BIOGRAPHICAL SKETCH

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NAME: Jeffrey J. Saucerman

eRA COMMONS USER NAME (credential, e.g., agency login): jjs3gnih

POSITION TITLE: Professor of Biomedical Engineering and Cardiovascular Medicine

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
Pennsylvania State University, University Park, PA	B.S. (Hons)	05/2000	Engineering Science
UC San Diego, La Jolla, CA	M.S.	05/2002	Bioengineering
UC San Diego, La Jolla, CA (w. Andrew McCulloch)	Ph.D.	08/2005	Bioengineering
Loyola University of Chicago (w. Don Bers)	Postdoc	06/2006	Physiology

A. Personal Statement

The overall goal of my research program is to advance the field of cardiac systems biology, which aims to develop a systems-level understanding of how signaling networks control cardiac remodeling. Our methods combine computational models of signaling networks and cardiac physiology with cellular imaging and biochemical approaches such as fluorescent protein biosensors, immunofluorescence and RNA sequencing. I have a strong quantitative background in engineering, computational modeling, and quantitative microscopy. Much of our recent work has focused on developing computational and imaging approaches scalable to large and poorly characterized networks regulating the heart. I have obtained grants from the NIH, NSF, AHA, and university/foundation/industry partnerships to support my research.

Mentoring undergraduate, graduate, and postdoctoral trainees is one of the most important and rewarding aspects of my job. I am committed to leading a laboratory that is committed to scientific rigor, training, mentoring, and to promoting inclusive, safe, and supportive scientific environment. I have mentored 49 undergraduate, 11 graduate, 7 postdoctoral trainees, 6 staff, and 4 faculty members. My trainees have won a range of internal (16) and external fellowships (14; NIH, AHA, NSF, Beckman). My trainees achieved subsequent placement in MS (3), PhD (14), MD (17) or MD/PhD (3) programs, medical residency (1), post-docs (4; HHMI/MIT, NIH, UCSD), and ultimately positions as tenure-track faculty (4; Clemson U., Rutgers, UC Boulder, Messiah College), industry (14; AstraZeneca, BMS, Novartis, Merck, Pfizer), and government (NIH, FDA).

<u>Highlighted current projects:</u>

NIIH/NHLBI R01-HL162925 (multiPIs Saucerman, Wolf) 4/01/2022-3/31/2027
Systems Pharmacology Model of Cardiac Hypertrophy

NIH/NHLBI R01-HL160665 (multiPIs Saucerman, van Berlo) 1/01/2022-12/31/2025
Computational and Experimental Modeling of Cardiomyocyte Proliferation

NIH/NHLBI R01-HL137755 (multiPIs Saucerman, Holmes) 7/01/2017-6/30/2023 (NCE)
Systems Pharmacology Model for Spatial Control of Cardiac Fibrosis

UVA School of Medicine Vivian Pinn Scholar Award (PI: Saucerman) 01/01/2018 – 12/30/2023
Systems biology of cardiac regeneration

NIH/NHLBI R01-HL158718 (PI: Wolf; co-I: Saucerman) 8/01/2021-6/30/2025
DYRK1a as a therapeutic target to treat myocardial infarction

NIH R01-AR050429 (PI: Yan; co-I: Saucerman) 8/01/2018-6/30/2023
AMPK-ULK1 in exercse-induced mitophay in skeletal muscle

NIH/NHLBI R01HL159945 (PI: Bilchick; co-I: Saucerman) 8/13/2021- 7/31/2025
Multiscale Models for Predicting Short and Long-term Outcome of Cardiac Resynchronization Therapy

Novartis (PI: Saucerman) 4/08/2021-4/07/2023
Hypothesis generation using cellular network models

UVA-AstraZeneca Alliance (PI: Wolf; Co-PI: Saucerman) 1/2021 – 12/2022
Enhancement of cardiomyocyte cycling by modified mRNA after myocardial infarction

B. Positions and Honors

Positions

2022	Interim Vice Chair of Biomedical Engineering, University of Virginia
2020-	Professor of Biomedical Engineering and Cardiovascular Medicine, University of Virginia
2013-2020	Associate Professor of Biomedical Engineering, University of Virginia, Charlottesville, VA
2006-2013	Assistant Professor of Biomedical Engineering, University of Virginia, Charlottesville, VA
2015-	Faculty Member, Center for Membrane Physiology, UVA
2008-	Faculty Member, Center for Public Health Genomics, UVA
2006-	Faculty Member, Robert M. Berne Cardiovascular Research Center, UVA
2005-2006	Postdoctoral Fellow, Stritch School of Medicine, Loyola University of Chicago, Maywood, IL

Other Experience and Professional Memberships

2022-	Associate Editor, Biophysical Journal
2020-	Co-Editor, JMCC Special Issue on Computational Models of Cardiovascular Regulation
2018-	Editorial Board, Cellular Signaling
2014-	Advisory Board, Keck Center for Cellular Imaging, UVA
2013-	Associate Editor, PLOS Computational Biology
2010-	American Heart Association Professional Member; Council on Basic CV Sciences
2015-	Cardiovascular Training Grant Advisory Committee, UVA School of Medicine
2002-	Biomedical Engineering Society, Member
2020-2021	NIH/NHLBI Mentored Transition to Independence (MTI) Study Section, Ad Hoc Member
2021	Reviewer, Dutch Research Council
2020	Interagency Multiscale Modeling Consortium Meeting, Program Committee
2019	Chair, Search Committee for General Faculty, UVA Biomedical Engineering
2019	Systems Pharmacology Session Chair, Interagency MSM Meeting, Bethesda, MD
2019	K-12 Dissemination Session Chair, Interagency MSM Meeting, Bethesda, MD
2018	Assistant Dean of Research Search Committee, UVA School of Medicine
2018	AHA Career Development Program Study Group
2016-2018	Chair, Dean's Research Advisory Committee, UVA School of Medicine
2017	NIH Predictive Multiscale Models U01 Study Section
2017	NSF Computer & Information Science & Engineering Study Section
2015-2016	Member, Dean's Research Advisory Committee, School of Medicine
2016-2017	Chair, AHA Bioengineering Bsc 3 Peer Review Study Group
2015-2017	Chair, UVA Biomedical Data Sciences Faculty Search Committee
2015	Cardiovascular Systems Biology Session Chair, AHA Scientific Sessions
2014-2017	Vice President for Research Internal Review Committee, UVA
2014-2015	Co-Chair, AHA Bioengineering Bsc 3 Peer Review Study Group
2014	Member, Big Data Faculty Search Committee, UVA Dept of Systems Engineering
2014	Participant, Leadership in Academic Matters course, UVA
2014	Reviewer, KU Leuven Research Council

2013 Reviewer, Danish Council for Strategic Research
2009-2013 Judge, Charlottesville Business Innovation Council Awards
2012 Reviewer, Wellcome Trust, UK
2012 Reviewer, Royal Society of New Zealand, Marsden Fund
2010 Reviewer, Biotechnology and Biological Sciences Research Council (United Kingdom)
2009 Reviewer, Netherlands Organisation for Scientific Research
2009 Visiting Fellow, Isaac Newton Institute for Mathematical Sciences, Cambridge University, UK
2007 Reviewer, Smithsonian Institution
2002 Research Visitor with Denis Noble and Peter Kohl, University of Oxford, UK

Honors

2018 Vivian Pinn Scholar Award, U. Virginia School of Medicine
2014 Thelma R. Swortzel Collaborative Research Award, with Zhen Yan
2014- Fellow of the American Heart Association, Council on Basic Cardiovascular Sciences
2013 NSF Faculty Early Career Development (CAREER) Award
2012- Member, Academy of Distinguished Educators, U. Virginia School of Medicine
2012 Dean's Excellence in Teaching Award, U. Virginia School of Medicine
2008 National Scientist Development Grant, American Heart Association
2007 FEST Distinguished Young Investigator Grant, University of Virginia
2000-2005 Whitaker Foundation Graduate Fellowship
2000 Francis H. Fenlon Award (outstanding undergrad thesis), The Pennsylvania State University
1997-2000 Schreyer Scholar, The Pennsylvania State University

C. Contributions to Science

1. Computational modeling of cardiomyocyte signaling networks. We have developed methods for building and analyzing large-scale computational models of cell signaling networks. We developed a new logic-based differential equations approach, which we showed to retain much of the predictive capability of a detailed biochemical model while requiring only network topology. We applied this method to develop and validate the first large-scale computational model of the cardiac signaling network, discovering a bow-tie control structure for myocyte hypertrophy involving Ras. We recently used a similar approach to model the cardiac fibroblast signaling network, identifying and validating context-dependent regulators of fibrosis. We have also applied this approach to model cardiac differentiation, revealing a hysteresis critical for robust performance.

a. Hota SK, Rao KS, Blair AP, Khalilimeybodi A, Hu KM, Thomas R, So K, Kameswaran V, Xu J, Polacco BJ, Desai RV, Chatterjee N, Hsu A, Muncie JM, Blotnick AM, Winchester SAB, Weinberger LS, Hüttenhain R, Kathiriya IS, Krogan NJ, Saucerman JJ, Bruneau BG. Brahma safeguards canalization of cardiac mesoderm differentiation. Nature. 2022 Feb;602(7895):129-134. PMCID: PMC9196993.

b. Saucerman JJ, Tan PM, Buchholz KS, McCulloch AD, Omens JH. Mechanical regulation of gene expression in cardiac myocytes and fibroblasts. Nat Rev Cardiol. 2019 Jun;16(6):361-378. PMCID: PMC6525041.

c. Khalilimeybodi A, Paap AM, Christiansen SLM, Saucerman JJ. Context-specific network modeling identifies new crosstalk in β-adrenergic cardiac hypertrophy. PLoS Comput Biol. 2020 Dec 18;16(12):e1008490. PMCID: PMC7781532.

d. Grabowska ME, Chun B, Moya R, Saucerman JJ. Computational model of cardiomyocyte apoptosis identifies mechanisms of tyrosine kinase inhibitor-induced cardiotoxicity. J Mol Cell Cardiol. 2021 Mar 3;155:66-77. PMCID: PMC8154673. Cover Image.

2. Computational modeling of inflammation and fibrosis signaling networks. Using our logic-based network modeling methods, we have created dynamic models of the cardiac fibroblast signaling network, identifying and validating context-dependent regulators of fibrosis. We have also applied this approach to model macrophage activation, finding that opposing cues generate a distinct cell phenotype.

a. Angela C. Zeigler, Anders R. Nelson, Anirudha S. Chandrabhatla, Olga Brazhkina, Jeffrey W. Holmes, Jeffrey J. Saucerman. Computational Model Predicts Paracrine and Intracellular Drivers of Fibroblast Phenotype After Myocardial Infarction. Matrix Biol. 2020 Sep;91-92:136-151. PMCID: PMC7434705.

b. Xiaji Lu, Jingyuan Zhang, Angela C. Zeigler, Anders R. Nelson, Merry L. Lindsey, Jeffrey J. Saucerman. Network analysis reveals a distinct axis of macrophage activation in response to conflicting inflammatory cues.. J Immunol. 2021 Feb 15;206(4):883-891. PMCID: PMC7854506.

c. Zeigler AC, Chandrabhatla AS, Christiansen SL, Nelson AR, Holmes JW, Saucerman JJ. Network model-based screen for FDA-approved drugs affecting cardiac fibrosis. CPT Pharmacometrics Syst Pharmacol. 2021 Feb 11. PMCID: PMC8099443.

d. Chowkwale M, Lindsey ML, Saucerman JJ. Intercellular model predicts mechanisms of inflammation-fibrosis coupling after myocardial infarction. J Physiol. 2022 Jul 21. doi: 10.1113/JP283346. PMC Journal – In Process.

3. High-throughput microscopy of large-scale cardiac signaling networks. We were among the first to perform high-throughput microscopy customized for cardiac myocyte phenotypes. We have applied these methods to validate computational model predictions, discover mechanisms regulating reversal of cardiac myocyte hypertrophy and identify pathways differentially controlling myocyte size, shape, gene expression, and sarcomeric organization, and screen for compounds that induce CM proliferation.

a. Bass GT, Ryall KA, Katikapalli A, Taylor BE, Dang ST, Acton ST, Saucerman JJ. Automated image analysis identifies signaling pathways regulating distinct signatures of cardiac myocyte hypertrophy. J Mol Cell Cardiol. 2012 May;52(5):923-30. PMCID: 3299901.

b. Ryall, K. A., V. J. Bezzerides, A. Rosenzwieg, Saucerman JJ. Phenotypic screen quantifying differential regulation of cardiac myocyte hypertrophy identifies CITED4 regulation of myocyte elongation. J Mol Cell Cardiol, 2014 Jul;72:74-84. PMCID: 4078663.

c. Sutcliffe MD, Tan PM, Fernandez-Perez A, Nam Y-J, Munshi NV, Saucerman JJ. High content analysis identifies unique morphological features of reprogrammed cardiomyocytes. Scientific Reports 2018 8:1258 doi:10.1038/s41598-018-19539-z. PMCID: PMC5775342.

d. Woo LA, Tkachenko S, Ding M, Plowright AT, Engkvist O, Andersson H, Drowley L, Barrett I, Firth M, Akerblad P, Wolf MJ, Bekiranov S, Brautigan DL, Wang QD, Saucerman JJ. High-content phenotypic assay for proliferation of human iPSC-derived cardiomyocytes identifies L-type calcium channels as targets. High-content phenotypic screen for compounds that induce proliferation of human iPSC-derived cardiomyocytes. J Mol Cell Cardiol. 2019 Feb;127:204-214. PMCID: PMC6524138.

4. *Modeling β-adrenergic signaling in heart.* As a graduate student, I developed the first computational model of a cardiac signaling pathway, focusing on β-adrenergic signaling and its regulation of cardiac excitation-contraction coupling. To our knowledge, these studies were the first mechanistic simulations of candidate therapies in a signaling pathway, integration of signaling with cell physiology, and effects of a gene mutation on the ECG (which was validated in a subsequent clinical case study). These models have been used by numerous academic labs and several companies. More recent work in my lab has extended these models with recently identified components of β-adrenergic signaling (e.g. phospholemman, CaMKII), a wide range of β-blockers (explaining how β-blockers can both suppress and enhance β-adrenergic responsiveness), receptor polymorphisms, and performing our own experimental validations in adult cardiomyocytes.

a. Saucerman JJ, Brunton LL, Michailova AP, McCulloch AD. Modeling beta-adrenergic control of cardiac myocyte contractility in silico. J Biol Chem. 2003;278(48):47997-8003.

b. Soltis AR, Saucerman JJ. Synergy between CaMKII substrates and beta-adrenergic signaling in regulation of cardiac myocyte Ca(2+) handling. Biophys J. 2010;99(7):2038-47. PMCID: 3042590.

c. Yang JH, Saucerman JJ. Phospholemman in a negative feed-forward regulator of Ca2+ in β-adrenergic inotropy. J Mol Cell Cardiol. 2012 May;52(5):1048-55. PMCID: PMC3327824.

d. Amanfu RK, Saucerman JJ. Modeling the Effects of β1-Adrenergic Receptor Blockers and Polymorphisms on Cardiac Myocyte Ca2+ Handling. Mol Pharmacol. 2014 Aug;86(2):222-30. PMCID: 4127930.

5. *Compartmentation of cellular signaling*. We have integrated computational models and live-cell imaging to identify new mechanisms for subcellular compartmentation of cell signaling, which is fundamental to the specificity of many signaling pathways. We were the first to integrate computational modeling of cell signaling with FRET biosensors, demonstrating that cAMP gradients lead to gradients in PKA-mediated phosphorylation. We found that these gradients were caused not only by cAMP degradation but also by physical barriers and cAMP buffering. We predicted and validated a nuclear PKA signaling complex, along with discovering a role for

nuclear PKA in cardiac myocyte hypertrophy. We developed the first computational models of signaling on A-kinase anchoring proteins (AKAPs) and developed the scaffold state-switching model which mechanistically explains how scaffold proteins can amplify, accelerate and insulate cell signaling.

a. Saucerman JJ, Zhang J, Martin JC, Peng LX, Stenbit AE, Tsien RY, McCulloch AD. Systems analysis of PKA-mediated phosphorylation gradients in live cardiac myocytes. Proc Natl Acad Sci U S A. 2006;103(34):12923-8. PMCID: 1568947.

b. 1Sample V, 1DiPilato LM, 1Yang JH, Ni Q, *Saucerman JJ, *Zhang J. Regulation of nuclear PKA revealed by spatiotemporal manipulation of cAMP. Nat Chem Biol. 2012;8(4):375-82. PMCID: 3307945.

c. [1]Greenwald EC, [1]Redden JM, *Dodge-Kafka KL, *Saucerman JJ. Scaffold state-switching amplifies, accelerates and insulates PKC Signaling. J Biol Chem. 2014 Jan 24;289(4):2353-60. PMCID: 3900978.

d. Yang JH, Polanowska-Grabowska RK, Smith JS, Shields CW, *Saucerman JJ. PKA catalytic subunit compartmentation regulates contractile and hypertrophic responses to β-adrenergic stimulation. J Mol Cell Cardiol, 2014 Jan;66:83-93. PMCID: 3927644.

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/jeffrey.saucerman.1/bibliography/40918420/public/