Juan Du, Ph.D. Professor, Department of Molecular Biosciences Northwestern University

Research Focus

I am broadly interested in how the human body senses external stimuli, conveys this signal to the brain and generates responses via neuronal ion channels, such as how we detect and respond to different temperatures. To address these fundamental questions, our lab uses a diverse set of biophysical approaches to study the structure and function of these important ion channels, including cryo-electron microscopy (Cryo-EM) and patch-clamp electrophysiology. Our long-term goals include understanding temperature sensation and regulation in the human body and structure-guided drug design relevant to mental illness, pain therapy, and temperature-related pathological conditions.

<u>Contact</u>

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Education

2008-2011	Ph.D.	University of Freiburg (Chemistry), Germany
		Mentor: Prof. Dr. Oliver Einsle
2003-2008	B.A. & M.A.(Diplom)	University of Göttingen (Chemistry), Germany

Postgraduate Training

2012/04-2015/10 Postdoctoral Research Fellow, HHMI & Vollum Institute, Oregon Health & Science University, Portland, Oregon, USA
2016/05-2017/10 Postdoctoral Research Fellow, HHMI & Vollum Institute, Oregon Health & Science University, Portland, Oregon, USA
2016/05-2017/10 Postdoctoral Research Fellow, HHMI & Vollum Institute, Oregon Health & Science University, Portland, Oregon, USA
2016/05-2017/10 Postdoctoral Research Fellow, HHMI & Vollum Institute, Oregon Health & Science University, Portland, Oregon, USA

Professional Experience

- 2024/09- Professor of Molecular Biosciences, Weinberg College of Arts and Sciences, Northwestern University, Evanston, Illinois, USA
- 2024/11- Professor of Pharmacology (secondary appointment), Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA
- 2024/01-2024/08 Adjunct Professor of Molecular Biosciences, Weinberg College of Arts and Sciences, Northwestern University, Evanston, Illinois, USA
- 2021/05-2024/08 Associate Professor, Department of Structural Biology, Van Andel Institute, Grand Rapids, Michigan, USA
- 2017/10-2021/05 Assistant Professor, Department of Structural Biology, Van Andel Institute, Grand Rapids, Michigan, USA

Honors and Awards

- 2020 Pew Biomedical Scholar Award
- 2020 Alfred P. Sloan Research Fellow in Neuroscience
- 2019 Klingenstein-Simons Award in the Neurosciences
- 2019 McKnight Scholar Award for neuroscience
- 2018 Van Andel Institute Employee Impact Fund
- 2012 Arthur Lüttringhaus Prize (doctoral prize)
- 2011 Chinese Government Award for Outstanding Self-financed Students Abroad
- 2011 Ph.D. in Chemistry, awarded Summa Cum Laude

Active and Pending Research Support:

NIH NINDS R01NS129804, J. Du (PI)

Structural Basis of Nociceptor Channel TRPM3 gating and pharmacology 09/01/2023 – 06/30/2028

NIH NINDS R01NS128180, J. Du (Multi-PI) Activation and Inhibition Mechanisms of Calcium-Activated Nonselective Cation Channels 06/01/2022 – 05/31/2027

NIH NINDS R01NS111031, J. Du (PI) Structural and Functional Studies of TRPM2 channel 04/01/2019 – 03/31/2025 (NCE)

McKnight Scholar Award for neuroscience, J. Du (PI) 07/01/2019 – 06/30/2025 (NCE)

Alfred P. Sloan Research Fellow in Neuroscience, J. Du (PI) 06/01/2020 – 07/31/2025 (NCE)

Pew Biomedical Scholar Award, J. Du (PI) 07/01/2020 – 06/30/2025 (NCE)

Completed Research Support:

Klingenstein-Simons Fellowship Award in the Neurosciences, J. Du (PI) 07/01/2019 – 06/30/2024

<u>Service</u>

Peer Review Grants

2024 – 2028	Standing member of NIH Biochemistry and Biophysics of Membranes (BBM)	
2024	Ad hoc reviewer, NIH Macromolecular Structure and Function C (MSFC)	
2023	Ad hoc reviewer, NIH Biochemistry and Biophysics of Membranes (BBM)	
2021	Ad hoc reviewer, NIH R03 ZRG1 BCMB G55	
2021	Ad hoc reviewer, NIH Biophysics of Neural Systems (BPNS)	
2021	Reviewer, Chan Zuckerberg Biohub Investigator Award	
2020	Ad hoc reviewer, NIH Metformin and Aging R01 Review Panel	
2019 – present	Review Board for Pacific Northwest National Laboratory for Cryo-EM Project Proposals	

Peer Review Journals

Nature, Science, Cell, eLife, Journal of General Physiology, Nature Structural & Molecular Biology, Nature Chemistry&Molecular Biology, PNAS, Angewandte Chemie, JMB

Scientific Society Memberships and Leadership

- 2026 Chair of the Channels, Receptors & Transporters Subgroup of the 70th bps in LA
- 2025 Co-Chair of cryo-EM sessions of ACA meeting in Lombard IL
- 2024 Chair of the inaugural Gateway Ion Channel Symposium in Grand Rapids MI
- 2023 Co-Chair of the 9th International Ion Channel Conference in China
- 2019-present Biophysical Society
- 2019-present American Heart Association
- 2019-present Review Board for Pacific Northwest National Laboratory for Cryo-EM Project Proposals

Invited Seminars as a Faculty Member:

The 43rd International School of Biophysics in Erice, Silily, May 13-19 2026 2025 TRP Channel Meeting (fifth edition), Leuven, Belgium, September 17-19 2025 Caltech Biochemistry Seminar Series, Pasadena, CA, May 28-30 2025 Beijing University, Beijing, China, April 23 Cold Spring Harbor Asia Conference on Membrane Proteins, Suzhou, China, April 14-18 2025 2025 Fred Hutch Basic Sciences Seminar, Seattle, WA, April 8 BPS Channels, Receptors and Transporters Subgroup Symposium, February 15 2025 2024 ASCB/EMBO meeting, San Diego, CA, December 14, 2024 2024 Washington University in St. Louis, CIMED seminar, St. Louis, MO, December 2 2024 Weill Cornell Medicine, 2024-2025 PBSB Seminar Series, September 18 2024 EMBO Practical Course lecture, Hamburg, Germany, September 9-16 2024 International Conference on Life Science, Guiyang, China, July 25-30 2024 University of Texas at Austin, Molecular Biology, Austin, TX, April 28 2024 GRC Ligand Recognition and Molecular Gating, Ventura, March 24-29 2024 Pew Biomedical Scholar Annual Meeting, Tucson, AZ, March 17-22 2024 Duke University, Biochemistry, Durham, NC, March 1 2023 UMass at Amherst, MCB, Amherst, MA, November 7 2023 Northwestern University, Molecular Biosciences, Evanston, IL, March 9 2022 Neurocrine, December 7, virtual 2022 GRC Ion Channels, Mount Holyoke College, July 10-15 2022 GRC Calcium Signaling, Ventura, CA, June 2022 FASEB Science Research Conferences (SRC) on NAD+ Metabolism and Signaling, 2022 Steamboat, CO, June 2022 McKnight Neuroscience Foundation Meeting, Aspen, CO, June 2022 Klingenstein-Simons Neuroscience Foundation Meeting, New York, May 2022 Vollum Institute, Oregon Health & Science University, Portland, OR, April 29th NIH Neuroscience Seminar, March 14th, virtual 2022 BPS Channel Receptors & Transporters Subgroup, San Francisco, CA, February 19-23 2022 2021 FMP Institute, Germany, November 03, virtual 2021 Society of General Physiologist (SGP) annual meeting, September 8-12, virtual 2021 The 8th International Ion Channel Conference, China, August 03, virtual 2021 FASEB Science Research Conferences (SRC) on the understudied druggable genome, June. virtual 2021 FASEB Science Research Conferences (SRC) NAD+ Metabolism and Signaling, June, virtual (keynote speaker) University of Washington, Seattle, WA, January 2020 Shanghai institute of Neuroscience, Shanghai, China, July 2019 2019 Shanghai Institute of Materia Medica, Shanghai, China, July 2019 The 7th International Ion Channel Conference, Zhejiang University, Hangzhou, China, June 2019 Hamburg Eppendorf Klinikum, Hamburg, Germany, May

Peer-Reviewed Publications:

*: co-corresponding author; #: co-first author

26. Kumar S[#], Jin F[#], Park SJ, Choi W, Keuning S, Massimino R, Vu S, Lü W* & <u>**Du J***</u>. Convergent Agonist and Heat Activation of Nociceptor TRPM3. *Under Review, BioRxiv* (2025).

25. Huang Y, Kumar S, Lee J, Lü W* & <u>Du J*</u>. Coupling enzymatic activity and gating in an ancient TRPM chanzyme and its molecular evolution. *Nat Struct Mol Biol*, **31**, 1509-1521 (2024).

24. Hu J, Park SJ, Walter T, Orozco I, O'Dea G, Ye X, <u>**Du J***</u> & Lü W*. Physiological temperature drives TRPM4 ligand recognition and gating. *Nature*, **630**:509-515 (2024).

23. Ruan Z, Lee J, Li Y & <u>**Du J***</u> & Lü W*. Human Pannexin 1 Channel is NOT phosphorylated by Src Tyrosine Kinase at Tyr199 and Tyr309. *eLife* (2024).

22. Muller C[#], Zhang L[#], Zipfel S, Topitsch A, Lutz M, Eckert J, Prasser B, Chami M, Lü W, <u>**Du J**</u> & Einsle O^{*}. Molecular interplay of an assembly machinery for nitrous oxide reductase. *Nature* **608**, 626-631 (2022).

21. Ruan Z[#], Haley E[#], Orozco IJ[#], Sabat M, Myers R, **Du J**^{*}, Lü W^{*}. Structures of TRPM5 channel elucidate mechanism of activation and inhibition. *Nat Struct Mol Biol* **28**, 604-613 (2021).

20. Yu J[#], Zhu HT[#], Lape R, Greiner T, <u>**Du**</u>, Lü W, Sivilotti L^{*}, Gouaux E^{*}. Mechanism of gating and partial agonist action in the glycine receptor. *Cell* 184(4):957-968.e21 (2021).

19. Ruan Z[#], Osei-Owusu J[#], <u>**Du**</u>, Qiu Z^{*}, Lü W^{*}. Structures and pH sensing mechanism of protonactivated chloride channel. *Nature* **588**, 350-354 (2020).

18. Ruan Z, Orozco I. J., **Du J***, Lü W*. Structures of human Pannexin 1 reveal ion pathways and mechanism of gating. *Nature* **584**, 646-651 (2020).

17. Lü W* & <u>**Du J***</u>. The N-terminal domain in TRPM2 channel is a conserved nucleotide binding site. *Journal of General Physiology* 152(5):e20192555 (2020).

16. Huang Y, Fliegert R, Guse A. H, Lü W*, <u>**Du J***</u>. A structural overview of the ion channel of the TRPM family. *Cell Calcium* 85(102111) (2020).

15. Choi W[#], Clemente N[#], Sun W, <u>**Du J**</u>^{*}, Lü W^{*}. The structures and gating mechanism of calcium homeostasis modulator2. *Nature* **576**, 163-167 (2019).

14. Huang Y, Roth B, Sun W, Lü W*, <u>**Du J***</u>. Ligand recognition and gating mechanism through three ligandbinding sites of human TRPM2 channel. *eLife* 8:e50175 (2019).

13. Haley E[#], Choi W[#], Fan C, Sun W, <u>**Du J***</u>, Lü W*. Expression and purification of the human lipidsensitive cation channel TRPC3 for structural determination by single-particle cryo-electron microscopy. *J. Vis. Exp.* (143), e58754 (2019).

12. Huang Y, Winkler PA, Sun W, Lü W*, <u>**Du J***</u>. Architecture of the TRPM2 channel and its activation mechanism by ADP-ribose and calcium. *Nature* **562**, 145-149 (2018).

11. Fan C[#], Choi W[#], Sun W, <u>**Du J**</u>^{*}, Lü W^{*}. Structure of the human lipid-gated cation channel TRPC3. *Elife* 7:e36852 (2018).

10. Winkler PA[#], Huang Y[#], Sun W[#], <u>**Du J**</u>, Lü W. Electron cryo-microscopy structure of a human TRPM4 channel. *Nature* **552**, 200-204 (2017).

9. Lü W[#], **Du J[#]**, Goehring A, Gouaux E. Cryo-EM structures of the triheteromeric NMDA receptor and its allosteric modulation. *Science* 355(6331)3729 (2017).

8. <u>Du J[#]</u>, Lü W[#], Wu S, Cheng Y, Gouaux E. Glycine receptor mechanism elucidated by electron cryomicroscopy. *Nature* **526**, 224-229 (2015).

7. Lee CH[#], Lü W[#], Michel JC, Goehring A, <u>**Du**</u>, Song X, Gouaux E. NMDA receptor structures reveal subunit arrangement and pore architecture. *Nature* **511**, 191-197 (2014).

6. Lü W, <u>**Du J**</u>, Schwarzer NJ, Wacker T, Andrade SL, Einsle O. The formate/nitrite transporter family of anion channels. *Biol Chem*, 394(6)715-727 (2013).

5. Lü W, Schwarzer NJ, **Du J**, Gerbig-Smentek E, Andrade SL, Einsle O. Structural and functional characterization of the nitrite channel NirC from Salmonella typhimurium. *Proc Natl Acad Sci USA* 109(45)18395-18400 (2012).

4. Lü W, **Du J**, Schwarzer NJ, Gerbig-Smentek E, Einsle O, Andrade SL. The formate channel FocA exports the products of mixed-acid fermentation. *Proc Natl Acad Sci USA* 109(33)13254-13259 (2012).

3. <u>Du J[#]</u>, Say RF[#], Lü W, Fuchs G, Einsle O. Active-site remodelling in the bifunctional fructose-1,6-bisphosphate aldolase/phosphatase. *Nature* **478**, 534-537 (2011).

2. Lü W, **Du J**, Wacker T, Gerbig-Smentek E, Andrade SL, Einsle O. pH-dependent gating in a FocA formate channel. *Science* 332(6027)352-354 (2011).

1. Lü W, **Du J**, Stahl M, Tzivelekidis T, Belyi Y, Gerhardt S, Aktories K, Einsle O. Structural basis of the action of glucosyltransferase Lgt1 from Legionella pneumophila. *J Mol Biol* 396(1)321-331 (2010).