Notes

Julian Echave

5/9/2020

Many ways of updating ENM...

LFENM

The LFENM does not change K. Thus, the structure changes, but not the normal modes, or entropy: there's a shift in the center of the potential energy well without any reorientation.

SC-LFENM

The SC-LFENM takes into account that by definition in ENM's K is built from the equilibrium conformation. Therefore, if we change the structure due to, for instance, a linearly-forcing term in the hamiltonian, the network's K should change accordingly. This was used in (Echave 2012) to derive the effect of mutations on normal modes.

Now, for running single-point mutation scans this is fine, but for longer evolutionary trajectories an issue arises: shall we use the updated K to calculate further deformations or just when we want to calculate changes in normal modes and/or entropies?

Thus, there are two possibilties: - Run LFENM simulation and update K only for calculating entropies and/or changes in dynamics (fast) - Run full SC-LFENM simulation, updating K at each step and using updated K to calculate deformations (slow)

Issues

- Rigorously, should I use K_{wt} or K_{mut} to calculate $\delta\mathbf{r}$?
- **reversibility:** Are mutations reversible?
- **path-independence:** Is the result of introducing two successive mutations independent of their order?

Connectivity changes

A problem with any method of self-consistently changing K is that in principle the network topology can change. This may result in relatively large changes in energy because of changes in the total number of contacts...

V_0 changes

Introducing a mutation adds stress to the network. Before recalculating a self-consistent relaxed network, we may want to add to the hamiltonian the δV_0 that results from the mutational stress that cannot be totally relaxed.