Protein Dynamics Reconstruction

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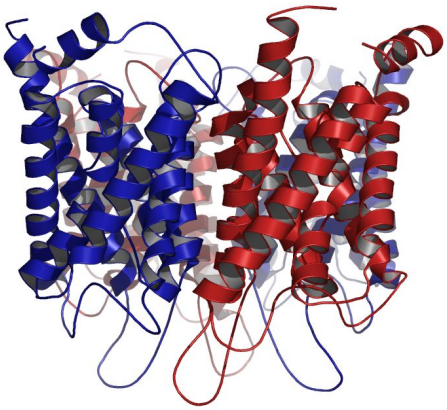
Introduction

Stanford Linear Accelerator Laboratory (SLAC) can generate 3D images of a specific protein, but each at different conformation and orientation (angle of object in image). This reveals static structural information about the protein, but cannot give insight into how the proteins might shift to different conformations over time.



The ultimate goal for our project would be to take these 3D images of a protein create a coherent 3D video describing not only the structure of the protein, but also the dynamics. To working towards this goal, we describe our project milestones below.

Methods

Schwander et al. proposed that protein conformations recovered from a scattering experiments (such as SLAC's) reside on data manifolds with specific symmetries. The properties of these manifolds then can be utilized to deduce the dynamics of the protein.

Our problem is different in nature, since we start working with spatial (X, Y, Z) locations of atoms rather than cryo-EM or raw electron density data. However, we believe that similar dimensionality reduction techniques can be used to yield more insightful data structures that then can be used to determine the sequence of images.

We can start with Schwander et al.'s procedure, by performing isomap and then comparing nearest neighbors in the reduced dimension. We can set a baseline of performance using linear techniques such as PCA and explore other tools such as autoencoders.

Goals & Milestones

Milestone 1: Video reconstruction of a horse galloping from a shuffled version of Eadweard Muybridge's photographs of a horse galloping.

Milestone 2: Create a 3D video of a simple oscillating structure (e.g. torus undergoing torsion) and then randomly sample the video at random time points and orientation. From the random sample we will try to reconstruct the 3D video of the oscillations. We will try to test the limits of reconstruction with the addition of noise and varying the sample rate.

Milestone 3: Sample a molecular dynamic simulation of a small peptide at random time points and orientation and try to reconstructive the protein dynamics. We will try to test the limits of reconstruction with the addition of noise and varying the sample rate. *

Milestone 4: Same as milestone 3, but attempt on a larger protein simulation, such as the G coupled protein receptor (GPCR). GPCR has been subject of extensive molecular dynamics simulations.

Milestone 5: Attempt reconstruction of 3D dynamics of a viral protein, data given from SLAC.

***Note: We expect to get to at least milestone 3.**

We will not use an Android device for this project.

References

[1] Schwander, P., Fung, R., & Ourmazd, A. (2014). Conformations of macromolecules and their complexes from heterogeneous datasets. *Phil. Trans. R. Soc. B*, *369*(1647), 20130567.

[2] Schwander P, Yoon CH, Ourmazd A, Giannakis D. 2012 The symmetries of image formation by scattering. II. Applications. Opt. Express. 20, 12 827 – 12 849. (doi:10.1364/OE.20.012827)

[3] Dashti, Ali, et al. "Trajectories of the ribosome as a Brownian nanomachine."*Proceedings of the National Academy of Sciences* 111.49 (2014): 17492-17497.