



## Merritt Maduke

Professor of Molecular and Cellular Physiology  
Molecular & Cellular Physiology

### Bio

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#### ACADEMIC APPOINTMENTS

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

#### ADMINISTRATIVE APPOINTMENTS

- Associate Director, Molecular and Cellular Physiology Graduate Program, (2021- present)
- Co-director, Neurosciences Interdisciplinary Graduate Program, (2021- present)
- President, Society of General Physiologists, (2018-2019)
- Executive Committee, Biophysics Interdisciplinary Program, (2012-2021)
- 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

- Founding Curator, Biophysics Colab (2021 - present)
- Editor, Biophysical Journal (2020 - present)
- Reviewing Editor, eLife (2019 - present)
- Associate Editor, Journal of General Physiology (2014 - 2019)
- Editorial Board, Journal of General Physiology (2010 - present)

#### PROFESSIONAL EDUCATION

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

## LINKS

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

## Research & Scholarship

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### 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. A 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. We additionally apply our expertise on ion-transport mechanisms to interdisciplinary collaborations to create novel chemical tools, to develop CLC-targeted therapies, and to understand the mechanism by which ultrasound modulates ion-transport to effect neuromodulation.

### PROJECTS

- Mechanisms of CLC Channels and Transporters - Stanford University
- Small-molecule probes for study of CLC-2 chloride-channel function in the central nervous system - Stanford University
- BRAIN Initiative - Neurostimulation by Ultrasound: Physical, Biophysical, and Neural Mechanisms - Stanford University
- Structure-based strategy for developing inhibitors of the kidney chloride channel CLC-Ka
- Inhibiting the CLC-Ka Cl<sup>-</sup> channel, a novel therapeutic target for hyponatremia - Stanford University

## Teaching

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### COURSES

#### 2023-24

- How Cells Work: Energetics, Compartments, and Coupling in Cell Biology: MCP 256 (Spr)

#### 2021-22

- How Cells Work: Energetics, Compartments, and Coupling in Cell Biology: MCP 156, MCP 256 (Win)

#### 2020-21

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

### STANFORD ADVISEES

#### Doctoral Dissertation Reader (AC)

Suzanna Bennett, Samantha Gumbin, Kyrstyn Ong, Andras Sagi

#### Postdoctoral Faculty Sponsor

Daniel Collins, Juergen Kreiter, Amy Nava, Shwetha Srinivasan

#### Doctoral Dissertation Advisor (AC)

Raymond McKoy

### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

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

- Neurosciences (Phd Program)

## Publications

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### PUBLICATIONS

- **Towards an ion-channel-centric approach to ultrasound neuromodulation.** *Current opinion in behavioral sciences*  
Prieto, M. L., Maduke, M.  
2024; 56
- **CryoEM structures of the human CLC-2 voltage-gated chloride channel reveal a ball-and-chain gating mechanism.** *eLife*  
Xu, M., Neelands, T., Powers, A. S., Liu, Y., Miller, S. D., Pintilie, G. D., Bois, J. D., Dror, R. O., Chiu, W., Maduke, M.  
2024; 12
- **Novel CLC-Kb pore mutation associated with defective glycosylation and renal tubulopathy**  
Sharma, Y., Dong, W., Liao, X., Venkataraman, A., Qiao, Y., Francisco, C. V., Maduke, M., Charu, V., Kambham, N., Pochynyuk, O., Govaerts, C., Bhalla, V.  
OXFORD UNIV PRESS INC.2022: 1026-1027
- **Development and validation of a potent and specific inhibitor for the CLC-2 chloride channel.** *Proceedings of the National Academy of Sciences of the United States of America*  
Koster, A. K., Reese, A. L., Kuryshev, Y., Wen, X., McKiernan, K. A., Gray, E. E., Wu, C., Huguenard, J. R., Maduke, M., Du Bois, J.  
2020
- **Spike frequency-dependent inhibition and excitation of neural activity by high-frequency ultrasound.** *The Journal of general physiology*  
Prieto, M. L., Firouzi, K., Khuri-Yakub, B. T., Madison, D. V., Maduke, M.  
2020; 152 (11)
- **LRRc8A:C/E Heteromeric Channels Are Ubiquitous Transporters of cGAMP.** *Molecular cell*  
Lahey, L. J., Mardjuki, R. E., Wen, X., Hess, G. T., Ritchie, C., Carozza, J. A., Bohnert, V., Maduke, M., Bassik, M. C., Li, L.  
2020
- **Expanding the membrane-protein NMR toolkit.** *Nature chemical biology*  
Cheng, R. C., Maduke, M.  
2020
- **An international gathering of physiologists in Valparaiso, Chile.** *The Journal of general physiology*  
Maduke, M. C., Rothberg, B. S.  
2020; 152 (6)
- **Special Issue: Molecular Biophysics of Membranes and Membrane Proteins Preface** *BIOCHIMICA ET BIOPHYSICA ACTA-BIOMEMBRANES*  
Thompson, L. K., Maduke, M.  
2020; 1862 (1): 183116
- **Spike-frequency dependent inhibition and potentiation of neural activity by ultrasound** *BioRxiv*  
Prieto, M. L., Firouzi, K., Khuri-Yakub, B. R., Madison, D. V., Maduke, M.  
2020
- **Development and validation of a potent and specific inhibitor for the CLC-2 chloride channel** *BioRxiv*  
Koster, A. K., Reese, A. L., Kuryshev, Y., Wen, X., McKiernan, K. A., Gray, E. E., Wu, C., Huguenard, J. R., Maduke, M., Du Bois, J.  
2020
- **A CLC-ec1 mutant reveals global conformational change and suggests a unifying mechanism for the Cl<sup>-</sup>/H<sup>+</sup> transport cycle.** *eLife*  
Chavan, T. S., Cheng, R. C., Jiang, T. n., Mathews, I. I., Stein, R. A., Koehl, A. n., Mchaourab, H. S., Tajkhorshid, E. n., Maduke, M. n.  
2020; 9
- **Dynamical model of the CLC-2 ion channel reveals conformational changes associated with selectivity-filter gating.** *PLoS computational biology*  
McKiernan, K. A., Koster, A. K., Maduke, M. n., Pande, V. S.  
2020; 16 (3): e1007530
- **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
- **Activation of Piezo1 but Not NaV1.2 Channels by Ultrasound at 43 MHz.** *Ultrasound in medicine & biology*  
Prieto, M. L., Firouzi, K. n., Khuri-Yakub, B. T., Maduke, M. n.  
2018
  - **Protein ligands for studying ion channel proteins.** *journal of general physiology*  
Chavan, T., Maduke, M., Swartz, K.  
2017
  - **CLC Chloride/Proton Transporters**  
Maduke, M.  
CELL PRESS.2017: 308A
  - **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
  - **An Outward-Facing Open Conformational State in a CLC Transporter**  
Abraham, S. J., Chavan, T., Cheng, R. C., Fenollar-Ferrer, C., Han, W., Islam, S. M., Jiang, T., Khantwal, C. M., Mathews, I. I., Stein, R. A., Roux, B., Forrest, L. R., Mchaourab, et al  
CELL PRESS.2016: 178A
  - **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
  - **Monitoring Substrate-Driven Structural Changes in a CLC Chloride-Proton Antiporter with Double Electron-Electron Resonance Spectroscopy**  
Cheng, R. C., Chang, P., Fenollar-Ferrer, C., Stein, R. A., Trone, K., Forrest, L. R., Mchaourab, H. S., Maduke, M. C.  
CELL PRESS.2014: 145A
  - **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
  - **Monitoring Substrate-driven Structural Changes in a CLC Chloride-Proton Antiporter with Double Electron-Electron Resonance Spectroscopy**  
Cheng, R. C., Chang, P., Stein, R. A., Trone, K., Mchaourab, H. S., Maduke, M. C.  
ROCKEFELLER UNIV PRESS.2013: 5A
  - **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
- **Characterization of a Novel CLC-ec1 Inhibitor**  
Matulef, K. I., Howery, A., Sanford, R., Phillips, S., Simpson, S., Abraham, S., Whitelegge, J., Du Bois, J., Andersen, O. S., Maduke, M.  
CELL PRESS.2012: 520A
- **Ultrasound-Induced Currents in Planar Lipid Blayers: Origins and Potential Physiological Significance**  
Prieto, M. L., Oralkan, O., Khuri-Yakub, B. T., Maduke, M. C.  
CELL PRESS.2012: 34A
- **CLC Transporters: The Search for Conformational Change**  
Maduke, M.  
CELL PRESS.2012: 407A
- **Monitoring Substrate-Driven Conformational Changes of CIC-ec1 by [Methyl-13C] Methionine NMR**  
Cheng, R. K., Elvington, S. M., Maduke, M. C.  
CELL PRESS.2012: 520A-521A
- **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.

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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