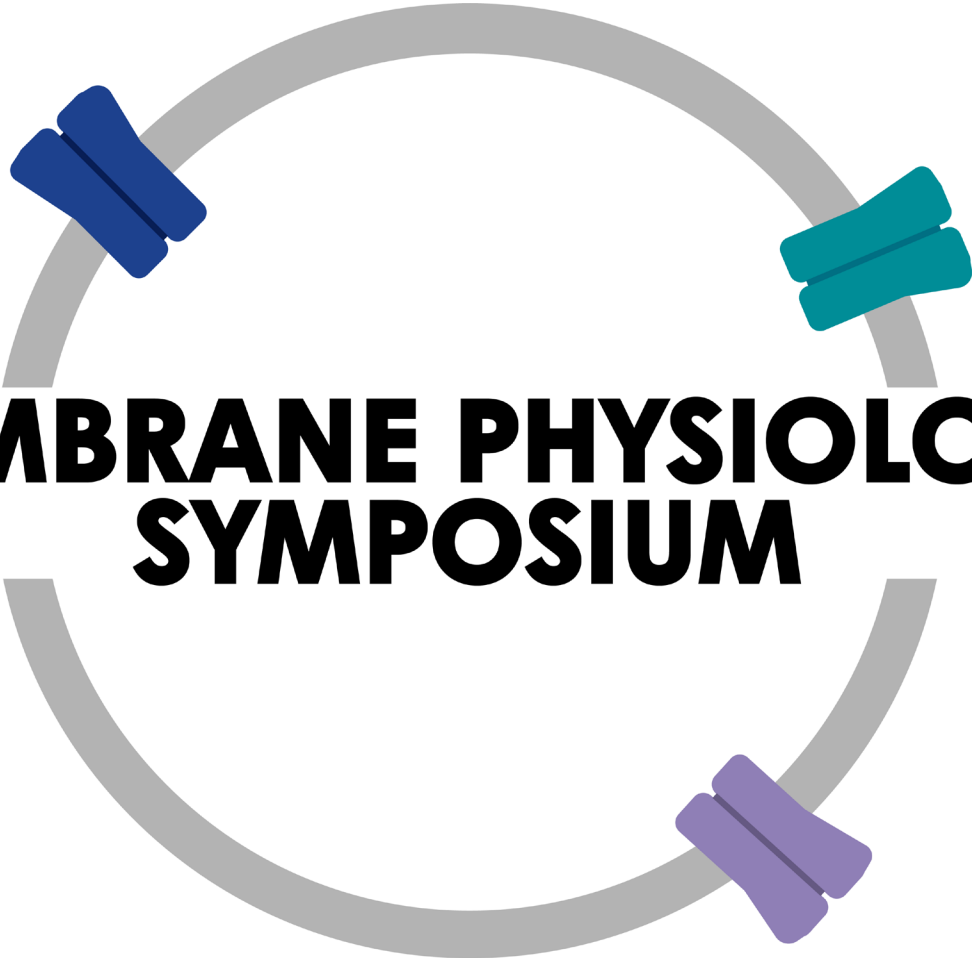




MEMBRANE PHYSIOLOGY SYMPOSIUM

Welcome to MPS

Napa Valley, California



MPS 2026 Schedule

Napa California,
April 14th - 15th

Tuesday, April 14th

8:00 - 9:00 am

Arrival, Breakfast, & Poster Set Up

9:00 - 9:15 am

**Dr. Niels Fertig - Nanion CEO, and
Wyatt Hall - Vice President of Sales**

Welcome Introduction

Keynote - 9:15 - 10:00 am

Dr. Ardem Patapoutian - Scripps Research

May the Force be with you! Piezo channels in
Mechanosensory Biology

10:00 - 10:30 am

Dr. Joseph C. Wu - Stanford Medicine

Stem Cells, Genomics, and AI for Drug Discovery

10:30 - 11:00 am

Dr. Tom Claydon - Simon Fraser University

Targeted Rescue of hERG Channel Variants Associated with
Long QT Syndrome.

11:00 am - 11:45 am

Networking Session & Morning Break

11:45 am - 12:00 pm

Dr. Francesca Puppo - MaxWell Biosystems

Advancing Functional Characterization of In-Vitro Neural
Models with Next Gene

12:00 - 12:30 pm

Dr. Ed Twomey - Johns Hopkins University

Structural and Molecular Basis for Ligand-gating in Delta-Type
Glutamate Receptors

12:30 - 1:00 pm

Dr. Jun Chen - Genentech

Subtype-Selective Modulation of HCN1 Channels

1:00 - 2:30 pm

Lunch Break & Networking Session

2:30 - 2:45 pm

Marine Moutia - Oria Labs

Unlocking Intracellular Targets: Native Organelle
Electrophysiology for Drug Discovery

2:45 - 3:15 pm

Dr. Yamuna Krishnan - University of Chicago

Exploring the Insides of the Insides of Our Insides

3:15 - 3:45 pm

Dr. Howard Young - University of Alberta

Conformation-dependent Regulation of the SERCA Calcium
Pump by Small Transmembrane Peptides

3:45 - 4:30 pm

Afternoon Break - Dedicated Poster Sessions

4:30 - 5:00 pm

Dr. Jeffrey Noebels - Baylor College of Medicine

Elucidating Downstream Effectors of mTOR Signaling Drive
Hyperexcitability

5:00 - 5:15 pm

Michael George - Nanion Technologies

From Automation to Interaction: Rethinking Patch Clamp
Workflows

6:30 - 9:00 pm

Dinner Hosted by Nanion Technologies

Wednesday, April 15th

8:00 - 9:00 am

Arrival, Breakfast, & Networking Session

Keynote - 9:00 - 9:45 am

Dr. Lori L. Isom - Michigan Neuroscience Institute

Developing Gene Modifying Therapies for Dravet Syndrome

9:45 - 10:15 am

Dr. Sagardip Majumder - Baker Lab - Washington

Engineering Life's Gatekeepers: De Novo Design of Membrane
Pores and Ion Channels

10:15 - 10:45 am

Dr. Ivy Dick - University of Maryland

Voltage gated Calcium Channel Dysregulation in
Calmodulinopathies

10:45 - 11:30 am

Networking Session & Morning Break

11:30 am - 12:00 pm

Dr. Matthew Coleman - Lawrence Livermore

Bilayer Systems for De Novo Cell-Free Synthesis and Validation of
Diverse Ion Channels.

12:00 - 12:30 pm

Dr. Jorge Contreras - University of California Davis

When Cardiac Connexin43 Is Remodeled, Stress Can Be Deadly

12:30 - 1:00 pm

Dr. Mauricio Lillo Gallardo - Rutgers University

When Redox Meets Electricity: GC1 and Connexin Coordinate
Endothelial Communication and Arterial Tone

1:00 - 2:15 pm

Networking Session & Lunch

2:15 - 2:45 pm

Dr. Lisa Ellerby - Buck Institute

CD38 Inhibition Delays Age-Related Cognitive Decline via a Cho-
roid Plexus-Cerebrospinal Fluid-Hippocampus Axis

2:45 - 3:15 pm

Dr. David K. Jones - University of Michigan

Mechanisms Regulating hERG1NP Physiology and
Pathophysiology

3:15 - 4:00 pm

Afternoon Break - Dedicated Poster Sessions

4:00 - 4:30 pm

Dr. Franck Kalume - Seattle Children's

Solving the Molecular Logistics of SCN1A Delivery: A Key to Inter-
neuron-specific AAV-based Gene Replacement Therapy in Dravet
Syndrome

4:30 - 5:00 pm

Dr. John Lueck - University of Rochester

Development of ACE-tRNA Therapeutics for
Nonsense-associated Diseases

5:00 - 5:30 pm

Exhibitor Booth Breakdown

5:15 - 6:45 pm

Wine Tasting - Wine Cave



April 14th

8:45 - 11:45 am



Keynote

Dr. Ardem Patapoutian

Scripps Research

May the Force be with you! Piezo Channels in Mechanosensory Biology

Mechanotransduction was perhaps the last major sensory modality not understood at the molecular level. Proteins/ion channels that sense mechanical force are postulated to play critical roles in sensing touch/pain (somatosensation), sound (hearing), shear stress (cardiovascular function), etc.; however, the identity of ion channels involved in sensing mechanical force had remained elusive. The Patapoutian lab identified PIEZO1 and PIEZO2, mechanically activated cation channels that are expressed in many mechanosensitive cell types. Genetic studies established that PIEZO2 is the principal mechanical transducer for touch, proprioception, baroreception, bladder, and lung stretch, and that PIEZO1 mediates blood-flow sensing, which impacts vascular development and iron homeostasis. Clinical investigations have confirmed the importance of these channels in human physiology. Current work in Patapoutian continues to explore the role of mechanosensation and interoception in physiology and disease.

Dr. Joseph C. Wu

Stanford Medicine

Stem Cells, Genomics, and AI for Drug Discovery

Drug discovery and development continue to face significant challenges, with over 90% of candidate drugs failing in clinical trials. These efficacy failures are primarily due to inherent species-specific differences, fundamental biological variances between model organisms and humans, and the limitations of existing models to accurately reflect the complexity of human disease and treatment responses. In this discussion, I will explore how the NIH and FDA are advocating for new alternative methodologies (NAMs) to reduce or replace animal testing. I will highlight recent advancements in technologies such as stem cells, organoids, and microphysiological systems (MPS), along with the roles of clinical genomics and AI/ML. Additionally, I will examine how these platforms can collaboratively enhance our understanding of rare orphan diseases, facilitate drug discovery, support precision medicine, and enable clinical trials in a dish (CTiD).



Dr. Tom Claydon

Simon Fraser University

Targeted Rescue of hERG Channel Variants Associated with Long QT Syndrome

Long QT syndrome (LQTS) is a cardiac electrical disorder wherein repolarization of the myocardium is delayed causing affected individuals to live with an elevated threat of arrhythmia. LQTS type 2 (LQTS2) is associated with inherited variants in the hERG K⁺ channel; however, the susceptibility to cardiac arrhythmia in patients carrying hERG channel genetic variants is often uncertain. Risk stratification and clinical management is therefore often challenging, and this is compounded by the presence of variants of uncertain significance (VUS) and variable expressivity of variant phenotype. For example, an estimated one third of variant carriers have an unremarkable QTc interval. Moreover, it is difficult to predict what might trigger an arrhythmia on a particular day at a particular time. There is, therefore, need for improved functional testing of hERG channel variants in translatable systems to explore arrhythmia mechanisms, trigger conditions, and tailored treatment options. I will describe recent studies in HEK cells and isolated CRISPR-edited human iPSC-derived cardiomyocytes that demonstrate a novel mechanism for triggered arrhythmias caused by hERG channel variants. This intriguing mechanism involves impaired protective responses to premature depolarization without significant impact on action potential duration. Interestingly, variant phenotype can be reversed by targeted channel activator compounds opening the possibility for high content automated patch screening for novel compounds that protect against arrhythmia vulnerability without overcorrection risk.

Networking Session & Morning Break - 11:00 am - 11:45 am

Take a break and connect:

Discuss - Share insights on cutting-edge research, techniques, and challenges in membrane physiology.

Interdisciplinary Insights - The sessions bring together experts from different fields (e.g., neuroscience, cardiology, pharmacology), facilitating interdisciplinary learning and innovation.



April 14th

11:45 am - 2:30 pm



Dr. Francesca Puppo
MaxWell Biosystems

Advancing Functional Characterization of In-Vitro Neural Models with Next Gene

Neural models derived from human induced pluripotent stem cells, including both 2D neuronal cultures and 3D organoids, are powerful systems for studying brain development, disease mechanisms, and drug discovery. Comprehensive characterization of these models requires advanced tools capable of capturing activity across multiple scales. MaxWell Biosystems' High-Density Microelectrode Array (HD-MEA) technology enables label-free, high-resolution recordings of neuronal activity at network, single-cell, and subcellular levels. Using the MaxOne and MaxTwo platforms, researchers can reliably assess electrophysiological properties and generate robust, reproducible datasets. This approach supports detailed functional characterization, enabling applications such as phenotyping and compound testing, and advancing next-generation electrophysiological analysis in neuroscience research.

Dr. Ed Twomey
Johns Hopkins University

Structural & Molecular Basis for Ligandgating in DeltaType Glutamate Receptors



Delta-type ionotropic glutamate receptors (iGluRs), or GluDs, are members of the iGluR ligand-gated ion channel family, yet their function remains enigmatic. Although GluDs are widely expressed in the brain, play key roles in synaptic organization, and harbor disease-linked mutations, whether they retain iGluR-like channel function is debated as currents have not been directly observed. Here, we define GluDs as ligand-gated ion channels via cryo-electron microscopy and single channel bilayer recordings. GluDs are cation channels gated by neurotransmitters (GABA & D-serine), with augmented function at physiological temperatures. Ataxia-linked mutations disrupt the ultrastructure of GluD2 and enable leak currents. Our findings demonstrate that GluDs possess the intrinsic biophysical properties of ligand-gated ion channels, reconciling prior conflicting observations to establish a framework for understanding their cellular regulation and for developing therapies targeting GluDs.



Dr. Jun Chen
Genentech

Subtype-Selective Modulation of HCN1 Channels

Subtype-selective modulation remains a major challenge for the therapeutic targeting of ion channels, particularly for the hyperpolarization-activated cyclic nucleotide-gated (HCN1–4) channels, which regulate rhythmic excitability in the heart, brain, and peripheral nerve system. Current agents—propofol and ivabradine—inhibit HCN isoforms indiscriminately, limiting their therapeutic utility. Here, we define the subtype selectivity and drug interaction mechanism for a first-in-class, potent, and highly selective HCN1 inhibitor. We identify a single residue underlying subtype selectivity, a drug binding pocket, and the dynamic remodeling of this pocket that accounts for state-dependent block of HCN1 wild-type channels, and the rescue of epilepsy-associated mutants.

Networking Session & Lunch Break - 1:00 - 2:30 pm



April 14th

2:30 - 4:30 pm

Marine Moutia

Oria Labs

Unlocking Intracellular Targets: Native Organelle Electrophysiology for Drug Discovery

An increasing number of intracellular organelle membrane proteins show strong potential as therapeutic targets in neurodegenerative diseases, immune-related diseases, and rare cardiopathologies. Collectively, these proteins represent a promising avenue for new therapeutic strategies that the scientific community must actively explore. However, functional electrophysiology characterization of these proteins remains challenging due to their intracellular localization. Microfluidic isolation of native organelles addresses these limitations by enabling direct electrophysiological recordings from intact membranes in their physiological lipid and protein environment, without artificial reconstitution or plasma membrane relocation. This approach yields higher-fidelity data and reveals endogenous protein behavior that is difficult to access using conventional methods.



Dr. Yamuna Krishnan

University of Chicago

Exploring the Insides of the Insides of our Insides

Currently, the largest number of FDA approved drugs work by manipulating the activity of ion channels at the plasma membrane. But the plasma membrane comprises 2–3% of the total cellular membrane, the remaining 98% is present in organelles, and the latter harbor hundreds of transmembrane proteins that can potentially transport ions. Organelles perform specific biochemistries within their lumens. This biochemistry is enabled by a specialized ionic microenvironment that is likely sculpted by organelle-resident channels and transporters. However, the precise ion levels were unknown until we developed a technology to measure organellar ions in live cells. We recently discovered that many organelles harbor membrane potential, indicating that vigorous ion transport occurs across organelle membranes. This means that many transmembrane organellar proteins that are risk genes for cardiovascular, neurodegenerative and immune diseases, that could potentially transport ions are yet to be identified as such and characterized. Their discovery and study in native organelles was intractable until we developed our technology to measure ions in organelles. By creating the means to study organellar ion transporting proteins in situ, a vast and unexplored landscape for biology and medicine is now accessible.

Dr. Howard Young

University of Alberta

Conformation-Dependent Regulation of the SERCA by Small Transmembrane Peptides

The sarco/endoplasmic reticulum Ca^{2+} -ATPase (SERCA) maintains low resting intracellular Ca^{2+} . During transport, SERCA cycles through multiple conformational states with different structures and substrate affinities, driven by Ca^{2+} and ATP binding and formation of an aspartyl-phosphate intermediate. Because Ca^{2+} regulates key processes such as skeletal and cardiac muscle contraction, SERCA activity is tightly controlled. Tissue-specific transmembrane regulators known as regulins, including SLN and MLN in skeletal muscle, PLN and DWORF in cardiac muscle, ELN in endothelial/epithelial tissues, and the ubiquitous ALN, modulate SERCA's apparent Ca^{2+} affinity and/or maximal activity. We found that regulins interact with SERCA in distinct modes depending on its conformational state, and that these interactions show "conformational memory," meaning the initial binding mode persists during steady-state SERCA turnover.



Networking Session & Afternoon Break - 3:45 - 4:30 pm



April 14th

4:30 - 9:00 pm



Dr. Jeffrey Noebels

Baylor College of Medicine

Elucidating Downstream Effectors of mTOR Signaling that Drive Hyperexcitability

Hyperexcitability is a biomarker and therapeutic target across a spectrum of brain network synchronization disorders, frequently in those with inflammatory involvement. Channelopathy drug discovery typically begins with analysis of solitary currents in heterologous cells, although cell type selectivity, degenerate circuit solutions and molecular plasticity bedevil genotype-phenotype correlations. Genetic deletions in epilepsy models reveal an intracellular interaction between the brain sodium channel $Na_v1.2$ and mechanistic target of rapamycin (mTOR) signaling, defining a novel target to modulate hyperexcitability in pharmacoresistant epilepsies. In HEK cells, we find hyperactive mTOR signaling directly stimulates $Na_v1.2$, one of three previously identified downstream phosphorylation targets of mTORC2 and a key regulator of membrane electrogenesis. Augmented $Na_v1.2$ channel function induced by hyperactive mTOR signaling requires the action of mTORC2 and is selective among major brain Na_v channel isoforms.



Michael George

Nanion Technologies

From Automation to Interaction: Rethinking Patch Clamp Workflows

Twenty years ago, the Patchliner set a new benchmark as a fully automated patch clamp system capable of recording from up to eight cells simultaneously. Since then, it has become a trusted workhorse across academia and industry - supporting everything from routine cardiac safety assays to intricate biophysical investigations of voltage-gated ion channels and heat activation of TRP channels. Now, two decades later, the Patchliner is undergoing a major transformation. With groundbreaking enhancements in assay versatility, hardware design, and software performance, this next-generation Patchliner redefines what is possible in automated electrophysiology, signifying a new era of precision, efficiency, and discovery.

Join Us For Dinner - 6:30 - 9:00 pm in the Vintners Room

Menu:

- Artisanal bread display with butter
- Grilled vegetables
- Potato leek soup
- Local farmer's lettuce
- Local charcuterie
- Artichokes, hummus
- Baby kale salad
- Prime tenderloin of beef
- Char grilled side of salmon
- Buttery pomme purée
- Heirloom carrots
- Assorted mini chocolate desserts



Patchliner^m

Simplicity multiplied

- | | |
|--|--|
| 1 Streamlined, manual Patchliner with complete experimental control | 5 Proven low-volume microfluidics technology |
| 2 Rapid operation for ultra-fast runs: up to 8 cells patched in under 2 minutes | 6 Intuitive software interface enabling fast setup and easy execution |
| 3 Plug-and-play, low-maintenance portable system for effortless daily use | 7 Software-controlled Bluetooth pipette for fast, precisely triggered ligand addition |
| 4 Brings the efficiency of manual patch clamp to the next level | 8 Versatile platform for training, assay development and exploratory research |



**Fast.
Simple.
Affordable.
Streamlined.
Built for exploration.**

Come by the Nanion Table
for a quick demo!,
visit our website: www.nanion.de



April 15th

9:00 - 11:30 am

Keynote

Dr. Lori L. Isom

Michigan Neuroscience Institute



Developing Gene Modifying Therapies for Dravet Syndrome

Dravet syndrome (DS) is a developmental & epileptic encephalopathy characterized by high seizure frequency & severity, intellectual disability, & a high risk of SUDEP. Most DS patients carry de novo variants in SCN1A causing haploinsufficiency of Nav1.1. Biallelic variants in SCN1B are also linked to DS or the more severe early infantile DEE (collectively termed DEE52). Targeted Augmentation of Nuclear Gene Output (TANGO) is an antisense oligonucleotide (ASO) technology that reduces non-productive mRNA splicing to increase productive mRNA & protein of the target gene. A single ICV dose of ASO-22 (TANGO-based, targeting exon 20N of Scn1a) at postnatal day 2 increased Nav1.1 expression & reduced electrographic seizures & SUDEP in DS mice. We then tested a surrogate, ASO-84, on cortical pyramidal & PV+ fast-spiking interneurons in DS mice at P21-25. In untreated DS mice, cortical pyramidal neuron firing was unchanged, while PV+ interneurons showed depolarization block & reduced sodium current density. Inhibitory post-synaptic current frequency in pyramidal neurons was also reduced, indicating impaired GABAergic signaling. ASO-84 restored PV+ interneuron excitability, sodium current density, & GABAergic signaling to pyramidal neurons. ASO-22, now Zorevunersen, is in Phase 3 clinical trials. Additionally, we developed an AAV-based SCN1B gene replacement strategy that reduces seizures & prolongs lifespan in DEE52 mouse models. Together, these findings advance precision medicine approaches for DS & related epileptic encephalopathies.



Dr. Sagardip Majumder

Baker Lab - University of Washington

Engineering Life's Gatekeepers: De Novo Design of Pores and Ion Channels

Membrane proteins, particularly pores and ion channels, are vital for cellular function by enabling the transport of ions and molecules across biological membranes. Although naturally occurring channels have been engineered for specific applications, their inherent limitations often restrict broader utility. De novo protein design presents a powerful alternative, allowing the creation of custom channels with precisely defined properties. This talk highlights recent advances in the design of trans-membrane β -barrel pores and ion channels. We have developed a flexible strategy to create pores with diverse shapes and sizes—including cylindrical, square, and oval—that are stably folded and exhibit conductance levels correlating with pore dimensions, efficiently transporting water and small molecules. Parallely, similar design principles for alpha-helical proteins have also been applied to create ion-selective channels, such as calcium channels with enhanced Ca^{2+} conductance. Furthermore, by integrating small-molecule binding domains into designed pores, we have developed ligand-gated biosensors capable of low-noise detection. These developments demonstrate the potential for designing membrane proteins with tailored functions for a range of applications, including biosensing, sequencing, synthetic biology, and therapeutics. Continued progress in computational design will enable the construction of increasingly sophisticated and functional membrane proteins

Dr. Ivy Dick

University of Maryland



Voltage Gated Calcium Channel Dysregulation in Calmodulinopathies

Calmodulinopathies are caused by mutations in calmodulin (CaM) and result in debilitating cardiac arrhythmias such as long-QT syndrome (LQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT). In addition, many patients exhibit neurological comorbidities, including developmental delay and autism spectrum disorder. Prior studies have identified the impairment of Ca^{2+} /CaM-dependent inactivation (CDI) of $\text{Ca}_v1.2$ channels as a major pathogenic mechanism leading to the LQTS phenotype in these patients. However, the impact of these mutations on other voltage-gated calcium channels (VGCCs) has yet to be fully explored. Here, we examine the potential for pathological CaM variants to impair the Ca^{2+} /CaM-dependent regulation of $\text{Ca}_v1.3$ and $\text{Ca}_v2.1$, both essential for neuronal function. We find that pathogenic mutations in CaM can impair the CDI of $\text{Ca}_v1.3$, with overlapping yet distinct disruption of the Ca^{2+} -dependent facilitation (CDF) of $\text{Ca}_v2.1$ channels.

Networking Session & Morning Break - 10:45 - 11:30 am





Dr. Matthew Coleman

Lawrence Livermore National Laboratory

Bilayer Systems for De Novo Cell-Free Synthesis and Validation of Diverse Ion Channels

Voltage-gated ion channels are large, complex membrane proteins whose study is limited by expression and stability challenges. We present a bilayer-based platform that enables de novo synthesis of full-length channels from cell-free lysates and their functional validation across complementary systems. Nanolipoprotein particles (NLPs) support co-translational insertion into native-like bilayers, while droplet interface bilayers (DIBs) provide an orthogonal platform for confirming electrophysiological activity. Using this approach, we generated reproducible data for $\text{Ca}_v2.2$, $\text{Na}_v1.2$, and GIRK1/2 channels, capturing conductance states, gating kinetics, and pharmacological sensitivity. Cross-validation between Nanion orbit and DIB platforms demonstrates the robustness of the workflow. By combining cell-free synthesis with bilayer functional assays, this strategy establishes a versatile toolkit for ion channel biophysics and accelerates applications in therapeutic discovery.

April 15th

11:30 am - 2:45 pm

Dr. Jorge Contreras

University of California Davis

When Cardiac Connexin43 Is Remodeled, Stress Can Be Deadly

Connexin-43 (Cx43) is essential for coordinated cardiac electrical conduction and contractile function. In heart disease, pathological remodeling of Cx43 is strongly associated with arrhythmias and sudden cardiac death. Using a mouse model of Duchenne muscular dystrophy (DMD), we previously showed that Cx43 redistributes from intercalated discs to the lateral membrane, where it forms undocked hemichannels. Here, we examine the role of Cx43 S-nitrosylation in mediating cardiac dysfunction during β -adrenergic stress. Our findings demonstrate that S-nitrosylation of laterally localized Cx43 promotes hemichannel opening, leading to impaired membrane excitability, arrhythmias, and myocardial injury in DMD cardiomyopathy. Genetic reduction of Cx43 S-nitrosylation preserves cardiac electrical stability and limits injury despite persistent Cx43 remodeling. These results identify S-nitrosylation-dependent activation of Cx43 hemichannels as a key pathogenic mechanism linking cardiac stress to lethal arrhythmias and highlight hemichannels as potential therapeutic targets in DMD-associated heart disease.



Dr. Mauricio Lillo Gallardo

Rutgers University

When Redox Meets Electricity: GC1 and Connexin Coordinate Endothelial Communication and Arterial Tone

Resistance arteries continuously adjust their diameter to control blood flow and pressure — a process known as vasomotor tone regulation. This fine control depends on the ability of endothelial cells to communicate and coordinate their electrical and redox signals. We discovered that soluble guanylyl cyclase (GC1), beyond its classical role as the nitric oxide receptor in smooth muscle, also acts within the endothelium to transfer nitric oxide-derived signals through a process called transnitrosation. Mice lacking this GC1 function displayed elevated blood pressure and impaired vessel relaxation due to defective calcium and potassium channel activation. We further found that this redox pathway preserves endothelial coupling through connexin proteins, which synchronize electrical activity and gene expression. Together, our findings reveal that GC1-driven transnitrosation and connexin-mediated coupling form a coordinated redox-electrical network essential for resistance artery relaxation and vascular homeostasis.

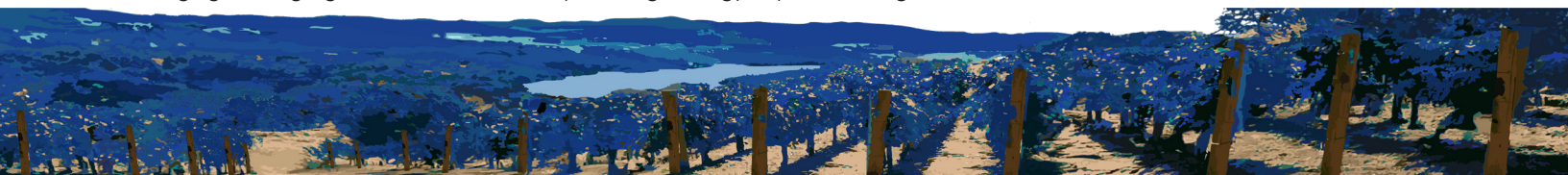
Networking Session & Lunch Break - 1:00 - 2:15 pm

Dr. Lisa Ellerby

Buck Institute

CD38 Inhibition Delays Age-Related Cognitive Decline via a Choroid Plexus–Cerebrospinal Fluid–Hippocampus Axis

Aging-related cognitive decline remains a major challenge. We identify the NAD^+ -degrading enzyme CD38 as a key driver of cognitive aging through a choroid plexus–CSF–hippocampus pathway. With age, CD38 increases in choroid plexus pericytes, lowering NAD^+ , impairing mitochondrial function, and promoting cellular senescence. Genetic deletion or pharmacological inhibition of CD38 restores NAD^+ , reduces senescence markers, and rejuvenates choroid plexus physiology, producing a more youthful, less inflammatory CSF profile. These improvements extend to the hippocampus, normalizing gene expression and enhancing synaptic plasticity. Treatment with NTX-748, a brain-permeable CD38 inhibitor, similarly boosts NAD^+ in blood and brain and improves cognition in aged mice. Overall, these findings position the choroid plexus as a key metabolic hub in brain aging and highlight CD38 inhibition as a promising strategy to preserve cognitive function.



April 15th

2:45 - 6:45 pm

Dr. David K. Jones

University of Michigan



Mechanisms Regulating hERG1NP Physiology and Pathophysiology

hERG1NP, encoded by KCNH2, is a polypeptide expressed in the nuclei of developing cardiomyocytes and neurons. KCNH2 variants that map to hERG1NP are linked with both sudden infant death syndrome (SIDS) and sudden unexplained death in epilepsy (SUDEP). The mechanisms regulating hERG1NP activity and the mechanistic relationship between hERG1NP variants and sudden death are unknown. In our most recent work, we demonstrate that biochemistry of the hERG1NP coiled-coil domain is critically important for normal hERG1NP nuclear trafficking and function. Further, early data from gene-edited cardiomyocytes demonstrate that hERG1NP regulates multiple systems associated with cardiac physiology. Collectively, these data suggest that hERG1NP has the capacity to broadly regulate human physiology.

Afternoon Break - Dedicated Poster Session - 3:15 - 4:00 pm



Dr. Franck Kalume

Seattle Children's

Solving the Molecular Logistics of SCN1A Delivery: A Key to Interneuron-Specific AAV-Based Gene Replacement Therapy in Dravet Syndrome

Dr. Franck Kalume's presentation highlights a major advance in AAV-based gene replacement therapy for Dravet syndrome (DS). His team at Seattle Children's, with the Allen Institute, developed an interneuron-specific dual-AAV strategy that restores SCN1A function and rescues epileptic phenotypes in DS mouse models. To address the large size of SCN1A, they used a dual-AAV system combined with split-intein technology to reconstitute Na_v1.1 after translation. A modified DLX2.0 enhancer ensured expression specifically in GABAergic interneurons. This approach provided complete protection from premature death, markedly reduced seizures, and maintained long-term effectiveness for over a year without detectable toxicity or off-target effects. The presentation will cover the design, implementation, and broader impact of this work, which represents a major step toward curative therapy for DS and a new framework for precision AAV treatments in monogenic neurological disorders.

Dr. John Lueck

University of Rochester



Development of ACE-tRNA Therapeutics for Nonsense-associated Diseases

Nonsense mutations or premature termination codons (PTCs) occur when a nucleotide codon is converted into a stop codon (TGA, TAG, or TAA). Approximately 10% of people with cystic fibrosis (CF) harbor a CFTR variant potentially responsive to PTC-targeting therapies, for which current modulators are ineffective. We have demonstrated that anticodon edited tRNAs (ACE-tRNAs) can suppress CF-causing PTCs in the CFTR gene in gene-edited human bronchial epithelial cells. A key advantage of ACE-tRNAs is their small (~125 bp) size, enabling encoding in non-viral DNA minivectors as small as 200 bp while producing robust PTC suppression. Our best-performing ACE-tRNA decodes all UGA PTCs to leucine, markedly rescuing CFTR function across immortalized airway cells and two primary CF patient-derived intestinal cell models. Notably, leucine substitution CFTR variants proved highly functional. ACE-tRNAs thus represent a promising platform therapeutic for CF and other nonsense-associated diseases.

Wine Tasting - 5:15 - 6:45 pm



AXOL - Liam Taylor

Human iPSC-derived motor neurons for ALS modeling on the high-throughput Nanion SyncroPatch 384 platform



Induced pluripotent stem cell (iPSC) technology enables the conversion of primary samples (blood or fibroblast) from a patient donor into a stem cell and from that stem cell, differentiated into functional cell types, including motor neurons. These motor neurons can be used in in vitro modeling when generated from high quality patient derived iPSCs and differentiated using a small molecule robust process to generate functionally qualified human iPSC-generated motor neurons.

Axol Bioscience has generated motor neurons from a number of patient and unaffected donor samples. We have previously reported ALS relevant phenotypes using low-throughput electrophysiology. To investigate the utility of iPSC-derived motor neurons in a high-throughput setting, we collaborated with Nanion Technologies. We successfully demonstrated the application of these cells on the SyncroPatch 384 system and report ALS relevant differences between motor neurons from an ALS patient C9orf72 affected line and that of an unaffected donor.

Anatomic - Vince Truong & Patrick Walsh

Scalable Human iPSC-Derived Trigeminal and DRG Neurons for Ion Channel Discovery and Screening



Human trigeminal neurons (TGNs) and dorsal root ganglion (DRG) neurons derived from induced pluripotent stem cells (hiPSCs) provide scalable human models for studying sensory neuron biology and pain mechanisms. We developed a rapid small-molecule differentiation protocol that generates high-purity sensory neurons within seven days without genetic manipulation. The resulting neurons express canonical sensory markers including ISL1, BRN3A, and TUJ1. RNA sequencing and qPCR profiling confirm expression of key sensory genes including TRPM8, NaV1.8, and TRPV1, along with a broad range of additional ion channel targets relevant to sensory signaling. Over four weeks in culture, neurons show increasing soma size, axonal density, and electrophysiological activity, with robust capsaicin responses observed in functional assays.

3Brain - Amber Jolly

Studying Single-Cell Behavior at Network Scale with HD-MEA



Three dimensional (3D) neuronal tissues and cultures such as brain organoids, brain slices, and neuronal assembloids offer advanced opportunities to investigate neuronal function and network properties in vitro. However, capturing the complex electrophysiological properties of these models requires highly sensitive recording technologies with high spatial resolution. CorePlate™ enabled high density multielectrode arrays (HD MEAs), including CorePlate™ 3D with its thousands of penetrating electrodes, provide a powerful solution for the functional assessment of 3D cultures, enabling detailed characterization at the cellular level and network scale.

This poster highlights the versatility of CorePlate™ platforms for characterizing activity across diverse 3D systems. First, we demonstrate the functional characterization of brain organoids in response to valproic acid and 4 aminopyridine. Second, we present recordings from cerebellar slices following exposure to potassium channel modulators. Finally, we showcase functional profiling of an assembloid model in response to bicuculline and tetrodotoxin (TTX).

Together, these examples show how CorePlate™ enabled HD MEA technology enables high resolution functional assessment of 3D cultures, and their responses to pharmacologically induced changes.

3Brain - Amber Jolly

Electrophysiological Analysis of axoCells™ Atrial and Ventricular Cardiomyocytes With CorePlate™ Enabled HD-MEA



Understanding the functional differences between atrial and ventricular cardiomyocytes is crucial for advancing cardiovascular research, particularly in the context of arrhythmias such as atrial fibrillation (AF). Induced pluripotent stem cell-derived cardiomyocytes (iPSC CMs) provide a powerful platform for modelling human cardiac tissue and enabling detailed electrophysiological studies across cardiac regions. In this dataset, CorePlate™ enabled high-density multielectrode arrays (HD MEAs) were used to characterize axoCells™ atrial and ventricular iPSC derived cardiomyocytes within a streamlined 7 day plating to assay workflow. Following baseline characterization, atrial cardiomyocytes were treated with 10 µM isoproterenol, resulting in increased field potential rate and R-S and T wave peak amplitudes, accompanied by decreases in inter beat field potential interval and R-T interval durations.

These findings highlight the ability of CorePlate™ enabled HD MEA technology to rapidly characterize and screen axoCells™ atrial and ventricular iPSC derived cardiomyocytes within a fast, time to results workflow.

Yen-Her Lai - University of California Davis

Molecular Modeling and Simulations of Cardiac Sodium Channel NaV1.5 Genetic Variants for Patient-Specific Anti-Arrhythmia Therapeutics

Voltage-gated sodium channel NaV1.5 is critical for cardiac electrical signaling and its loss or gain of function genetic variants have been implicated in a wide spectrum of arrhythmogenic disorders. Multiple NaV1.5 mutations are linked to Brugada and long QT syndromes as well as other inherited arrhythmias. To uncover the molecular mechanisms underlying altered physiology and pharmacology of these pathogenic variants, we employed molecular modeling, molecular docking, and molecular dynamics (MD) simulations to examine how mutations alter channel structure, gating, and drug binding. We tested several potentially pathogenic NaV1.5 pore-domain mutants via MD simulations as well as AutoDock 4 and OpenEye FRED drug docking and found that these mutations affect channel structural stabilities and anti-arrhythmic drug quinidine binding. By integrating mutation-specific structural insights with computational drug screening, this work aims to support precision medicine, tailoring antiarrhythmic therapy to a patient's molecular genetic profile.



Posters

Dr. David Baez - *Broad Institute*

A Subtype-Selective TTA-2 Interaction Reveals Structural Coupling of Drug Binding and Inactivation in Ca_v3 Channels

T-type calcium channels ($\text{Ca}_v3.1-3.3$) are important drug targets, yet subtype-selective modulation remains challenging due to limited structural information. Cryo-EM analyses of Ca_v3 in complex with TTA-2 revealed a $\text{Ca}_v3.3$ -specific interaction mediated by Ile1722. Functional mutagenesis demonstrated that this interaction critically shapes TTA-2 state-dependent block and channel inactivation, altering the window current. Additionally, Q1718 residue stabilizes TTA-2 across all T-types; changes in this residue also modify state-dependent blockade, indicating a key overlap between the inactivation machinery and the TTA-2 binding site. Together, these findings establish a structural framework for the development of next-generation subtype-specific T-type channel therapeutics.

Shrinivasan Raghuraman - *University of Utah*

Conotoxin kM-R111J Reveals Novel Function of Heteromeric $\text{K}_v1.2$ Channel in Proprioception

Voltage-gated potassium (K_v) channels are among the most diverse ion channel families, with ~70 genes encoding α -subunits that assemble into tetrameric complexes. Distinct combinations of these subunits generate heteromeric channels with unique biophysical and physiological properties, yet the functional roles of such heteromers remain largely unexplored due to the lack of subtype-selective tools.

Using the cone snail-derived peptide kM-R111J as a selective pharmacological probe and applying the constellation pharmacology platform, we identified heteromeric $\text{K}_v1.2/1.1$ channels as key regulators of excitability in proprioceptive neurons of the dorsal root ganglion (DRG). Inhibition of these channels caused increased calcium influx and tonic firing, revealing that $\text{K}_v1.2/1.1$ heteromers oppose persistent sodium currents to maintain neuronal stability. *In vivo*, kM-R111J impaired proprioception in mice, uncovering a previously unrecognized role for $\text{K}_v1.2/1.1$ heteromers in sensory signaling.

Jiaying Yan - *University of California Davis*

Modeling Drug Binding to the hERG Channel Across Conformational States, Isoforms, and Patient-Specific Variants

The hERG (KCNH2) potassium channel is responsible for the major repolarizing current in cardiomyocytes and is critical for normal cardiac repolarization. Many small-molecule drugs block hERG and can cause QT prolongation and arrhythmias, but the structural basis of arrhythmogenic risk remains unclear. Our work uses a computational framework that combines cryo-EM structures, AlphaFold and Rosetta modeling, molecular docking, and all-atom molecular dynamics simulations to study hERG channel - drug binding. I examine how binding differs across functional states, including open and inactivated conformations, and across isoforms such as hERG1a and hERG1b. I also study disease-associated mutations and variants of unknown significance, including channel pore and selectivity filter mutations. Together, these studies aim to define the molecular basis of hERG block and improve prediction of drug-induced arrhythmia risks.

Kyle C. Rouen - *University of California Davis*

Arrhythmia Risk Predictions From Molecular Simulations of Cardiac Ion Channel-Drug Interactions

Unintended blockade of cardiac ion channels, especially hERG ($\text{K}_v11.1$), is a major safety concern due to its link to fatal arrhythmias. We examined drug interactions with open and inactivated hERG and assessed whether interactions with $\text{Na}_v1.5$ and $\text{Ca}_v1.2$ channels can mitigate arrhythmia risk. Cryo-EM-based ion channel structures were modeled using Rosetta, and SILCS (Site Identification by Ligand Competitive Saturation) docking was applied to predict drug binding affinities. Bayesian machine learning (ML) refined SILCS scoring using IC50 data from 53 hERG blockers, outperforming standard docking methods. Random forest ML models trained on ~300 CredibleMeds drugs achieved accurate arrhythmia risk classification. Cationic nitrogen SILCS fragment energies were identified as key proarrhythmic risk predictors, enabling rapid, structure-independent assessment of cardiac safety for drug design.

Adam Laurence - *Lawrence Livermore National Laboratory*

Cell-Free Expression and Electrophysiology Platforms for Functional Analysis of Membrane Proteins

Membrane proteins, including ion channels, make up nearly one-third of the proteome and constitute the majority of pharmaceutical drug targets. Yet their biophysical and biochemical characterization remains constrained by challenges in expression and stability. Advances in cell-free protein synthesis (CFPS) have enabled new workflows for the efficient production and stabilization of membrane proteins. By co-expressing target proteins with the scaffold protein ApoA1 and the lipid DMPC in scalable lysate systems, we achieve *in vitro* production of stable membrane protein complexes. Functional validation is achieved using electrophysiology platforms including the Nanion Orbit mini and Droplet Interface Bilayers (DIB), enabling characterization of voltage-gated ion channels such as $\text{Ca}_v2.2$ and $\text{Na}_v1.2$. The integration of CFPS with bilayer-based electrophysiology establishes a versatile toolkit for biochemical and biophysical studies. Together, these methods provide a pathway to probe membrane protein dynamics, benchmark activity across membrane mimetics, and accelerate discovery in both basic science and therapeutic development.



Notes



Notes



Nanon User Meeting 2026

Science Workshops Networking

Join us in Munich!
October 20-21st, 2026



Thank you to our Sponsors

AXOL

maxwell
BIOSYSTEMS



ORIA
BIOSCIENCE



ANATOMIC



3 Brain



elements
enabling technologies for Life Science

