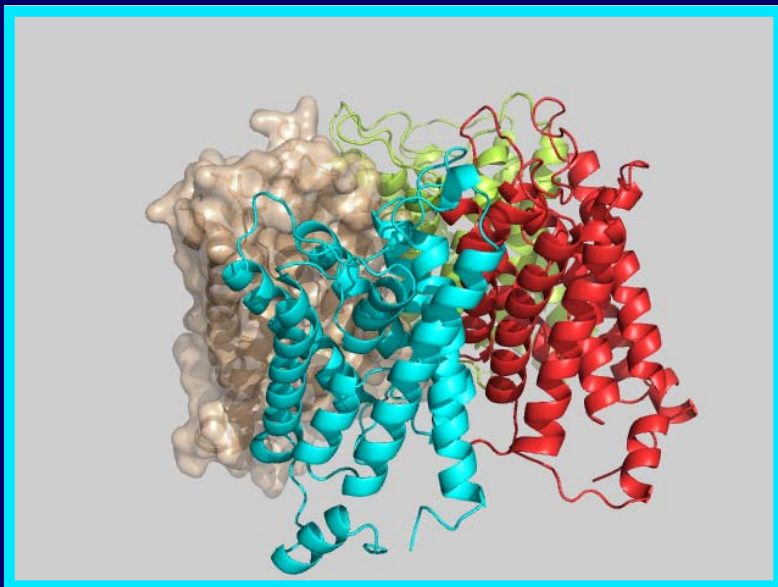


GAS CHANNELS WORKSHOP



September 6 - 7, 2012

*Case Western Reserve University
School of Medicine
Cleveland, Ohio*

*SPONSORED BY
THE OFFICE OF NAVAL RESEARCH*

Gas Channels Workshop

Thursday, September 6 &
Friday, September 7, 2012

*Department of Physiology and Biophysics
Case Western Reserve University
School of Medicine*

*Sponsored by
The Office of Naval Research*

Welcome to the Workshop on Gas Channels, sponsored by the Office of Naval Research and the Department of Physiology and Biophysics in the School of Medicine at Case Western Reserve University.

The ONR handles the science and technology programs of the US Navy and Marine Corps. Divers, submariners, and individuals ascending to altitude may face a range of medical issues related to dissolved (or undissolved) gases. These include decompression illness, N₂ narcosis, O₂ toxicity, CO₂ narcosis, and hypoxia. Thus, the ONR has a strong and longstanding interest in gas transport.

The Department of Physiology and Biophysics at Case Western Reserve University is one of the few in the world that studies physiological problems from the level of the atom—through molecules, cellular organelles, whole cells, tissues, and organs—to the whole organism. We focus on the nervous, cardiovascular, and renal systems. In the past few years, we have recruited eight outstanding new faculty members. In addition, we completed a major renovation of about 40,000 gross square feet of space. We have also established three major core facilities to support our work: A Protein Expression, Purification, and Crystallization Core (PEPCC, 5th floor), a Molecular Biophysics Core (6th floor), and a Mouse Physiological Phenotyping Core (MPPC, basement).

We hope that you enjoy the Workshop. If during your visit you would like to see our facilities, we would be happy to arrange a tour.



WORKSHOP AGENDA
Thursday, September 6, 2012

7:45 - 8:15am

Registration & Continental Breakfast

8:15am - 8:20am

Welcome/ Introduction

-Walter F. Boron, M.D., Ph.D.

8:20am - 9:00am

Walter Boron, M.D., Ph.D.

Title: "Gas Channels"

9:00am - 9:10am:

Question/Answer Session

9:10am - 9:50am

Emad Tajkhorshid, Ph.D.

Title: "Visualizing gas permeation pathways through proteins at sub-Angstrom resolution"

9:50am - 10:00am:

Question/Answer Session

10:00am - 10:25am:

Morning Break

10:25am - 11:05am

Gerolf Gros, Ph.D.

Title: "Measuring cellular CO₂ permeability by ¹⁸O exchange—methodology and results on red blood cells"

11:05am - 11:15am: *Question/Answer Session*

11:15am - 11:55am

Volker Endeward, Ph.D.

Title: "Intrinsic CO₂ permeability of cell membranes and effect of cholesterol and aquaporin"

11:55am - 12:05pm: *Question/Answer Session*

12:05pm - 1:05pm

Lunch –On your own

(Lunch provided for invited speakers in E-504)

1:05pm - 1:45pm

Bhanu Jena, Ph.D.

Title: “Involvement of elevated membrane cholesterol on G-protein regulated water and gas transport in biological membranes”

1:45pm- 1:55pm: Question/Answer Session

1:55pm - 2:35pm

Jeffrey Garvin, Ph.D.

Title: “NO transport by aquaporin I”

2:35pm - 2:45pm: Question/Answer Session

2:45pm - 3:10pm: Afternoon Break

3:10pm - 3:50pm

David Weiner, M.D.

*Title: “Role of Rh glycoproteins in gas transport
— lessons from in vitro model systems”*

3:50pm - 4:00pm: Question/Answer Session

4:00pm - 5:00pm

Robert Stroud, Ph.D.

Title: “What do structures of the Aquaporins, and Ammonia transporters tell us about conduction of gases?”

WORKSHOP AGENDA
Friday, September 7, 2012

8:00am - 8:30am

Continental Breakfast

8:30am – 8:35am

Introduction/Welcome

-Dr. Walter Boron, M.D., Ph.D.

8:40am – 9:00am

Speaker: Ryan Geyer, Ph.D.

Title: “Role of membrane proteins in oxygen transport in red blood cells”

9:05am – 9:25am

Speaker: Rossana Occhipinti, Ph.D.

Title: “Mathematical modeling of gas movements in an oocyte ”

9:30am - 9:50am

Speaker: Xue Qin, Ph.D.

Title: “Structure determinants for CO₂ transport of human aquaporin 5”

10:00am – 10:30am

Morning Break

(Refreshments served)

10:30am - 1:00pm

Gas Workshop Meeting

1:00pm - 2:00pm

Lunch

2:00pm - 3:30pm

Gas Workshop Meeting

3:30pm –End of Meeting

Walter F. Boron, M.D., Ph.D.
–Case Western Reserve University
Cleveland, Ohio



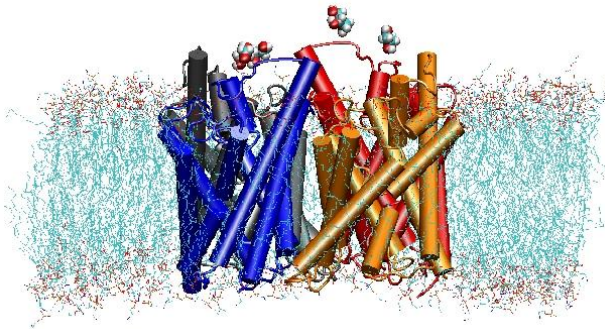
Dr. Boron is the David N. and Inez Myers/ Antonio Scarpa Professor & Chairman of the Department of Physiology and Biophysics at Case Western Reserve University. He earned his AB in chemistry at Saint Louis University, and his M.D. and Ph.D. (Physiology & Biophysics) at Washington University in St. Louis. He joined Yale University as a post-doctoral fellow with Emile Boulpaep in 1978, and remained there for the next 29 years, serving as Chairman of the Department of Cellular & Molecular Physiology for three 3-year terms (1989-1998). In 2007 he returned to his hometown of Cleveland. He is the former President of the American Physiological Society (APS) and is currently Secretary-General of the International Union of Physiological Sciences (IUPS). He is the former editor-in-chief of Physiological Reviews and is the former editor-in-chief of Physiology. He and Emile Boulpaep co-edit the textbook Medical Physiology. He developed his life-long interest in acid-base transport and intracellular-pH regulation with his Ph.D. mentor Albert Roos as well as Paul De Weer, and his complementary interest in renal HCO_3^- transport with Boulpaep. His group currently focuses on three related areas: the molecular physiology of the Na^+ -coupled HCO_3^- transporters, molecular $\text{CO}_2/\text{HCO}_3^-$ sensors, and gas channels. Among his previous honors are a Young Investigator Award (American Society of Nephrology/American Heart Association, 1986), the Robert F. Pitts Award (IUPS, 1993), the Gottschalk Award (APS, 1998), an NIH MERIT Award (2002), the Homer Smith Award (ASN, 2005), the Sharpey-Schafer Award (The Physiological Society, 2008), and the Palade Gold Medal (shared with William Catterall and Richard Tsién, Wayne State University, 2010).

Emad Tajkhorshid, Ph.D.
-University of Illinois at Urbana-Champaign
Urbana, Illinois



Emad Tajkhorshid received his initial training as a pharmacist from Tehran University. After attending two Ph.D. programs, one in medicinal chemistry and pharmacology at Tehran University of Medical Sciences and another one in molecular biophysics at the University of Heidelberg, he started his postdoctoral

training in Computational Biophysics in the Theoretical and Computational Biophysics Group at the University of Illinois at Urbana-Champaign in 2001. In 2003 he became the assistant director of research of the NIH Center for Macromolecular Modeling and Bioinformatics at the Beckman Institute for Advanced Science and Technology. He started his independent career as an assistant professor of biophysics, biochemistry, and pharmacology in 2007 and was promoted to associate professor in 2010. The primary focus of his research is on understanding the structural and dynamical properties of membranes and membrane proteins as a basis for their biological function. Employing computational methodologies, his group investigates a wide range of membrane proteins and membrane-associated phenomena in biological systems, in particular the mechanisms of passive and active transport across the membrane.



Gerolf Gros, M.D., Ph.D.
–Hannover Medical School
Hannover, Germany



Dr. Gros is Professor of Physiology at the Department of Physiology at the Medizinische Hochschule Hannover/Germany. He was Professor and Chairman of this Department from 1986 to 2008. He earned his MD degree in 1969 at the University of Tübingen/Germany, followed by one year of practical clinical work. In 1970 he joined Hannover Medical School as a postdoc with Waldemar Moll, and joined his mentor when he moved to the Department of Physiology at the University of Regensburg in 1972. Intermittently, he worked at the Department of Physiology with Robert E. Forster in 1973-1974. He obtained his "Habilitation" in Physiology after returning to Regensburg in 1976. From 1978-1986 he was Associate Professor of Physiology at the University of Essen, and thereafter moved to Hannover to become Full Professor and Department Chairman. He was President of the German Physiological Society in 2007, and President of the Annual Congress of Physiology held in Hannover in 2007. He developed a life-long interest in CO_2 and O_2 transport in the body, in carbonic anhydrases and in acid-base physiology, initially stimulated by Waldemar Moll and Robert E. Forster. After his move to Hannover, he developed a second field of interest in studying the molecular mechanisms of skeletal muscle plasticity. His work was continuously supported by the Deutsche Forschungsgemeinschaft. His most recent interest is in the field of CO_2 channels in biological membranes, in combination with developing a novel method to determine the CO_2 permeability of cell membranes, and in the molecular mechanism of HCO_3^- transfer across the red cell membrane.

Volker Endeward, Ph.D.
–Hannover Medical School
Hannover, Germany



Dr. Endeward is presently Asst. Professor of Physiology in the Department of Physiology of the Medizinische Hochschule Hannover/Germany. From 1983-1995 he studied Physics at the University of Hannover and obtained his "Diplom" in 1995. Partly simultaneously, he studied Medicine at the Medizinische Hochschule Hannover from 1986-1995. From 1996 to 1997 he practiced Surgery at the Agnes-Karll hospital in Laatzen/Hannover. In 1998 he joined the Department of Physiology of Hannover Medical School and developed his research interests in CO₂ and O₂ transport and acid-base physiology in Gerolf Gros' laboratory. He has worked and published on several topics in these areas, but his main interest over the last years has been CO₂ channels in biological membranes. He has essentially contributed to the development of the mass spectrometric ¹⁸O exchange technique to measure CO₂ permeabilities of cell and vesicle membranes, including the complex mathematical description of this process and a numerical procedure to derive CO₂ and bicarbonate permeabilities from mass spectrometric measurements. He has further developed this technique by an analysis of the size and role of unstirred layers and by modelling the intracellular processes influencing the process of ¹⁸O exchange. He has presented a comprehensive experimental analysis of the role of aquaporin 1 as a CO₂ channel in the human red cell membrane, as well as the first report that the red cell Rhesus protein RhAG also acts as a CO₂ channel. Most recently he has shown that the intrinsic permeability of many biological membranes is low and identified the molecular cause of this property. In addition, he has presented a comprehensive reinvestigation of the so-called metabolon hypothesis, which proposes the existence of a functionally relevant complex of the anion exchanger 1 and carbonic anhydrase 2 in the red cell membrane. His scientific success was recognized by a special personal grant awarded to him by the Deutsche Forschungsgemeinschaft in 2009.

Bhanu Jena, Ph.D.

**–Wayne State University School of Medicine
Detroit, Michigan**



Dr. Bhanu Jena was born in a small town in Orissa, India, on November 1, 1955, to Manju Prova and Prafulla K. Jena, a chemist. He spent his early childhood in several remote villages in India, where his grandfather practiced medicine. The dedication of his father and grandfather to science and medicine and their service to humanity greatly influenced his choice

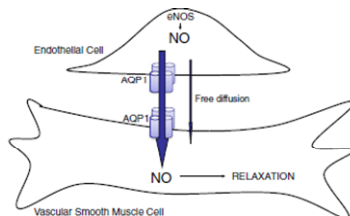
for a career in science. Dr. Jena majored in Chemistry, Zoology and Botany from BJB College in India (B.Sc., 1975) and studied Reproductive Endocrinology at Utkal University, (M.Sc., 1978). He graduated top of his class in the Masters program receiving the Prasant Ku. Memorial Prize and the Utkal University Gold Medal. In December 1988, Dr. Jena received his Ph.D. degree in Reproductive Endocrinology, and the Research Excellence Award from Iowa State University. Following postdoctoral training at Yale University, he joined Yale University as an Assistant Professor. In 2000, Dr. Jena moved to the Department of Physiology, at Wayne State University School of Medicine, as a tenured Professor, and Founder-Director of the Institute of NanoBioScience. His foray into science began 40 years ago, when he published his first scientific paper. His enquiry on how cells secrete, led to the serendipitous discovery of the “porosome” - a new cellular structure universally present in all secretory cells at the cell plasma membrane, and involved in secretion. In early 2012, the neuronal porosome proteome was determined. The current focus of the laboratory is to further determine the structure and conformation of the neuronal porosome using cryo electron crystallography.

Jeffrey Garvin, Ph.D.
-Henry Ford Hospital
Detroit, Michigan



Jeffrey Garvin, Ph.D. is currently Professor of Physiology at Wayne State University and Division Head of the Hypertension and Vascular Research Division of Henry Ford Hospital. He received his B.S. from the University of Miami in Biology and Chemistry in 1979 and his Ph.D. from Duke University in 1984. Dr.

*Garvin did his postdoctoral training in the Laboratory of Kidney and Electrolyte Metabolism at the National Institutes of Health under Maurice Burg, Mark Knepper and Kenneth Spring where he was supported by a National Kidney Foundation fellowship and two National Research Service Awards. In 1988 he joined the Hypertension and Vascular Research Division of Henry Ford Hospital and became Division Head in 2009. His research deals with the regulation of transport processes in the kidney and how dysregulation of these systems can contribute to hypertension. Currently he has more than 125 original publications on renal physiology. Dr. Garvin is a fellow of the Council for High Blood Pressure Research of the American Heart Association and has served on several NIH study sections. He also is an Associate Editor of *The American Journal of Physiology: Renal Physiology*. His research is now supported by three NIH grants, including a Program Project Grant entitled “Blood Pressure Regulation: Novel Roles for the Kidney.”*



David Weiner, M.D.
-University of Florida
Gainesville, Florida



Dr. Weiner's primary research interests involve examining the mechanisms and regulation of renal ammonia metabolism and transport. Ammonia plays a central role in acid-base homeostasis, as it is the primary component of basal net acid excretion and changes in ammonia excretion comprise almost 90% of the renal response to acid-base alterations. Renal ammonia transport has traditionally been believed to involve "ammonium (NH_4^+) trapping" and diffusive NH_3 movement.

Dr. Weiner's laboratory examines the specific mechanisms of renal NH_3 movement, and has shown that, in contrast to previously thought models, that NH_3 transport involves specific proteins, namely, Rh glycoproteins. These proteins are widely expressed in ammonia transporting tissues, and Dr. Weiner's studies, using a variety of in vivo and in vitro models, including transgenic animal models utilizing cell-specific gene deletion, have shown the central role of these proteins in renal ammonia, and thereby acid-base, homeostasis.

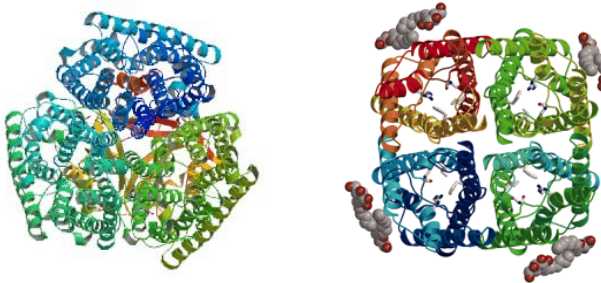


Robert Stroud, Ph.D.
-University of California San Francisco
San Francisco, California



Dr. Stroud was the first to discover fundamental mechanisms of transmembrane proteins by 'Aquaporins' at atomic resolution. These included GlpF, AqpZ, the eye lens AQP0, the H₂S channel, and the essential glycerol channel of the malaria parasite P.falciparum. He defined the structure and regulatory mechanisms of the ammonia channel AmtB and the 'Rh factors'. He revealed the atomic basis for 'signal sequence' dependant membrane protein synthesis, signaling by EPO (erythropoietin) via its receptors. Stroud also determined the mechanisms of enzyme drug targets thymidylate synthase, HIV protease, HIV integrase, and KSHV protease and used these to facilitate drug discovery for human health.

He was elected to the National Academy of Sciences (of the USA) in 2003, President of the Biophysical Society (of the United States) from 1986-1987, and Founding Fellow of the Society in 2000. Dr. Stroud is a member of the Committee for the International Union of Pure and Applied Biophysics. In 1984 he was elected the DeWitt Stetten Lecturer of the National Institutes of Health (NIH). Dr. Stroud was elected as a Fellow of the Royal Society of Medicine (United Kingdom) in 1992.



Case Western Reserve University Boron Lab Post-doctorates



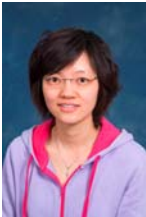
R. Ryan Geyer, Ph.D. is currently a postdoctoral research fellow in the Department of Physiology and Biophysics at Case Western Reserve University. He received his B.A. in biology from Earlham College in 1998 and his Ph.D. in biochemistry and molecular biology from Wright State University in 2007. In 2008,

Dr. Geyer joined Dr. Boron's laboratory and has focused his attention towards elucidating the role of membrane proteins in red blood cell oxygen transport. Dr. Geyer is currently supported by a postdoctoral fellowship from the Office of Naval Research.



Rossana Occhipinti, Ph.D. joined Dr. Boron's laboratory as a postdoctoral fellow in October of 2009 shortly after obtaining her Ph.D. in Applied Mathematics from Case. During her Ph.D. studies she developed mathematical models of cellular brain metabolism and numerical methods combining optimization algorithms with Bayesian statistics. She is currently developing mathematical

models to investigate the movement of acid-base equivalents across the plasma membrane. In 2009, she received the Melvin H. Knisely International Award and in 2012 the Cell & Molecular Physiology Section Research Recognition Award. Her work is currently supported by an AHA Postdoctoral Fellowship.



Xue Qin, Ph.D. earned her Ph.D. in Pathophysiology at Peking University in China. In 2008 she joined Case Western Reserve University in Dr. Boron's lab. Dr. Qin's Ph.D. work was about the signaling pathway of Nitric Oxide, cGMP and Protein Kinase G in coronary arteries. In Dr Boron's Lab, her research has mainly focused on gas channels. Dr. Qin uses surface pH method to study the structural functional relationships of human aquaporin 5.

Her work has been supported by American Heart Association Postdoctoral Fellowship. In 2010 she won the Cell & Molecular Physiology Section Research Recognition Award.

