Rengasayee (Sai) Veeraraghavan, PhD, FAHA, FHRS
Principal Investigator
Associate Professor, Department of Biomedical Engineering,
Davis Heart & Lung Research Institute,
The Ohio State University
Director (Biological Sciences), Microscopy Society of America

Nanocardiology Lab

Who am I? I am, in equal parts, a biomedical engineer, a cardiac physiologist, and microscopist. My team and I are working to understand how protein nanomachines – structures 10,000 times smaller than the width of human hair – contribute to the spread of electrical signals through the heart. The goal of this research is to develop novel treatments to prevent life-threatening arrhythmias (irregular heartbeats). In pursuing this scientific mission, we are often challenged by the limits of current microscopy and image analysis methods. Therefore, the efforts of my laboratory are divided between cardiac research and the development of new imaging and image analysis techniques.

Research Interests: Cardiac electrophysiology ▪ Arrhythmia mechanisms ▪ Action potential Propagation ▪ Super-resolution microscopy ▪ Computational image analysis ▪ Gap Junctions ▪ Ion channels ▪ Indirect correlative light & electron microscopy (*iCLEM*) ▪ Glioblastoma ▪ Sudden death in epilepsy ▪ Vascular Barrier Function

CONTACT

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EDUCATION/TRAINING

2011 **Ph.D. in Biomedical Engineering**
University of Utah, Salt Lake City, UT

2005 **B.Tech in Chemical Engineering**
Anna University, Chennai, India.
(Ranked 11th among >6000 Chem Engg. graduates.)

EMPLOYMENT

2022 – Associate Professor, Dept. of Biomedical Engineering, The Ohio State University, OH
2017 – 2022 Assistant Professor, Dept. of Biomedical Engineering, The Ohio State University, OH
2016 – 2017 Research Assistant Professor, The Virginia Tech Carilion Research Institute, VA
2012 – 2016 Postdoctoral Research Associate, The Virginia Tech Carilion Research Institute, VA
2011 – 2012 Postdoctoral Research Fellow, Math Biology Group, University of Utah, UT
2005 – 2011 Graduate Research Assistant, Dept. of Biomedical Engineering, University of Utah, UT

SELECTED AWARDS & HONORS

2024 Elected fellow of the Heart Rhythm Society
2024 JACC: Clinical EP confers the *2023 Young Author Achievement Award* on my former student Dr. Heather Struckman for our paper (PMID: 37498248)
2024 Elected Director, Biological Sciences [2024-26], Microscopy Society of America
2024 Strategic Initiative Award ($8,000) from the Microscopy Society of America to fund a professional development program for postdoctoral fellows.
2024 Strategic Initiative Award ($5,000) from the Microscopy Society of America to fund electron microscopy-based education outreach in central Ohio [Partner: Metro Early College High School].
2023 Elected fellow of the American Heart Association
2022 Lumley Interdisciplinary Research Award (along with Drs. Przemysław Radwański, Sandor Györke) from the Ohio State University College of Engineering.
2021 Lumley Research Award from the Ohio State University College of Engineering.
2020 Microscopy & Microanalysis awards our article (PMID: 31931893) "*Best biological sciences paper of the year*"
2020 Strategic Initiative Award ($20,000) from the Microscopy Society of America to fund microscopy-based education outreach.
2017 George Palade Award for distinguished contributions to the field of microscopy and microanalysis in the life sciences, Microscopy Society of America
2017 Young Investigator Award (Basic Science) from the Cardiac Electrophysiology Society

RESEARCH SUPPORT

Ongoing:

NIH R01 Veeraraghavan (Subcontract) 06/15/23-03/31/27
Critical sorting steps and pathways in the trafficking of cardiac sarcoplasmic reticulum proteins

NIH R01 Veeraraghavan (MPI) 04/01/23-03/31/28
Distinct Ion Channel Pools and Intercalated Disk Nanoscale Structure Regulate Cardiac Conduction

NIH R01 Veeraraghavan (PI) 07/01/20-06/30/25
Targeting Vascular Leak and Intercalated Disk Nanodomains to Prevent Atrial Fibrillation

NIH R01 Veeraraghavan (Co-I) 03/01/20-02/28/25
Abnormal intracellular calcium release in heart failure

NIH R01 Veeraraghavan (Co-I) 09/01/21-08/31/26
Regulation and dysregulation of cardiac EC coupling by calmodulin

NIH R01 Veeraraghavan (Co-I) 12/01/21-11/30/26
Defining novel mechanisms of sudden death in Dravet syndrome: Dysregulation of sodium channels in the heart

NIH R01 Veeraraghavan (Co-I) 09/01/21-08/31/26
Regulation and dysregulation of sodium channels by calmodulin

Completed (Selected)

NIH R01HL141855-01 Veeraraghavan (Subcontract) 07/01/18-06/30/22
The Role of the Sodium Channel Beta Subunit in Cardiac Conduction

AHA Transformative Project Grant Veeraraghavan (PI) 01/01/21-12/31/21
Preventing Atrial Fibrillation by Preserving the Vascular Barrier and Intercalated Disk Nanodomains (Relinquished due to overlap with R01)

AHA Scientist Development Grant Veeraraghavan (PI) 07/01/16-06/30/19
Modulation of cardiomyocyte ultrastructure by vascular barrier function - a novel mechanism for atrial arrhythmias

AHA Post-Doctoral Fellowship Veeraraghavan (PI) 07/01/13-06/30/15
The Role of the Perinexus in Ephaptic Coupling between Cardiac Myocytes.

SELECTED PUBLICATIONS

Peer-reviewed Publications (h-index: 23, 1531 citations)

Struckman HL, Moise N, Vanslembrouck B, Rothacker N, Chen Z, van Hengel J, Weinberg SH, **Veeraraghavan R**. Indirect Correlative Light and Electron Microscopy (iCLEM): A Novel Pipeline for Multiscale Quantification of Structure from Molecules to Organs. Microsc Microanal. 2024 Mar 25.

Soltisz AM, Craigmile PF, **Veeraraghavan R**. Spatial Pattern Analysis using Closest Events (SPACE) – A Nearest Neighbor Point Pattern Analysis Framework for Assessing Spatial Relationships from Image Data. Microsc Microanal. 2024 Mar 18.

King DR, Demirtas M, Tarasov M, Struckman HL, Meng X, Nassal D, Moise N, Miller A, Min D, Soltisz AM, Anne MNK, Wagnon JL, Weinberg SH, Hund TJ, **Veeraraghavan R**, Radwański PB. Cardiac-specific deletion of Scn8a mitigates Dravet syndrome-associated sudden death in adults. JACC Clin Electrophysiol. 2024 Feb 15.

Adams, W.P., Raisch T.B., Zhao Y., Davalos R., Barrett S., King D.R., Bain C.B., Colucci-Chang K., Blair G.A., Hanlon A., Lozano A., **Veeraraghavan R.**, Wan X., Deschenes I., Smyth J.W., Hoeker G.S., Gourdie R.G., Poelzing S. Extracellular perinexal separation is a principal determinant of cardiac conduction. Circ Res. 2023 Sep 29;133(8):658-673.

Mezache L, Soltisz AM, Johnstone SR, Isakson BE, **Veeraraghavan R**. Vascular Endothelial Barrier Protection Prevents Atrial Fibrillation by Preserving Cardiac Nanostructure. *JACC Clin Electrophysiol. 2023 Nov 8:S2405-500X(23)00804-6*.

Struckman HL, Moise N, King DR, Soltisz A, Buxton A, Dunlap I, Chen Z, Radwański PB, Weinberg SH, **Veeraraghavan R**. Unraveling Chamber-specific Differences in Intercalated Disc Ultrastructure and Molecular Organization and Their Impact on Cardiac Conduction. *JACC Clin Electrophysiol. 2023 Jul 12:S2405-500X(23)00387-0*.

Tarasov M*, Struckman HL*, Olgar Y*, Soltisz AM, Miller A, Bogdanov V, Györke S, **Veeraraghavan R**, Radwański PB. Nav1.6 dysregulation within myocardial T-tubules by D96V calmodulin enhances proarrhythmic sodium/calcium mishandling. J Clin Invest. 2023 Feb 23:e152071. *Co-first authors. [Featured on journal cover]

Che J, DePalma T, Sivakumar H, Mezache L, Tallman MM, Venere M, Swindle-Reilly K, **Veeraraghavan R**, Skardal A. αCT1 Peptide Sensitizes Glioma Cells to Temozolomide in a Glioblastoma Organoid Platform. *Biotechnol Bioeng*. 2023 Apr;120(4):1108-1119.

Mezache L, Nuovo GJ, Suster D, Tili E, Awad H, Radwański PB, **Veeraraghavan R**. Histologic, viral, and molecular correlates of heart disease in fatal COVID-19. *Annals of Diagnostic Pathology*. 2022:151983.

Bogdanov V*, Soltisz AM*, Moise N, Ivanova M, Andreev I, Skuta G, Weinberg SH, Davis JP, **Veeraraghavan R**†, Györke S†. Distributed synthesis of sarcolemmal and sarcoplasmic reticulum membrane proteins in cardiac myocytes. Basic Res Cardiol. 2021 Oct 28;116(1):63. *Co-first authors. †Co-corresponding authors.

Moise N, Struckman HL, Dagher C, **Veeraraghavan R**, Weinberg SH. Intercalated disk nanoscale structure regulates cardiac conduction. J Gen Physiol. 2021 Aug 2;153(8):e202112897.

Mezache L, Struckman HL, Greer-Short A, Baine S, Györke S, Radwański PB, Hund TJ, **Veeraraghavan R**. Vascular Endothelial Growth Factor Promotes Atrial Arrhythmias by Inducing Acute Intercalated Disk Remodeling. Sci Rep. 2020 Nov 24. 10 (1), 1-14.

Munger MA, Olğar Y, Koleske M, Struckman HL, Mandroli J, Lou Q, Bonilla I, Kim K, Mondragon RR, Priori SG, Volpe P, Valdivia HH, Biskupiak J, Carnes CA, **Veeraraghavan R**, Györke S, Radwański PB. Tetrodotoxin-sensitive neuronal-type Na+ Channels: A Novel and Druggable Target for Prevention of Atrial Fibrillation. J Am Heart Assoc. 2020 Jun 2;9(11):e015119.

Struckman HL, Baine S, Thomas J, Mezache L, Mykytyn K, Györke S, Radwański PB, **Veeraraghavan R**, Super-resolution Imaging Using Novel High Fidelity Antibody Reveals Close Association of Neuronal Sodium Channel Nav1.6 with Ryanodine Receptors in Cardiac Muscle. Microsc Microanal. 2020 Jan 14:1-9. [Featured on journal cover]

Bonilla IM, Belevych AE, Baine S, Stepanov A, Mezache L, Bodnar T, Liu B, Volpe P, Priori S, Weisleder N, Sakuta G, Carnes CA, Radwański PB, **Veeraraghavan R***, Gyorke S. Enhancement of Cardiac Store Operated Calcium Entry (SOCE) within Novel Intercalated Disk Microdomains in Arrhythmic Disease. Sci Rep. 2019 Jul 15;9(1):10179. *Co-corresponding author

Veeraraghavan R*, Hoeker GS, Alvarez-Laviada A, Hoagland D, Wan X, King DR, Sanchez-Alonso J, Chen C, Jourdan J, Isom LL, Deschenes I, Smyth J, Gorelik J, Poelzing S, Gourdie RG. The adhesion function of the sodium channel beta subunit (β1) contributes to cardiac action potential propagation. Elife. 2018 Aug 14;7:e37610. *Co-corresponding author

Raisch TB, Yanoff MS, Larsen TR, Farooqui MA, King DA, **Veeraraghavan R**, Gourdie RG, Baker JW, Arnold WS, AlMahameed ST, Poelzing S. Intercalated Disc Extracellular Nanodomain Expansion in Patients with Atrial Fibrillation. Front Physiol. 2018 May 4;9:398.

Patents

Soltisz A, **Veeraraghavan R**, Craigmile P, Systems and Methods for Data Analysis. Provisional patent filed March 2024.

Soltisz A, **Veeraraghavan R**, Craigmile P, Systems and Methods for Single Molecule Localization Microscopy. Provisional patent filed March 2024.

Skardal A, Swindle-Reilly K, **Veeraraghavan R**, Sustained Adjunct Therapy to Improve Chemotherapy Efficacy in Glioblastoma in a Cerebrovascular-Tumor-On-A-Chip Model. Pending; PCT filed June 2023.

Mezache L, **Veeraraghavan R**, Compositions and Methods for Treating Atrial Fibrillation. Pending; PCT filed May 2021, Published Nov 2021.

Poelzing S, **Veeraraghavan R,** Smoot A, X-ray attenuating compositions and methods. U.S. Patent 8808668; filed April 2009.

Poelzing S, **Veeraraghavan R**, Raisch R. Automatic Centerline Isolation and Continuous Width Measurements Between Two Edges. U.S. Patent Application No: 62/405,554 filed 10/7/2016.

Gourdie RG, **Veeraraghavan R**, Poelzing S. Pharmacologic Targeting of Cell Adhesion to Modulate Conduction. U.S. Patent Application No: 62/299,817 filed 02/25/2016.

Veeraraghavan R, Gourdie RG. Two Novel Methods for the Assessment of Relative Protein Localization from Three Dimensional Single Molecule Localization Data. U.S. Patent Application No: 62/295,672 filed 02/16/2016.

SELECTED INVITED PRESENTATIONS

Nanocardiology: What is it and how does it help treat arrhythmia?, Invited Seminar, College of Medicine, University of South Carolina, 2024.

Rapid, Hyperparameter-free Point Pattern Analysis of Single Molecule Localizations in 3D using VoronoiTessellation-Based Clustering, Biophysics Colloqium, Dept. of Physics, Case Western Reserve University, 2024.

Nanocardiology: What is it and why physicians need care?, Cardiology Grand Rounds, OSU Wexner Medical Center, 2024.

Ion Channel-Rich Nanodomains and Their Dynamic Influence on Cardiac Rhythm, Gordon Research Conference on Cardiac Regulatory Mechanisms, 2024.

Voronoi Tessellation-Based Clustering Enables Rapid, Hyperparameter Free Point Pattern Analysis of Single Localizations in 3D, DIJON - COMPLEXBIODYN 2024 (Complex Kinetics And Dynamics From Single Molecule To Cells).

Developing computational image analysis approaches to unlock the investigative power of high-resolution microscopy, Keynote Talk, Annual Biophysics Symposium, University of Michigan – Ann Arbor, May 2024.

Unlocking the investigative power of high-resolution microscopy through computational image analysis, 66th Annual May Conference of the Microscopy Society of Northern Ohio, May 2024.

COVID-19 and Cardiac Arrhythmias: Developing Therapies to Protect Cardiac Nanostructure. 2023 Connor Senn Symposium: Sudden Cardiac Arrest in the Athlete, OSU.

Eavesdropping on cardiac muscle cells using multi-scale light and electron microscopy. Plenary Talk, 2023 Midwest Microscopy and Microanalysis Society Meeting.

Discovering (through) Microscopy: A Scientific Metamorphosis Story, Microscopy & Microanalysis 2023: Pre-meeting Congress for Students and Early-Career Professionals.

Nanocardiology: How the heart's nanoscale structure dynamically determines macroscale physiology, UCLA Cardiac Arrhythmia Center & Neurocardiology Research Program of Excellence – Research & Innovation Lecture Series, 2023.

Visualizing Nanopathies: The connection between channels and discs, American Heart Association Annual Scientific Sessions, 2022.

Leveraging correlative multi-modal multi-scale microscopy to understand the heart in health and disease, Gordon Research Conference on Liquid Phase Electron Microscopy, 2022.

Nanoscale Organization of Ion Channels: A Dynamic Determinant of Cardiac Electrophysiolgy. FASEB Conference on Ion Channel Regulation, 2022

Variability in Channel Isoform Expression Determines Pathology and Drug Response. Heart Rhythm 2022.

Nanocardiology: A Microscopy-Driven Approach to Cardiac Biology and Physiology, Seminar at Fralin Biomedical Research Institute, Virgnia Tech, 2022.

Inflammation-induced vascular leak and progression of AF. American Heart Association Annual Scientific Sessions, 2021.

Linking Cardiac Nanostructure and Molecular Organization to Function, Webinar organized by Bruker Fluorescence Microscopy Inc, 2021.

Confocal Imaging to Characterize Structural Underpinnings of Local Calcium Entry Events, Heart Rhythm 2021.

Targeting Vascular Leak and Intercalated Disk Nanodomains to Prevent Atrial Fibrillation, American Heart Association Annual Scientific Sessions, 2020.

Dynamic Reorganization of Cardiac Nanodomains: A New Mechanism for Arrhythmia, Biomedical Engineering Department Seminar Series, Pennsylvania State University, 2020.

Confocal Imaging to Characterize Local Calcium Entry Events, Heart Rhythm 2020.

Structural Changes in Sodium Channel-Rich Nanodomains Contribute to the Progression of Atrial Fibrillation, Microscopy & Microanalysis 2018.

STORM and TEM Identify the Cardiac Ephapse: An Intercalated Disk Nanodomain with Previously Unanticipated Functions in Cardiac Conduction, Microscopy & Microanalysis 2017.

Integrating Imaging Tools From Single Molecule to Whole Organ Scales to Investigate the Heart's Structure and Function, Microscopy & Microanalysis 2017: Pre-Meeting Congress for Students and Early-Career Professionals.

STORM-based Quantitative Assessment of Sodium Channel Localization Relative to Junctional Proteins within the Cardiac Intercalated Disk, Microscopy & Microanalysis 2016.

Spatial Organization of Proteins: Above and Below Abbe's Diffraction Limit, Heart Rhythm 2016.