Interview Assessment #2

Student Name: Aiswharyaa Lalgudi Nagarajan

Name of Professional: Kris Dammen-Brower and Sam Schulte

Profession/Title: Phd Candidate (currently working on dissertation)/ Senior in College

Business/Company name: Dr. Kevin Yarema's Lab at JHU/Michigan State University

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Through my interview with Sam Schulte and Kriss Dammenbrower, I learned how computational tools are used to analyze protein structure and protein–protein interactions in modern drug design. A significant takeaway was the importance of having accurate protein structures before attempting any modeling or docking work. Experimentally solved structures are stored in the Protein Data Bank (PDB), which serves as a foundational resource for structural biology. However, when experimental structures are unavailable, predictive tools such as AlphaFold3 can be used to generate highly accurate structural models.

I also learned that post-translational modifications, particularly glycosylation, play a critical role in protein function and binding. Not all NxS/T motifs are glycosylated, and tools like NetNGlyc can predict whether newly introduced glycosylation sites are likely to be modified. Additionally, I gained an understanding of protein–protein docking tools such as ClusPro and HADDOCK, which can simulate how two proteins bind and provide scores, binding poses, and interface residue data. These methods allow researchers to compare wild-type proteins to engineered variants and evaluate how mutations affect binding affinity and interaction behavior.

This information is directly relevant to my learning and my ISM journey within RVG's AI-powered drug design focus. My project focuses on understanding how molecular changes can influence protein behavior, particularly in therapeutic contexts. Knowing how to locate or predict

protein structures enables me to work independently with real biological data rather than relying on simplified models. The discussion about glycosylation is particularly applicable because engineered glycovariants can significantly alter protein stability, immune recognition, and receptor binding. Learning to use predictive tools like NetNGlyc allows me to evaluate whether a proposed mutation is biologically plausible before investing time in downstream analysis. Docking tools such as ClusPro and HADDOCK provide a practical workflow for testing hypotheses by comparing wild-type proteins with modified versions and observing changes in docking scores and binding interfaces.

The information from the interview can be broken down into three major components: structural modeling, modification prediction, and interaction analysis. Structural modeling includes accessing experimentally solved data from the PDB or using AlphaFold3 when data is missing. Modification prediction focuses on determining whether changes such as glycosylation are likely to occur and affect function. Interaction analysis involves docking simulations that evaluate how proteins bind to receptors. Each tool serves a specific purpose, but also connects to the others. Accurate structure prediction enables reliable docking, while understanding glycosylation helps explain why specific binding interactions may improve or weaken. Compared to my previous knowledge, which was conceptual primarily, this interview shifted my understanding toward a more workflow-based approach. Instead of viewing protein interactions as static diagrams, I now see them as testable, variable systems influenced by structure, chemistry, and computational modeling.

Using this new knowledge, I can plan a clear experimental strategy for my project. First, I would identify the wild-type protein structure using the PDB or AlphaFold3. Next, I would introduce

glycosylation variants and evaluate their likelihood using NetNGlyc. Then, I would perform docking simulations between the protein and its receptor using ClusPro and HADDOCK, comparing results across variants. Blending this information with my previous understanding of biology and AI allows me to form a more integrated research approach. I am now interested in exploring how different docking tools compare in terms of scoring reliability, and how glycan-structure visualization tools like GlycoShape might further inform binding analysis. This interview also raised new questions about how molecular dynamics simulations could complement docking results in future projects.

Overall, the knowledge gained from this interview was efficient in helping me move toward my goals. It was motivating and encouraging to see how advanced computational tools are actively used by researchers and students working at a high level. The advice to test multiple docking platforms and compare outputs was especially valuable, as it emphasized scientific rigor rather than relying on a single result. I found the discussion both challenging and inspiring, as it highlighted the complexity of protein interactions while also showing that these problems are approachable with the right tools and methodology. This interview strengthened my confidence in pursuing computational drug design and confirmed that this field aligns well with my interests and long-term academic goals.