BIOGRAPHICAL SKETCH

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NAME: Yoram Rudy

POSITION TITLE: Fred Saigh Distinguished Professor of Engineering; Director, Cardiac Bioelectricity & Arrhythmia Center

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

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
Technion, Haifa, Israel	B.Sc.	1971	Physics
Technion, Haifa, Israel	M.Sc.	1973	Physics
Case Western Reserve University	Ph.D.	1978	Biomedical Engineering

A. Personal Statement

My research interests are in cardiac electrophysiology, arrhythmias, and sudden death. I have been active in this field for many years and research in my laboratory spans the entire spectrum from the molecular/cellular mechanisms of cardiac arrhythmias to clinical studies in patients using novel imaging techniques developed in my lab. The research on molecular/cellular mechanisms of arrhythmias has been supported by the NIH-NHLBI grant “Cardiac Excitation and Arrhythmias”. Mathematical models of cardiac cells, developed under this grant, have been used for cardiac electrophysiology and arrhythmia simulation studies in many laboratories worldwide. The development of a novel noninvasive imaging modality for cardiac electrophysiology (ECG Imaging, ECGI) and its application in the study of human arrhythmia mechanisms has been supported by the NIH-NHLBI grant “Inverse and Forward Problems in Electrocardiography” - an NIH MERIT award recipient. I have trained many graduate students and post-doctoral fellows (in basic science and clinical departments) to become independent researchers. I am also the director of the Cardiac Bioelectricity and Arrhythmia Center (CBAC) that includes 37 faculty members and fosters interdisciplinary research, from cell to bedside, in the cardiac electrophysiology and arrhythmia field.

B. Positions and Honors

Positions

1981-1986 Assistant Professor, Department of Biomedical Engineering, Case Western Reserve University
1986-1989 Associate Professor, Department of Biomedical Engineering, Case Western Reserve University
1989-2004 Professor, Department of Biomedical Engineering, Case Western Reserve University
1991-2004 Professor, Department of Physiology & Biophysics, Case Western Reserve University
1992-2004 Professor, Department of Medicine, Division of Cardiology, Case Western Reserve University
1994-2004 Director, Cardiac Bioelectricity Research and Training Center, Case Western Reserve University
2001-2004 The M. Frank and Margaret C. Rudy Professor of Cardiac Bioelectricity, Case Western Reserve Univ.
2004- The Fred Saigh Distinguished Professor of Engineering, Professor of Biomedical Engineering, Medicine, Cell Biology & Physiology, Pediatrics, and Radiology, Washington University in St. Louis
2004- Director, Cardiac Bioelectricity and Arrhythmia Center (CBAC), Washington University in St Louis

Visiting Professorships

Technion - Israel Institute of Technology, Haifa, Israel, Department of Biomedical Engineering (Dec. 1982 - Mar. 1983).
University of Parma, Italy, Institute of General Physiology (July 1986 and July 1987).
University of Berne, Switzerland, Department of Physiology (May 1990).
University of Utah, Salt Lake City, The Nora Eccles Harrison Cardiovascular Research and Training Institute (Oct.1990).
Tel-Aviv University, Israel, Department of Physics and Astronomy (June - July, 1991).
Columbia University, College of Physicians and Surgeons, Department of Pharmacology, New York, August 1994.
Cornell University, Department of Physiology, Ithaca, New York, October 1994.
Masonic Medical Research Laboratory, Utica, New York, December 1995.
Russian Academy of Sciences, St. Petersburg, June 1997.
University of Szeged, Department of Pharmacology and Pharmacotherapy, Szeged, Hungary, September 2004.

Reynolds Visiting Professor, The Reynolds Cardiovascular Research Center, Johns Hopkins School of Medicine, Baltimore, March 2005.
Columbia University, College of Physicians and Surgeons, Department of Pharmacology, New York, June 2005.
Nagoya University, Research Institute of Environmental Medicine, Nagoya, Japan, October 2005.
Columbia University College of Physician and Surgeons, Department of Pharmacology, New York, April 2006.
University of Berne, Switzerland, Department of Physiology, December 2006.
Stanford University Cardiovascular Institute, December 2007.
University of California, San Francisco, Department of Medicine, March 2008.
Maastricht University, The Netherlands, September 2008 and September 2009.
The Cleveland Clinic, Cleveland, Ohio, July 2010.
University of Pavia and Instituto di Analisi Numerica del C.N.R., Italy, September 2012.
University of Milano, Department of General Physiology and Biochemistry, Department of Biomolecular Sciences and Biotechnology, and Department of Mathematics, Italy, September 2012.
Slovak Academy of Sciences, Bratislava, Slovak Republic, September 2012.
Oxford University, Institute of Mathematics and Department of Computer Science, Aug. 2013, Sept. 2015 and Oct. 2016.

NIH and Government Committees

Member, Cardiovascular & Pulmonary Study Section, NIH-NHLBI (7/84-6/88)
Member, National Institutes of Health Reviewers (7/88-6/92)
NIH Task Force on Medical Imaging Research
Committee on Bioengineering – Building the Future of Biology & Medicine
Committee on Biomedical Imaging – Visualizing the Future of Biology & Medicine
Review of Grants for Centers of Excellence in Computational Biology
NIH Special Emphasis Review Panels
Organized and chaired an NHLBI Workshop “Systems Approach to Understanding Electromechanical Activity in the Human Heart”
Panel, Medicare Evidence Development & Coverage Advisory Committee, Centers for Medicare & Medicaid Services.
FDA Cardiotoxicity Working Group, Development and Use of Computer Models.
Reviewer and member of site-visit teams for Program Project Grants
Ad hoc member of various study sections

Selected Awards

- Member of the National Academy of Engineering (since 2003). Citation: “For leadership in the engineering sciences of cardiac excitation at the genetic and molecular levels and for introducing new methods in clinical diagnosis and therapy”
- Distinguished Scientist Award, Heart Rhythm Society, 2010
- NIH MERIT Award, September, 1998
- Distinguished Alumni Award, Case Western Reserve University, October 2009. For contributions to basic science in biomedical engineering.
- University of Oxford, Astor Visiting Professor in Computational Medicine in the Mathematical, Physical and Life Sciences Division and the Department of Computer Science, 2014-
- The Hein Wellens Distinguished Professor in Cardiology, University of Maastricht, The Netherlands, 2008-2009.
- The Tawara Lecture Award, 36th International Congress of Physiological Sciences (IUPS2009), Kyoto, Japan, July 2009.
- President, the Cardiac Electrophysiology Society, November 2006 – November 2008
- The Biomedical Engineering Society (BMES) 2001 Distinguished Lectureship Award
- Fellow of the Academy of Science – St. Louis
- Fellow of the American Physiological Society – Cardiovascular Section
- Fellow of the Institute of Electrical and Electronics Engineers (IEEE). Citation: "For contributions to mathematical descriptions and solutions applicable to cardiac electrophysiology"
- Fellow of the American Institute of Medical and Biological Engineering (AIMBE). Citation: "In recognition of outstanding contributions to the field of medical and biological engineering"
- Fellow of the Biomedical Engineering Society (BMES). Citation: “For research of cellular mechanisms underlying cardiac electrophysiology and arrhythmias using computational biology and mathematical modeling, and for development of Electrocardiographic Imaging (ECGI) for cardiac arrhythmias”
- Fellow of the American Heart Association
- Fellow of the Heart Rhythm Society

- The Gordon K Moe Professorship Award, Masonic Medical Research Laboratory, 1997. Citation: "In recognition of outstanding contributions to science and medicine in the fields of cardiac electrophysiology and arrhythmias"
- Keynote Presentation, SPIE Medical Imaging, San Diego, CA, February 2006.
- Keynote Presentation, International Society for Heart Research, Manchester, UK, June 2006.
- Keynote Presentation, International Congress on Electrocardiology, Cologne, Germany, June 2006.
- Keynote Presentation "Noninvasive ECG Imaging (ECGI) of Cardiac Arrhythmia", Fields Institute Conference on Mathematics of Medical Imaging, University of Toronto, Canada, June 2011.
- Keynote Presentation "The Molecular Basis of Cardiac Action Potential Repolarization", 4th Cardiac Physiome Workshop, Oxford University Merton College, Oxford, England, July 2011.
- Michael and Ada Anbar Lecturer in Biophysical Sciences, University at Buffalo, The State University of New York, October 11, 2012.
- University of Michigan, Frontiers in Cardiovascular Science Lecturer, Ann Arbor, October 29, 2012.
- Keynote Presentation "Noninvasive Mapping of Human Cardiac Arrhythmias with ECGI", 40th International Congress on Electrocardiology, Glasgow, Scotland, August 2013.
- Keynote Presentation, University of Milano Department of Biotechnology and Biosciences, Department Day Celebration, "Mechanisms of Human Cardiac Arrhythmias: Noninvasive Studies with Electrocardiographic Imaging (ECGI)",Milan, Italy, December 5, 2013.
- Keynote Presentation "Multiscale Integration of Cardiac Excitation: From Molecular Structure to the Human Heart", Virtual Physiological Human Conference, Norwegian University of Science and Technology, Trondheim, Norway, September 11, 2014.
- Keynote Presentation "Noninvasive Mapping of Cardiac Electrophysiology and Arrhythmias in the Intact Human Heart" Simula School of Science and Innovation, Oslo, Norway, September 16, 2014.
- Keynote Presentation "Arrhythmogenic substrates and arrhythmia mechanisms in the human heart – insights from noninvasive mapping in patients" Symposium Honoring Matthew N. Levy, Case Western Reserve University School of Medicine, Department of Physiology & Biophysics, Cleveland, Ohio, October 2014.
- Keynote Presentation "A Noninvasive Imaging Modality for Electrical Excitation of the Heart (And Possibly Other Excitable Tissues)" March of Dimes and Burroughs Wellcome Fund 5th Symposium on Preventing Prematurity: Establishing a Network for Innovation and Discovery. Newport Beach, CA, December 2014.
- Keynote Presentation "Noninvasive Imaging of Cardiac Electrophysiology and Arrhythmias" Israel Society for Medical and Biological Engineering Annual Meeting, February 24, 2016.
- Keynote Presentation "Multi-scale modeling and imaging cardiac electrophysiology: A potential approach for drug development and evaluation" Sanofi – Mount Sinai Systems Pharmacology Symposium. New York, NY, June 2016.
- Keynote Presentation "Hereditary repolarization disorders: ECG imaging of the clinical substrate and mathematical modeling of the molecular mechanism" The 40th meeting of the European Society of Cardiology Working Group on Cardiac Cellular Electrophysiology. Glasgow, UK, September 2016.
- Keynote Presentation "ECGI – Principles, Methodology and Validation" ECG Imaging Workshop, Barts Heart Center and University College London, September 2016.
- Dutch Heart Foundation Keynote Lecture "Towards a multi-scale understanding of cardiac arrhythmogenesis: Integration of mathematical modeling with electrocardiographic imaging" Frontiers in Computational Electrocardiology, Maastricht, The Netherlands, September 2016.
- Elected for Top Ten in Cardiology; Lausanne, Switzerland, October 2nd, 2015.

C. Contribution to Science

My contributions to science can be grouped into two areas of cardiac electrophysiology: 1. Studies of basic mechanisms using mathematical modeling, and 2. Development of a novel noninvasive imaging modality for cardiac electrophysiology (Electrocardiographic Imaging, ECGI) and its application to study mechanisms of cardiac arrhythmias in patients.

1. My laboratory pioneered the development and application of detailed, physiologically accurate mathematical models of cardiac myocytes. These species-specific models have been used by us and in other laboratories worldwide for research and training. The first published model of the guinea pig ventricular cell (Circulation Research 1991 and 1994) has been included in textbooks in many languages. To date, we have published models of the canine and the human myocytes which simulate the cell electrophysiology and calcium cycling and include regulatory pathways (the CaMKII pathway and beta-adrenergic cascade). We have used modeling to connect genotype to phenotype in hereditary cardiac arrhythmias, thereby providing a new computational-biology approach for relating phenotype to phenotype in other pathologies. Simulations were conducted to study the electrophysiological consequences and mechanisms in various pathologies (e.g. ischemia and infarction, calcium

overload). We also established basic principles of intercellular communication and action potential propagation in cardiac tissue, including definitions of important quantitative parameters such as the safety factor for conduction and the vulnerable window for unidirectional block and reentry. Recently, we have integrated molecular dynamics simulations with electrophysiology modeling to study structure – function relationships during ion-channel gating, starting from the channel protein molecular structure. Representative publications:

a. C. E. Clancy, Y. Rudy, "Linking a genetic defect to its cellular phenotype in a cardiac arrhythmia" *Nature* 1999;400:566-569.
b. J. R. Silva, H. Pan, D. Wu, A. Nekouzadeh, K. Decker, J. Cui, N. A. Baker, D. Sept, Y. Rudy, "A Multiscale Model Linking Ion-Channel Molecular Dynamics and Electrostatics to the Cardiac Action Potential" *Proc Natl Acad Sci USA (PNAS)* 2009;106:11102-11106.
c. T.J. O'Hara, L. Virág, A. Varró, Y. Rudy, "Simulation of the undiseased human cardiac ventricular action potential: Model formulation and experimental validation" PLoS Computational Biology 2011; 7(5): e1002061.doi:10.1371/journal.pcbi.1002061
d. R.M. Shaw and Y. Rudy, "Ionic Mechanisms of Propagation in Cardiac Tissue: Roles of the Sodium and L-Type Calcium Currents during Reduced Excitability and Decreased Gap-Junction Coupling" Circ Res 1997; 81:727-741.
e. A. Nekouzadeh, Y. Rudy, "Conformational changes of an ion–channel during gating and emerging electrophysiologic properties: application of a computational approach to cardiac Kv7.1" Progress in Biophysics & Molecular Biology 2016;120:18-27.

2. The only noninvasive method for assessing cardiac electrical function has been the electrocardiogram, which was introduced 112 years ago. While very useful in clinical practice, it is severely limited in resolution, sensitivity and specificity because it records a few signals on the body surface, far away from the heart. To overcome these limitations, we developed a novel imaging modality (similar in concept to CT or MRI) for noninvasive mapping of the electrical activity of the human heart and cardiac electrophysiologic substrate. After a long period of validation in animal experiments and in patients undergoing cardiac surgery and catheter ablation, we published the first human application in 2004 (Nature Medicine). This new method is called Electrocardiographic Imaging (ECGI); its resolution is about 6mm on the heart surface. The technology has already been translated to clinical application by CardioInsight Technologies. In my lab, we are using ECGI to study in patients the mechanisms of various cardiac arrhythmias, the properties of arrhythmic substrates, the manifestation of hereditary disorders, and the consequences of therapeutic interventions such as catheter ablation of atrial fibrillation and cardiac resynchronization therapy in heart failure. The following are representative publications:

a. C. Ramanathan, R.N. Ghanem, P. Jia, K. Ryu, Y. Rudy, "Electrocardiographic Imaging (ECGI): A Noninvasive Imaging Modality for Cardiac Electrophysiology and Arrhythmia" Nature Medicine 2004;10:422-428.
b. Y. Wang, P.S. Cuculich, J. Zhang, K. A. Desouza, R. Vijayakumar, J. Chen, M. N. Faddis, B. D. Lindsay, T. W. Smith, Y. Rudy, "Noninvasive Electroanatomic Mapping of Human Ventricular Arrhythmias Using ECG Imaging (ECGI)" Science Translational Medicine 2011 (31 August); Volume 3 (issue 98):191-200 (98ra84).
c. P.S. Cuculich, Y. Wang, B.D. Lindsay, M.N. Faddis, R.B. Schuessler, R.D. Damiano, L. Li, Y. Rudy, "Noninvasive Characterization of Epicardial Activation in Humans with Diverse Atrial Fibrillation Patterns" Circulation 2010;122:1364-1372.
d. Y. Rudy, "Noninvasive Electrocardiographic Imaging of Arrhythmogenic Substrates in Humans" Circulation Research, 2013;112:863-874.
e. J Zhang, F Sacher, K Hoffmayer, T O'Hara, M Strom, P Cuculich, J Silva, D Cooper, M Faddis, M Hocini, M Haissaguerre, M Scheinman, Y Rudy, "The Cardiac Electrophysiologic Substrate Underlying the ECG Phenotype and Electrogram Abnormalities in Brugada Syndrome Patients" Circulation 2015; 131:1950-1959. PMID: 25810336

List of Published Work is in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40548203/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIH-RO1-HL033343 Rudy (PI) 07/01/85 - 05/31/17
Inverse and Forward Problems in Electrocardiography
Development of a novel noninvasive imaging modality for cardiac electrical activity (ECG Imaging, ECGI) and its application in the study of human arrhythmia mechanisms
Role: PI

NIH-RO1-HL049054 Rudy (PI) 02/01/93 - 11/30/17
Cardiac Excitation and Arrhythmias
Under this grant we develop and use mathematical models to study mechanisms of cardiac excitation and arrhythmia at the ion-channel, cell, and tissue levels
Role: PI

Completed Research Support

FONDATION LEDUCQ Rudy (Member) 10/01/08-12/31/13
Alliance for CaMK2 Signaling in Heart Disease
Role: Member

NATIONAL SCIENCE FOUNDATION CBET-0929633 Rudy (PI) 08/15/09-07/31/13
Modeling Spatial Organization of Cardiac Cell Function: Application to Calcium Waves and Arrhythmia
Role: PI