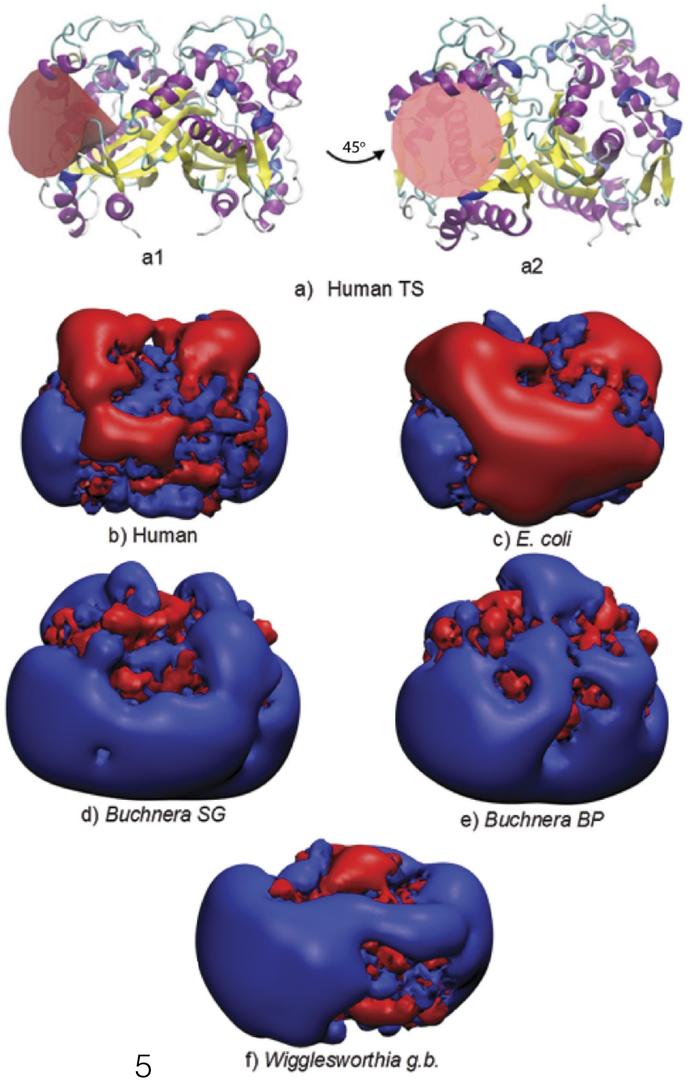
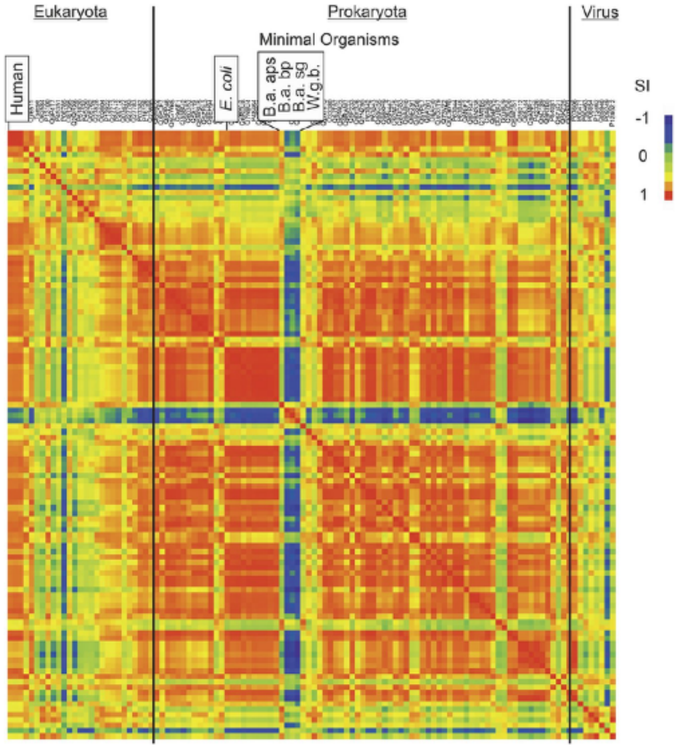
Summary of “Conservation and Role of Electrostatics in Thymidylate Synthase”

- Built 110 homology models
- Calculated and compared electrostatic potential of the enzyme across species
- Found minimal organisms, including Wigglesworthia glossinidias brevipalpis (W.g.b.), to have divergent potential
- Rationalized W.g.b. TS to be functional and unsuccessfully tried to express and purify it
- Mutated E. coli TS to be more like W.g.b. TS and found the enzyme to be less active





Left: Figure 1 of Garg *et al.* (2015) Electrostatic potentials and definition of region for comparative analysis. Above: Figure 2 of Garg *et al.* (2015). Heat map of pairwise similarity index

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.