BIOGRAPHICAL SKETCH

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NAME:	Robert S. MacLeod
eRA COMMONS USER NAME:	rsmacleod
POSITION TITLE:	Professor of Bioengineering

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and 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
Dalhousie University, Halifax, N.S., Canada	BSc	1979	Engineering Physics
Technische Universität Graz, Graz, Austria	MSc	1985	Electrical Engineering
Dalhousie University, Halifax, N.S., Canada	Ph.D.	1990	Physiology & Biophysics
CVRTI, University of Utah, Salt Lake City, Utah	Postdoctoral	1992	Electrophysiology

A. Personal Statement

I have over 30 years of experience in basic and translational cardiac electrophysiology, biomedical simulation, image based modeling, and visualization. My approaches include human and animal experimental studies using a wide range of technologies, especially multichannel measurement of electrical signals, image analysis, image based modeling, and numerical techniques for large scale computations. For 13 years I have been the co-director of an NIH funded Center for Integrated Biomedical Computing (CIBC), in which we develop open source software for use by a range of biomedical scientists and engineers. One focus of my recent research is on all aspects of atrial fibrillation detection, evaluation, and treatment and our software has had a major impact in the clinical management of this disease. My current research funding is over $600,000 per year and I mentor 5 PhD students, a post doctoral fellow, 10 undergraduates, and several software developers. I have extensive past experience mentoring over 20 graduate students, post doctoral fellows, and junior faculty and am the Vice-chair and Director of Undergraduate Studies in Bioengineering. This proposal for Ravi Ranjan builds directly on all this research and mentorship experience and is the ideal next step after Ravi's successful K award and his outstanding progress in the last three years. I am enthusiastic about this opportunity, especially with the chance to continue to collaborate closely with Ravi. He is an outstanding young researcher with unparalleled pedigree and an already outstanding track record, one that is advancing very nicely since his arrival in Utah.

The specific approaches in this proposal match very well my own expertise and the well established capabilities at the University of Utah. There exists deep expertise and long experience in both MRI imaging (at the Utah Center for Advanced Imaging Research, UCAIR) and image analysis (at the Scientific Computing and Imaging, SCI, Institute) and in the development and use of high density electrocardiographic mapping techniques (at the Cardiovascular Research and Training Institute, CVRTI). As Co-Director of the NIH/NIGMS funded Center for Integrative Biomedical Computing (CIBC), I have also guided the development of software that will be extremely useful for the proposal research, especially the image and signal analysis components. My role as Associate Director of both SCI and CVRTI along with the close collaborations with Dr. Ranjan create the uniquely ideal environment for the proposed research into mechanisms of persistent AF and improvements in ablation based management of this debilitating and costly condition.

B. Positions and Honors

Positions and Employment

1980–86	Research Assistant Professor and Computer System Manager, Institut für Medizinische Physik und Biophysik, Universität Graz, Graz, Austria
1986–90	Graduate Research Assistant, Department of Physiology & Biophysics, Dalhousie University, Halifax, N.S., Canada, Postdoctoral Research Associate, Nora Eccles Harrison Cardiovascular Research and Training Institute, University of Utah School of Medicine, Salt Lake City, Utah, 1990-1992
1992–1998	Research Assistant Professor, Nora Eccles Harrison Cardiovascular Research and Training Institute, University of Utah School of Medicine, Salt Lake City, Utah
1993–1997	Research Assistant Professor, Department of Bioengineering, University of Utah, Salt Lake City, Utah
1998–2003	Assistant Professor, Department of Bioengineering, University of Utah, Salt Lake City, Utah
2003–2012	Tenured Associate Professor, Department of Bioengineering, University of Utah, Salt Lake City, Utah
1999–2003	Acting Co-Director, Cardiovascular Research and Training Institute, University of Utah
2003–present	Associate Director, Cardiovascular Research and Training Institute, University of Utah
2002–present	Associate Director, Scientific Computing and Imaging (SCI) Institute, University of Utah
2006–present	Associate Chair and Head of Undergraduate Studies, Dept. of Bioengineering, U of Utah
2009–present	Co-founder and Associate Director Comprehensive Arrhythmia Research and Management (CARMA) Center
2012–present	Full Professor, Department of Bioengineering, University of Utah, Salt Lake City, Utah

Other Experience and Professional Memberships

1990–	Member, IEEE Engineering in Medicine and Biology Society (EMBS)
1999–	Member Biomedical Engineering Society (BMES)
2008–	Member, Heart Rhythm Society (HRS)
1999–	International Society of Electrocardiology (ISE)
2002–	ISE International Council member
1979–	Computing in Cardiology (CinC) Society
2014–	CinC Council member
1995–	International Society of Computerized Electrocardiology
1995–	Ad hoc NIH study section member
2005–	Editorial Board, Journal of Electrocardiology

Honors

1975–79	Dalhousie University Academic Scholarships
1979	Dalhousie University Medal in Engineering Physics
1980–85	Austrian Student Union Scholarships
1986–90	Izaak Walton Killam Memorial Scholarship
1987–90	Medical Research Council of Canada Studentship
1990–92	Heart and Stroke Foundation of Canada Postdoctoral Fellowship

C. Contribution to Science)

Electrocardiographic Inverse Problems: I have spent my entire career exploring novel approaches to inverse problems in electrocardiography, *i.e.,* the estimation of cardiac electrical activity from body-surface ECG. I have pursued a wide variety of approaches and used both computational and experimental methods to develop and validate a range of approaches, and most recently have applied uncertainty quantification approaches to evaluate the role of parameter variation on the accuracy of the resulting solutions to the forward and inverse problems.

1. M. Milanic and V. Jazbinsek and R.S. MacLeod and D.H. Brooks and R. Hren. Assessment of regularization techniques for electrocardiographic imaging in *J Electrocardiol* 47(1):20–28, 2014. PMCID: PMC4154607.
2. D. Wang, R.M. Kirby, R.S. MacLeod, and C.R. Johnson. Inverse electrocardiographic source localization of ischemia: An optimization framework and finite element solution. *J. Comp. Phys.* 250:403–424, 2013. PMCID: PMC3727301
3. D.J. Swenson, S.E. Geneser, J.G. Stinstra, R.M. Kirby, and R.S. MacLeod. Cardiac Position Sensitivity Study in the Electrocardiographic Forward Problem Using Stochastic Collocation and BEM. *Ann. Biomed. Eng.*, 39(12):2900–2910, 2011. PMCID: PMC3362042.
4. Y. Serinagaoglu, D.H. Brooks, and R.S. MacLeod. Improved performance of Bayesian solutions for inverse electrocardiography using multiple information sources. *IEEE Trans. Biomed. Eng.* 53(2):2024–2034, 2006.

Image based biomedical modeling: This research direction stemmed from the recognition of the absence of tools for conducting patient specific, imaged based modeling and simulation of physiology. To extend and make openly available the tools we have developed for the purpose, we have received NIH support since 1999 and now release a complete pipeline of software for image based modeling and simulation. We conduct courses each year (some under separate NIH funding) and have identified over 300 publications from researchers who use our software and techniques for their research.

1. J. Blauer, D.J. Swenson, K. Higuchi, G. Plank, R. Ranjan, N. Marrouche, and R.S. MacLeod. Sensitivity and Specificity of Substrate Mapping: an in silico Framework for the Evaluation of Electroanatomical Substrate Mapping Strategies in *J. Cardiovasc. Electrophys.* 25(7): 774–780, 2014. PMCID: PMC4107007.
2. B.M. Isaacson, J.G. Stinstra, R.D. Bloebaum, COL P.F. Pasquina, and R.S. MacLeod. Establishing Multiscale Models for Simulating Whole Limb Estimates of Electric Fields for Osseointegrated Implants. *IEEE Trans. Biomed. Eng.* Oct;58(10):2991–4, 2011. PMCID: PMC3179554.
3. R.S. MacLeod, J.G. Stinstra, S. Lew, R.T. Whitaker, D.J. Swenson, M.J. Cole, J. Kruger, D.H. Brooks, and C.R. Johnson. "Subject-specific, multiscale simulation of electrophysiology: a software pipeline for image-based models and application examples. *Phil. Trans. Royal Soc.* 367(1896):2293–2310, 2009. PMCID: PMC2696107.
4. S.E. Geneser, R.M. Kirby, and R.S. MacLeod. Application of Stochastic Finite Element Methods to Study the Sensitivity of ECG Forward Modeling to Organ Conductivity, In *IEEE Transactions on Biomedical Engineering*, 55(1):31–40, 2008.

Simulation of cardiac arrhythmias and defibrillation: We have conducted, in collaboration with physicians and other simulation researchers, studies based on simulation of both cardiac arrhythmias and the therapeutic management of their extreme forms through defibrillation. Our arrhythmia simulations focus on identifying the role of abnormal tissue substrate in supporting tachycardia and fibrillation. The goals of our defibrillation studies have focused on optimizing electrode and device placement in order to minimize energy needs while achieving successful defibrillation.

1. K.S. McDowell, S.S. Zahid, F. Vadakkumpadan, J. Blauer, R.S. MacLeod, and N.A. Trayanova. Virtual Electrophysiological Study of Atrial Fibrillation in Fibrotic Remodeling, *PLoS ONE*,10(2), 2015. PMCID: PMC4333565.
2. K.S. McDowell, F. Vadakkumpadan, R. Blake, J. Blauer, G. Plank, R.S. Macleod, and N.A. Trayanova. Mechanistic inquiry into the role of tissue remodeling in fibrotic lesions in human atrial fibrillation. *Biophys. J.* 104(12):2764–2773, 2013. PMCID: PMC3686346.
3. M. Jolley, J. Stinstra, J. Tate, S. Pieper, R. Macleod, L. Chu, P. Wang, and J.K. Triedman. Finite element modeling of subcutaneous implantable defibrillator electrodes in an adult torso. *Heart Rhythm.* 7(5):692–698, 2010. PMCID: PMC3103844.
4. B. Taccardi, B.B. Punske, E. Macchi, R.S. MacLeod, P.R. Ershler. Epicardial and Intramural Excitation During Ventricular Pacing: Effect of Myocardial Structure. *Am J Physiol Heart Circ Physiol* April 294(4), H1753–1766, 2008.

Electrocardiology of acute ischemia: Myocardial ischemia remains a leading cause of mortality and morbidity and has been a physiological focus of my research career. We have applied inverse electrocardiography (ECG Imaging) to identify and localize ischemia in humans; we have carried out animal research studies to characterize the electrical changes induced by ischemia at the tissue and whole heart scale; we have proposed novel concepts of the location of acute ischemia and its evolution over time that contradict long held beliefs.

1. K. Aras, B. Burton, D. Swenson, and R. MacLeod, Sensitivity of epicardial electrical markers to acute ischemia detection. *J. Electrocardiol.* 47(6): 836-41, 2014. PMCID: PMC4252649.
2. S, Shome, R.L. Lux, B.B. Punske, and R.S. MacLeod. Ischemic preconditioning protects against arrhythmogenesis through maintenance of both active as well as passive electrical properties in ischemic canine hearts. *J Electrocardiol.* 40(6):S150-9, 2007.
3. Shibaji Shome and Rob MacLeod. Characterization of the transmural myocardial electrocardiographic response in in vivo canine working hearts under reduced flow and increased heart rate *J Electrocardiol.* 40(4):S5-6, 2007.
4. J.G. Stinstra, S. Shome, B. Hopenfeld, R.S. MacLeod. Modeling the passive cardiac conductivity during ischemia. *Med. Biol. Eng. Comput.* 43(6): 776-782, 2005.

Image analysis for cardiac arrhythmias: MRI imaging approaches have made enormous progress in evaluating the substrate changes that arise in patients suffering from cardiac arrhythmias. We have developed novel approaches to analyze cardiac MRI in patients with atrial fibrillation, including the ability to predict treatment outcome and thus guide clinical management of this very common arrhythmia. Ongoing studies are expanding these capabilities to evaluate the effectiveness of ablation strategies and determine the mechanistic relationships between tissue pathology and the nature of the resulting arrhythmias.

1. B.R. Parmar, T.R. Jarrett, N.S. Burgon, E.G. Kholmovski, N.W. Akoum, N. Hu, R.S. MacLeod, N.F. Marrouche, and R. Ranjan. Comparison of Left Atrial Area Marked Ablated in Electroanatomical Maps with Scar in MRI *J Cardiovasc. Electrophys.* 25(5):457–463, 2014. PMCID: PMC4090328.
2. C. McGann, N. Akoum, A. Patel, E. Kholmovski, P. Revelo, K. Damal, B. Wilson, J. Cates, A. Harrison, R. Ranjan, N.S. Burgon, T. Greene, D. Kim, E.V.R. DiBella, D. Parker, R.S. MacLeod, and N.F. Marrouche. Atrial Fibrillation Ablation Outcome Is Predicted by Left Atrial Remodeling on MRI. *Circ A & E*, Feb 1;7(1):23-30, 2014. PMCID: PMC4086672.
3. R. Karim, Y. Gao, A. Tannenbaum, D. Rueckert, J. Cates, T. Schaeffter, D. Peters, R.S. MacLeod, and K. Rhode. Evaluation of current algorithms for segmentation of scar tissue from late Gadolinium enhancement cardiovascular magnetic resonance of the left atrium: an open-access grand challenge. *J Cardiovasc Magn Reson* 15:105, 2013. PMCID: PMC3878126.
4. N. Akoum; C. McGann; G. Vergara; T. Badger; R. Ranjan; C. Mahnkopf; E. Kholmovski, R.S. MacLeod and N.F. Marrouche. Atrial Fibrosis Quantified Using Late Gadolinium Enhancement MRI is Associated with Sinus Node Dysfunction Requiring Pacemaker Implant. *J. Cardiovasc. Electrophys.* 23(1):44-50, 2012.

List of Published Work: To see a full list of my publications, please visit the SCI Institute publications cite (and carry out a search for "MacLeod") at `http://www.sci.utah.edu/scipubs.html`.

D. Research Support

Ongoing Research Support

2 P41 RR12553 (Johnson) Date: 9/1/15–8/30/2020
NIH/NCRR Center for Integrated Biomedical Computation
Role: Co-PI
This Center is national research resource (P-41) that has existed since 1999. The goals of the current edition are to address biomedical research problems in bioelectric fields, imaged-based anatomy, multi-scale tissue modeling and simulation, and scientific visualization. We will accomplish these goals by creating state-of-the- art computational techniques and innovative, well-engineered software, which, in combination with and freely distributed to the science community, will significantly advance biomedical computing research.

British Heart Foundation PG/15/8/31130 (Aslanidi) Date: 5/1/2015–4/30/2018
Dissecting multifactorial mechanisms of atrial fibrillation: Predictive modelling framework for evaluating medical treatments
Role: Co-Investigator
This project will investigate AF genesis and treatments using in silico 3D canine atria models validated by canine experimental models of AF. The 3D atria models will integrate major structural and functional factors associated with AF fibrosis, innervation and electrical remodelling. They will be applied to dissect (i) multifactorial mechanisms of electrical activations sustaining AF, (ii) typical locations of electrical drivers during AF progression, and (iii) optimal drug and ablation treatments that can terminate various AF scenarios. Model predictions will be applied for evaluating key factors underlying successful treatments in two retrospective cohorts of AF patients. Hence, the genesis of predictive models in silico will assist in evaluating medical strategies.

No ID Number (MacLeod) Date: 7/1/13–6/30/17
Nora Eccles Treadwell Foundation
Role: PI
Title: Electrocardiographic Characterization of Myocardial Ischemia
The overarching goal of this research is to recognize and diagnose all forms of myocardial ischemia using the ECG. The overarching hypothesis of this project is that current electrocardiographic descriptions of myocardial ischemia are incomplete and that, as a result, the clinical interpretation of the electrocardiogram fails to achieve its potential as a diagnostic and monitoring approach. We seek, therefore, through measurements, experiments, and simulations to achieve the most complete understanding possible of the full spectrum of ischemia in terms of its bioelectric source, its electrical interaction with surrounding tissues, and its reflection on the body surface.

R25GM107009-01 (MacLeod, Weiss, Whitaker) Date: 7/1/2013–6/30/2016
Image Based Modeling, Simulation, and Visualization Summer Course for Biomedical Researchers
Role: Co-PI
The goal of this proposed program is to expand the scope of current Center for Integrative Biomedical Computing (CIBC) and Muskuloskeletal Research Lab (MRL) training to create a dedicated two-week course in the area of image based modeling and simulation applied to bioelectricity and biomechanics.

R25GM107009-01 (Aylward, Cates) Date: 7/1/2013–6/30/2016
WEB-Based Infrastructure for Comparison and Validation of Image Computing Methods
Role: Co-Investigator
The goal of this project is to develop the infrastructure for and deploy a commercial installation of an Algorithm Evaluation Service (AES) to help bridge the gap between algorithm researchers and commercial product developers. We will support a novel mechanism for algorithm submission based on virtual machine technology that addresses clinical integration, security, and computational resource scalability to support extensive testing. We will make the submission of algorithms to challenges an inherent and effortless part of algorithm development for researchers. We will validate the resulting system using additional grand challenges, and we will deliver it to and receive feedback from our first commercial customer as part of the proposed work.

Siemens Medical Solutions (MacLeod) Date: 09/12/2012–12/31/2015
Overlay and registration of MRI-derived scar maps to real-time fluoroscopy for repeat atrial fibrillation (AF) ablation
Role: PI
This is an industry funded project to develop a means to merge previously acquire MRI images and content derived from those images with real time fluoroscopy displays in the catheterization laboratory for atrial ablation treatments. The goal of the project will be to develop a combination of custom and available software tools that will perform all the necessary steps of registering (aligning) the scar map with fluoroscopic images captured from fluoroscopy performed as part of a repeat ablation procedure.

Recently Completed Research Support

2 P41 RR12553 (Johnson) Date: 9/1/2010–8/30/2015
NIH/NCRR Center for Integrated Biomedical Computation
Role: Co-Investigator and Center Co-director
This Center is national research resource (P-41) that has existed since 1999. The goals of the current edition are to address biomedical research problems in bioelectric fields, imaged-based anatomy, multi-scale tissue modeling and simulation, and scientific visualization. We will accomplish these goals by creating state-of-the- art computational techniques and innovative, well-engineered software, which, in combination with and freely distributed to the science community, will significantly advance biomedical computing research.

U54E B005149-06 (Kikinis) Date: 10/1/10–9/30/14
NIH/Roadmap Initiative National Alliance for Medical Image Computing: DBP Atrial Fibrillation
Role: Co-Investigator and DBP PI
NA-MIC is a multi-institutional, interdisciplinary team of computer scientists, software engineers, and medical investigators who develop computational tools for the analysis and visualization of medical image data. The purpose of the Center is to provide the infrastructure and environment for the development of computational algorithms and open-source technologies, and then oversee the training and dissemination of these tools to the medical research community.