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SEMINAR SERIES 2025

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Professor Juan Du

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Juan Du earned her Diploma degree in chemistry from University of Göttingen and her Ph.D. from the Institute of Organic Chemistry & Biochemistry at the University of Freiburg, in the laboratory of Dr. Oliver Einsle. In 2012, she joined the Gouaux Lab at Oregon Health & Science University's Vollum Institute as a Postdoctoral Fellow. In October 2017, Juan became an Assistant Professor at Van Andel Institute, where she was promoted to Associate Professor in May 2021. In September 2024, she joined the Department of Molecular Biosciences at Northwestern University as a Professor. Juan's research explores the molecular mechanisms that enable the human body to sense and respond to external stimuli, particularly how we detect and respond to different temperatures. Temperature sensation is crucial for survival, guiding our responses to environmental changes and protecting us from harm. Her lab focuses on understanding how neuronal ion channel receptors detect temperature changes and convey these signals to the brain. Using techniques such as cryo-electron microscopy (Cryo-EM) and patch-clamp electrophysiology, the lab seeks to illuminate the processes underlying temperature regulation and its broader implications, including pain perception. This research not only deepens our understanding of these essential biological functions but also informs the development of new therapies for pain.

The importance of Physiological Temperature in Biomedical & Biophysical Research

Temperature profoundly affects macromolecular function, particularly in proteins with temperature sensitivity. However, its impact is often overlooked in biophysical studies typically performed at non-physiological temperatures, potentially leading to inaccurate mechanistic and pharmacological insights. Using single-particle cryo-EM at physiological temperature, we investigated temperature-sensitive ion channel TRPM4, uncovering thermally driven conformations and modes of ligand recognition. In TRPM4, we discovered a "warm" conformation driven by a temperature-dependent Ca^{2+} binding site in the intracellular domain (ICD), essential for physiological gating. Ligands such as decavanadate (a positive modulator) and ATP (an inhibitor) bind to different sites at physiological temperature than at lower temperatures, revealing a previously unrecognized dimension of ligand recognition. Structural snapshots captured at physiological temperature also revealed the elusive open state of TRPM4, not observed at cryogenic preparation conditions. Our findings underscore the importance of studying thermosensitive proteins under physiological temperature to obtain accurate mechanistic and pharmacological insights.