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Biophysical Society 2025 Annual Meeting Summary

The Biophysical Society 2025 Annual Meeting was a conference packed with knowledge from all areas of molecular biology research. The first day of the conference started with a session on transmembrane protein molecular biology. The most important talk in this session was by a woman named Dr. Bianca Moise from Ohio State University. She presented on a mutation in the cardiac sodium ion channel (my main protein of study) that leads to Brugada syndrome. Other important talks from this day were a scientist from UC Irvine who was studying the effects of Native American medicines on the potassium ion channel. The specific compounds he tested affected the voltage sensing ability of the potassium ion channel. Since the voltage dependence of ion channels are a focus of my lab's research, I pointed this compound out to one of my colleagues working on small molecule effects on the sodium ion channel.

The following day, I spent the morning going to talks about modeling lipid interactions with proteins, an area of research my lab is moving towards. In these talks, I learned about new ways to model protein lipid interactions and how specific lipid molecules affect proteins. Later that day, I had my poster presentation on three C-terminal domain interactions that we observed in our model of the cardiac sodium ion channel. Dr. Johnson would go find his collaborators and bring them to my poster, so I had the opportunity to talk to some big names in the field. I saw that my poster was near Dr. Moise's poster, whose talk I saw the day before. I talked to her about her research and pointed her to our modeling work, which she seemed interested in. I gave her name to Dr. Johnson as a reviewer for our upcoming papers. I found two other reviewers at my poster (one was a modeler; the other was an ion channel scientist).

On day three, I started the morning with sessions on protein-small molecule interactions. I heard an interesting talk by a Ph.D. student at UC Davis named Kyle Rouen. He was using a program called SILCSBio to create energy maps of proteins for small molecule design. I gave my colleague working on our small molecule research the name of this program, so he could design small molecules to test specific ion channel mechanisms. At the poster sessions this day, I walked through the cardiac ion channel section and wrote down about five mutations and their physiological effects to test in our modeling research.

The fourth day was the most productive day. I began the morning at a talk about sodium/proton exchangers, which provided interesting insights into cytosolic control of sodium ion channels, specifically the control of the voltage dependence of ion channels by the cytosol. At the poster session this day, I spent most of my time talking to modeling people and finding new tools for me to use in analyzing our structures.

The fifth day was only a half day. I went to the poster sessions in the morning and talked to some sodium ion channel scientists about their work, but I did not find much information to use in my research. Once the conference concluded, my lab decided to get away from science in the afternoon and took a bus tour around Hollywood. This was relaxing until our bus broke down in Beverly Hills, which was not too bad because we were able to explore the area until they got the bus to work again.

Overall, the conference was tremendously beneficial to me. I met about twenty scientists through the wide array of networking opportunities available. Additionally, I was able to find tons of new concepts to use in my research, most of which I would never have known to look for on my own. What I learned from this conference is going to push my research much further than it would have gone otherwise and the connections I made will help my accelerate my research career in the upcoming years.

Day 1

Mechanical Activation of OSCA/TMEM63 Channels Opens a Lipid Lined Pore that can Scramble Lipids – Ben Corry (Australian National University) – Used AlphaFold2 to predict the binding conformation of two different proteins. It would be interesting to see if we can do this with accessory proteins and our all-atom models, but I am not sure how reliable AlphaFold2 is.

Pisiferic Acid Ligand-Gates the Kv1.1 Potassium Channel to Correct Episodic Ataxia Type 1 – Rian Manville (University of California Irvine) – Pisiferic acid originated from an herbal medicine used by Native Americans. He found that the small molecule binding in the voltage sensing regions of Kv1.1. It could be interesting for Randy to try and dock it in the voltage sensing regions of NaV and CaV. Eventually, if we are able to put a potential across the membrane or capture channels in an open state, docking this small molecule could highlight voltage sensor mechanisms. Paper – Manville et al. 2025

I didn't get all of this guy's information and it was not on the BPS 2025 program. He was the second to last guy in the membrane transporters talk. He used Chai 1 and AlphaFold3 to model ligands and post translational modifications. This could be an interesting method to try docking with. I am not sure how reliable it is.

Day 2

Interplay Between Lipids and Ligand Activation in STHK Channels – Philipp A.M. Schmidpeter (UT San Antonio) – Charge of lipid head group affects voltage gated ion channels. This doesn't seem too important for our work, but it is interesting to keep in mind when we start focusing on conduction.

Allosteric Modulation of ELIC by POPG and POPE; Distinguishing Overlapping Phospholipid Binding Modes Using SAFEP – Ezry Santiago-McRae (Rutgers University) – Slowly turned off interaction between the lipid ligand and the protein to determine the delta G between the bound and unbound state. Using the delta G, he determined binding probability of the ligand. I am not sure how developed this method is, but it could be useful for Randy's small molecule project. Here is the link to the methods https://livecomsjournal.org/index.php/livecoms/article/view/v5i1e2067.

Combining CHARMM36M and OPC to Improve Accuracy – Nicolai Kozlowski (Max Planck-Germany) – Found that CHARMM36M used with OPC was an accurate method for modeling coiled regions of protein. If we ever decide to put a charge on the lipid membrane, CHARMM would be the best system to do that, so having the knowledge the OPC is compatible is useful.

A De Novo Designed Miniprotein Prevents Ca Feedback of CaV1 Channels – Marc Yehya (Columbia University)– Mentioned that CaV1.2 had an IQ motif, which could be an area of interest for the CaV1.2 projects.

Characterizing CCO-TX3 Toxin Binding Site in NaV1.5 Channel – Wendy Gonzalez (University of Talca) – Found that TX3 toxin only affects NaV1.5. When we get Randy's docking project working, it would be interesting to try to dock this molecule onto our isoforms and see if there are any major differences in docking.

Posters

- Michael Green (CCNY) – Potassium channel guy who seemed knowledgeable on all things ion channel, could be a potential reviewer.
- Soumya Dutta (Arizona State University) - Had a brief talk with him. He was a modeling guy for the TRP channel. He was the guy you discussed our GPU capabilities with. Could be a nice reviewer for our modeling papers.
- Eduardo Guadarrama (Northwestern) – Gave me the idea to compare our defined cytosolic regions to areas that lack resolution in CryoEM structures.

Day 3

Disrupting Resistance: A Novel Inhibitor Targeting Antimicrobial Efflux – Tania Szal (Fraunhofer ITMP) – Used an in silico repurposing screen, which uses molecular dynamics simulations to find effective small molecules for eliciting desired channel responses. It would be nice to keep this method at the back of our minds for futures small molecule work.

Comparative Molecular Modeling and Simulations of Beta-Adrenergic Receptor-Drug Interactions – Kyle Rouen (UC Davis) – Used a program called SILCSBio to find 3D free energy maps to aid in small molecule design. This would also be good further down the line if we wanted to make small molecules to test specific ion channel functions in silico.

Unexpected Nanostructural Remodeling in Hearts of Mice with a Loss-of-function Defect in the NaV1.5 Sodium Channel – Bianca Ioana Moise (Ohio State University) – This is the lady we heart on the first day talk about the DEKA to DEEA mutation in NaV1.5, leading to Brugada Syndrome. It may make a nice discussion piece to look at the K in DEKA and see if we can determine what its purpose is to select only for sodium. Sara also mentioned to me that a poster she saw for another sodium ion channel had a selectivity filter lysine mutation to a different residue, leading to potassium conduction to the pore. The lysine seems to play an important role in sodium selectivity.

Posters

- RyR2-V2475F Mutation in Rabbit Alters on Cardiomyocyte Electrophysiology – Garance E. Gerard (Paris Saclay University, University of Wisconsin) – This mutation would be interesting to look at when we make the RyR2 model.
- Enhanced Molecular Visualization Dynamics and Structural Analysis Tools for Biomolecular Studies with VMD 2 – Diego Gomes (Auburn University) – He is a developer at VMD. VMD2 releases in 2025 with new features and GUI.

Day 4

Hydrophobic Gating of Ion Channels – Jianhan Chen (UMass Amherst) – Used modeling to suggest that potassium channels gate by desolvating the pore, which prevents potassium ion flow. I am speculative of this concept since I am not sure how the channel can remove all water except by displacing it with an activation gate, which would mean that the loss of conductance is due to gating rather than a lack of solvation. Nevertheless, we can look at pore solvation near the activation gate of NaV and CaV in our models and see if we find anything interesting.

Developmental Encephalopathy-Associated Mutations Cause Constitutive Opening of the Kv7.2 Channel Inner Pore Gate – Agnese Roscioni (Polytechnic University of Marche) – Also suggested desolvation theory of potassium channel gating.

Lipid and Voltage Regulation of Na/H Exchangers – Dravid Drew (Stockholm University) – This was surprisingly interesting talk. He compared the voltage sensors to the Na/H exchanger to the NaV1.7 voltage sensors. The Na/H Exchangers S4 voltage sensing helices moved upwards and curved slightly to the channel, which matches closely with our theory of S4 helix movement in NaVs. Additionally, the Na/H exchanger is regulated by a cytosolic accessory protein that holds the bottom part of the S4 helix, keeping the helix from moving up. This is interesting because the N639D and N639TP mutations for CaV1.2 seem like they have a similar situation since they form a salt bridge with a cytosolic lysine.

Posters

- Molecular Dynamics Trajectory Analysis for Permeation (MDTAP) – Suthri Sundaresan (Indian Institute of Technology Hyderabad) – Created a tool for determining if an ion conducted through the pore. Her work is under review, but I scanned her barcode to keep track of when she publishes. This would be a great tool for analyzing whether ion conduct through our channels or not.
- At the Crossroads of Disease and Treatments: Targeting NaV Channels for Both Breast Cancer and Chronic Pain Therapy – Khoa Ngo (UC Davis) – Studies isoform differences with tarantula and scorpion toxins on NaV isoforms. Used a program called RosettaDock which performs both low and high resolution docking depending on how many small molecules one wants to dock.
- A CACNA1C Variant Associated with Cardiac Arrythmias Provides Mechanistic Insights in the Calmodulation of L-Type Ca Channels – Juan Zhao (Montreal Heart Institute) – She studied the effects of calmodulin on the G419R mutation (a variant of Timothy Syndrome). I tried to get some speculation out of her about what she through was occurring structurally to the protein due to the mutation, but she didn't have good English and didn't understand my question. Her work is published under the same title and author as the poster. I am going to give this to Caden for him to review.

Day 5

Molecular Simulations of State-Specific Drug Interactions with NaV1.5, CaV1.2, and HERG Channels for in silico Predictions of Drug-Induced Arrhythmogenesis - Kyle Rouen (UC Davis) – Did docking of common functional groups to form affinity maps of functional groups on ion channels, we could use this to create an affinity map of the cytosolic regions. He used SILCS to do this. This program would be useful further down the line in our small molecule studies.

Posters

- Functional Role of Positive Charges on the Extracellular Side of S4 in HCN Channels – Kaei Ryu (Jichi Medical University) - S4 forms salt bridges with S5 and S2 near the extracellular portion of HCN channels. Analogs for these residues in our NaV channels may be interesting to look at.

- Structural Insights into RyR1 Variant T4709M Linked to Congenital Myopathy – Gunnar Weninger (Columbia University) – RyR1 T4709M mutation linked to congenital myopathy. An analog of this mutation may be interesting to make in our future RyR2 model.
- MemPro: Membrane Protein Orientation in Lipid Bilayers – Matyas Parrag (University of Warwick) – Used MemPro to place transmembrane proteins in a membrane. We could compare the results of this program to PPM2.0 and our model to determine if it will be useful for channel placement in the membrane in the future.
- Structural and Functional Investigation of Ryanodine Receptor 1 with Endogenous Ligands and Drugs – Kookjoo Kim (Columbia University) – Cavitracker uses algorithms modified from MOLE2 to define cavities in proteins. This is compatible with the ProDy program, but all of our .nc files would have to be adapted to fit ProDy formats.
- Structural Insights into Amyloid-Beta Oligomers and their Impact on Membrane Integrity Using AlphaFold and Molecular Dynamics Simulations – Yiru Qian (University of Chicago) – Healthy neurons have 18.1% cholesterol content. She also found helix position in the membrane by finding the average position of the lipid head group across her simulations and compared helix positions to this value.