

Plan for reproducing key results from “Conservation and Role of Electrostatics in Thymidylate Synthase”

- To reproduce the key results, we'll need computational models of thymidylate synthase from *homo sapiens*, *E. coli*, and W.g.b.
 - For the former two, there are many structures of TS in the PDB. Garg et. al. used PDB ID 1HVY for *homo sapiens* and 2G8O for *E. coli*
 - For the latter, we will use a model from the I-TASSER web server
- Next, we'll align the models with the MultiSeq module in VMD
- We'll then calculate the electrostatic potential with PDB2PQR and APBS
- Finally, we'll visualize the results in VMD
- In interest of time, I will not ask you to do every step. Instead, I will guide you through what I did and ask you to download results from previous calculations.

- Getting structures from the PDB (<https://www.rcsb.org/>) is pretty straightforward.
- For a particular crystal structure, you can just click on “Download Files” and select “PDB format”
- We will use the PDB files for 1HVY and 6NNR, which has superceded 2G8O.
- Next, let’s go through getting a model for W.g.b. thymidylate synthase.

The screenshot displays the RCSB Protein Data Bank (PDB) website. At the top, there is a search bar with the text "Search by PDB ID, author, macromolecule, sequence, or ligands" and a "Go" button. Below the search bar, there are logos for PDB-101, PDB, EMDataResource, and the Worldwide Protein Data Bank Foundation. The main navigation bar includes tabs for "Structure Summary", "3D View", "Annotations", "Sequence", "Sequence Similarity", "Structure Similarity", and "Experiment". The "Structure Summary" tab is selected, showing the entry 1HVY. The entry title is "Human thymidylate synthase complexed with dUMP and dUMP in the closed conformation". The DOI is 10.2210/pdb1HVY/pdb. The classification is TRANSFERASE, the organism is Homo sapiens, and the expression system is Escherichia coli. The deposition date is 2001-01-08 and the release date is 2001-01-31. The deposition author(s) are Phan, J., Koli, S., Minor, W., Dunlap, R.B., Berger, S. The experimental data snapshot shows the method as X-RAY DIFFRACTION, resolution as 1.9 Å, R-Value Free as 0.244, and R-Value Work as 0.201. The wwPDB Validation section shows metrics for Rfree, Clashscore, Ramachandran outliers, Sidechain outliers, and RSRZ outliers. A dropdown menu for "Download Files" is open, showing options like FASTA Sequence, PDB Format, PDB Format (gz), PDBx/mmCIF Format, PDBx/mmCIF Format (gz), PDBML/XML Format (gz), Biological Assembly 1, Biological Assembly 2, Structure Factors (CIF), Structure Factors (CIF - gz), 2fo-fc Map (DSN6), fo-fc Map (DSN6), and Map Coefficients (MTZ format).