Team DRINK: Examining the binding mechanism and public health implications of alcohol consumption and poisoning

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Overarching Research Question: How does alcohol impact college students physiologically, socially, and emotionally?

Alcohol is a commonly abused drug, especially in the United States, with over 2,000 deaths from alcohol poisoning a year (CDC). Alcohol poisoning, which is defined as excessive alcohol diffusion into the brain, results in a BAC level of 0.25-0.4% (NIAA, 2019). Social binge drinking is highly prevalent in college campuses, and binge drinking may lead to alcohol poisoning. In this condition, ethanol molecules diffuse through the blood brain barrier (BBB) and bind to extrasynaptic gamma aminobutyric acid type A (GABA-AR) receptors (Abrahao et al., 2017). This causes neuronal inhibition, leading to nausea, breathing difficulties, and potential death. However, the specific mechanism by which this binding occurs is unknown. To analyze both the biological and social impact of this issue, our team is divided into two subteams: computational modeling and public health.

Computational Modeling

The computational subteam aims to examine the binding of ethanol to the GABA-AR receptor through a molecular dynamics approach, which uses Newton's Laws of Motion to model the movements of atoms and molecules through time. We used a coarse-grain model, which simplifies individual atoms into groups of atoms.

Methodology

(1) Performed a literature review to determine the lipid composition of a neuronal cell membrane (2) Constructed lipid bilayer using CHARMM-GUI's martini builder to specify lipid ratios (3) Ran minimization steps and final molecular dynamics simulation product run for lipid bilayer (4) Performed bilayer analysis looking at properties such as lipid aggregation (5) Visualized protein (PDB ID: 6I53) in VMD and used PyMOL to fix missing regions and remove unnecessary ones from protein (6) Currently working on inserting protein into lipid bilayer

Figure 1. Lipid ratios within bilayer

Lipid	Outer Layer (#)	Inner Layer (#)
DPPC	268	72
DPPE	240	228
DPPI	0	24
DPPS	0	228
DPPA	0	60
CHOL	288	144

Figure 2. Graph of example bilayer analysis of cholesterol aggregation. No aggregation was found, which aligns with previous work.
Figure 3. Visual Molecular Dynamic simulation of lipid bilayer
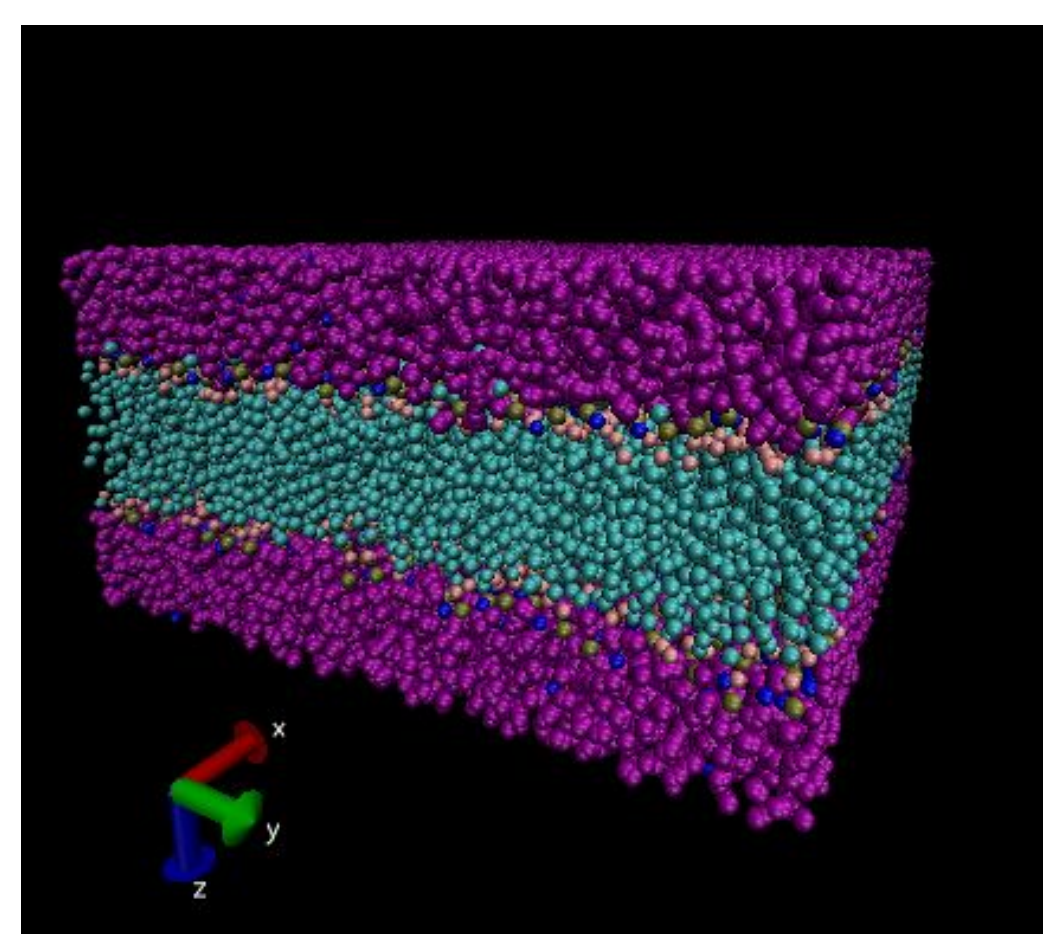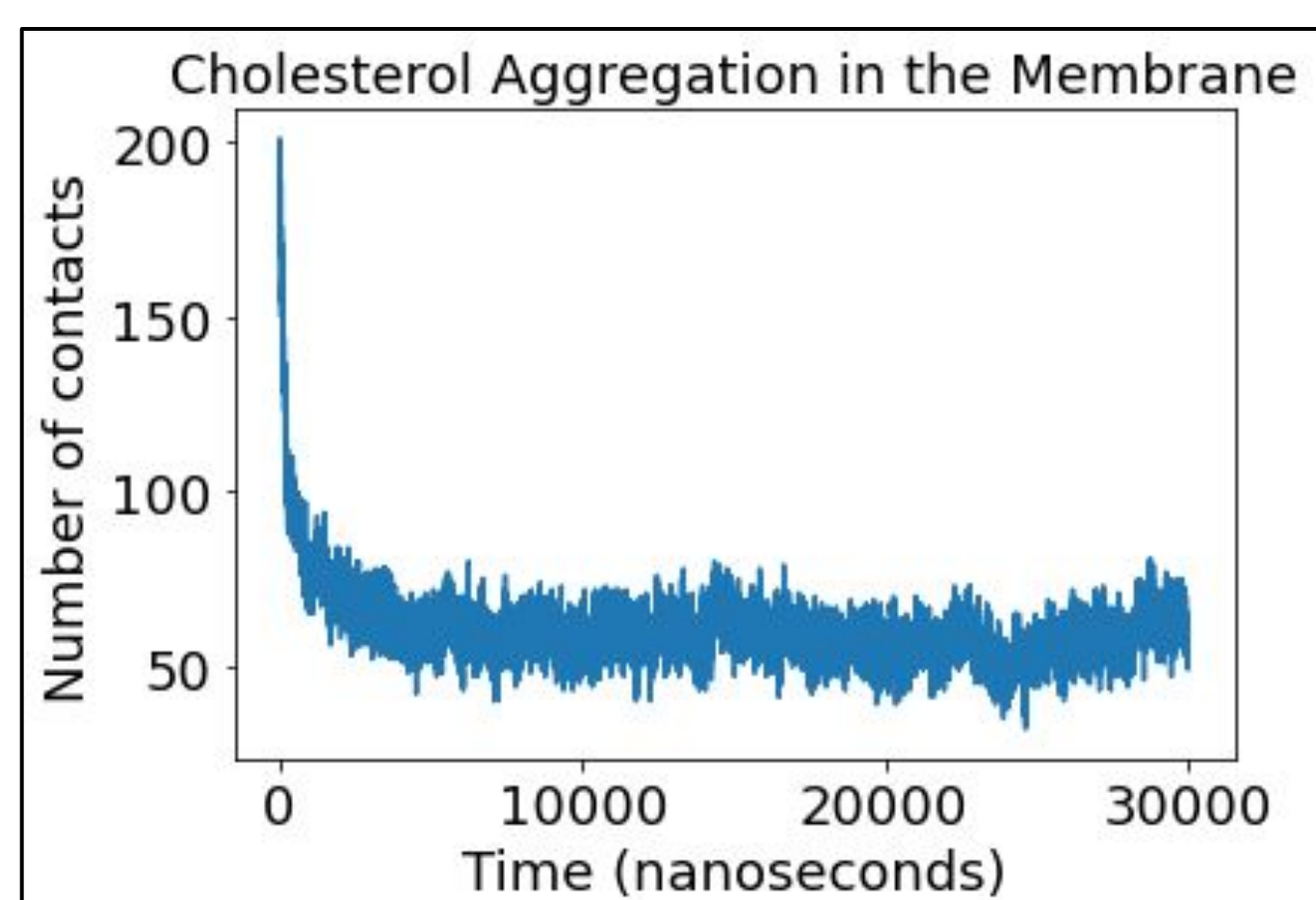
Future Research Goals

- Complete protein insertion and run simulation with complete parameters
- Conduct root mean square deviation (RMSD) and the root mean square fluctuation (RMSF) to study protein configuration and tilt in membrane
- Add ethanol concentration closely mimicking a state of alcohol poisoning to simulation box

Public Health

The public health subteam's focus is on how this issue impacts UMD's campus to better understand the impacts of alcohol consumption on college students.

Methodology

- An anonymous survey asking UMD students about their alcohol consumption habits and knowledge of alcohol poisoning and other drinking related behaviors and consequences was created (see Figures 1-3)
- IRB approval was obtained to distribute the survey to UMD students
- The survey is currently being disseminated through social media and flyers around campus and has received 147 responses as of 3/25/2022
- Statistical analysis and data visualization will be completed upon collection of 500 survey responses
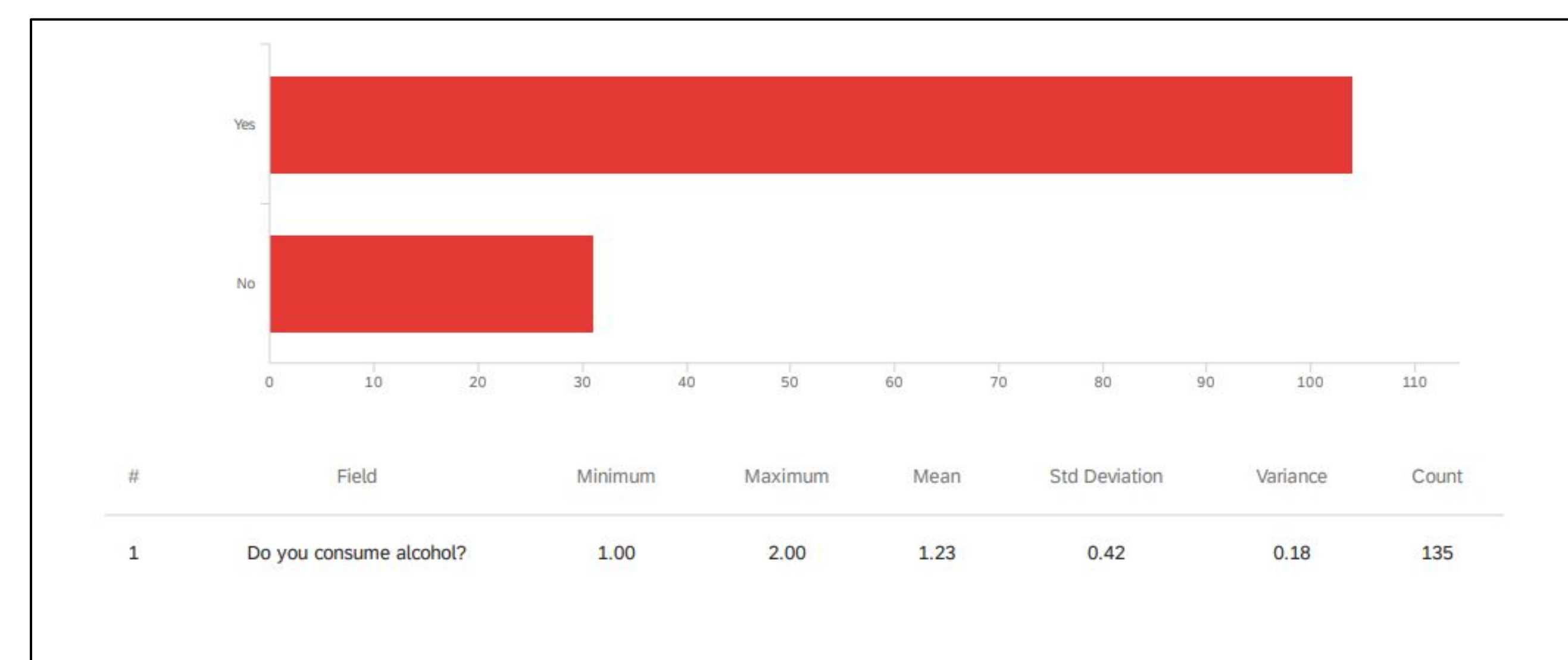- Participants will be rewarded through a raffle

Figure 4. Preliminary Data from Public Health Survey as of March 12, 2022 Figure 3 poses the question "Do you consume alcohol?" which 77% of respondents said yes to. This indicates that a large portion of the sample consumes alcohol, which may help provide insight into how alcohol impacts UMD students.

Question 7: Do you consume alcohol?

#	Field	Minimum	Maximum	Mean	Std Deviation	Variance	Count
1	Do you consume alcohol?	1.00	2.00	1.23	0.42	0.18	135

Future Research Goals

- Statistically analyze data by coding responses for high/low alcohol use/exposure
- Draw conclusions about the trends represented by the data

References