



Complex Biosystems Seminar Series

Date: September 19, 2024, Time: 4-5pm Place: Beadle N176

Zoom: <https://unl.zoom.us/j/99493999289>

“Structural and Evolutionary Mechanisms of the Sensory TRPM2 Channel by Cryo-EM”

The TRPM2 ion channel is a polymodal receptor that senses chemical compounds, temperature, and redox changes, playing a crucial role in maintaining core body temperature in mammals. Uniquely activated by Ca^{2+} and ADP-ribose (ADPR), TRPM2 has evolved from a dual-function channel-enzyme in invertebrates to a thermal sensor in mammals. Dysfunction of TRPM2 has been linked to various neurodegenerative diseases, including Alzheimer's and Parkinson's. Using single-particle cryo-EM, we determined high-resolution structures of TRPM2 from unicellular choanoflagellates, zebrafish, and humans in different conditions. This study uncovered a novel, conserved ligand-binding site and revealed the ligand recognition and gating mechanisms. Additionally, it elucidated the coupling mechanisms between the channel and enzyme functions by capturing the channel-enzyme TRPM2 in various functional states using time-resolved cryo-EM analysis, offering an atomic perspective on the molecular evolution of TRPM2.

Bio: Yihe Huang earned his Ph.D. from Peking University, China, specializing in X-ray crystallography. He then moved to the United States for postdoctoral training at UT Southwestern Medical Center in Dallas, Texas, and the Van Andel Institute in Grand Rapids, Michigan. He is currently an assistant professor in the Department of Biochemistry and serves as a project leader at the Nebraska Center for Integrated Biomolecular Communication (CIBC) and a member of the Buffett Cancer Center at the University of Nebraska Medical Center (UNMC). His lab focuses on studying the structural and evolutionary mechanisms of transmembrane signaling in human health and disease, with a particular emphasis on signaling pathways involved in development and regeneration.

