Zentrum Physiologie

Medizinische Hochschule Hannover

Invitation

to the Physiology Seminar

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An auto-mechanics approach to dissecting and understanding ion-channel regulation

Voltage-gated ion channels (NaVs and CaVs) are complex macromolecular proteins that generate the upstroke of an action potential in excitable cells. Appropriate function is necessary for many physiological processes such as a heartbeat (NaV1.5 and CaV1.2), voluntary muscle contraction (NaV1.4), nerve conduction and neurological function (NaV1.2 and NaV1.6). Dysfunction can have debilitating and/or life-threatening consequences. Mechanistic understanding of the allosteric communication between cytosolic portions of these channels and amino acids that govern ion conduction are lacking and areas of significant interest. During the past decade, there have been several advancements with ion channel structural characterization by CryoEM; yet descriptions of extracellular and cytosolic components are often lacking. Many investigations have characterized the biophysics of reconstituted component interactions, however, extrapolating the structural alterations and allosteric communication within a full-length intact ion channel can be challenging. To address this, my group has developed a series of all-atom, all residue models of human ion channels (NaVs and CaVs) in lipid bilayers with explicit salt and water. Leveraging the latest advancements of the AMBER force field (ff19sb and Lipid21) and water model (OPC), our simulations contain descriptions of cytosolic components that are poorly predicted by AlphaFold and lacking in many CryoEM structures. Our simulations improved prediction of protein backbone torsion angles and consider structural details across time (four independent one microsecond simulations for each model). With these predictions we have designed solution NMR experiments to interrogate the assembly of these interactions and explain calcium regulation of channel function. I will share our latest preliminary data and current approaches aimed at generating in silico membrane potentials, as well as discuss our hypothesis of amphipathic lipid surfing as a mechanism of channel regulation and/or ion channel endocytosis. Lastly, I will highlight our recent advancements with characterizing downstream consequences of modified channel function, with consideration for changes in cellular energetics as well as discuss a plant molecule that can resynchronize intracellular calcium release.

Date: **Tuesday, 31st of March 2026**

Place: **Lecture Hall G**

Building: I01-01-1130

Scheduled at: **15 Uhr c.t.**

Guests are welcome!

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