iMODS
http://imods.chaconlab.org/

Internal coordinates normal mode analysis server

➢ QUICK REFERENCE
   Basic NMA
   Advanced NMA
   Morphing

➢ TUTORIALS
   Basic NMA
   Advanced NMA
   Morphing
**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.

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

<table>
<thead>
<tr>
<th>CG</th>
<th>Description</th>
<th>Sketch</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA</td>
<td>Cα atoms accounting for whole residue mass.</td>
<td></td>
</tr>
<tr>
<td>C5</td>
<td>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)</td>
<td></td>
</tr>
<tr>
<td>HA</td>
<td>All heavy atoms, each one accounting for its own mass.</td>
<td></td>
</tr>
</tbody>
</table>

*For nucleic acids this HA is automatically selected.*

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**JSmol plugin:** The JSmol implementation offers three display modes:

<table>
<thead>
<tr>
<th>JSmol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTML5</td>
<td>JavaScript based Jmol, compatible with new handheld devices and major browsers. However, slow visualization is expected for large macromolecules.</td>
</tr>
<tr>
<td>JAVA</td>
<td>Standard Jmol Java applet. It is the fastest and memory efficient mode.</td>
</tr>
<tr>
<td>WebGL</td>
<td>JavaScript &amp; OpenGL mode. Despite very developmental, it will be likely the new standard for on-line 3D graphics.</td>
</tr>
</tbody>
</table>
### 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 \((\phi,\psi)\) 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:

<table>
<thead>
<tr>
<th>ENM</th>
<th>Comments</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sigmoid</td>
<td>Smooth distance dependence ((Cutoff = x0))</td>
<td>(x &lt; c \Rightarrow f(x) = k/(1+(x/x0)^p)) (x \geq c \Rightarrow f(x) = 0) ((k=1, x0=3.8\text{Å}, c = x0+5\text{Å}, p=6))</td>
</tr>
<tr>
<td>Tirion</td>
<td>Simple distance cutoff ((Cutoff = c))</td>
<td>(x &lt; c \Rightarrow f(x) = k) (x \geq c \Rightarrow f(x) = 0) ((k=1, c(\text{CA})=10\text{Å}, c(\text{C5})=7\text{Å}, c(\text{HA})=5\text{Å}))</td>
</tr>
<tr>
<td>Hinsen</td>
<td>Derived from Amber94 force field. (only for CA model)</td>
<td>K. Hinsen et al., Chem. Phys. 261, 25 (2000)</td>
</tr>
</tbody>
</table>

### 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.*
**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 ($\phi,\psi$) to be randomly fixed. The removal of up to 50% does not affect much and speeds up a lot the calculations.

**7. ΔCa-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.*
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 directly 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, you 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.
Introduce the job ID and click submit button to retrieve previous results.

Pull-down to explore the collective motions of the pre-computed examples.

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.

More information (See next)
Residues with high deformability values may be part of “hinges”.

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

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

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

Eigenvalues plot evidences the relative modal stiffness.

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

All generated files can be downloaded.
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 (\(\phi\) and \(\psi\)) 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 (\(\phi\) and \(\psi\)) 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!**
Results tab is the same for Basic and Advanced interfaces, check the results and more information pages for details.
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. ΔCa-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.
iMOLS 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.

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.

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.

All files can be downloaded:

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