



No. 1, Spring 2006 issue

Yoram Rudy, Director

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The **Cardiac Bioelectricity & Arrhythmia Center (CBAC)** is pleased to publish its first Newsletter. The CBAC Newsletter will include important information, research updates, news, and achievements of the center and its members. The Newsletter will add to CBAC's already popular informational and educational dissemination sources that currently include the **CBAC website** which is located at <http://cbac.wustl.edu>, the **CBAC Seminar Series**, and the **CBAC Video Archives** (downloadable video files of the CBAC seminars).

CBAC is an interdisciplinary center set up to foster intellectual interactions and collaborations between researchers and clinicians from the Washington University Hilltop and Medical School campuses in an effort to understand the heart's irregular rhythms and to prevent their fatal consequences.

The CBAC center includes 31 faculty members from various departments in the Hilltop and Medical School campuses. [CBAC Faculty member directory can be found on Pages 4-5].

The Fall of 2005 marked the inaugural CBAC seminar series. The seminars are held most Monday afternoons at 5:30 pm during the academic year (September through May) and have proven to be an important vehicle for education and outreach, collaborations, and advancement of knowledge in the research and clinical fields supported by the center. The CBAC seminars are video-taped with permission from the speakers, and MPEG and DIVX formats of the video files can be downloaded and viewed from the CBAC website. [CBAC seminar schedule can be found on Pages 6-7].

Cardiac Bioelectricity & Arrhythmia Center (CBAC)

Washington University in St. Louis



Whitaker Hall



The School of Medicine

Providing an "arch" in cardiology and cardiovascular research between the School of Engineering & Applied Science and the School of Medicine

Published by the Cardiac
Bioelectricity and Arrhythmia
Center (CBAC)

Washington University in St. Louis
Whitaker Hall, Room 290
1 Brookings Dr., CB 1097
St. Louis, MO 63130-4899



FROM THE DIRECTOR'S DESK

The Heart of all creatures is the foundation of their life, from whence all strength and vigour flows.

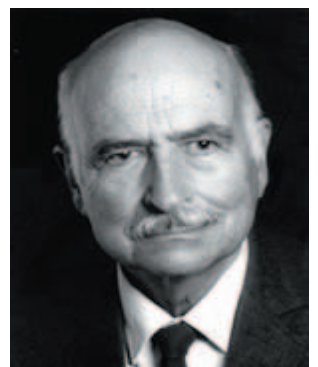
--William Harvey: An anatomical disputation concerning the movement of the heart and the blood in living creatures, 1653



Yoram Rudy, Ph.D., F.A.H.A., F.H.R.S.

A little over a year has passed since we established the **Cardiac Bioelectricity and Arrhythmia Center (CBAC)** at Washington University in St. Louis. The research retreat on May 12 serves not only to bring us together for a day, but to also celebrate our first anniversary. The idea behind **CBAC** was to provide a platform for discussion of research and clinical topics among Washington University faculty members who share an interest in cardiac electrophysiology and arrhythmias. To achieve this goal, we invited to the Center faculty from both campuses of the university, encompassing the entire spectrum from molecular biology and cellular physiology to clinical cardiology, surgery and imaging. Our Monday evening seminars (thanks to Jennifer and my laboratory members for the logistics involved) were designed to facilitate the dialogue between basic researchers and clinicians, covering topics such as cardiac ion channels, calcium cycling, molecular and organ-level imaging, risk stratification for sudden death, and mapping/ablation of cardiac arrhythmias. I am grateful to the seminar speakers, both members of **CBAC** and guests from other universities, who made it an informative and very stimulating learning experience. The long and thought-provoking discussions that followed every seminar testify to the interest in this series and to its evolving role as a place for scientific exchange among us (the seminars can be viewed on the **CBAC** website at <http://cbac.wustl.edu/pageEducationVideo.asp>). My hope is that the seminars and retreat will also help to identify common interests among our members that can lead to collaborative efforts in the study and treatment of cardiac arrhythmias.

The field of cardiac electrophysiology has recently lost two of its pioneers and visionaries: **Professor Silvio Weidmann** (University of Bern, Switzerland; 1921-2005) and **Professor Seymour Furman** (Albert Einstein College of Medicine and Montefiore Hospital, New York; 1931-2006). Professor Weidmann recorded the first cardiac action potential in 1949 and was also the first to demonstrate that cardiac cells communicate electrically through conductive pathways (now called connexons). His work and ideas opened the fascinating era of cellular cardiac electrophysiology that many of us continue to explore. Professor Furman pioneered many of the concepts and techniques of cardiac pacing in patients, initially using a stimulating catheter electrode of his own design. He ran the earliest pacemaker clinics of 1958 and from his clinical experience proposed the virtual electrode hypothesis of stimulation, a concept that underlies our present understanding of cardiac pacing and defibrillation. Silvio Weidmann was a basic scientist motivated by clinical problems; Seymour Furman was a clinician that based his approach to therapy on the mechanistic understanding provided by Weidmann and his followers. My hope is that within **CBAC** we will continue their efforts, even if in a small way, to develop better diagnosis and treatments for cardiac arrhythmias based on understanding of the basic science of cardiac electrophysiology.



Silvio Weidmann*



Seymour Furman**



Physician taking the pulse of a young woman (oil painting by J. Steen [1626-1679]).

ABOUT CBAC

The CBAC Mission Statement

The Cardiac Bioelectricity and Arrhythmia Center, CBAC, is an interdisciplinary center whose goals are to study the mechanisms of rhythm disorders of the heart (cardiac arrhythmias) and to develop new tools for their diagnosis and treatment. Cardiac arrhythmias are a major cause of death (over 300,000 deaths annually in the US alone; estimated 7 million worldwide) and disability, yet mechanisms are poorly understood and treatment is mostly empirical. Through an interdisciplinary effort, CBAC investigators apply molecular biology, ion-channel and cell electrophysiology, optical mapping of membrane potential and cell calcium, multi-electrode cardiac electrophysiological mapping, Electrocardiographic Imaging (ECGI) and other noninvasive imaging modalities, and computational biology (mathematical modeling) to study mechanisms of arrhythmias at all levels of the cardiac system. Our mission is **"To battle cardiac arrhythmias and sudden cardiac death through scientific discovery and its application in the development of mechanism-based therapy"**.

Research Goals

Research projects at CBAC cover the entire spectrum from molecular and cellular processes to mechanisms, diagnosis and treatment of arrhythmias in patients. The cross-disciplinary structure of CBAC promotes collaborations between researchers and clinicians and fosters a multiple-approach strategy to the study, diagnosis and treatment of cardiac arrhythmias. Approaches include molecular, single-cell and whole-animal experiments, mathematical modeling and computer simulations, and patient studies during imaging, catheterization and open-heart surgery. Among the state-of-the-art techniques employed are genetics, biomolecular structural analysis, patch clamp recordings from single ion channels, ion-selective electrode measurements, high resolution electrical mapping, optical mapping of cardiac activation and cell-calcium, Electrocardiographic Imaging, supercomputing and computer graphics, signal processing and image analysis.

Projects include:

- Molecular structure and electrophysiological function of cardiac ion channels
- Development of mathematical models of cardiac ion channels, cells and tissues
- Regulatory pathways in cardiac cells
- Mechanisms of hereditary cardiac arrhythmias
- Arrhythmias in myocardial ischemia and infarction
- Cell-to-cell communication and action potential propagation in the diseased heart
- Structure and function of the atrio-ventricular node
- Mechanisms of cardiac (ventricular and atrial) fibrillation and new strategies for defibrillation
- Development and application of a novel imaging modality for cardiac arrhythmias
- Mechanisms of cardiac resynchronization therapy for heart failure

Education and Training Goals

An important goal of CBAC is to enhance and promote education and training in biomedical engineering, life sciences, and clinical medicine. The cross-disciplinary structure of CBAC facilitates a synergistic relationship between training, research and clinical medicine. The educational component of CBAC builds on graduate programs in the Department of Biomedical Engineering and the Medical School. Through CBAC, graduate students and scientists in engineering and life sciences can participate in clinical lectures, seminars, case presentations and clinical procedures such as diagnosis and treatment of arrhythmias in the catheterization laboratory. Similarly, post-M.D. clinical fellows can participate in lectures and seminars in the basic science departments and in research projects in the basic science laboratories.

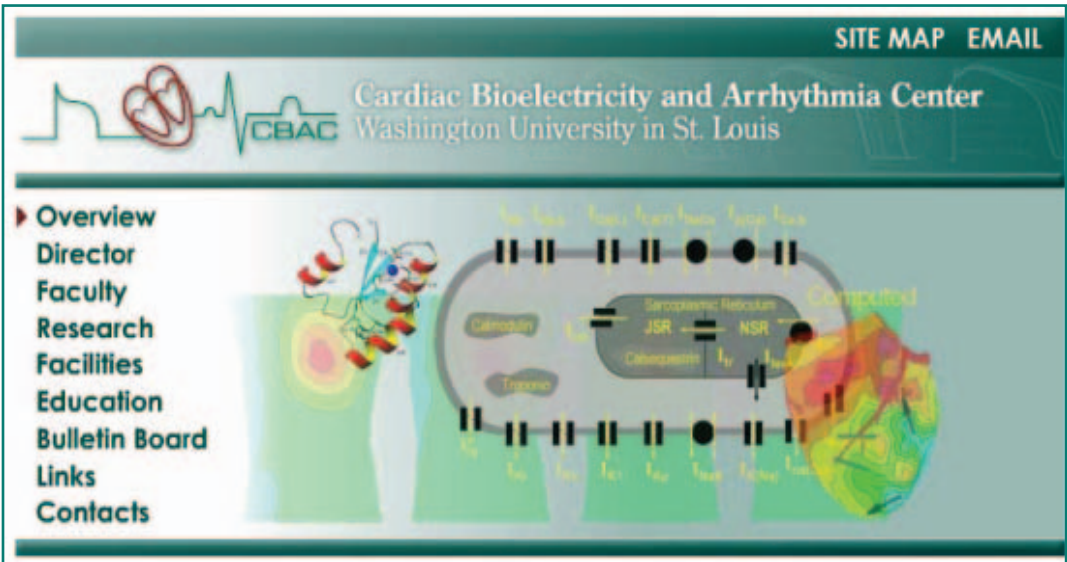
Support and Facilities

Research is supported through grants to affiliated faculty. Funding agencies include: NIH, AHA, VA, Whitaker Foundation and NSF. A number of projects are funded through industrial support (pharmaceutical- and device-related studies). Facilities include state-of-the-art laboratories for genetics, molecular biology, cellular and subcellular electrophysiology, optical mapping of action potentials and cell-calcium, multi-electrode mapping of cardiac electrical activity, and theoretical and computer simulations using supercomputing. Studies can also be conducted in clinical facilities for MRI, CT and Ultrasound imaging, and for electrophysiology studies and arrhythmia treatment during cardiac catheterization and surgery.

CBAC Website

The Cardiac Bioelectricity and Arrhythmia Center (CBAC) website is located at <http://cbac.wustl.edu>.

The CBAC website contains information about the center, a complete Faculty listing including research and clinical interests, related current research publications, and course listings. The CBAC seminar schedules and the CBAC brochure are posted on the website, as well as a Bulletin Board section containing announcements, news, and events. An important addition to the website is the Video Archives located under the Education section. The Video Archives contain downloadable MPEG and DIVX video files of the CBAC seminars. We are using the videotaped seminars as an education and outreach tool to enhance learning and knowledge in the areas supported by the center. The CBAC website consists of the following sections and content: • **Overview** <CBAC Mission, Research Goals, Education and Training Goals, Support and Facilities, Center Directory, CBAC brochure (pdf)>; • **Director**; • **Faculty**; • **Research** <Research Areas, Representative Publications, Work in Progress (password required)>; • **Facilities**; • **Education** <Course Listings, Seminars and Journal Clubs, Research Retreat, Video Archives>; • **Bulletin Board** <Announcements, News, Seminars and Journal Clubs, Upcoming Events, Recent Events, Faculty Meetings>; • **Links**; • **Contacts**.



The CBAC website is continuously updated, so check back often.

CBAC Faculty Members

Director - Yoram Rudy, Ph.D., F.A.H.A., F.H.R.S.

The Fred Saigh Distinguished Professor of Engineering; Professor of Biomedical Engineering, Cell Biology & Physiology, Medicine, Radiology, and Pediatrics; Director of the Cardiac Bioelectricity and Arrhythmia Center (CBAC)

Amir A. Amini, Ph.D.

Associate Professor; Director, Cardiovascular Image Analysis Lab

R. Martin Arthur, Ph.D.

Newton R. and Sarah Louisa Glasgow Wilson Professor of Engineering; Professor of Electrical and Systems Engineering; Professor of Biomedical Engineering

Kyongtae T. Bae, M.D., Ph.D.

Associate Professor of Radiology, Assistant Professor of Biomedical Engineering

Philip V. Bayly, Ph.D.

Lilyan and E. Lisle Hughes Professor of Mechanical Engineering, Aerospace Engineering, and Biomedical Engineering

John P. Boineau, M.D.

Professor of Surgery, Medicine, and Biomedical Engineering

Michael E. Cain, M.D.

Tobias and Hortense Lewin Professor of Medicine; Director, Cardiovascular Division

Jianmin Cui, Ph.D.

Associate Professor of Biomedical Engineering on the Spencer T. Olin Endowment

Ralph J. Damiano, Jr., M.D.

John M. Shoenberg Professor of Surgery; Chief of Cardiac Surgery

Victor G. Davila-Roman, M.D.

Associate Professor of Medicine, Anesthesiology, and Radiology; Medical Director, Cardiovascular Imaging and Clinical Research Core Laboratory

Igor R. Efimov, Ph.D.

The Stanley and Lucy Lopata Associate Professor of Biomedical Engineering, Cell Biology & Physiology, and Radiology

Mitchell N. Faddis, M.D., Ph.D.

Assistant Professor of Medicine, Radiology; Clinical Cardiac Electrophysiologist, Barnes Hospital

ABOUT CBAC cont.

CBAC Faculty Members cont.

Richard W. Gross, M.D., Ph.D.

Professor of Medicine, Chemistry, and Molecular Biology & Pharmacology; Director, Division of Bioorganic Chemistry and Molecular Pharmacology (Joint Appointment with the School of Medicine), Department of Internal Medicine, Department of Molecular Biology and Pharmacology and Department of Chemistry, Washington University School of Medicine

Patrick Y. Jay, M.D., Ph.D.

Assistant Professor of Pediatrics and Genetics

R. Gilbert Jost, M.D.

Elizabeth Mallinckrodt Professor of Radiology; Chairman, Department of Radiology; Director, Mallinckrodt Institute of Radiology

Daniel Kelly, M.D.

Alumni Endowed Professor in Cardiovascular Diseases; Professor of Medicine, Pediatrics, and Molecular Biology & Pharmacology; Director, Center for Cardiovascular Research; Co-Director, Cardiovascular Division, Department of Medicine, Washington University School of Medicine

Sándor J Kovács, Ph.D., M.D.

Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering

Bruce D. Lindsay, M.D.

Associate Professor of Medicine; Director, Clinical Electrophysiology Laboratory at Washington University

Achi Ludomirsky, M.D.

The Louis Larrick Ward Professor of Pediatrics and Biomedical Engineering; Director, Pediatric Cardiology, Washington University School of Medicine and St. Louis Children's Hospital

Arye Nehorai, Ph.D.

Chairman of the Department of Electrical & Systems Engineering; Eugene and Martha Lohman Professorship of Electrical Engineering

Jeanne M. Nerbonne, Ph.D.

Alumni Endowed Professor of Molecular Biology and Pharmacology

Colin G. Nichols, Ph.D.

Professor of Cell Biology and Physiology

Joseph A. O'Sullivan, Ph.D.

The Samuel C. Sachs Professor of Electrical Engineering; Professor of Radiology and Biomedical Engineering; Director of Electronic Systems and Signals Research Laboratory; Associate Director of Center for Security Technologies

Edward K. Rhee, M.D.

Assistant Professor of Pediatrics, Washington University School of Medicine; Director, Arrhythmia Services, St. Louis Children's Hospital

Richard B. Schuessler, Ph.D.

Associate Research Professor of Surgery; Associate Research Professor of Biomedical Engineering; Director, Cardiothoracic Surgery Research Laboratory

Jinyi Shi, Ph.D.

Research Faculty, Biomedical Engineering

Timothy W. Smith, D.Phil., M.D.

Assistant Professor of Medicine

Jason W. Trobaugh, D.Sc.

Research Instructor in Medicine, Electrical and Systems Engineering

Samuel A. Wickline, M.D.

Professor of Medicine; Adjunct Professor of Physics and Biomedical Engineering; Co-Director of Cardiology

Pamela K. Woodard, M.D.

Associate Professor, Diagnostic Radiology, Cardiovascular Imaging Laboratory, Mallinckrodt Institute of Radiology

Kathryn A. Yamada, Ph.D., F.A.H.A.

Research Associate Professor of Medicine

SPRING 2006 SEMINAR SCHEDULE

The Cardiac Bioelectricity and Arrhythmia Center (CBAC) seminars are held on Monday afternoons at 5:30 PM, with refreshments served beforehand from 5:00 PM - 5:30 PM, in room 218 of Whitaker Hall on the Washington University Hilltop Campus.

Contact Jennifer Godwin-Wyer (jlgodwin@biomed.wustl.edu) for more information, or visit the CBAC website at <http://cbac.wustl.edu/pageBulletinBoardClubs.asp>.

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CBAC Seminar Series Spring 2006 Schedule

Date: January 9, 2006

Geoffrey S. Pitt, M.D., Ph.D.
Assistant Professor of Pharmacology and Medicine, Columbia University Department of Pharmacology, New York, NY
“Modulation of Calcium Channels by Accessory Subunits”

Date: January 23, 2006

Michael Cain, M.D.
Tobias and Hortense Lewin Professor of Medicine; Director, Cardiovascular Division, Washington University School of Medicine, St. Louis, Missouri
“Risk Stratification For Sudden Arrhythmic Death: Is Ejection Fraction Alone Sufficient?”

Date: February 6, 2006

Daniel Kelly, M.D.
Alumni Endowed Professor in Cardiovascular Diseases; Director, Center for Cardiovascular Research, Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, Department of Medicine, Washington University School of Medicine, St. Louis, Missouri
“PGC-1: A Physiologic Transducer Linked to Gene Regulatory Networks Controlling Cardiac Metabolism and Function”

Date: February 20, 2006

Samuel A. Wickline, M.D.
Professor of Medicine; Adjunct Professor of Physics and Biomedical Engineering; Co-Director of Cardiology, Washington University School of Medicine, St. Louis, Missouri
“Molecular Imaging and Targeted Therapeutics: Prospects For High Payload Drug Delivery With Novel Pharmacokinetic/Pharmacodynamic Profiles”

Date: February 27, 2006

Donald Bers, Ph.D.
Chairman, Dept. of Physiology; Professor, Cellular & Molecular Physiology, Loyola University, Chicago, Illinois
“Calcium Regulation in Cardiac Myocytes: Systolic Dysfunction and Arrhythmogenesis in Heart Failure”

Date: March 6, 2006

William Gregory Stevenson, M.D.
Director, Clinical Cardiac Electrophysiology Program, Brigham and Women's Hospital, Cardiovascular Division, Boston, Massachusetts
“Scar-Related Ventricular Arrhythmias”

Date: March 20, 2006

Kyongtae T. Bae, M.D., Ph.D.
Associate Professor of Radiology, Assistant Professor of Biomedical Engineering
“Applications of Engineering Concepts in Medical Imaging”

continued on Page 7...

SPRING cont.

CBAC Seminar Series Spring 2006 Schedule cont.

Date: March 27, 2006

Craig Henriquez, Ph.D.

W.H. Gardner Jr. Professor of Biomedical Engineering; Associate Professor of Computer Science; Co-Director of the Center for Neuroengineering, Duke University, Durham, North Carolina

"Multiscale Modeling of Cardiac Electrical Activity"

Date: April 3, 2006

Madison Spach, M.D.

James B. Duke Professor of Pediatrics, Emeritus, Duke University, Durham, North Carolina

"Mechanisms for Complex Atrial Conduction Disturbances Generated Near Premature Stimuli Sites in Aging Human Bundles"

Date: April 10, 2006

Henk E.D.J. ter Keurs, M.D., Ph.D., Leiden

Professor of Physiology and Biophysics; Member of the Cardiovascular Research Group, University of Calgary, Canada

"Arrhythmogenic Calcium Release from Cardiac Myofilaments"

Date: May 1, 2006

Albert Waldo, M.D.

The Walter H. Pritchard Professor of Cardiology, Professor of Medicine, and Professor of Biomedical Engineering, Case Western Reserve University, Cleveland, Ohio

Director of the Clinical Cardiac Electrophysiology Program, University Hospitals of Cleveland

"Mechanisms of Atrial Fibrillation"

Date: May 22, 2006

Bruno Taccardi, M.D., Ph.D.

Research Professor of Medicine, University of Utah School of Medicine; Associate Director, Cardiovascular Research and Training Institute (CVRTI), Salt Lake City, Utah

"Three-Dimensional Mapping of Intraventricular Repolarization"

The Fall 2006 Seminar Schedule will be posted and distributed this summer. Please check our website at <http://cbac.wustl.edu/pageBulletinBoardClubs.asp> for the most current seminar schedule.

Focus On... Dr . Henk ter Keurs



Dr . Henk ter Keurs was born in Delft, The Netherlands. He received his Ph.D. in 1970 in Physiology, his M.D. in 1972 from Leiden, and trained in Cardiology (1983) where he started basic research of heart function. Dr. ter Keurs was the Established Investigator of the Netherlands Heart Foundation from 1976-1981. In 1984, he moved to Calgary, Canada and joined the Foothills Hospital and the Faculty of Medicine where he combines research with patient care as a practicing cardiologist with support of the Alberta Heritage Foundation for Medical Research. Dr. ter Keurs is an AHFMR Medical Scientist and holds the Merck Frosst Chair in Cardiovascular Research, and is a Professor in the Departments of Medicine and Medical Physiology and Cardiac Sciences at the LIBIN Institute of Alberta.

Dr. ter Keurs' research focuses on the interaction between excitation and contraction of the heart, and his laboratory studies issues such as: initiation of a rise of the intracellular calcium concentration by electrical activity of cardiac cells, which then triggers contraction; the determinants of force development and the velocity of shortening at the level of the contractile proteins; triggering of arrhythmias in damaged cardiac muscle; and the pathophysiology of excitation contraction coupling in heart failure. He has received many citations of merit and recognition, including a Dutch knighthood. Dr. ter Keurs is the April 10, 2006 CBAC seminar speaker.

Focus On... continued on Page 12...

New Members:

The CBAC center would like to welcome our newest members, **Dr. Arye Nehorai** and **Dr. Richard Gross**.



Dr. Arye Nehorai became the new Chair of the Department of Electrical & Systems Engineering on January 1, 2006, and holds the Eugene and Martha Lohman Professorship of Electrical Engineering. Dr. Nehorai received his B.Sc. in 1976, and M.Sc. in 1979, in Electrical Engineering from the Technion, Israel Institute of Technology, and his Ph.D. in 1983 in Electrical Engineering from Stanford University. Dr. Nehorai's research deals with analysis of space-time data obtained from sensors distributed in space, and taking temporal measurements from each of them. He is a fellow of the IEEE and the Royal Statistical Society, and served 10 years as a professor at the University of Illinois in Chicago and 10 years on the faculty at Yale University (from 1985-1995).

From <http://ese.wustl.edu/~nehorai/overview.html>:

"Our processing is statistical, since there is noise in the measurements. However, unlike most researchers in our field, we also compute physical models for the measurements. A common example of the problems we solve is finding the positions of sources emitting energy. Such problems appear in defense, communications, biomedicine, and environmental monitoring. In defense, we develop methods for locating targets using novel sensors that provide full information in time and space. These are used in radar and sonar applications. In communications, our methods can be used to locate a 911 caller, using an array of antennas or GPS and triangulation. In biomedicine, we develop methods for locating electrical sources in the brain using arrays of electrodes (EEG) or magnetometers (MEG) placed around the head. Our solutions are important for clinical applications such as finding origins of seizures, or in neuroscience for mapping the brain functions. We are developing procedures that find the stiffness of the heart wall using MRI. We also estimate the electrical current density in the heart with ECG and MCG sensor arrays. In environmental monitoring, we introduce techniques for detecting and locating sources emitting chemical substances. We apply our methods to biochemical defense and finding land-mines. Our models can predict the space-time dispersion of a biochemical agent after it is released. In summary, our research is interdisciplinary, encompassing physical and statistical modeling, algorithm development, performance analysis, and simulations. We solve diverse problems arising in engineering and sciences."



Dr. Richard Gross is a Professor of Medicine, Chemistry, and Molecular Biology & Pharmacology, and the Director of the Division of Bioorganic Chemistry and Molecular Pharmacology (with joint appointment with the School of Medicine). Dr. Gross received his M.D. from New York University Medical School in 1976, was a Cardiology Fellow from 1978-1981 at Barnes Jewish Hospital, and received his Ph.D. in 1982 from Washington University in St. Louis.

Dr. Gross's research is focused on the chemical biology of membranes in health and disease. Biologic membranes are comprised of a structurally diverse array of thousands of distinct chemical entities in a bilayer configuration that are in constant motion providing a rich repertoire of chemical forces that can be used to modulate the conformation and function of transmembrane proteins such as ion channels and ion pumps. Through adaptation of a bilayer structure, membranes serve as a hydrophobic scaffold for the organization of complex supramolecular chemical assemblies that are used in biologic systems as signaling platforms.

Visit <http://cbac.wustl.edu/pageFaculty.asp> and <http://cbac.wustl.edu/pageResearch.asp> for more information on the CBAC Faculty members.

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CBAC Alumni:

We would like to say good-bye to two of the CBAC members, Dr. Jeffrey Saffitz and Dr. Vladimir Nikolski. Dr. Saffitz joined the Beth Israel Deaconess Medical Center at Harvard University as Professor and Chair of Pathology in 2005, and Dr. Nikolski has recently joined Medtronic.



Dr. Vladimir Nikolski



Dr. Jeffrey Saffitz

FACULTY NEWS

The installation ceremony for **Dr. Arye Nehorai**, chair of Dept. of Electrical & Systems Engineering, was held on March 6, 2006 in Whitaker Hall. Dr. Nehorai was installed as the first Eugene and Martha Lohman Professor of Electrical Engineering. On January 1, 2006 Dr. Nehorai replaced R. Martin Arthur (who was serving as interim chair since July 2003) as Chair of the Dept. of Electrical & Systems Engineering.

The installation ceremony for **Dr. Philip V. Bayly**, was held on March 8, 2005 in Whitaker Hall. Dr. Bayly was installed as the first Lilyan and E. Lisle Hughes Professor in Engineering.



Dr. Philip Bayly's research was in an article featured in *The Record* [Jan. 27, 2006, vol. 30, no. 19] written by Tony Fitzpatrick, Sr. Science Editor.

"New imaging technique stands brain injury research on its head" article is about understanding brain deformation after impact by using a technique originally developed to measure cardiac deformation to image deformation in human subjects during repeated mild head decelerations. (This article also ran in the *St. Louis Post Dispatch*, Science & Medicine section, on Thursday, August 11, 2005 [written by Sam Kean].)

Dr. Igor Efimov was selected to receive the Chancellor's Hartwell Prize for Innovative research. The project will focus on Low-voltage Defibrillation - A New Paradigm. Dr. Efimov also received a one-year \$100,000 research contract from Medtronic, Inc. entitled "Understanding defibrillation mechanisms using optical mapping".

Dr. Daniel Kelly is leading the planning program on research for a proposal to develop a center for treatment of diabetics with heart disease and to develop new methods for early detection of the disease in these patients. If selected, the university could receive more than \$20 million over five years in renewable grants for research on heart problems in diabetics [as reported in the featured article in the *St. Louis Business Journal*, Aug. 12, 2005 edition **"Washington U. team seeks \$20 million in grant money"** by Victoria SÆland].



[Exerpt taken from <http://wup20.wustl.edu/rfa/rfa.htm>]:

"Washington University was recently selected to receive an NIH Roadmap P20 Planning Grant to develop an Interdisciplinary Research Center (IRC) focused on diabetic cardiovascular disease. The overall goal of the WU P20 Planning Center is to develop novel interdisciplinary strategies to rapidly translate discovery to reduce the burden of diabetic cardiovascular disease, a serious and

common medical problem with profound implications for world health."

"The Pilot Project Program comprises a chief component of the P20 planning process. Two year pilot projects will be jointly supported by the P20 grant and the WU BioMed21 initiative. The pilot research will be conducted by groups of investigators representing multiple scientific disciplines."

[Exerpt taken from <http://wup20.wustl.edu/overview/overview.htm>]:

"The overall goal of this planning program (NIH #P20RR20643) is to establish a planning process to develop novel interdisciplinary strategies to rapidly translate discovery to reduce the burden of diabetic cardiovascular disease, a serious and common medical problem with profound implications for world health. This planning proposal, led by Dr. Daniel P. Kelly, will involve the collective efforts of an interdisciplinary team spanning across 13 departments and 4 colleges at Washington University in St. Louis in partnership with a national population outcomes group."

Dr. Yoram Rudy gave The Kazuo Yamada Lecture at the Japanese Society of Electrocardiology meeting Oct. 7, 2005 in Toyama, Japan. The title was "Noninvasive Electrocardiographic Imaging of Cardiac Electrophysiology and Arrhythmia." He also conducted a workshop on the ion-channel basis of cardiac arrhythmia at Nagoya University on Oct. 10, 2005.

Dr. Rudy presented at the Keystone Symposium on Cardiac Arrhythmias in January 2006 in Tahoe City, California. The title of his presentation was "Modeling Cardiac Arrhythmias". He also gave the keynote presentations at the SPIE Medical Imaging conference in San Diego, California, February 2006 ("Electrocardiographic Imaging (ECGI): a new noninvasive imaging modality for cardiac electrophysiology and arrhythmia"), and at the International Society for Computerized Electrocardiology in Niagara-on-the-Lake, Canada, April 2006 ("Noninvasive Electrocardiographic Imaging (ECGI) of cardiac resynchronization therapy in heart-failure patients").

Dr. Samuel Wickline was featured in the article **"Nanotechnology cancer center is formed via grant"** by Gwen Ericson published in *The Record* [Oct. 14, 2005, vol. 30, no. 10].

"The National Cancer Institute (NCI) has awarded \$16 million over five years to the School of Medicine to establish the Siteman Center of Cancer Nanotechnology Excellence (SCCNE). The center will be headed by Samuel A. Wickline, M.D., professor of medicine and of cellular biology in the School of Medicine; of biomedical engineering in the School of Engineering & Applied Science; and of physics in Arts & Sciences. He and Gregory M.


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FACULTY NEWS cont.; FACULTY PUBLICATIONS

Faculty News continued from Page 9...

Lanza, M.D., Ph.D., associate professor of medicine, developed nanoscale particles that can home in on tumor cells to carry imaging agents and drug therapies directly to tumor sites."

 **Dr. Pamela Woodard** will serve on the WUSTL Senate Council Roster for 2005-2006.

 **Dr. Kathryn Yamada** was featured in the article "**Heart failure linked to altered communication channels**" by Gwen Ericson [Feb. 2, 2006, School of Medicine News and Information, Medical Public Affairs located at <http://mednews.wustl.edu/tips/page/normal/6464.html>].



"Failing hearts develop interference in their communication channels, according to research conducted at Washington University School of Medicine in St. Louis. The problem involves a subtle change in the pores that connect heart muscle cells. When the scientists duplicated this change in mice, the mice became susceptible to ventricular tachycardia, a dangerous heart rhythm disorder that can lead to sudden cardiac death."

This research was published in the January issue of the *American Journal of Physiology-Heart and Circulatory Physiology*.

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Grants:

Dr. Arye Nehorai: Principal Investigator, Multi-university Research Initiative (MURI) grant on Adaptive Waveform Design for Full Spectral Dominance, AFOSR, 2005 to 2010.

Dr. Igor Efimov
Pending grants: 2006-2011 NIH R01, "Structure/function of the pacemaking and conduction system of the heart", Principal investigator;
2006-2011 NIH, R01 HL67322 "Virtual Electrode Hypothesis of Defibrillation", Principal investigator, competitive renewal pending.

Honors:

Dr. Arye Nehorai was the Distinguished Lecturer, IEEE Signal Processing Society, 2004 to 2005.

Dr. Yoram Rudy received the Kazuo Yamada Lectureship Award, The Japanese Society of Electrocardiology, Toyama, Japan, October 2005, and was the Keynote Speaker at the SPIE Medical Imaging, San Diego, February 2006. He also became a Fellow of The Heart Rhythm Society, and a Fellow of the Academy of Science – St. Louis.

Faculty Publications

[Reference Cut-off Date: 01/01/2006 - 02/01/2006;
References retrieved from www.pubmed.gov]

Submitted or in Press:

Boineau, JP, "The early repolarization variant - An ECG enigma with both QRS and J-STT anomalies", *J Electrocardiol* (submitted).

Boineau JP, "The early repolarization variant – Normal or a marker of heart disease in certain subjects", *J Electrocardiol* (submitted).

C. Ramanathan, P. Jia, R.N. Ghanem, K. Ryu, **Y. Rudy**, "Activation and repolarization of the normal human heart under complete physiological conditions" *Proc. Natl. Acad. Sci., U.S.A. (PNAS)* 2006 (in press).

Y. Rudy, J.R. Silva, "Computational biology in the study of cardiac ion channels and cell electrophysiology" *Q Revs Biophys* 2006 (in press).

Recent Peer-Reviewed Journal Publications:

2006:

Tustison NJ, **Amini AA.**, "Biventricular myocardial strains via nonrigid registration of anfigatomical NURBS models", *IEEE Trans Med Imaging*. 2006 Jan;25(1):94-112.

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CBAC RESEARCH RETREAT; FOCUS ON...



The first inaugural Cardiac Bioelectricity & Arrhythmia Center (CBAC) Research Retreat will be held Friday, May 12, 2006 from 7:30 am - 5:00 pm in Whitaker Hall.

This is an annual event whose idea and form is carried over from Dr. Yoram Rudy’s first cardiac center, the Cardiac Bioelectricity Research and Training Center (CBRTC), Case Western Reserve University, Cleveland, Ohio.

The Research Retreat will be a full day of exciting lectures and presentations from various CBAC faculty members whose interests range in both research and clinical studies and will include talks by:

- **Thomas Hund, Ph.D.** from the Dept. of Surgery, “CaMKII Regulation of Cardiac Cell Excitation in Normal and Diseased Myocardium: A Computational Biology Approach”;
- **Patrick Jay, M.D., Ph.D.** from Pediatrics & Genetics, “Function Follows Form: The Role of Development in Cardiac Conduction”;
- **Bruce Lindsay, M.D.**, the Director of the Clinical Electrophysiology Laboratory, “Development of Magnetic Catheter Navigation for Ablation of Complex Arrhythmias”;
- **Jeanne Nerbonne, Ph.D.** from the Dept. of Molecular Biology & Pharmacology, “Molecular Insights Into Repolarization and Remodeling in the Ventricular Myocardium”;
- **Richard Schuessler, Ph.D.**, the Director of the Cardiothoracic Surgery Research Laboratory, “Atrial Fibrillation: Revisiting The Critical Mass Hypothesis”;
- **Pamela Woodard, M.D.** from the Mallinckrodt Institute of Radiology, “Delayed Contrast-Enhanced Imaging of the Myocardium in Determining Cause and Source of Arrhythmogenic Foci”.

Colin Nichols, Ph.D., Professor of Cell Biology and Physiology will be the Morning Session Moderator, and **Michael Cain, M.D.**, Tobias and Hortense Lewin Professor of Medicine; Director, Cardiovascular Division will be the Afternoon Session Moderator.

The keynote speaker for this year’s Retreat will be Dan Roden, M.D., Professor of Medicine and Pharmacology, and the Director of the Oates Institute for Experimental Therapeutics at Vanderbilt University School of Medicine.

Dr. Roden will be giving the presentation titled “Hereditary and Drug-Induced Arrhythmias: From Gene to Bedside, and Back Again”. [See “Focus On: Dan Roden” on Page 13].

Also during the Retreat there will be poster presentations given by various CBAC students, fellows, and laboratory members hi-lighting important research that occurs in the laboratories and facilities of the CBAC faculty members. The Retreat promises to be a full and interesting day of informal talks and dialogue, of important and novel research by the CBAC faculty members, and will hi-light the CBAC center’s interdisciplinary philosophy and show how the center really does build a bridge in cardiology and cardiovascular research between the School of Engineering & Applied Science and the School of Medicine.

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Focus On... Madison Spach, M.D.



Dr. Madison Spach, a Winston-Salem native, has had a most impressive career at Duke University, North Carolina for over 59 years since he first came to the university as a freshman in 1946. He received his M.D. from Duke in 1954 and served on the faculty of the Departments of Pediatrics and Physiology from 1960-1996. While at Duke Dr. Spach was a medical student, a pediatrics resident, and a pediatric cardiology fellow. He was the first chief of the Division of Pediatric Cardiology (1960-1983, and 1986-1991). He retired in 1996 but continues to work full-time in laboratory research as the James B. Duke Professor of Pediatrics, emeritus.

During Dr. Spach’s later career, his research efforts focused on the development of a research component in pediatric cardiology, and he is known for his research studies of electrophysiology and NIH-funded research on the mechanisms underlying cardiac conduction and dysrhythmias.

“His conceptual framework will provide the basis for future molecular studies and potential interventions that may lead to new and successful treatments.” *Duke University Medical School, Medical Alumni News, Fall 2000.*

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Focus On... cont.

Focus On... Dr. Madison Spach continued from Page 12...

Dr. Spach is a member of the Alpha Omega Alpha Medical Honor Society (an honor medical society organized to “recognize and perpetuate excellence in the medical profession.”) in Pediatrics for his distinguished achievement in that field. He also received the Supercomputing award in February 2000 for his proposal which gave him a supercomputing account at the North Carolina Supercomputing Center (NCSC). Dr. Spach was also recognized by Duke University as achieving a “Duke University Pediatric Research Milestone [in the 1960’s]” for performing one of the first pediatric cardiac catheterizations. He was also the recipient of the NASPE (now called the Heart Rhythm Society) Distinguished Scientist Award.

Dr. Spach will be the April 3, 2006 CBAC seminar speaker.

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Focus On... Dan Roden, M.D.



Dan M. Roden, M.D. is a Professor of Medicine and Pharmacology, and the William Stokes Professor of Experimental Therapeutics at Vanderbilt University Medical Center, Nashville, Tennessee. Dr. Roden received his M.D. in 1974 from McGill University in Canada. His research specialty is in mechanisms and treatment of cardiac arrhythmias, and he also has clinical interests in the variability in arrhythmia presentations and their response to therapies, particularly as a function of genetic background. Dr. Roden received the 2005 Distinguished Scientist Award from the Heart Rhythm Society (HRS) at its annual meeting in May 2005 in New Orleans, Louisiana. This HRS award honors an individual who has made major contributions to the advancement of scientific knowledge in the field of cardiac pacing and/or cardiac electrophysiology.

The overall theme of research in the Roden laboratory is mechanisms underlying variability in response to drug therapy, with a particular focus on therapies used to treat cardiac arrhythmias. The individual projects focus on emerging models in molecular medicine and genetics, and often incorporate the expertise of the laboratory in electrophysiologic methods; studies in human populations are also undertaken. Examples of individual projects underway at this time include definition of the functional consequences of sodium channel deletion in zebrafish; development of methods to establish function of non-coding variants in ion channel and other genes; exploitation of a new method to very rapidly generate mice with variant cardiac sodium channels; and studies of structure-function relations of wild-type and variant ion channels. Dr. Roden has a special interest in the role of defined genetic abnormalities in heart diseases associated with arrhythmias (such as the long QT syndromes or the hypertrophic cardiomyopathies).

The laboratory’s research focus is also being translated into studies of arrhythmia genomics, and pharmacogenomics. Dr. Roden directs the Pharmacogenomics of Arrhythmia Therapy (PAT) program, the Vanderbilt site of the NIH Pharmacogenetics Research Network. The site’s efforts are directed at studies of drugs used to treat cardiac arrhythmias as well as on testing the hypothesis that the increasingly well-recognized effect of certain drugs to unexpectedly provoke potentially fatal arrhythmias includes a genetic component. Work in PAT identifies common polymorphisms and genomic structures in arrhythmia candidate genes (ion channel and other), establishes function of these variants, and studies association between DNA variants and large databases of patients with defined arrhythmia and drug response phenotypes. Dr. Roden serves as US coordinator for a Leducq Foundation Trans-Atlantic Network focusing on application of contemporary genomic tools to identify novel risk factors and new drug targets to prevent Sudden Cardiac Death.

“Abnormalities of cardiac rhythm are a common and serious public health problem. However, the therapies used to treat arrhythmias are often ineffective, and can sometimes even exacerbate arrhythmias. Research in this laboratory is directed at elucidating mechanisms underlying abnormalities of cardiac rhythm and mechanisms underlying variable responses to antiarrhythmic drug treatments. Since antiarrhythmic drugs affect the function of cardiac ion channels, it is one working hypothesis in the laboratory that variable responses to drug therapy may reflect variable function or expression of genes encoding ion channels or proteins involved in drug disposition. Thus, a major focus of work in the laboratory is elucidation of factor(s) that determine ion channel gene expression in cardiac tissue. Approaches include identification of new genes, identification of DNA polymorphisms and characterization of their functional effects on disease and drug responses, and modulation of expression in cultured heart cells (e.g. by antisense) and gene knockout in mice.” [quote from https://medschool.mc.vanderbilt.edu/facultydata/php_files/part_dept/show_part.php?id3=861.]

Dr. Roden will be the Keynote Speaker for this year’s inaugural CBAC Research Retreat held on Friday, May 12, 2006.

SPOTLIGHT ON...

DR. PAMELA WOODARD

Dr. Pamela Woodard is an Associate Professor of Diagnostic Radiology in the Cardiovascular Imaging Laboratory, Mallinckrodt Institute of Radiology, Washington University School of Medicine in St. Louis, Missouri. She received her M.D. in 1990 from Duke University School of Medicine in Durham, North Carolina. Dr. Woodard was one of the first faculty members to join the Cardiac Bioelectricity and Arrhythmia Center (CBAC) when it first opened in September 2004. Her research and collaborative efforts with the CBAC center have proven extremely valuable, and her hard work and dedication to her research and staff is why Dr. Pamela Woodard was chosen to be the first CBAC Newsletter "Spotlight On..." faculty member.



Dr. Pamela Woodard at the Mallinckrodt Institute of Radiology (East Building)

"I first became interested in cardiovascular MR and CT research in 1991 as a resident at Duke University. Dirk Sostman, now Executive Vice Dean at the Cornell Weill Medical Center, was Vice Chairman there and had been one of the investigators on the NIH PIOPED (Prospective Investigation in Pulmonary Embolism Diagnosis) project. He was principal investigator on an NIH R01 grant to investigate CT and MRI for the detection of pulmonary emboli. He started me on a project where I would come into the hospital at 3:00 AM and do pulmonary CT angiography and MRI on animals who had received pulmonary emboli. It was my job to administer the emboli and then take the animals to CT and MRI. We had a research MRI scanner, but no research spiral CT scanner, so we used the clinical single detector spiral CT scanner – we had to be off of the CT scanner before the first patient arrived at 7:00 AM."

"Our results showed that CT had better sensitivity and specificity for the detection of pulmonary emboli than MRI. In 1992, CT for assessment of pulmonary emboli was not routinely performed as it is now. We submitted the article to the journal Radiology, where I believe it was reviewed by an expert in MRI. The article was counterintuitive to what was then believed and was rejected, but [it was] later published in a smaller subspecialty journal (preliminary data on what was later proved by others in human subjects)."

"This initial work lead to involvement with the PIOPED investigators and the submission and award of the multicenter R01 PIOPED II and, most recently PIOPED III."

"I developed a clinical interest in cardiac imaging through James T.T. Chen at Duke University and Fernando Gutierrez here at Washington University. Both are highly talented individuals with tremendous clinical expertise. During my Cardiothoracic Imaging Fellowship, I applied for and received funding from the Radiological Society of North America (RSNA) to pursue research in cardiac MRI. This initial funding lead to research in coronary MR angiography, and then later to work on MR perfusion imaging, myocardial infarction, and atherosclerotic plaque assessment. With the recent developments in multidetector CT, we have returned to the modality of CT for the assessment of atherosclerosis of coronary arteries."

"I am extremely indebted to all of my research colleagues and fellows in the Cardiovascular Imaging Laboratory. I think collaborators are key to any successful grant and research project. No investigator can do it all – or has the expertise to do it all. A successful clinical investigator needs good physicists, chemists and engineers as collaborators and visa versa. Good research teams are multidisciplinary. Rob Gropler's lab (the Cardiovascular Imaging Laboratory, of which I am a member), for instance, is an excellent example of a research team where radiologists, cardiologists, cardiothoracic surgeons, physicists, engineers and chemists all work together in collaboration to produce excellent research. Our collaborators include mathematicians at Worcester Polytechnic, physicists in Seattle and pathologists in Boston."

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SPOTLIGHT ON... *cont.*; CONTACT INFORMATION

“I have immensely enjoyed our collaborative efforts with Dr. Rudy on his ECGI projects, and look forward to continue to collaborate as a part of his multidisciplinary team.”

Dr. Woodard will be one of the speakers at the May 12 CBAC Research Retreat and will present a talk titled “*Delayed Contrast-Enhanced Imaging of the Myocardium in Determining Cause and Source of Arrhythmogenic Foci*”.



Dr. Pamela Woodard



The Mallinckrodt Institute of Radiology
(East Building)

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Want to Be Added to the CBAC Email List?

If you would like to be added to the CBAC email list to receive information on upcoming seminars, events, and news, or to be added to the CBAC mailing list to receive future newsletters, email Jennifer Godwin-Wyer at jlgodwin@biomed.wustl.edu or call (314) 935-7887.

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The CBAC newsletters can also be found on the CBAC website at <http://cbac.wustl.edu>.

This newsletter is produced on behalf of the Cardiac Bioelectricity and Arrhythmia Center (CBAC) by the CBAC office. Editors: **J. Godwin-Wyer** <jlgodwin@biomed.wustl.edu> and **Y. Rudy** <rudy@wustl.edu>.



The Atrium in Whitaker Hall
(Department of Biomedical Engineering, and the CBAC offices)

