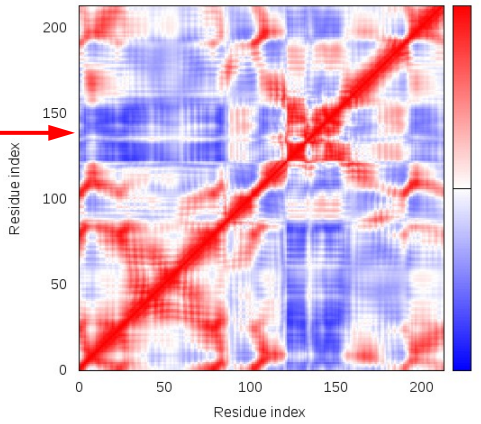
The variance associated to each normal mode is inversely related to the eigenvalue. Colored bars show the individual (red) and cummulative (green) variances.



The variance associated to the modes indicates their relative contribution to the equilibrium motions.

Covariance map

Covariance matrix indicates coupling between pairs of residues, i.e. whether they experience correlated (red), uncorrelated (white) or anti-correlated (blue) motions.



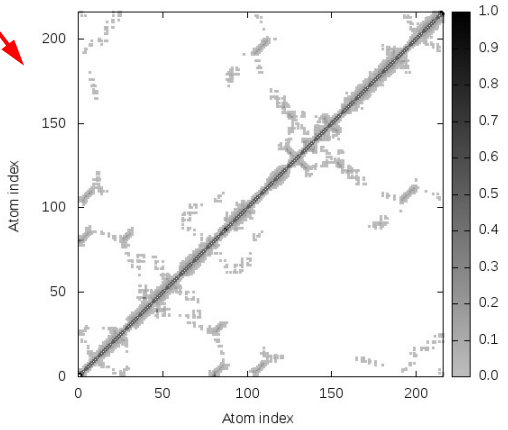
Covariance matrix indicates which parts of the macromolecule move in a correlated, uncorrelated or anti-correlated fashion.

The correlation matrix is computed using the Cα Cartesian coordinates and the equation 2 in: Ichiye T, Karplus M. Collective Motions in Proteins: a Covariance Analysis of Atomic Fluctuations in Molecular-Dynamics and Normal Mode Simulations. Proteins 11 205-217 (1991).

The elastic network model used to compute the normal modes can be illustrated as a linking matrix.

Elastic network

The elastic network model defines which pairs of atoms are connected by springs. Each dot in the graph represents one spring between the corresponding pair of atoms. Dots are colored according to their stiffness, the darker grays indicate stiffer springs and vice versa.



All generated files can be downloaded.

Download Files

Description	Format	Filename
Deformability/Mobility tabulated data	ASCII	imode_defmob.txt
Deformability C-alpha (temperature field)	PDB	imode_def.pdb
Mobility C-alpha PDB (temperature field)	PDB	imode_mob.pdb
Eigenvectors/values in Internal Coords.	ptraj ASCII	imode_ic.evec
Eigenvectors/values in Cartesian Coords.	ptraj ASCII	imode_cart.evec
Log-file	ASCII	logfile.txt
All computed files	TAR + GZIP	job1105194422916.tgz

iMODS tutorial – Advanced NMA interface: Input

Advanced NMA interface:
Using the advanced interface, NMA can be further customized. In contrast to the previous example, where default parameters were selected, in this brief tutorial we are going to compute the 10 lowest frequency modes of the human lactoferrin (1lfh), a 691 aminoacids protein, using the HA atomic model and Tirion´s elastic network with a 5.5 Å distance cutoff. To speed up calculations, the 50% of the dihedral angles (ϕ and ψ) will be randomly frozen and the time consuming deformability calculations will be disabled.

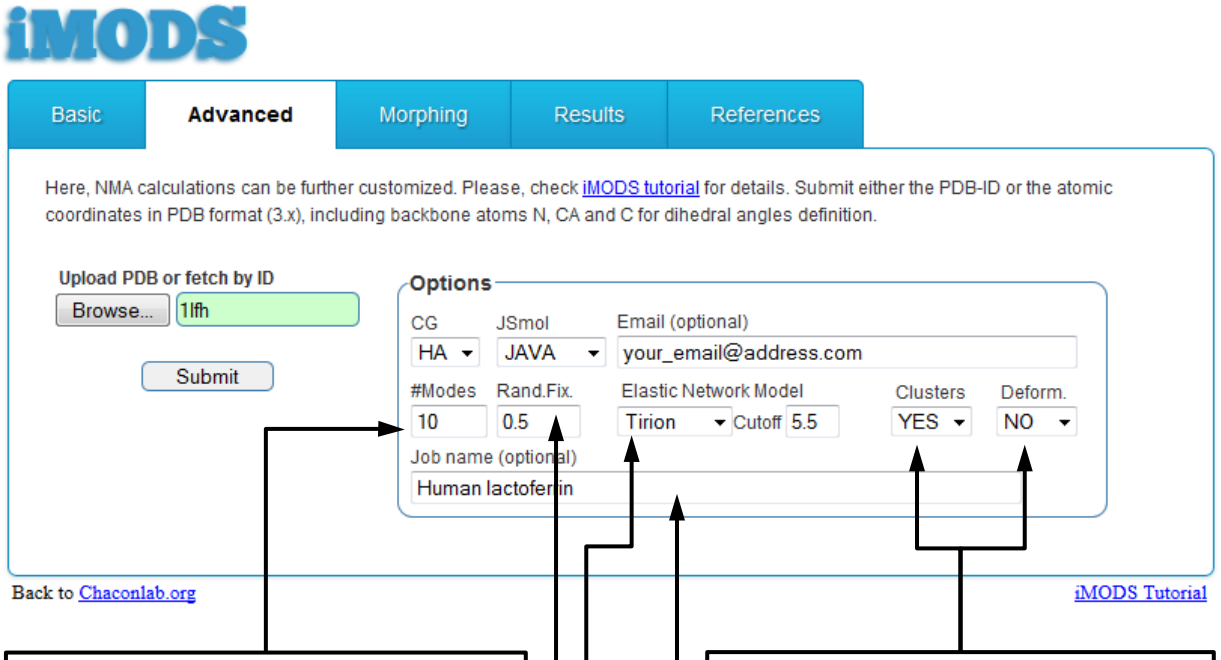
The first four steps are equivalent to those detailed for the Basic tutorial:

1. Introduce atomic coordinates.
Type the PDB ID: **1lfh**
(No chain IDs are required in this case)

2. Select atomic model.
Choose the **HA** model. Please check the *Basic NMA quick reference* for details.

3. Select JSmol plugin mode.
Select the **JAVA** mode, it will provide the fastest 3D experience. If your browser does not allow Java, use HTML5 instead.

4. Introduce your email
If you wish, a link to results page will be sent to this address.



5. Introduce number of modes.
Now only **10** modes are requested. Any number from 1 to 100 is valid.

6. Introduce fixed angles ratio.
To randomly freeze the 50% of the backbone dihedral angles (ϕ and ψ) type this percentage as a ratio: **0.5**

7. Select elastic network model.
Change the default Sigmoid function to the **Tirion**´s elastic network model and introduce **5.5** as distance cutoff [Å]. Please, check the Advanced NMA quick reference for details.

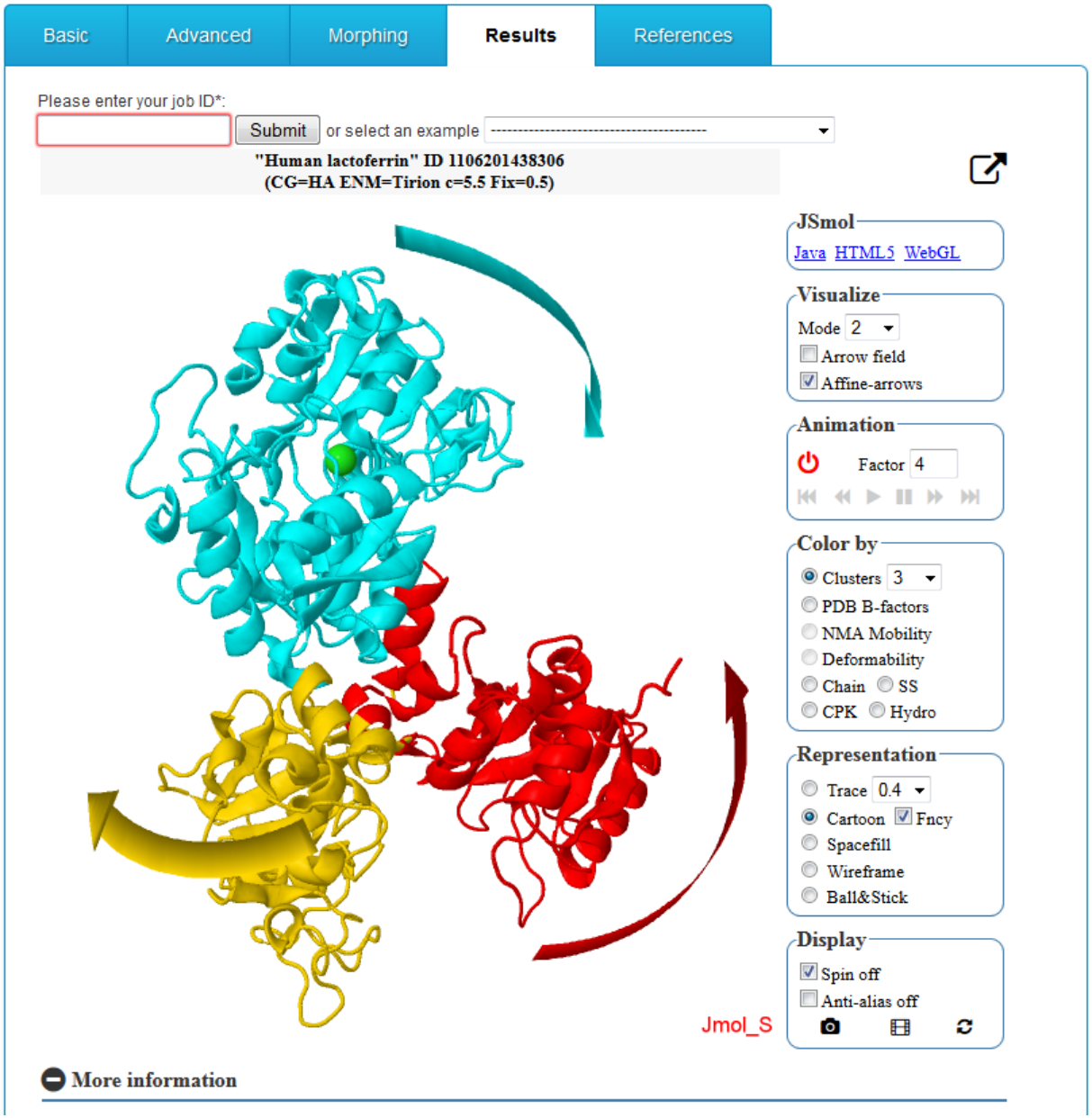
8. Disable deformability.
Select **NO** in the *Deform.* (deformability) selector. Further speed ups can be obtained by disabling affine models based calculations. To this end, select NO in the *Clusters* selector.

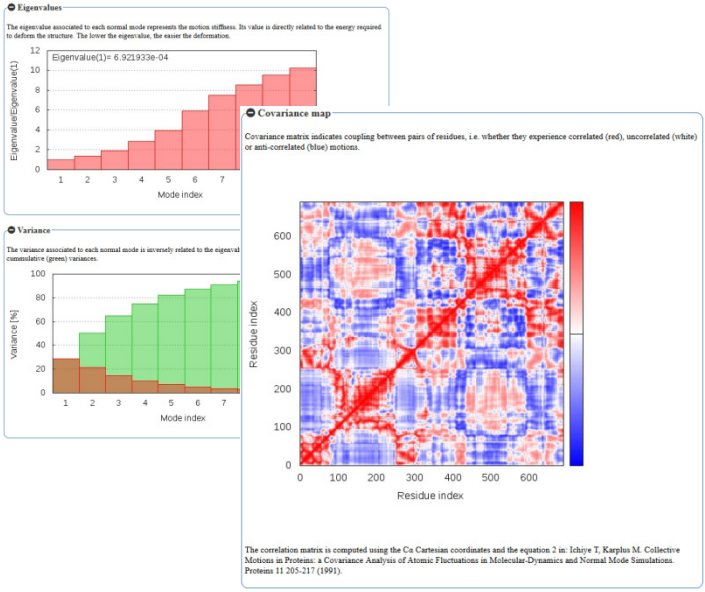
9. Job name.
Optionally, type some description to identify your job easily.

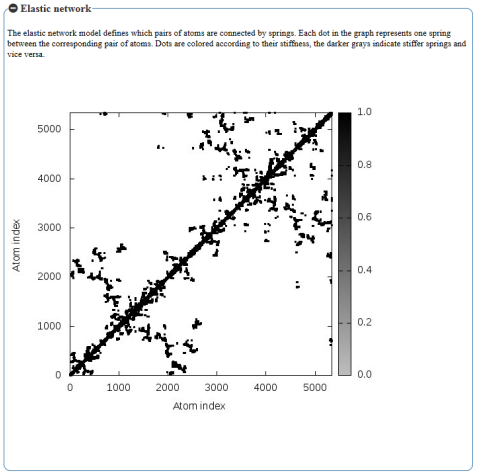
10. Submit the job!

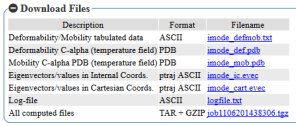
iMODS tutorial – Advanced NMA interface: Results

Results tab is the same for Basic and Advanced interfaces, check the results and more information pages for details.





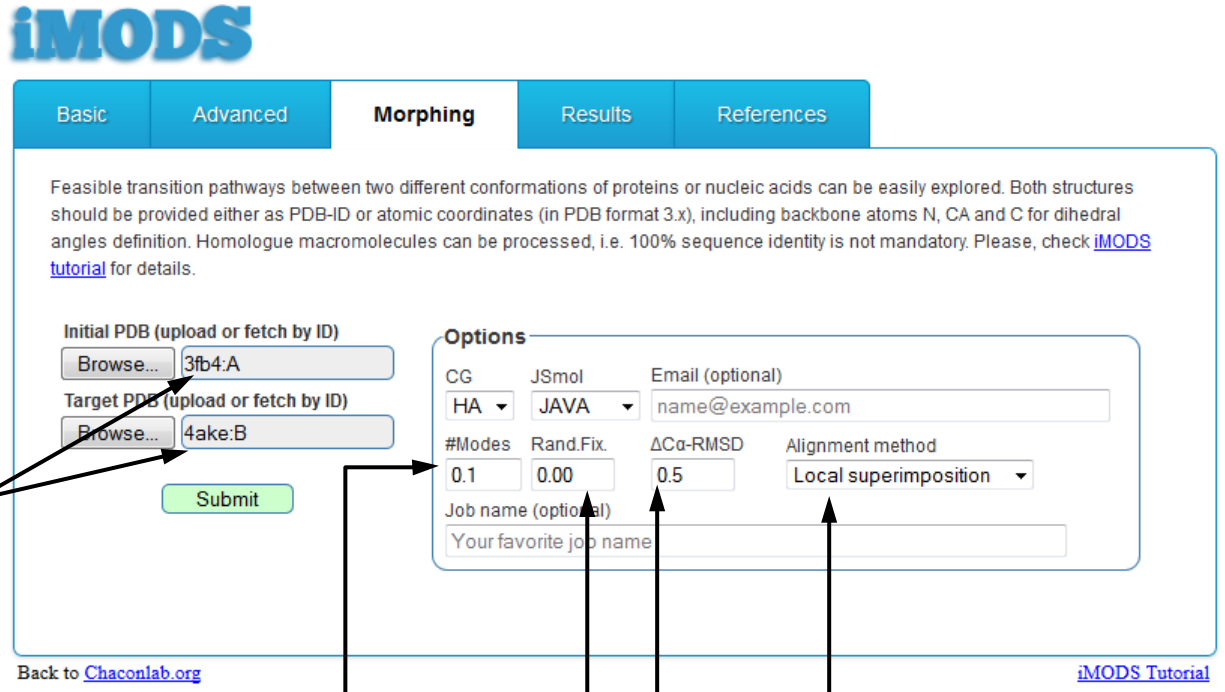




iMODS tutorial – Morphing interface: Input

Morphing interface

We are going to obtain a transition trajectory between the closed (3fb4) and open (4ake) homolog structures of the adenylate kinase from Marinibacillus marinus and Escherichia coli, respectively.



1. Introduce atomic coordinates
Type the PDB and chain IDs for initial **3fb4:A** and final **4ake:B** structures in the corresponding input boxes. The same considerations given in the Basic tutorial are valid here.

The steps 2, 3 and 4 are equivalent to those detailed in the Basic tutorial:

2. Select atomic model.
Choose the **HA** model. Please check the *Basic NMA quick reference* for details.

3. Select JSmol plugin mode.
Select the **JAVA** mode if possible, otherwise use HTML5 instead.

4. Introduce your email
Optionally, a link to results will be emailed.

5. Introduce number of modes
Besides specifying some integer number of modes [1,100], a fraction of the total available can be selected as well. In this example, the default value of **0.1** will consider the 10%.

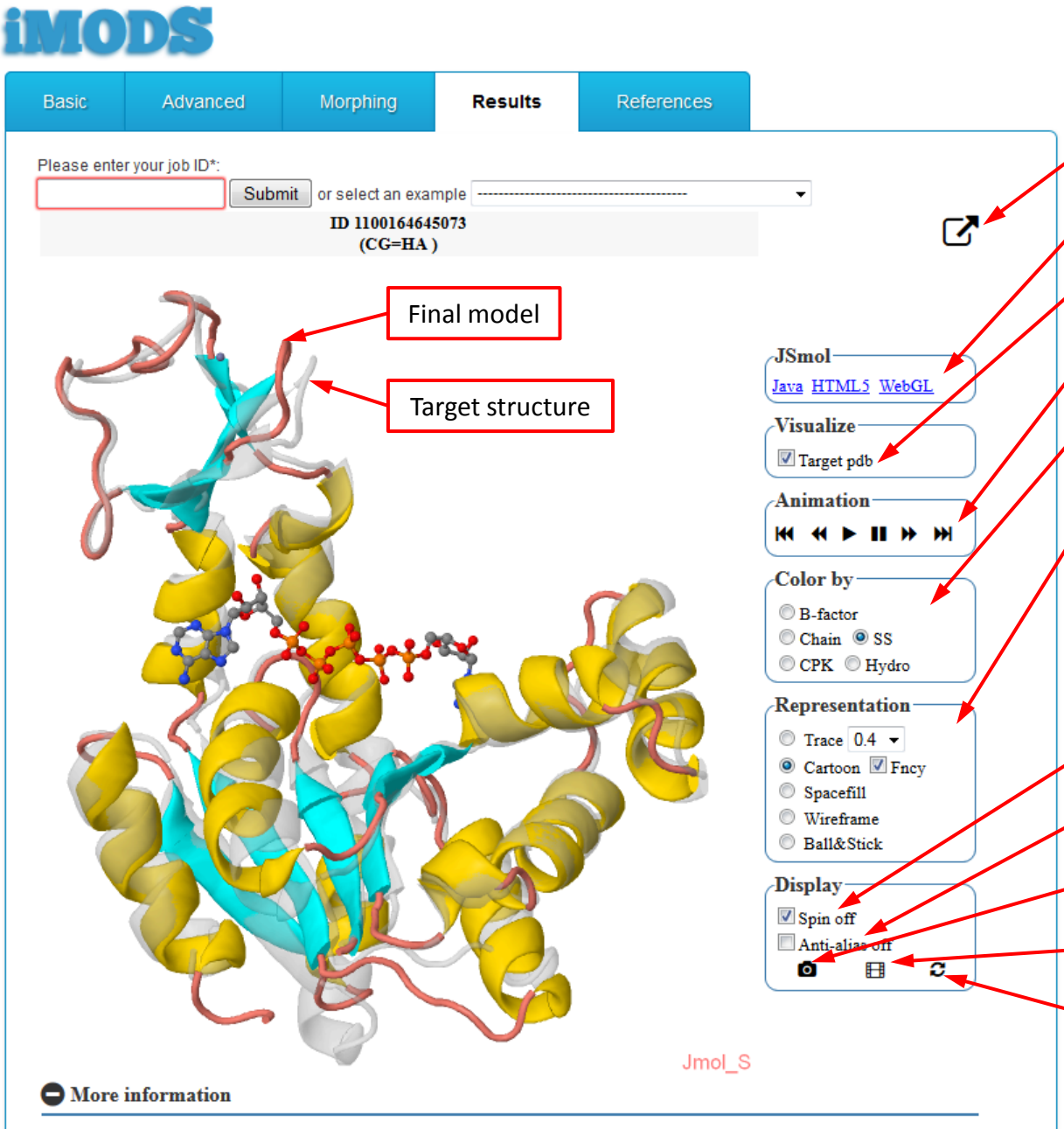
6. Introduce fixed angles ratio
Use the default value **0.00**%, all ϕ and ψ dihedral angles will be considered.

7. ΔCα-RMSD between frames
It controls RMSD distance between consecutive models (frames) in the saved trajectory. Use the **0.5** Å value to obtain a smoother trajectory.

8. Alignment method
Select the ***Local superimposition*** method, the RMSD of the most similar regions will be minimized. Alternatively, the *Global* method will minimize the RMSD of all pairs of atoms. The *User defined* option keeps the input orientation as starting pose.

10. Submit the job!
Once submitted, the score profile will be updated to monitor progress. You will be redirected to results in a couple of minutes.

iMODS tutorial – Morphing interface: Results



- Opens a new re-sizeable window.
- JSmol plugin selection.
- Toggles target macromolecule visualization.
- Standard playback controls.
- Color scheme selection: *Chain*, Secondary Structure (*SS*), *CPK* or Hydrophobicity (*Hydro*).
- Macromolecular representation scheme selection: *Trace*, *Cartoon*, *Spacefill*, *Wireframe* or *Ball&Stick*. The later two are not available for CA atomic model. To improve *Cartoon* representation mark the "*Fncy*" box. The pull-down box controls *Trace* thickness.
- Toggles spinning around vertical axis
- Toggles Antialiasing
- Takes a snapshot
- Takes one snapshot per movie frame.
- Resets orientation.

iMODS tutorial – Morphing interface: “More information”

The sequence alignment illustrates the homology between initial and target structures. When both sequences are not identical, like in this case, only the Cα atoms of fully conserved (*) and strongly similar (:) residues are considered for score computation. WARNING! Low homology may lead to artifacts.

Sequence alignment

Clustal sequence alingment is automatically performed to define the residue correspondence between input structures and compute the scoring (RMSD). In case sequences are not identical, only the Cα atoms of fully conserved (*) and strongly similar (:) residues are considered.

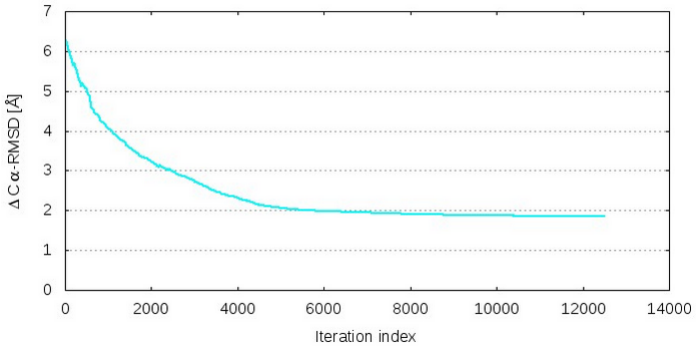
```
CLUSTAL 2.1 multiple sequence alignment


initial          MNIVLMGLPGAGKGTQAEQIIEKYEIPHISTGDMFRAAIKNGTELGLKAKSFMDQGNLVP
target_up        MRIILLGAPGAGKGTQAQFIMEKYGIPQISTGDMLRAAVKSGSELGKQAKDIMDAGKLVT
                 *.*:*:* *********: *:*** **:******:***:*.*:*** :**.:** *:**.

initial          DEVTIGIVHERLSKDDCQKGFLLDGFPRTVAQADALDSLLTDLGKKLDYVLNIKVEQEEL
target_up        DELVIALVKERIAQEDCRNGFLLDGFPRTIPQADAMK----EAGINVDYVLEFDVPDELI
                 **:.*.:*:**::::**::**********:.****:.    : * ::****::.* :* :

initial          MKRLTGRWICKTCGATYHTIFNPPAVEGICDKDGGELYQRIDDKPETVKNRLDVNMKQTQ
target_up        VDRIVGRRVHAPSGRVYHVKFNPPKVEGKDDVTGEELTTRKDDQEETVRKRLVEYHQMTA
                 :.*:.** :  ..* .**. **** ***  *  * **  * **: ***::**    : *

initial          PLLDFYSQKGVLKD-----IDGQQDIKKVFVDINDLLGGL
target_up        PLIGYYSKEAEAGNTKYAKVDGTKPVAEVRADLEKILG--
                 **:.:**::.   :     :** : : :* .*::.:**
```

Click Here to download the alignment.

The Cα-RMSD between current and target structures is computed every iteration to monitor convergence. If final RMSD values were not sufficiently low, try again increasing the number of modes and/or reducing the percentage of frozen dihedral angles.

Score profile

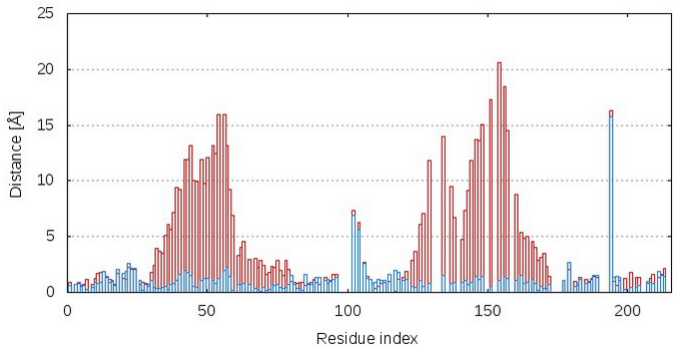
Morphing trajectory convergence can be monitored here. At every iteration the Cα-RMSD is computed. In case final RMSD values are not around 1 or 2 Å, try increasing the number of modes.



Distance profiles between target and either initial (red) or final (blue) structures show the fitting quality at each residue. The differences between initial and final profiles indicate the motion amplitude. For example, in our test case the regions around residues 50 and 150 experience displacements in the order of 10-15 Å. Blue peaks around residues 100 and 190 are probably sequence alignment artifacts. Residue indices were referenced to initial structure.

Distance profile

The Cα-based distance profile indicates the fitting differences between target and initial (red) or final (blue) structures. Residue indices are referenced to initial structure.



All files can be downloaded:

Download Files

Description	Format	Filename
Morphing trajectory	GZipped Multi-PDB	imorph_movie.pdb.gz
Sequence alignment	ASCII	initial_target.aln
Initial CG structure	PDB	imorph_model.pdb
Aligned target structure	PDB	target.pdb
Final fitted model	PDB	imorph_fitted.pdb
Log-file	ASCII	logfile.txt
All computed files	GZipped TAR	job1100164645073.tgz