Web Server For External Force Perturbation And Normal Mode Analysis of Proteins

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Elastic Network Models

- Coarse-Grained at the residue level

- Residues are connected via elastic springs within a cutoff distance

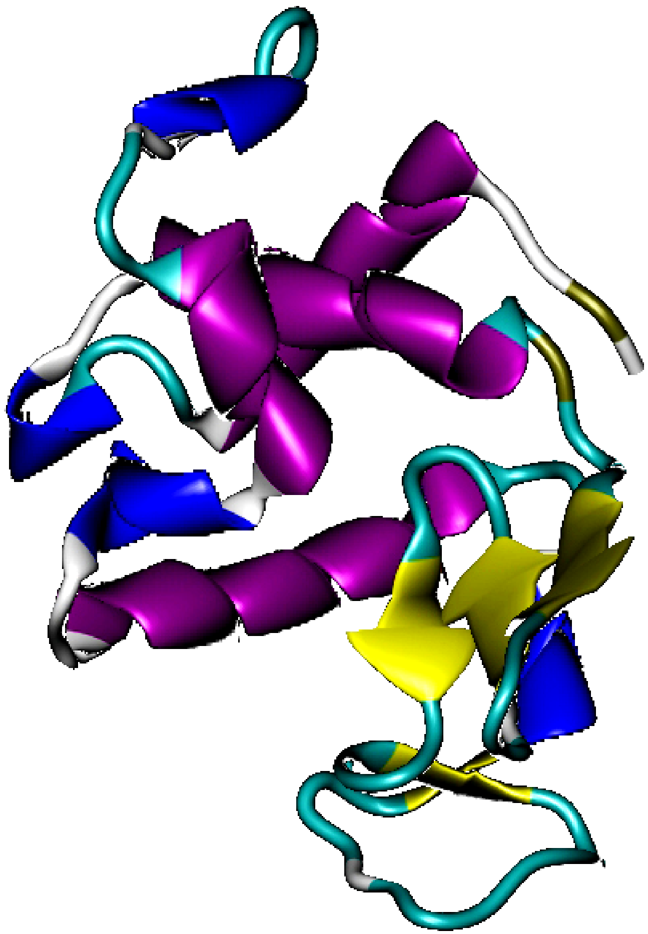
- Interactions are governed by harmonic potentials

Two main models:

- GNM (Gaussian Network Model)

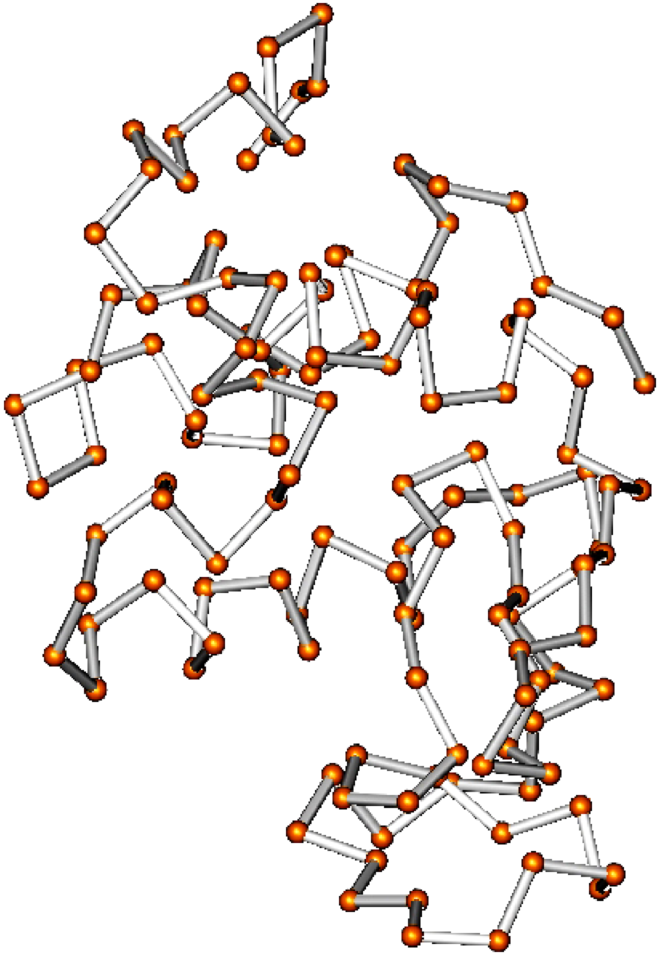
- ANM (Anisotropic Network Model)

Elastic Network Models



Given a protein structure

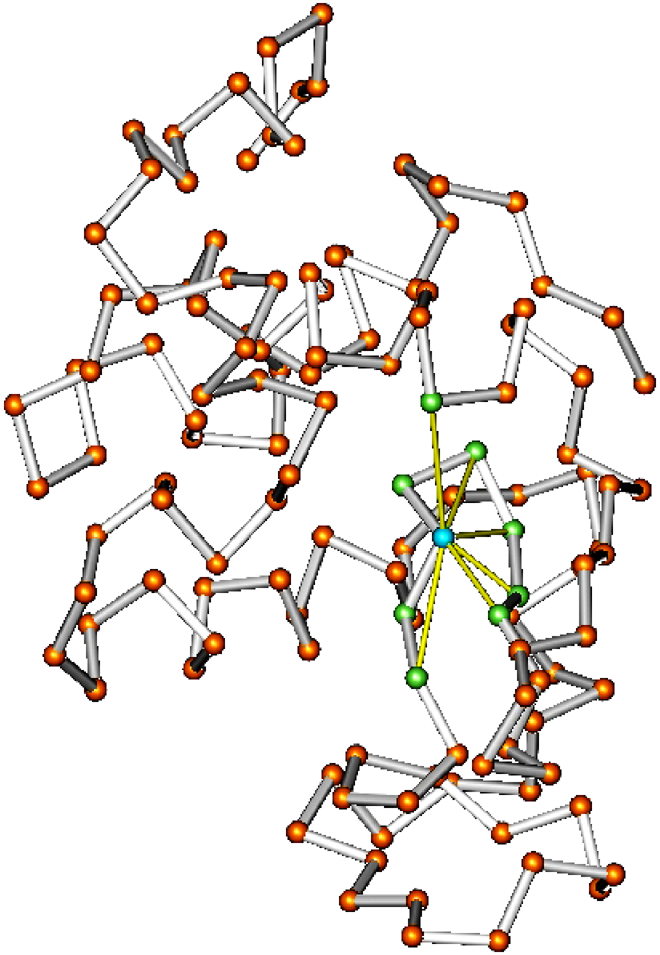
Elastic Network Models



Coarse grain at residue level

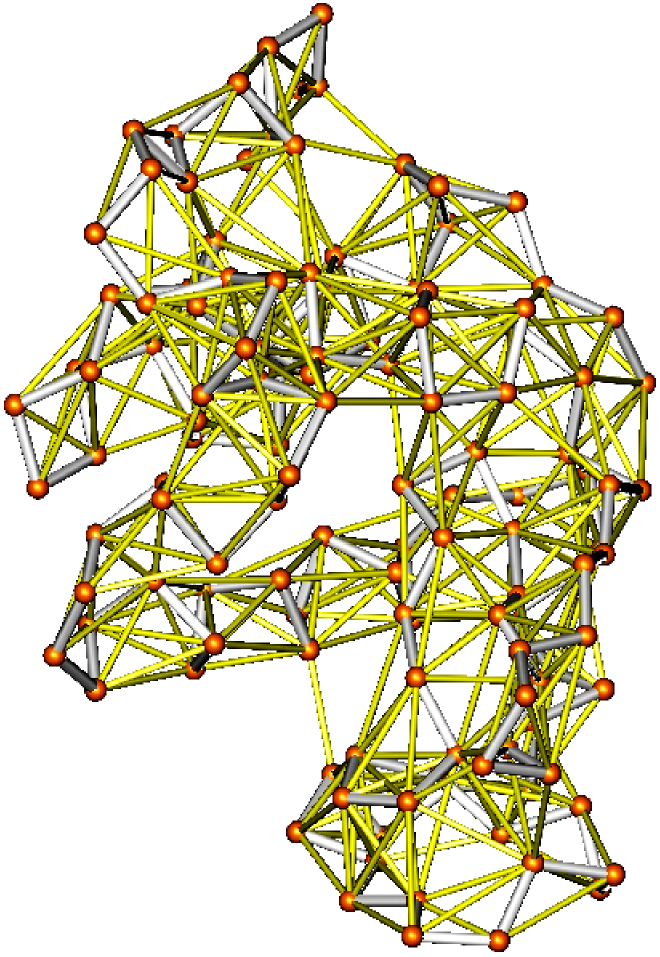
C_α (or C_β) atoms are selected as representative points

Elastic Network Models



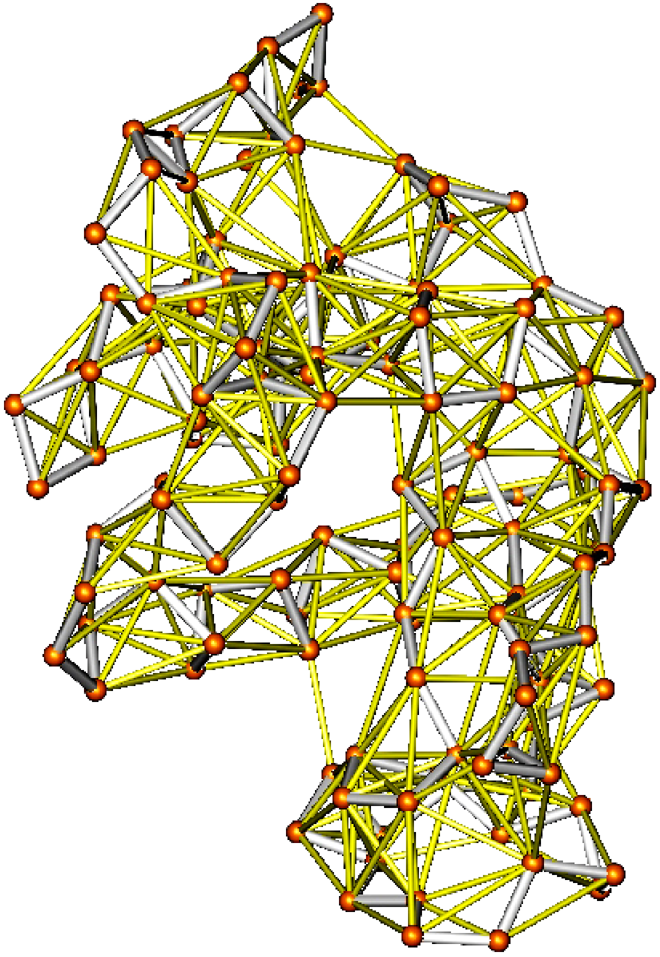
Connect residues that are closer than a selected cutoff (r_c)

Elastic Network Models



Connect residues that are closer than a selected cutoff (r_c)

Anisotropic Network Model



Assuming harmonic potentials for each spring:

$$V_{i,j} = \frac{\gamma}{2}\left(s_{i,j} - s_{i,j}^{0}\right)^2$$

Force constant matrix (Hessian) is the second derivative of the potential:

$$\mathbf{H}_{i,j} = \begin{bmatrix} \frac{\partial V^2}{\partial X_i \partial X_j} & \frac{\partial V^2}{\partial X_i \partial Y_j} & \frac{\partial V^2}{\partial X_i \partial Z_j} \\ \frac{\partial V^2}{\partial Y_i \partial X_j} & \frac{\partial V^2}{\partial Y_i \partial Y_j} & \frac{\partial V^2}{\partial Y_i \partial Z_j} \\ \frac{\partial V^2}{\partial Z_i \partial X_j} & \frac{\partial V^2}{\partial Z_i \partial Y_j} & \frac{\partial V^2}{\partial Z_i \partial Z_j} \end{bmatrix}_{3x3}$$

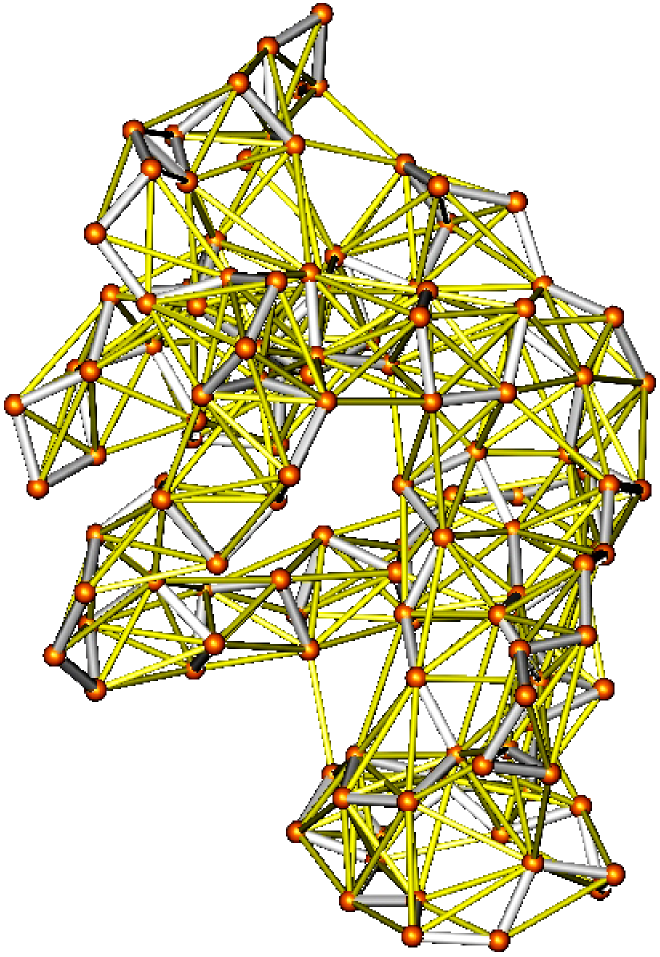
Which also can be written as:

$$\mathbf{H}_{3Nx3N} = \mathbf{B}_{3NxM} \mathbf{K}_{MxM} \mathbf{B}^{T}_{Mx3N}$$

B : Direction Cosine Matrix
K : Coefficient Matrix

Atilgan AR, Durell SR, Jernigan RL, Demirel MC, Keskin O, et al. (2001) Anisotropy of fluctuation dynamics of proteins with an elastic network model. Biophysical Journal 80: 505–515. doi: 10.1258/ebm.2009.009230.

Anisotropic Network Model



3x3 super element of the inverse Hessian will give the fluctuation correlations:

$$\mathbf{H}^{-1}_{i,j} = \Delta \mathbf{R}_i \Delta \mathbf{R}_j^{\mathbf{T}}$$

The diagonal super element will correspond to the self-correlations.

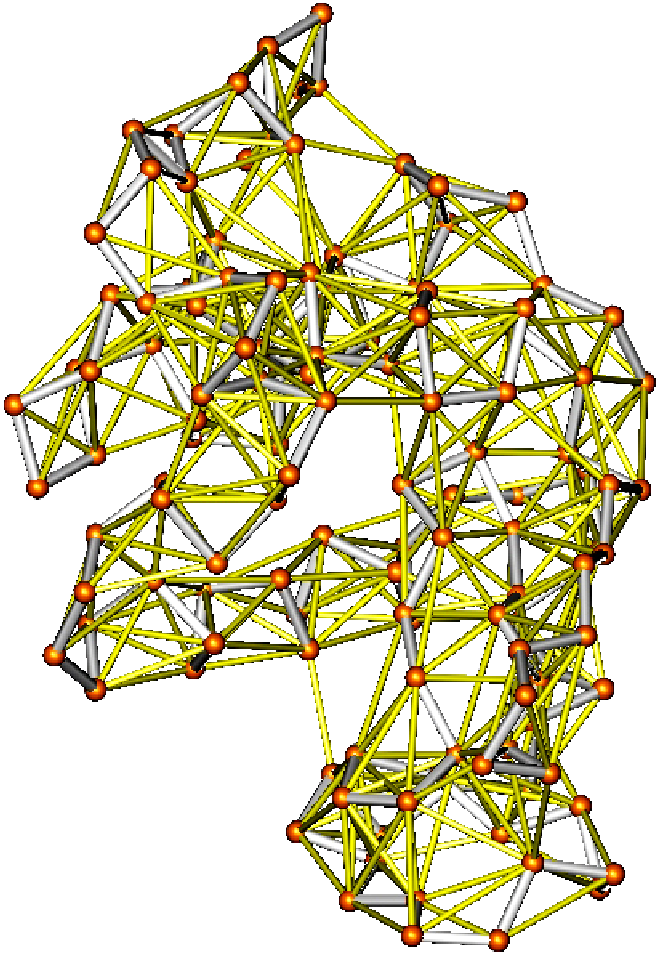
Normal modes are given by eigenvalue decomposition;

$$\mathbf{H} = \mathbf{U} \mathbf{\Lambda} \mathbf{U}^{\mathbf{T}}$$

Diagonals matrix **Λ** will give the frequencies
Columns of **U** will be the normal modes

Atilgan AR, Durell SR, Jernigan RL, Demirel MC, Keskin O, et al. (2001) Anisotropy of fluctuation dynamics of proteins with an elastic network model. Biophysical Journal 80: 505–515. doi: 10.1258/ebm.2009.009230.

Perturbation Response Scanning



In the presence of an external force, following equation holds:

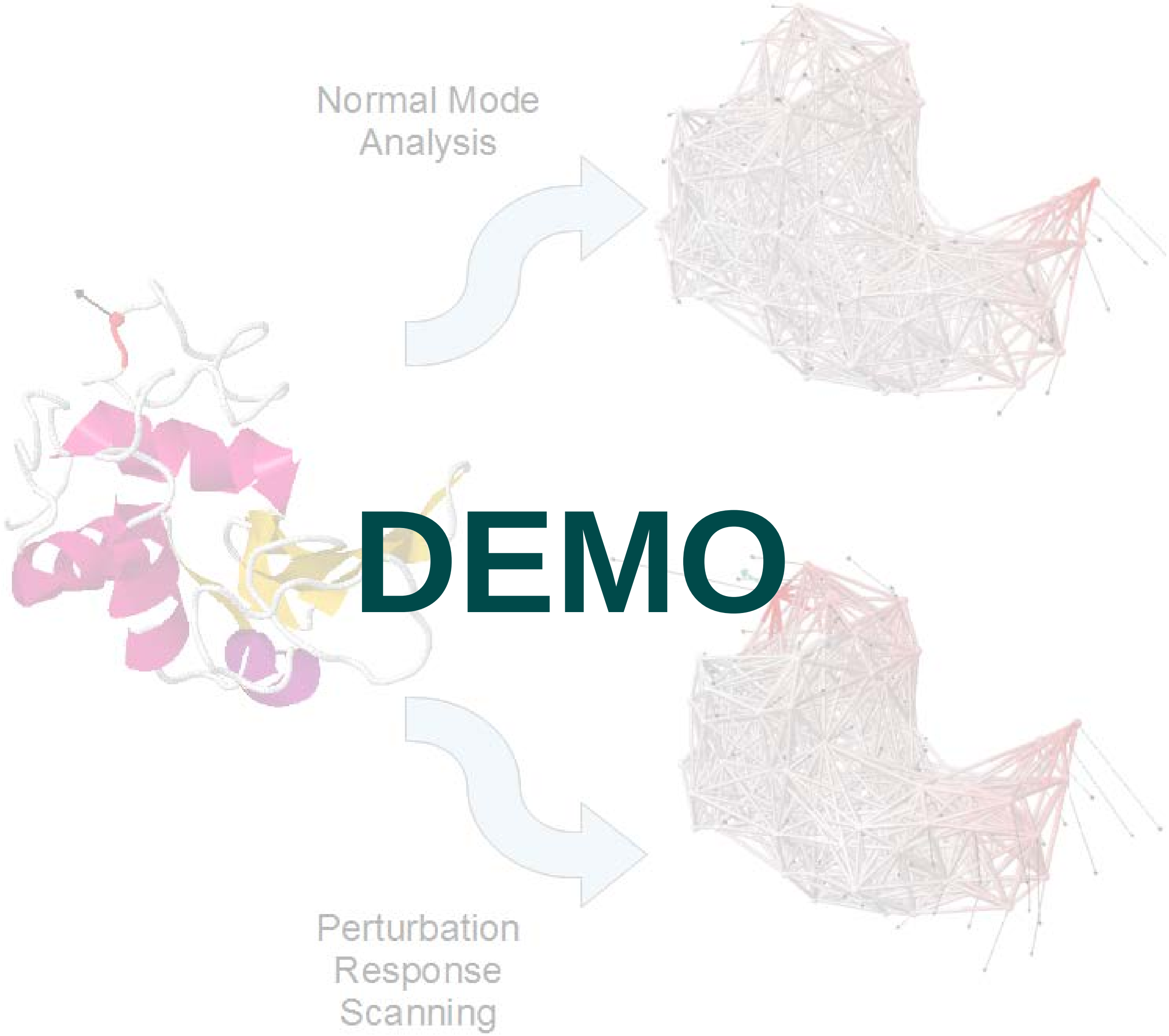
$$\mathbf{H}_{3Nx3N}\,\Delta\,\mathbf{R}_{3Nx1} = \Delta\,\mathbf{F}_{3Nx1}$$

ΔR : Displacement vector
ΔF : External force vector

Therefore, one can find the individual displacements for a given force

$$\Delta\,\mathbf{R} = \mathbf{H}^{-1}\Delta\,\mathbf{F}$$

Atilgan C, Atilgan AR (2009) Perturbation-Response Scanning Reveals Ligand Entry-Exit Mechanisms of Ferric Binding Protein. PLoS Comput Biol 5(10): e1000544. doi:10.1371/journal.pcbi.1000544



DEMO

Visualizations by Jmol: an open-source Java viewer for chemical structures in 3D.
http://www.jmol.org/

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