**Mail**

Hi Amit,

Thank you for the feedback.

We have taken a closer look at the subject. In the attached PDF we give a detailed explanation of our plan, progress and goals.

Please let us know if you have any questions, ideas or suggestions.

Have a great week,  
Amnon and (O|U)ri

**Introduction**

1. Proteins are composed of multiple chains of amino acids. In nature, and especially during enzymatic reactions, the angles between different chains change, whilst each chain also changes its internal structure. We will assume that each chain is static and that structural transformation occurs only between chains.
2. We will use the method described in <https://www.ncbi.nlm.nih.gov/pubmed/26422261> , which applies optimal virtual bonds between the chains, that will be used as pivots for the movement between the chains.
3. The paper defines the optimal virtual bonds as the most stable bonds, i.e. the bonds which satisfy:

Where and are the indices of the current chains, and are the indices of the current atoms, and are the amount of atoms in chains and respectively, is an array of atom coordinates of a chain in the first conformation, is an array of atom coordinates of a chain in the last conformation.

Hence, for getting the whole protein to be connected with the most stable connections and with minimum number of connections, minimum spanning tree algorithm can be applied (With as edges weights and chains as vertices). The paper treats those virtual bonds as biological bonds, thus their length does not change, and the change in angle appears only in the torsion angles, and (see: <https://en.wikipedia.org/wiki/Molecular_geometry>).

1. Since we would like to add viable physical joints, we would like to add a regularizer for the length of the virtual bonds.

**Project Blueprint**

1. The input is a pdb file containing two structural conformations of the same protein.
2. Process each conformation into a three-dimensional matrix containing the location of atoms of amino acids that the proteins are made of.
3. Calculate edges of a minimum spanning tree and use them as virtual bonds which best describe the protein movement between the two conformations.
4. For each bond, calculate the delta of the torsion angles, and , as angle constraints for the movement of that bond.
5. The output will be the locations of the joints (the virtual bonds) and the constraints on the angles for each joint.
6. Based on the method described in paper "*jointfit*", one can use the output of our implementation to add the locations of the joints and their angles as constraints, in order to fabricate a viable 3D model of the first conformation which can move and to be transformed into the second conformation (PDB files can easily be loaded into a 3D printing software as shown in <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5408980/> or in Maya - <https://clarafi.com/tools/mmaya/>).

**Progress**

Until now we have managed to make a good progress in the first three steps.

In the third step, we used the distance between the atoms in the first conformation as a regularizer. I.e.

For example, for the *AbaA3-DKP-insulin* protein (PDB ID: *2JUV*), the suggested virtual bond can be shown in the attached Gif. Note that although the suggested amino acids are not the closest pair, the distance between them is stable during the movement and only the angles between them seem to change. One can look at the connection between them as a pivot to the movement between the two chains.

We are also planning to try more regularizers.

**Possible Future Work**

* Try other methods of finding virtual bonds, instead of MST. For example, forcing one chain to contain all the bonds (as described in paper).
* Add a validation step for validating that the virtual bonds do not intersect with the protein itself.
* Discard the assumption that the chains are static and take into account the movement inside the chains.