



Merritt Maduke

Associate Professor of Molecular and Cellular Physiology
Molecular & Cellular Physiology

Bio

ACADEMIC APPOINTMENTS

- Associate Professor, Molecular & Cellular Physiology
- Member, Bio-X
- Member, Wu Tsai Neurosciences Institute

ADMINISTRATIVE APPOINTMENTS

- Chair, Provost's Advisory Committee on Postdoctoral Affairs, Stanford University, (2012-2016)

HONORS AND AWARDS

- Faculty Scholar, Esther Ehrman Lazard (2003-2005)
- Scientist Development Award, American Heart Association (2004-2007)
- Cranefield Award, Society of General Physiologists (2008)
- Spark Scholar, Stanford University (2010)

BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Past President, Society of General Physiologists (2020 - 2020)
- Reviewing Editor, eLIFE (2019 - present)
- President, Society of General Physiologists (2018 - 2019)
- Associate Editor, Journal of General Physiology (2014 - 2019)

PROFESSIONAL EDUCATION

- Ph.D., UCSD , Chemistry & Biochemistry (1995)
- B.S., Wheaton College , Chemistry (1989)

LINKS

- My Lab Site: <http://maduke.stanford.edu>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Ion transport across the hydrophobic barrier of the cell membrane is a primary challenge faced by all cells. Such transport sets up and exploits ion gradients, thus providing the basic energy and signaling events that are the foundation of life. My laboratory studies the molecular mechanisms of ion channels and transporters, the

proteins that catalyze this transport. Our major research focus is on the chloride-selective CLC family, which contains both types ion-transport protein. CLC proteins are expressed ubiquitously and perform diverse physiological functions in cardiovascular, neuronal, muscular, and epithelial function. We use a combination of biophysical methods to investigate membrane-protein structure and dynamics together with electrophysiological analyses to directly measure function.

A major direction includes developing NMR approaches for studying CLC structure and dynamics and combining these studies with molecular dynamics simulations (in collaboration with Emad Tajkhorshid, University of Illinois). As part of this endeavor, we are part of the Membrane Protein Structural Dynamics Consortium, a multidisciplinary team focused on elucidating the relationship between structure, dynamics and function in a variety of membrane proteins - <http://memprotein.org/>.

We are also developing novel small-molecule inhibitors as tools for studying the CLC proteins, in collaboration with Prof Justin Du Bois (Chemistry). These molecules will be used as biophysical probes to advance our understanding of CLC mechanisms, as cellular probes to study CLC-mediated physiological processes, and as lead compounds for treating several types of CLC-related diseases. The latter effort is in collaboration with Prof Alan Pao (Medicine) and funded by the Stanford SPARK program.

In a new multidisciplinary team effort, we are working in the emerging field of non-invasive ultrasonic neural modulation, with the goal of developing ultrasound technology for non-invasive brain stimulation in experimental and clinical applications. Research is in collaboration with Profs Baccus (Neurobiology), Butts-Pauly (Radiology) and Khuri-Yakub (Electrical Engineering). Our lab is addressing the problem and the molecular level, studying the effects of ultrasound on ion channels in reduced systems using electrophysiological recording techniques.

Teaching

COURSES

2019-20

- Neuroscience Journal Club and Professional Development Series: NEPR 280 (Win, Spr)

2018-19

- How Cells Work: Energetics, Compartments, and Coupling in Cell Biology: MCP 256 (Spr)
- MCP Journal Club and Professional Development Series: MCP 208 (Aut)
- Neuroscience Journal Club and Professional Development Series: NEPR 280 (Aut, Win, Spr)

2017-18

- Neuroscience Journal Club and Professional Development Series: NEPR 280 (Aut, Win, Spr)

2016-17

- How Cells Work: Energetics, Compartments, and Coupling in Cell Biology: MCP 156, MCP 256 (Spr)
- Neuroscience Journal Club and Professional Development Series: MCP 300, NEPR 280 (Aut, Win, Spr)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Thomas Chew, Andras Sagi, Chase Wood

Postdoctoral Faculty Sponsor

Tanmay Chavan, Wei Feng, Xianlan Wen

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biophysics (Phd Program)

- Molecular and Cellular Physiology (Phd Program)
- Neurosciences (Phd Program)

Publications

PUBLICATIONS

- **Special Issue: Molecular Biophysics of Membranes and Membrane Proteins Preface** *BIOCHIMICA ET BIOPHYSICA ACTA-BIOMEMBRANES*
Thompson, L. K., Maduke, M.
2020; 1862 (1): 183116
- **A selective class of inhibitors for the CLC-Ka chloride ion channel** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Koster, A. K., Wood, C. P., Thomas-Tran, R., Chavan, T. S., Almqvist, J., Choi, K., Du Bois, J., Maduke, M.
2018; 115 (21): E4900–E4909
- **Focused Ultrasound Activates Task Potassium Channels, Increases Membrane Capacitance, and Modulates Action Potential Waveform and Firing Properties in Hippocampal Brain Slices**
Prieto, M. L., Madison, D. V., Khuri-Yakub, B. T., Maduke, M.
CELL PRESS.2018: 669A
- **Activation of Piezo1 but Not NaV1.2 Channels by Ultrasound at 43 MHz.** *Ultrasound in medicine & biology*
Prieto, M. L., Firouzi, K., Khuri-Yakub, B. T., Maduke, M.
2018
- **Protein ligands for studying ion channel proteins.** *journal of general physiology*
Chavan, T., Maduke, M., Swartz, K.
2017
- **Molecular Basis for Differential Anion Binding and Proton Coupling in the Cl(-)/H(+) Exchanger CIC-ec1.** *Journal of the American Chemical Society*
Jiang, T., Han, W., Maduke, M., Tajkhorshid, E.
2016; 138 (9): 3066-3075
- **Revealing an outward-facing open conformational state in a CLC Cl-/H+ exchange transporter** *ELIFE*
Khantwal, C. M., Abraham, S. J., Han, W., Jiang, T., Chavan, T. S., Cheng, R. C., Elvington, S. M., Liu, C. W., Mathews, I. I., Steins, R. A., Mchaourab, H. S., Tajkhorshid, E., Maduke, et al
2016; 5
- **C-13 NMR detects conformational change in the 100-kD membrane transporter CIC-ec1** *JOURNAL OF BIOMOLECULAR NMR*
Abraham, S. J., Cheng, R. C., Chew, T. A., Khantwal, C. M., Liu, C. W., Gong, S., Nakamoto, R. K., Maduke, M.
2015; 61 (3-4): 209-226
- **Water access points and hydration pathways in CLC H+/Cl- transporters** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Han, W., Cheng, R. C., Maduke, M. C., Tajkhorshid, E.
2014; 111 (5): 1819-1824
- **Dynamic Response of Model Lipid Membranes to Ultrasonic Radiation Force** *PLOS ONE*
Prieto, M. L., Oralkan, O., Khuri-Yakub, B. T., Maduke, M. C.
2013; 8 (10)
- **Novel diuretic targets** *AMERICAN JOURNAL OF PHYSIOLOGY-RENAL PHYSIOLOGY*
Denton, J. S., Pao, A. C., Maduke, M.
2013; 305 (7): F931-F942
- **Dynamic response of model lipid membranes to ultrasonic radiation force.** *PloS one*
Prieto, M. L., Ömer, O., Khuri-Yakub, B. T., Maduke, M. C.
2013; 8 (10)
- **A Designed Inhibitor of a CLC Antiporter Blocks Function through a Unique Binding Mode** *CHEMISTRY & BIOLOGY*

Howery, A. E., Elvington, S., Abraham, S. J., Choi, K., Dworschak-Simpson, S., Phillips, S., Ryan, C. M., Sanford, R. L., Almqvist, J., Tran, K., Chew, T. A., Zachariae, U., Andersen, et al
2012; 19 (11): 1460-1470

- **Structural investigations of CIC-ec1, a large integral membrane protein, using solution-state NMR and nanodisc technology** *Experimental Biology Meeting 2012*
Chew, T., Abraham, S., Elvington, S., Maduke, M.
FEDERATION AMER SOC EXP BIOL.2012
- **Biochemistry to the Rescue: A CIC-2 Auxiliary Subunit Provides a Tangible Link to Leukodystrophy** *NEURON*
Maduke, M. C., Reimer, R. J.
2012; 73 (5): 855-857
- **Substrate-driven conformational changes in CIC-ec1 observed by fluorine NMR** *EMBO JOURNAL*
Elvington, S. M., Liu, C. W., Maduke, M. C.
2009; 28 (20): 3090-3102
- **Proton-coupled gating in chloride channels** *PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B-BIOLOGICAL SCIENCES*
Lisal, J., Maduke, M.
2009; 364 (1514): 181-187
- **Ion Channel Targets - Select Biosciences' Fourth Annual Conference** *IDRUGS*
Holmqvist, M., Maduke, M.
2008; 11 (11): 795-98
- **Thinking outside the crystal Complementary approaches for examining transporter conformational change** *CHANNELS*
Elvington, S. M., Maduke, M.
2008; 2 (5): 373-379
- **The CIC-0 chloride channel is a 'broken' Cl⁻/H⁺ antiporter** *NATURE STRUCTURAL & MOLECULAR BIOLOGY*
Lisal, J., Maduke, M.
2008; 15 (8): 805-810
- **A Cytoplasmic Domain Mutation in CIC-Kb Affects Long-Distance Communication Across the Membrane** *PLOS ONE*
Martinez, G. Q., Maduke, M.
2008; 3 (7)
- **Discovery of potent CLC chloride channel inhibitors** *ACS CHEMICAL BIOLOGY*
Matulef, K., Howery, A. E., Tan, L., Kobertz, W. R., Du Bois, J., Maduke, M.
2008; 3 (7): 419-428
- **The role of a conserved lysine in chloride- and voltage-dependent CIC-0 fast gating** *JOURNAL OF GENERAL PHYSIOLOGY*
Engh, A. M., Faraldo-Gomez, J. D., Maduke, M.
2007; 130 (4): 351-363
- **The mechanism of fast-gate opening in CIC-0** *JOURNAL OF GENERAL PHYSIOLOGY*
Engh, A. M., Faraldo-Gomez, J. D., Maduke, M.
2007; 130 (4): 335-349
- **The CLC 'chloride channel' family: revelations from prokaryotes** *MOLECULAR MEMBRANE BIOLOGY*
Matulef, K., Maduke, M.
2007; 24 (5-6): 342-350
- **Inhibition of CLC-ec1 by DIDS hydrolysis products** *51st Annual Meeting of the Biophysical-Society*
Matulef, K., Howery, A. E., Ganesan, R., Martinez, G., Du Bois, J., Maduke, M.
CELL PRESS.2007: 347A-347A
- **Side-dependent inhibition of a prokaryotic CIC by DIDS** *BIOPHYSICAL JOURNAL*
Matulef, K., Maduke, M.
2005; 89 (3): 1721-1730

- **Cysteine accessibility in CIC-0 supports conservation of the CIC intracellular vestibule** *JOURNAL OF GENERAL PHYSIOLOGY*
Engh, A. M., Maduke, M.
2005; 125 (6): 601-617
- **The poststructural festivities begin** *NEURON*
Maduke, M., Mindell, J. A.
2003; 38 (1): 1-3
- **Projection structure of a CIC-type chloride channel at 6.5 angstrom resolution** *NATURE*
Mindell, J. A., Maduke, M., Miller, C., Grigorieff, N.
2001; 409 (6817): 219-223
- **CIC chloride channels** *GENOME BIOLOGY*
Mindell, J. A., Maduke, M.
2001; 2 (2)
- **A decade of CLC chloride channels: Structure, mechanism, and many unsettled questions** *ANNUAL REVIEW OF BIOPHYSICS AND BIOMOLECULAR STRUCTURE*
Maduke, M., Miller, C., Mindell, J. A.
2000; 29: 411-438
- **High-level expression, functional reconstitution, and quaternary structure of a prokaryotic CIC-type chloride channel** *JOURNAL OF GENERAL PHYSIOLOGY*
Maduke, M., Pheasant, D. J., Miller, C.
1999; 114 (5): 713-722
- **Formation of CLC-0 chloride channels from separated transmembrane and cytoplasmic domains** *BIOCHEMISTRY*
Maduke, M., Williams, C., Miller, C.
1998; 37 (5): 1315-1321
- **IMPORT OF A MITOCHONDRIAL PRESEQUENCE INTO P-DENITRIFICANS - INSIGHT INTO THE EVOLUTION OF PROTEIN-TRANSPORT** *FEBS LETTERS*
ROISE, D., Maduke, M.
1994; 337 (1): 9-13
- **IMPORT OF A MITOCHONDRIAL PRESEQUENCE INTO PROTEIN-FREE PHOSPHOLIPID-VESICLES** *SCIENCE*
Maduke, M., ROISE, D.
1993; 260 (5106): 364-367