

Gentile group research projects, summer 2021

If it is safe to do so (COVID), we will be in the lab doing research this summer. If it is not safe to do so, we will be working on different computational aspects of each of these projects remotely

1. ***Mapping antidepressant binding sites on ionotropic glutamate receptor proteins (iGluRs) to understand their mechanism of action.*** Using fluorescence spectroscopy, members of my research group have shown that therapeutics from 3 classes of antidepressants (tricyclic antidepressants, selective serotonin reuptake inhibitors, and selective norepinephrine reuptake inhibitors) bind to an extracellular domain of ionotropic glutamate receptors (iGluRs). Current members of the group are working computationally to determine where these antidepressant binding pockets are on iGluRs so that we can answer the following types of questions: do drugs from the 3 classes all bind to the same protein pocket on iGluRs, is the binding pocket the same for all iGluR family members, and does this binding pocket overlap with that for glutamate and glycine, natural agonists of iGluRs? These computational results will dovetail nicely with future experimental work by providing specific binding interactions to probe in the wet lab.
2. ***Upper division lab development.*** I will be working on the design of an upper division biochemistry lab and welcome the help from interested students.
3. ***Mapping the pregnenolone sulfate (PS) and pregnanolone sulfate (Pregas) binding sites on ionotropic glutamate receptor proteins (iGluRs) to understand regulation of the receptors.*** Glutamate (which binds to iGluRs) is the major excitatory neurotransmitter in the CNS, and its regulation is important in neurodegenerative diseases as well as depression. PS and Pregas are endogenous neurosteroids which bind to different subunits of iGluRs and differentially regulate them.
4. ***Understanding the mechanism by which amyloid precursor protein is transported to neurons by exploring the potential of the cargo binding domain of kinesin motor proteins (the tetratricopeptide repeat of the kinesin light chain) to bind to the amyloid precursor protein.***
5. ***Protein engineering of a spectroscopic probe into malate dehydrogenase (a protein involved in many metabolic pathways, including the citric acid cycle), MDH.*** To better understand the function of MDH, we have to be able to visualize it. In proteins, the prime amino acid that allows for spectroscopic characterization is tryptophan (trp). MDH does not have any trp residues. Our goal is to clone MDH mutants that have specific amino acids mutated to trp. We are currently working on characterizing isoleucine 319 mutated to tryptophan (I319W) and valine 189 mutated to tryptophan (V189W).