BIOGRAPHICAL SKETCH

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NAME: Da-Neng Wang, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): wangd01

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Northeastern University, Shenyang, China	B.Sc.	1982	Physics
Academia Sinica, Shenyang, China	M.Sc.	1984	Crystallography & Electron Microscopy
University of Stockholm, Sweden	Ph.D.	1988	Structural Chemistry & Crystallography
European Molecular Biology Laboratory (EMBL), Heidelberg, Germany	Postdoc	1988-1991	Structural Biology

A. Personal Statement

I aim to understand the molecular mechanism of membrane transporters that are involved in key biological processes in the cell, using a combination of crystallographic, biochemical and biophysical approaches. My research on membrane proteins started when I was a postdoc at the European Molecular Biology Laboratory (EMBL) in Heidelberg. After joining the NYU faculty, my lab has focused on the mechanistic understanding of membrane transporters using structural and biochemical approaches. Over the years, the lab has been very fortunate in being able to recruit some very talented young scientists, who made breakthroughs in crystallizing and determining the structures of a number of membrane transporters and channels. All these membrane proteins play key roles in the cell. Their structures, along with biochemistry and computational characterizations, greatly advanced the molecular mechanisms of these membrane proteins and shed light on their biological role in the cell.

a. Mancusso, R.L., Gregorio, G.G., Liu, Q. and Wang, D.N. (2012) Structure and mechanism of a bacterial sodium-dependent dicarboxylate transporter. ***Nature***, 491, 622-626. PMC3220791

b. Czyzewski, B.K. and Wang, D.N. (2012) Identification and characterization of a bacterial hydrosulfide ion channel. ***Nature***. 483, 494-497. PMC3711795

c. Zhou, Z., Zhen, J., Karpowich, N.K., Goetz, R.M., Law, C.J., Reith, M.E.A. and Wang, D.N. (2007) LeuT-desipramine structure reveals how antidepressants block neurotransmitter reuptake. ***Science***. 317, 1390-1393. PMC3711652

d. Huang, Y., M.J. Lemieux, J.M. Song, M. Auer and D.N. Wang. (2003) Structure and mechanism of the glycerol-3-phosphate transporter from *Esherichia coli*. ***Science,*** 301, 616-620. PMID: 12893936

B. Positions and Honors

Positions and Employment

1982 – 1985	M.Sc. Student, Chinese Academy of Sciences, Shenyang, China
1985 – 1988	Ph.D. Student, Department of Structural Chemistry, Arrhenius Laboratory, University of Stockholm, Stockholm, Sweden
1988 – 1991	Postdoctoral Associate, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany
1991 – 1995	Staff Scientist, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

1995 – 2004	Assistant Professor, Skirball Institute of Molecular Medicine and Department of Cell Biology, New York University School of Medicine, New York
2002 – 2007	Graduate Advisor, NIH-NYU Joint Ph.D. Program in Structural Biology
2003 – present	Guest Professor, National Key Laboratory of Biomembrane and Membrane Biotechnology, Tsinghua University, Beijing, China
2005 – 2008	Associate Professor with tenure, Skirball Institute of Molecular Medicine and Department of Cell Biology, New York University School of Medicine, New York
2005 – 2015	Head, Division of Crystallography, New York Consortium of Membrane Protein Structure (NYCOMPS), New York
2007 – 2011	Graduate Advisor, NYU Ph.D. Program in Structural Biology
2008 – present	Professor, Skirball Institute of Molecular Medicine and Department of Cell Biology, New York University School of Medicine, New York
2008 – 2014	Program Coordinator, Structural Biology Program, Skirball Institute of Molecular Medicine, New York University School of Medicine, New York
2011 – 2012	Graduate Advisor, NYU Ph.D. Program in Molecular Biophysics
2014 – present	Program Coordinator, Metabolic Signaling Program, Skirball Institute of Molecular Medicine, New York University School of Medicine, New York

Other Experience and Professional Memberships

1985 – 1988	Member, Scandinavian Electron Microscopy Society
1993 – present	Member, American Association for the Advancement of Sciences
1994 – present	Member, The Biophysical Society
1997 – present	Member, the Harvey Society
2001 – 2013	Member, Editorial Board, *Journal of Chinese Electron Microscopy Society*
2002 – 2007	Member, Biology Proposal Study Penal, National Synchrotron Light Source, Brookhaven National Laboratory, Upton, NY
2002	*ad hoc* Member, NIH Study Section ZRG1 BBCB
2004	Member, Macromolecular Crystallography Review Penal, DOE
2006	*ad hoc* Member, NIH Study Section ZRG1 BCMB-B
2006 – present	Member, Publications Committee, the Biophysical Society
2006 – 2014	Member, the Protein Society
2006 – 2014	Member, the Society for Neuroscience
2007	*ad hoc* Grant Reviewer, NIH/NIDA
2007	*ad hoc* Member, NIH Study Section on Biochemistry and Biophysics of Membranes (BBM)
2008 – 2012	Permanent Member, NIH Study Section on Biochemistry and Biophysics of Membranes (BBM)
2008 – 2013	Referee, European Research Council (ERC) Review Panel LS1 (Molecular and Structural Biology and Biochemistry)
2010 – 2015	External Advisor, Membrane Protein Structural Biology Consortium, University of Buffalo – University of Rochester – University of Virginia
2011 – present	Member, Scientific Advisory Board for Swiss National Science Foundation NCCR Center "From Transporter Physiology to Therapeutic Targets", University of Bern, Switzerland
2011 – present	Member, College of Reviewers for the Canada Research Chairs Program
2011 – 2017	Member, Commission on Electron Crystallography (CEC), International Union of Crystallography (IUCr)
2011 – 2014	Chair, IUCr-CEC Sub-Committee on Biological Cryo-Microscopy
2012 – 2015	Member (*ex officio*), Finance Committee, the Biophysical Society
2012 – 2015	Chair, Publications Committee, the Biophysical Society
2014	Member, NIH Study Section ZAT1 TT-M (S1)
2014	External Evaluator for Faculty Recruitment, Department of Biochemistry and Biophysics, University of Stockholm
2015 – present	Chair, Biophysical Journal Sub-Committee, the Biophysical Society
2015	Member, NIH Study Section ZGM1 CBB-0, "Regional Consortia for High Resolution Cryo-Electron Microscopy" (U24)
2015	*ad hoc* Member, Board of Scientific Counselors, National Institute of Neurological

	Disorders and Stroke (NINDS)
2016 – present	Member, Faculty of 1000, Section on Membrane Proteins & Their Functional Complexes
2016	Member, NIH Special Emphasis Panel/Scientific Review Group 05 ZRG1 MOSS-R (56) R, Director's New Innovator Award Program (DP-2)
2016	Member, NIH Study Section ZRG1 MDCN-C (05), "Ion Channels and Synapses"
2017	Member, NIH Special Emphasis Panel/Scientific Review Group 05 ZRG1 MOSS-R (56) R, Director's New Innovator Award Program (DP-2)
2017	Member, NIH Study Section ZRG1 CBR 30, "Cryo-EM and Ancillary Equipment" (S10)
2017 – present	Member, American Epilepsy Society
2017 – present	Member, Biophysical Society-Institute of Physics Advisory Board on eBooks
2017 – present	Member, Award Committee, Chinese Cryo-Electron Microscopy Society
2018	Member, NIH Special Emphasis Panel/Scientific Review Group 05 ZRG1 MOSS-R (56) R, Director's New Innovator Award Program (DP-2)
2018	*ad hoc* Member, NIH Study Section Biochemistry and Biophysics of Membranes (BBM)
2018 – present	Member, NSLS-II Structural Biology Proposal Review Panel
2019	Member, NIH Special Emphasis Panel/Scientific Review Group 05 ZRG1 MOSS-R (70) R, Director's New Innovator Award Program (DP-2)

Honors

1986	Kazato Young Electron Microscopist Travel Award, Scandinavian Society of Electron Microscopy
1987	National Science Medal, First Class, State Council of Science and Technology, China
1987	Chien-Shiung Wu Prize for Young Experimental Physicists, Chinese Physics Society
1988 – 1989	Postdoctoral Fellowship, European Molecular Biology Laboratory (EMBL)
1989 – 1991	Postdoctoral Fellowship, German Research Council (DFG)
1997 – 1998	Whitehead Fellowship for Junior Faculty in Biomedical or Biological Sciences, New York University
2002	K.H. Kuo Prize, Chinese Electron Microscopy Society
2003	Outstanding Overseas Chinese Young Scientist Award, National Science Foundation of China
2007	Lennart Philipson Award, Skirball Institute, New York University School of Medicine
2009	Lennart Philipson Award, Skirball Institute, New York University School of Medicine
2014	The Peter C. Maloney Lectuer, Johns Hopkins University School of Medicine

C. Contributions to Sciences:

1. Crystal structure and mechanism of the glycerol-3-phosphate transporter

Joanne Lemieux and Yafei Huang, a graduate student and a postdoc in my lab, were able to crystallize and determine the structure of GlpT, a member of the major facilitator superfamily (MFS). MFS is the largest secondary transporter family, and the 3.2Å GlpT structure, published back-to-back with the LacY structure by Ron Kaback, were the first two structures solved for any secondary transporters. The GlpT structure allowed us to propose a "Rocker-Switch" mechanism of transport, which later has been shown to be accurate and applicable to the entire MFS family. In collaboration with Dr. Emad Tajkhorshid's lab in UIUC, we also characterized the structural basis of the substrate specificity.

a. Huang, Y., M.J. Lemieux, J.M. Song, M. Auer and D.N. Wang. (2003) Structure and mechanism of the glycerol-3-phosphate transporter from *Esherichia coli*. ***Science,*** 301, 616-620. PMID: 12893936

b. Law, C.J., Yang, Q., Soudant, C., Maloney, P.C. and Wang, D.N. (2007) Kinetic evidence is consistent with the rocker-switch mechanism of membrane transport by GlpT. ***Biochemistry***, 46, 12190-12197. PMCID: PMC2435215

c. Law, C.J., Almqvist, J., Bernstein, A., Huang, Y., Goetz, R.M., Soudant, C., Laaksonen, A., Hovmöller, S. and Wang, D.N. (2008). Salt bridge dynamics upon substrate binding to GlpT participate in conformational change during transport. ***J. Mol. Biol***., 378, 826-837. PMCID: PMC2426824

d. Law, C.J., Enkavi, G., Wang, D.N. and Tajkhorshid, E. (2009). Structural basis of substrate selectivity in the glycerol-3-phosphate:phosphate antiporter GlpT. ***Biophys. J.,*** 97, 1346-1353. PMCID: PMC2749764

2. Crystal structure and mechanism of the Na^+-driven dicarboxylate transporter

Romina Manccuso, a graduate student in the lab, crystallized and solved the structure of the bacterial Na+-dependent dicarboxylate transporter VcINDY. The protein is a homolog of the human Na^+-driven citrate transporter NaCT in the plasma membrane, which regulates the intracellular levels of citrate for fatty acid synthesis. The crystal structure revealed one citrate and one Na^+ ion bound. Again this was the first structure solved from that transporter superfamily. In collaboration with Joe Mindell, we characterized the substrate specificity and driving force in reconstituted proteoliposomes. This structure has been used to help inhibitor design as anti-obesity drug leads. More recently, the structure has been used to understand how mutations in the homologous human citrate transporter cause early-onset pediatric epilepsy.

a. Mancusso, R.L., Karpowich, N.K., Czyzewski, B.K. and Wang, D.N. (2011) Simple screening method for improving membrane protein thermostability. ***Methods***. 55, 324-329.

b. Mancusso, R.L., Gregorio, G.G., Liu, Q. and Wang, D.N. (2012) Structure and mechanism of a bacterial sodium-dependent dicarboxylate transporter. ***Nature***, 491, 622-626. PMCID: PMC3220791

c. Mulligan, C., Fitzgerald, G.A., Wang, D.N. and Mindell, J.A. (2014) Functional characterization of a Na^+-dependent dicarboxylate transporter from *Vibrio cholerae.* ***J. Gen. Physiol****.,* 143, 745-759. PMCID: PMC4035743

3. Structure and drug-binding site in leucine transporter

LeuT is a homolog of the human serotonin transporter and dopamine transporter in the brain. The structures of LeuT, in complex with various antidepressant molecules, were determined by Zheng Zhou, a postdoc in the lab. These structures revealed an allosteric drug binding site in the transporter protein.

a. Zhou, Z., Zhen, J., Karpowich, N.K., Goetz, R.M., Law, C.J., Reith, M.E.A. and Wang, D.N. (2007) LeuT-desipramine structure reveals how antidepressants block neurotransmitter reuptake. ***Science***, 317, 1390-1393. PMCID: PMC2758934

b. Zhou, Z., Zhen, J., Karpowich, N.K., Law, C.J., Reith, M.E.A. and Wang, D.N. (2009) Antidepressant specificity of serotonin transporter suggested by three LeuT-SSRI structures. ***Nat. Struct. Mol. Biol.***, 16, 652-657. PMCID: PMC2758934

4. Structural basis of ion selectivity and gating mechanism of formate and hydrosulphite channels

Andrew Waight and Bryan Czyzewski, two graduate students in the lab, crystallized and solved the structures of two acid channels that are involved in cellular metabolism in bacteria. Both formate and hydrosulphite are produced during bacterial metabolism. These structures revealed the structural basis of the ion selectivity and gating mechanisms of these two channels.

a. Waight, A.B., Love, J. and Wang, D.N. (2010) Structure and mechanism of a pentameric formate channel. ***Nat. Struct. Mol. Biol****.,* 17, 31-37, doi:10.1038/nsmb.1740. PMCID: PMC3613427

b. Czyzewski, B.K. and Wang, D.N. (2012) Identification and characterization of a bacterial hydrosulfide ion channel. ***Nature***, 483, 494-497. PMCID: PMC3711795

5. 3.4 Å cryo-EM structure of the plant light-harvesting complex

As a postdoc in the group of Werner Kühlbrandt at the European Molecular Biology Laboratory (EMBL), I was able to determine the 3.4 Å structure of the plant light-harvesting chlorophyll-protein complex (LHC-II), using cryo-EM from two-dimensional crystals. The protein complex is the main antenna for photosynthesis in the chloroplast membrane and the energy it absorbs is funneled to the reaction center to power photosynthesis. The 3.4 Å structure reveals, besides the transmembrane α-helices and their side chains, the positions and orientations of all 13 bound chlorophyll molecules. The structure was able to explain the high efficiency of energy transfer in photosynthesis. It was the 5th membrane protein structure ever solved, and the 1st eukaryotic one ever to high resolution.

a. Kühlbrandt, W. and Wang, D.N. (1991) Three-dimensional structure of plant light-harvesting complex determined by electron crystallography. ***Nature,*** 350, 130-134. PMID: 2005962

b. Wang, D.N. and Kühlbrandt, W. (1991) High-resolution electron crystallography of the light-harvesting chlorophyll a/b-protein complex in three different media. ***J. Mol. Biol***., 217, 691-699. PMID: 2005619

c. Nussberger, S., Dörr, K., Wang, D.N. and Kühlbrandt, W. (1993) Protein-lipid interactions in crystals of plant light-harvesting complex. ***J. Mol. Biol***., 232, 347-356. PMID: 8230219

d. Kühlbrandt, W., Wang, D.N. and Fujiyoshi, Y. (1994) Atomic structure of plant light-harvesting complex determined by electron crystallography. ***Nature,*** 367, 614-621. PMID: 8107845

Complete list of published work

http://www.ncbi.nlm.nih.gov/sites/myncbi/daneng.wang.1/bibliography/40755472/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

1R01GM121994 09/01/17 - 08/31/21
NIH/NIGMS
PI: D. N. Wang
Mechanism of Ragulator activation of the Rag GTPase for the recruitment of mTORC1
There is no overlap with the current project.

R01 NS108151-01 07/01/18 - 06/30/23
Molecular mechanism of citrate transporter NaCT and its mutations that cause pediatric epilepsies
PI: D. N. Wang

AES2017SD3 01/01/18 – 12/31/18
American Epilepsy Society
PI: D. N. Wang
Characterization of the neuronal citrate transporter – a gene mutated in pediatric epilepsy

PF0000000 01/01/18 – 12/31/18
Pfizer Inc.
PI: D. N. Wang
Crystallization and structure determination of the human citrate transporter NaCT in complex with inhibitor PF2

Completed Research Support (in the past three years)

R01DK099023 03/01/13- 2/28/17
NIH/NIDDK
PI: D. N. Wang
Structural and mechanistic studies of INDY proteins

R01DA019676 04/01/12 - 03/31/17
NIH/NIDA
PI: M. Reith (Co-PI: D. N. Wang)
Dopamine transporters and ions, substrates, blockers

U54GM095315 07/01/10 - 06/30/15
NIH/NIGMS
PI: W. A. Hendrickson (Co-PI: D. N. Wang *et al.*)
Structural genomics of membrane proteins

Pending

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
David B. Sauer, Ph.D.	Postdoctoral Fellow
eRA COMMONS USER NAME sauerd01	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Purdue University, West Lafayette, IN	B.S.	2005	Chemistry
UT Southwestern Medical Center at Dallas, TX	Ph.D	2012	Molecular Biophysics
NYU School of Medicine, NY	Postdoc	2015	Structural Biology

A. Personal Statement

Dr. Sauer has been studying cell membranes for 10 years, focusing on the structure and mechanism of membrane proteins. His most recently completed work focused on the mechanisms of ion channel folding and selectivity utilizing high-resolution X-ray crystallography in conjunction with bioinformatics and functional studies. His current work aims to address the mechanisms of eukaryotic transporters by X-ray crystallography.

B. Positions and Honors

Positions and Employment

2002 – 2002 Undergraduate Research Assistant, Department of Chemistry, University of Missouri
2003 – 2005 Undergraduate Research Assistant, Department of Chemistry, Purdue University
2006 – 2012 Graduate Research Assistant, Department of Physiology, UT Southwestern
2012 – present Postdoctoral Fellow, Skirball Institute of Biomolecular Medicine, New York University School of Medicine

Other Experience and Professional Memberships

Member, Biophysical Society

Honors

2013 Outstanding Poster Presentation, New York University Skirball Institute Retreat
2007 – 2010 Predoctoral Training Grant, NIH and UT Southwestern Molecular Biophysics
2005 Dale W. Margerum Undergraduate Research Award, Purdue University Dept. of Chemistry
2005 Outstanding Research Award, Purdue Undergraduate Research and Poster Symposium
2004 Harrison M. Stine Memorial Scholarship, Purdue University Department of Chemistry
2004 Best Science Paper Award, Butler University and Eli Lilly

C. Selected Peer-reviewed Publications

Most relevant to the current application

Additional recent publications of importance to the field (in chronological order)

1. M.C. Hull, D.B. Sauer, and J.S. Hovis. “The Influence of Lipid Chemistry on the Osmotic Response of Cell Membranes: Effect of Non-Bilayer Forming Lipids,” **J. Phys. Chem. B**, 108, 15890 -15895 (2004).

2. M.G. Derebe*, D.B. Sauer*, W. Zeng, A. Alam, N. Shi and Y. Jiang. “Tuning the Ion Selectivity of Tetrameric Cation Channels by Changing the Number of Ion Binding Sites” **Proc. Natl. Acad. Sci. USA**, 108, 598-602 (2011).

*- authors contributed equally

3. D.B. Sauer, W. Zeng, S. Raghunathan and Y. Jiang. “Protein Interactions Central to Stabilizing the K+ Channel Selectivity Filter in a 4-sited Configuration for Selective K+ Permeation” **Proc. Natl. Acad. Sci. USA**, 108, 16634-16639 (2011).

4. J. Liao, H. Li, W. Zeng, D.B. Sauer, R. Belemares, Y. Jiang. “Structural Insight into the Ion Exchange Mechanism of Sodium/Calcium Exchanger” **Science**, 335, 686-690 (2012).

5. C. Kong, W. Zeng, S. Ye, L. Chen, D.B. Sauer, Y. Lam, M.G. Derebe, Y. Jiang. “Distinct Gating Mechanisms revealed by the structures of a multi-ligand gated K^+ channel” **eLife**, 1 (2012).

6. D.B. Sauer, W. Zeng, J. Canty, Y. Lam, Y. Jiang “Sodium and potassium competition in potassium-selective and non-selective channels” **Nat. Commun.** 4:2721 doi: 10.1038/ncomms3721 (2013).

7. Y. Lam*, W. Zeng*, D.B. Sauer*, Y. Jiang “High Resolution Structural Views of Rubidium, Cesium and Barium Binding within a Potassium Selective Channel Filter” **J. Gen. Physiol.**, 144, 181-192 (2014).

8. D.B. Sauer, N.K. Karpowich, J. Song, D.N. Wang “Rapid Bioinformatic Identification of Thermostabilizing Mutations” submitted.

D. Research Support

Ongoing Research Support

None.

Completed Research Support (in the past three years)

None.