DynOmics Portal and ENM server

1. URLs of the DynOmics portal, ENM server, ANM server, and iGNM database.

DynOmics portal:  http://dynomics.pitt.edu/
ENM server:       http://enm.pitt.edu/
ANM server:       http://anm.csb.pitt.edu/
iGNM database:   http://gnmdb.csb.pitt.edu/

2. Introduction to the ENM server usage

Tutorial:  http://enm.pitt.edu/Tutorial.php

(1) How to submit a query to the server?

![Screenshot of ENM server interface]

You can submit a job by entering the PDB ID (e.g., 1XNB, xylanase or 4NIH, DNA bound AlkB family demethylase).

Note: You can click “Advanced options” and “Considering Environment” to view the options. If the submitted PDB structure is a membrane protein included in the OPM database, the ENM server can
build a coarse-grained membrane model as ‘environment’ for ANM/GNM analysis of the membrane protein. Or, users can specify a portion of the structure as the **system** and the rest as the **environment**.

For example, γ-secretase (PDB ID: 5FN2) is a membrane protein which can be submitted to the server using the option “**in the presence of membrane**” under the “**Considering Environment**”. And the pre-calculated results for the example can be loaded onto the ENM home page by clicking the load examples button of “**MembrANM**”. 
(2) How does the results page look like?
(3) How to view the motions in selected modes?

“Molecular Motions - Animations” – Viewing the ANM motions of structures.

Display properties:

Users can select different ANM modes from the Mode index dropdown menu. The thickness of the network edges (bond radius), the size of the network nodes (atom size), size of the deformation vector along the mode (magnitude) and the speed of vibrations (frequency) can be adjusted by the user.

Viewing and saving the motions at full atomic scale:

ANM motions are evaluated (and displayed) at single-node-per-residue level. By clicking the “Full Atomic Structures for ANM-Driven Conformers” button, users can generate the full atomic. The size of the motion along a given mode can be readjusted by defining the RMSD between the initial and target conformer. The movie for ANM motions can be viewed by downloading the PDB or PyMol session (Pse) files.
(4) How to evaluate the MS fluctuations of residues (and compare with experiments)?

Click the “Main result” button on the front page to load the results for a protein-DNA complex (oxidoreductase/DNA; PDB ID: 4NIH). Note that ms fluctuations scale with B-factors (reported for X-ray crystallographic structures)
Color-coded diagrams are shown for the theoretical (left) and experimental (right) B-factors in 3D JSMol windows. The correlation between the predicted/theoretical B-factors and experimental B-factors is given in the lower/middle part of the page (here it is 0.8). The corresponding B-factor profiles as a function of residue index are displayed in the lower portion. Users can click the curve to see the identity of the chain (if there are multiple chains, e.g. A, B,..). The residues selected on the curve are simultaneously displayed and labelled in the diagram of 3D JSMol window (e.g. Proline137 is labeled).

The curves in the lower chart can be hidden or displayed by clicking a set of buttons in the control panel. The images in the JSMol window and the charts can be exported and downloaded using the “Export image” and “Export” buttons.
(5) **How to view the extent of motion in selected modes?**

The interactive features of the chart and JSMol windows are similar to those on the “Mean-Square Fluctuations of Residues” results page. Besides, the color-coded ribbon diagrams of mode shapes can be changed to any selected modes using the dropdown menu above the JSMol window.
(6) “Cross-correlations between Residue Fluctuation”

**Note:** Users can calculate the cross-correlations map based on any selected ranges of modes by specifying the range of modes and clicking the “Calculate” button located on the top of page.

For a structure with < 1000 nodes (e.g., PDB: 4NIH), two cross-correlation maps are displayed. When clicking a point on the left map, the map on the right is updated with a zoom in view. The residues information and the value of correlation can be read while the cursor is hovering on the right map. By clicking a point on the right map, the corresponding pair of residues in the 3D JSMol window are labelled.
For structures above 1000 nodes (e.g., PDB id: 5FN2), only the left cross-correlation map will be displayed and the 3D JSMol can be loaded only when the “Open with 3D viewer” button is clicked.
(7) “Properties of GNM Mode Spectrum” – Frequency and collectivity of Modes

**Frequency Dispersion of Global Modes**

10% (or at least 20) global (low frequency) modes are displayed for both the dispersion and the collectivity.

**Degree of Collectivity of Global Modes**

High collectivity indicates parts of the protein move together in this mode.
(8) “Potential Functional Sites”

Display or hide the Potential Functional Sites in the color-coded diagram on the main results page by clicking the "Potential Functional Sites" button.
(9) “Sensors and Effectors” – Perturbation response scanning (PRS)

Sensors and effectors are based on the perturbation-scanning response (PRS) method. Click the “PRS” button on the front page to load the example of HSP70 (PDB ID: 4B9Q).

Users can to calculate the PRS results based on any selected ranges of modes by specifying the range of modes and clicking the “Calculate” button.

The color-coded diagrams for both sensors and effectors are displayed in JSmol windows on the top part of the results page.

Residue identities can be read by hovering the cursor on the charts or maps.
Results for 4B9Q.pdb:

Perturbation Response Scanning (PRS) based on modes: 1 to 527 Calculate
* Select a range of modes to calculate the PRS.
(10) MembrANM: A case study: the γ-secretase (PDB ID: 5FN2):

Comparison of the motion of the isolated molecule and that in an environment (e.g. membrane):

By clicking the “Effect of environment” button, the overlap map between ANM modes of the isolated protein and those of the protein in the presence of membrane environment can be viewed below the JSMol window.

The effect of the membrane environment can be evaluated using two alternative approaches: envANM-membrANM or Substructure-membrANM:

(a) envANM-membrANM: System-environment computations are performed by considering the membrane as environment (and the membrane protein is the system). The ANM modes represent the collective motions of the membrane protein as affected by the presence of the membrane.

(b) Substructure-membrANM. The computations are performed for the entire network, composed of membrane protein and membrane. Only the portion of the results (e.g. eigenvectors) corresponding to the membrane protein is reported on the “Substructure-membrANM” results page. To observe the full dynamics including the membrane motions, please use the item of “Substructure-membrANM (full)”