mismatch effects on individual M2 homotrimers. Mixtures of lipids with characteristic Lo and Ld states combined with cholesterole are used to study the preferential aggregation of M2 homotrimers in the boundaries of Lo/ Ld segregated phases with preference for the Ld lipid. The coarse grained representation of the protein is tested for selected simulations via backmapping into the atomistic OPLS forcefield, used to check the induced curvature effects of a few systems of interest.

Last, we show how these simulations may be used in order to estimate coverage fractions, i.e. the number of M2 homotrimers required to induce the process of budding at the biological scale.

2363-Pos Board B500
Hydrogen Bond Flexibility and Water Dynamics in the Far Red Fluorescent Protein TagRFP675
Prem Chapagain, Chola K. Regmi, Bernard S. Gerstman.
Physics, Florida International University, Miami, FL, USA.

Next-generation far-red emitting fluorescent proteins (FPs) with enhanced fluorescence quantum yields and high photostability are highly desirable. They would enable deeper tissue penetration and lengthened imaging times given a lower autofluorescence background, lower light scattering, and higher transmission beyond 650 nm. The far-red emitting FP engineered to date is TagRFP675, which has a 77 nm Stokes shift. The red emission of TagRFP675 is attributed to several H-bonding contacts involving Q41 and S28 at the N-acylimine position with additional H-bonds at the phenoxo end of the chromophore with N143, N158, and R197. We used molecular dynamics (MD) simulations to explore the relationship between flexibility of the chromophore environment and the large Stokes shift in TagRFP675 and related variants mKate and its mutant mKate-M41Q. With TagRFP675 and mKate-M41Q have large Stokes shifts compared to mKate. Analysis of the hydrogen bonds around the chromophore reveal that in both TagRFP675 and mKate-M41Q have an extended hydrogen bond network connecting Q106-water-F65-Q41-S28 whereas in mKate, this network does not extend beyond F65. The water molecule involved in the hydrogen bond network shows significantly larger flexibility and mobility in TagRFP675 as compared to mKate-M41Q, highlighting the role of the chromophore environment for large bathochromic shifts.

2364-Pos Board B501
Molecular Dynamics Study of the Biodegradation Process of the Biopolymer Poly (LACTIC)/Poly (VINYL) Scaffold for Bone Tissue Engineering
Samara M. Oña, Ana C. Cadena, Miguel M. Mendez.
Grupo de Quimica Computacional y Teorica USFQ, USFQ, Quito, Ecuador.

The biomaterial chosen for the design of the scaffold is poly (lactic acid) (PLA), this type of polyester together with poly(glycolic) acid (PGA) and Poly(lactic-co-glycolic acid) (PLGA) are widely used in tissue engineering because of their ability to tailor mechanical properties, degradation kinetics and also because its morphology and shape that can be easily manipulated in order to improve osteo-conduction and osteoinduction. It is important to emphasize that this biopolymer can be found as a racemic mixture. In vitro degradation experiments showed that stereochromic composition has an important role on the rate of degradation, concluding that L(-)-PLA degrades much better than D(-)-PLA.

The common process of biodegradation of this type of synthetic polymers is hydrolysis of its ester bonds producing lactic acid. Then this product enters the tricarboxylic acid cycle generating water and carbon dioxide which are non-toxic products present in human body. It is important to highlight that the scaffold degradation process should occur at the same rate of new bone tissue proliferation and the scaffold should keep its mechanical functionality during all the procedure. Previous experiments showed that the width of the biopolymer is directly proportional to the rate of hydrolysis. This is because water molecules can spread quicker throw all the scaffold if it has a wide surface instead of a folded one. Another aspect to consider is the molecular weight and the Young module of the material which determines the degree of elasticity of the bone-scaffold system. Here we report the use of molecular dynamics simulation to estimate several of these parameters from the data generated from these simulations. For instance, we address the solvent accessibility of the polymer and how it changes during the degradation process.

2365-Pos Board B502
A Molecular Dynamics Study on SSRI Antidepressant Drugs
Mohsen Ramezanpour1, Hamed Seyed-Allaei2.
1Department of Biological Sciences, University of Calgary, Calgary, AB, Canada, 2School of Cognitive Science, Institute for Research in Fundamental Sciences (IPM), Tehran, Iran, Islamic Republic of.

Selective serotonin reuptake inhibitors (SSRIs) are a rationally designed class of antidepressants which act via inhibition of the serotonin transporter (SERT), resulting in increased serotonin concentrations in the synaptic cleft. This group of drugs is thought to be selective for SERT rather than norepinephrine and dopamine transporters (respectively NET and DAT).

We used a computational approach to determine the drugs with the highest affinity and selectivity for SERT. We used molecular docking, energy minimization, molecular dynamics simulations and umbrella sampling to estimate the Gibbs binding free energy for each protein-drug complex. Our results qualitatively agree with corresponding experimental data. Among the SSRIs we studied, paroxetine has the highest affinity for SERT and NET, and sertraline for DAT. Our results confirmed the selectivity of this class of drugs for SERT rather than NET and DAT. We found citalopram was the most selective drug for SERT in this class. These results can be used for future studies on designing SSRIs with higher affinity and selectivity.

2366-Pos Board B503
Molecular Dynamics Simulations Helps to Rationalize CopB Mutations and their Relationships to Wilson Disease
Samuel Jayakantana1, Megan M. McEvoy2, Thomas B. Woolf2.
1Physiology, Johns Hopkins University, Baltimore, MD, USA, 2Chemistry & Biochemistry, University of Arizona, Tucson, AZ, USA.

The regulation of copper levels is central to physiology. Mutations in the ATP7B copper transporter are known to lead to Wilson's disease in humans. How these mutations lead to the disease is not fully characterized at a molecular level. An excellent model system for exploring the changes in structure and dynamics for Wilson disease mutations for the ATP binding domain is provided by CopB from A. fulgidus. This domain has high sequence similarity with the P- and N-domains and hinge regions of ATP7B. Mutations to each region have previously been characterized by in vitro experimental measurements such as ATPase assays and intrinsic tryptophan fluorescence. In this presentation we highlight a net ~5 µs of implicit and explicit solvent simulations conducted on the National supercomputer resource XSEDE (Stampede, Kraken, Keene- land and Lonestar) of the CopB wild-type and 13 Wilsons disease mutations found across each of these three regions. Solvent accessible surface area measurements, H-bonds analysis and schlenz entropy calculations showed that the mutations induced changes in the dynamics of the Closed conformations of CopB with respect to the Open structure revealing conformational transitions at different rates about the hinge region. While the mutations in the P and N-domains caused mild to moderate deviations with respect to the WT, the mutations in the Hinge region caused significant deviations. The results shed new light on how the disease mutations impact on conformational change, on ATP-binding, and on phosphorylation within these domains.

2367-Pos Board B504
Molecular Understanding of the Binding of Macrolide Antibiotics to the Ribosome using Site-Identification via Ligand Competitive Saturation Meagan C. Small1, Sirish Kaushik Lakkaraju1, E. Prabhu Raman1, Rodrigo B. Andrade2, Alexander D. MacKerell, Jr.1.
1Department of Pharmaceutical Sciences, University of Maryland, Baltimore, Baltimore, MD, USA, 2Department of Chemistry, Temple University, Philadelphia, PA, USA.

Microbial resistance is a major challenge in antibiotic development. Newer generation macrolide antibiotics avoid efflux and drug metabolism-based resistance mechanisms, yet ultimately succumb to resistance due to modification of their target, the 50S subunit of the ribosome. Site-Identification via Ligand Competitive Saturation (SILCS) harnesses the power of force field-based simulations to map the functional group affinities of a protein or any other macromolecule and has demonstrated its ability to identify classes of protein-ligand interactions that are observed in crystal structures. Recently, the use of Grand Canonical Monte Carlo/MD (GCMC- MD) simulations for SILCS has shown that multiple molecules inserted into an occluded binding pocket yield satisfactory overlap with known crystallographic ligands. Hence, the SILCS GCMC-MD method has been applied to the macrolide binding pocket of the E. coli 50S ribosomal subunit. Simulations were performed using the small molecules benzene, propane, formamide, acetaldehyde, acetate, methyloxonium, imidazole, and methanol. From these simulations, 3D probability maps for the fragment types (FragMaps) were calculated. Comparison of the FragMaps with the binding modes of known crystallographic macrolide antibiotics showed good agreement, especially the overlap of aromatic fragment maps presumably due to the hydrophobic nature of macrolide antibiotics. Notable is the ability of the FragMaps to capture the flexibility of telithromycin’s alkyl-aryl chain (ARM) from various crystal structures. Future extensions of the SILCS methodology to the ribosome will focus on addressing A2058-based modifications for drug design.