Application

01962 - The GEM Challenge 2015

02123 - High resolution, low power retinal prosthetic

Collaborative awards with IEM

Status:	Submitted
Submitted Date:	12/05/2014 2:01 PM

Primary Contact

First Name*	William First Name	R Middle Name	Freeman Last Name
Degree	MD		
Faculty Rank*	Full Professor Faculty Rank - Other		
Email:	cbarkley@ucsd.edu		
eRA Commons Name			
Area of Specialty	retina		

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Information

PI Name (Last Name, First Name)	*Freeman, William*
CO-PI Name (Last name, First name)	*Cauwenberghs, Gert ; Silva, Gabe*
Project Title	*High resolution, low power retinal prosthetic*
PI Contact information - include email and campus phone number	*wrfreeman@ucsd.edu* *858-534-3513*

PI Biosketch

File Name	Description	File Size
Biosketch- Silva.pdf	*Silva*	
Biosketch_GC.pdf	*Cauwenberghs*	
Biosketch_WF.pdf	*Freeman*	

Narrative

File Name	Description	File Size
GEM Challenge Final.pdf	*High resolution, low power retinal prosthetic*	

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
William R. Freeman, M.D.	**Distinguished Professor of Ophthalmology**
eRA COMMONS USER NAME **optwrf**	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(IF APPLICABLE)*	YEAR(S)	FIELD OF STUDY
Columbia University, New York, N.Y.	B.A.	1975	Cell Biology
Mount Sinai School of Medicine, N.Y.	M.D.	1979	Medicine
Cedars-Sinai/UCLA, Los Angeles, CA	Internship	1980	Internship/Medicine
Lenox Hill Hospital, N.Y., N.Y.	Residency	1983	Ophthalmology
Proctor Foundation, UCSF, San Francisco, CA	Fellowship 1yr	1984	Uveitis/Immunology
Univ. of Southern Calif., Doheny Eye Fd., LA, CA	Fellowship 2yrs	1986	Vitreoretinal Surgery

A. PERSONAL STATEMENT:

Dr. Freeman has had a longstanding interest in retinal disease and has been funded by the NIH for over 20 years in the area of retinal pathological structural analysis and animal models of retinal disease. He is Co-Director of the Retinal Engineering Center at UCSD where for the past four years he has been collaborating with engineering faculty on development of retinal prosthesis. He has published over 500 peer-reviewed papers and has held between one and two R01 grants at a given time. He works closely with Dr. Khraiche, and other members of engineering and Ophthalmology faculties on analysis of retinal structures and experimental approaches to retinal diseases. He has been an investigator on several multicentered randomized pharmaceutical trials of drugs for retinal disease. Dr. Freeman has worked in animal models of retinal diseases and is intimately familiar with surgical approaches to implantation of ocular devices. Dr. Freeman is committed to conducting and overseeing this research, designing experiments and participant in analysis of data.

B. POSITIONS AND HONORS:

1986-1990	Assistant Professor, Univ. of California, San Diego, Dept. of Ophthalmology
1990-1994	Associate Professor, Univ. of California, San Diego, Dept. of Ophthalmology
1994-Present	Professor, Univ. of California, San Diego, Dept. of Ophthalmology
2003-Present	Director, Jacobs Retina Center, Univ. of California, San Diego, Dept. of Ophthalmology
2012-Present	Distinguished Professor and Vice Chairman, Univ. of California, San Diego, Dept. of Ophthalmology

ACADEMIC HONORS AND AWARDS:

Alpha Omega Alpha Honor Medical Society, Mount Sinai School of Medicine,1979; Award for Clinical and Research Excellence, UCSD Medical Center, 1988; Who's Who Among Younger Americans Listing,1990; American Academy of Ophthalmology Honor Award Recipient, 1991; Steering Committee NEI sponsored SOCA trial, 1991; Editorial Board Member: Retina, Ophthalmology; ARVO Retina Program Committee Co-chair, 2005; Foundation Fighting Blindness Honor Award, 2008; ARVO Fellow, 2009, Distinguished Professor of Ophthalmology 2012.

PROFESSIONAL SOCIETIES:

American Academy of Ophthalmology; American Medical Association; American Uveitis Society; Aspen Retinal Detachment Society; Association for Research in Vision and Ophthalmology; Association of Proctor Fellows, Association of University Professors of Ophthalmology; American Society of Retina Specialists; Association for Research in Vision and Ophthalmology; Retina Society; Macula Society.

C. SELECTED PEER-REVIEWED PUBLICATIONS (in chronological order):

(Publications selected from over 500 peer-reviewed publications):

1. Kuppermann BD, Quiceno JI, Flores-Aguilar M, Connor JD, Capparelli EV, Sherwood CH, **Freeman WR**: Intravitreal ganciclovir concentration after intravenous administration in AIDS patients with cytomegalovirus retinitis: Implications for therapy. Journal of Infectious Diseases. 1993;168:1506-9.
2. Flores-Aguilar M, Huang JS, Wiley CA, De Clercq E, Vuong C, Bergeron-Lynn G, Chandler B, Munguia D, **Freeman WR**: Long acting therapy of viral retinitis with (s)-1- (3-hydroxy-2-phosphonylmethoxypropyl) cytosine (HPMPC). Journal of Infectious Diseases. 1994; 169:642-7.
3. Besen G, Flores-Aguilar M, Assil KK, Kupperman BD, Gangan P, Pursley M, Munguia D, Vuong C, De Clercq E, Bergeron-Lynn G, Azen SP, **Freeman WR**: Long term therapy of herpes retinitis in an animal model with high concentrated liposome encapsulated (s)-1-(3-hydroxy-2-phosphonyl methoxypropyl) cytosine (HPMPC). Archives of Ophthalmology. 1995; 113:661-8.
4. Kirsch LS, Arévalo JF, De Clercq E, Chavez de la Paz E, Munguia D, Garcia R, **Freeman WR**: A phase I/II study of intravitreal cidofovir (HPMPC) for the treatment of cytomegalovirus retinitis in patients with the acquired immune deficiency syndrome. American Journal of Ophthalmology. 1995; 119(4):466-76.
5. Banker AS, De Clercq E, Taskintuna I, Keefe KS, Bergeron-Lynn G, **Freeman WR**: Influence of Intravitreal Injections of HPMPC and Related Nucleoside Analogues on Intraocular Pressure in Guinea Pig Eyes. Investigative Ophthalmology & Visual Science. 1998; 39(7): 1233-1242.
6. Cheng L, Hostetler KY, Gardner MF, Avila Jr. CP, Bergeron-Lynn G, Severson GM, **Freeman WR**: Intravitreal pharmacokinetics in rabbits of the foscarnet lipid prodrug: 1-0-octadecyl-sn-glycerol-3-phosphonoformate (ODG-PFA). Current Eye Research. 1999; 18 (3):161-167.
7. Koh HJ, Bessho K, Cheng L, Bartsch DU, Jones TR, Bergeron-Lynn G, **Freeman WR**: Inhibition of Choroidal Neovascularization in Rats by the Urokinase-derived Peptide A6. Invest Ophthalmol Vis Sci. 2004;45(2):635-40.
8. Koh HJ, **Freeman WR**, Azen SP, Flaxel CJ, LaBree LD, Wills M, Jones TR: Effect of a Novel Octapeptide Urokinase Fragment, Å6, on Experimental Choroidal Neovascularization in the Monkey. Retina 26: 202-209, 2006.
9. Kozak, I, Silva G, Freeman WR: Testing of intraocular drugs for Clinical Use. Investigative Ophthalmology and Visual Science 2007: 48: 4861-63.
10. Cheng L, Anglin E, Cunin F, Kim D, Sailor MJ, Falkenstein I, Tammewar A, Freeman WR: Intravitreal properties of porous silicon photonic crystals: a potential self-reporting intraocular drug-delivery vehicle. British Journal of Ophthalmology. 2008;92(5):705-11.

11. Cheng LC, Lingyun Cheng1, Karl Hostetler2, Nadya Valiaeva2, Ajay Tammewar1, Iryna Falkenstein1, James Beadle2, Kathy Aldern2, **Freeman WR**: Intravitreal crystalline drug delivery for intraocular proliferation diseases." Investigative Ophthalmology 2010; 51; 474-81.
12. Andrew JS, Anglin EJ, Wu EC, Cheng LC, **Freeman WR**, Sailor M,: Sustained Release of a Monoclonal Antibody from Electrochemically Prepared Mesoporous Silicon Oxide. Adv Funct mater 2010 20: 4168-4174.
13. Hou J, Li Y, Zhou Z, Valiaeva N, Hostetler K, **Freeman WR**, Cheng LC,: Antiproliferative property of Hexadecyloxypropyl 9-[2-(phosphonomethoxy) ethyl] guanine (HDP-PMEG) for unwanted ocular proliferation. Molecular Vision 2011: 17:627-37.
14. Wu EC, Andrew JS, Cheng L, **Freeman WR**, PearsonL, Sailor MJ: Real-time monitoring of sustained drug release using the optical properties of porous silicon photonic crystal particles. Biomaterials 2011:32, 1957-60.
15. Kraiche ML, Lo Y, Wang D, Cauwenberghs G, **Freeman WR** and Silva GA: Ultra-High Photosensitivity Silicon Nanophotonics for Retinal Prosthesis: Electrical Characteristics. Conf Proc IEEE Eng Med Biol Soc. 2011;2011:2933-6.
16. Kraiche ML, ElEmam S, Akinin A, Cauwenberghs G, **Freeman WR** and Silva GA. Visual Evoked Potential Characterization of Rabbit Animal Model For Retina Prosthesis Research.Conf Proc IEEE eng Med Biol Soc. 2013;2013:3539-42.
17. Kozak I, Sasik R, **Freeman WR**, Sprague L, Gomez ML, Cheng L, ElEmam S, Mojana F, Bartsch DU, Bosten, J, Ayyagari R, Hardiman G: A novel degenerative retinal process in HIV associated Non-infectious Retinopathy. PLOSone 2013: 8: 1-12.

D. RESEARCH SUPPORT:

Ongoing Research Support

5 R01 EY07366-26 (Freeman) 04/01/2010 -- 03/31/2014
NIH/NEI
Studies of Retinopathy of AIDS in the HAART Era
Major Goals: Application of the latest molecular biological, immunological, and clinical study to better understand the changing retinal manifestations of HIV infection. To develop a new drug delivery system to treat resistant CMV retinitis that is the most common cause of infectious retinitis and vision loss in HIV patients.
Role: PI

5 R01 EY020617-02 (Cheng) 09/01/2011 – 08/31/2016
NIH/NEI
Porous Silicon Particles for Sustained Intravitreal Drug Delivery
Major Goals: To develop and evaluate a porous silicon based eye drug delivery system which is minimally invasive, slow releasing and long-lasting. The system could eliminate the need for frequent intravitreal injections or invasive intraocular implant surgeries for many of the refractory eye diseases such as macular degeneration, diabetic or trauma induced retinal scarring, and chronic uveitis.
Role: Investigator

5U10 EY014660-07 (Holbrook) 06/01/2012 – 04/30/2017
NIH/NEI/Johns Hopkins University Subcontract
Multicenter Uveitis Steroid Treatment Trial
Major Goals: Randomized clinical trial comparing intra-ocular fluocinolone acetonide implants to standard systemic therapy for the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis.
Role: Consortium PI

5 R01 EY016323-07 (Bartsch) 09/30/2011 – 08/31/2014
NIH/NEI
Mechanistic-Based Non-Invasive Assessment of Retinal Damage in HAART Era
Major Goals: Major Goals: To create a method of automatically mapping the presence of retinal damage associated with HIV infection. A high-resolution eye camera will be used to systematically image the back of the eye. The study will compare structural information to functional information to find a possible correlation.
Role: Investigator

1P30 EY022589-01 (Freeman) 07/01/2012 – 06/30/2017
NIH/NEI
Tissue Processing and Confocal Microscopy
Major Goal: This is one of four modules within the P30 grant aimed at improving the efficiency and productivity of vision scientists at UCSD by facilitating multidisciplinary collaboration among investigators, and providing core services to vision researchers that are unavailable to individual investigators. This module provides rapid characterization of eye tissues with respect to histology, immunohistochemistry, light microscopy and confocal microscopy by supporting a technician who is familiar with ocular anatomy and techniques required to properly process ocular tissues.
Role: Module Director

Completed Research Support

5 R01 EY018589-04 (Freeman) 09/30/2008 – 07/31/2013 (NCE)
NIH/NEI
Crystalline Antiproliferative Drugs for Intraocular Diseases
Major goals: To develop a long-acting intraocular injection that will prevent retina detachment and reduce damage due to scarring from age-related macular degeneration via small antiproliferative molecules.
Role: PI

NNSP-CTEC-0309-0038-UCSD-NER (Freeman) 08/01/2009 – 06/30/2012
NNRI/Foundation Fighting Blindness
New Therapeutic Approaches to Retinal Dystrophies
Major Goals: To recruit patients in a clinical trial and build phenotype/genotype database of various retinal diseases to analyze the biological processes leading to pathology; to provide treatment outcomes using visual acuity, peripheral visual field examination and electro-physiology, as well as identifying individuals at risk to develop disease and offer genetic counseling.
Role: PI

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Gert Cauwenberghs	Professor
eRA COMMONS USER NAME gcauwenberghs	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Brussels, Belgium	Eng. Degree	1988	Applied Physics
California Institute of Technology	M.S.	1989	Electrical Engineering
California Institute of Technology	Ph.D.	1994	Electrical Engineering

A. Personal Statement

One of the greatest challenges in neuroengineering, whether towards new therapies for neurological diseases or towards new means of human-computer interaction, is to advance our fundamental understanding of how the brain functions to the point where we may effectively interface the human brain with engineered systems.
My group has pioneered the design and implementation of highly energy efficient, massively parallel microchips that emulate function and structure of adaptive neural circuits in silicon. A main focus of our current work is on extending integrated sensing and actuation to dynamical interfaces to neural and brain activity. Recent developments include implantable and wireless microelectrode arrays for distributed recording of electrical and chemical neural activity, and biopotential sensor arrays and integrated signal processing for electroencephalogram and electrocorticogram functional brain imaging. These dynamical interfaces between living and artificial nervous systems offer tremendous opportunities for transformative, integrative neuroscience and neuroengineering that are the focus of continued research in our laboratory, in collaboration with partners in academia, industry, and the clinical sector.

B. Positions and Honors

Positions and Employment

1/94-6/98 Assistant Professor, Department of Electrical and Computer Engineering, The Johns Hopkins University, Baltimore MD 21218
7/98-6/02 Associate Professor, Department of Electrical and Computer Engineering, The Johns Hopkins University, Baltimore MD 21218
6/98-8/99 Visiting Professor, Center for Biological and Computational Learning, Department of Brain and Cognitive Science, Massachusetts Institute of Technology, Cambridge MA 02142, (sabbatical leave from Johns Hopkins University)
7/02-6/05 Professor, Department of Electrical and Computer Engineering, The Johns Hopkins University, Baltimore MD 21218
7/05-6/09 Professor, Neurobiology Section, Division of Biological Sciences, University of California San Diego, La Jolla CA 92093
7/09-present Professor, Department of Bioengineering, Jacobs School of Engineering, University of California San Diego, La Jolla CA 92093

Other Experience and Professional Memberships

9/08-present Co-Director, Institute for Neural Computation, University of California San Diego, La Jolla CA 92093

Editorial Boards

2011-present Editor-in-Chief, IEEE Transactions on Biomedical Circuits and Systems
2004-present Senior Editor, IEEE Sensors Journal
2011-present Senior Editor, IEEE Journal of Emerging Topics in Circuits and Systems
1999-2003 Associate Editor, IEEE Transactions on Circuits and Systems II: Analog and Digital Signal
2004-2008 ProcessingAssociate Editor, IEEE Transactions on Circuits and Systems I: Regular Papers
2006-present Associate Editor, IEEE Transactions on Neural Systems and Rehabilitation

Honors

1988 Francqui Fellow, Belgian American Educational Foundation
1997 Career Award, National Science Foundation
1999 Young Investigator Award, Office of Naval Research
2000 Presidential Early Career Award for Scientists and Engineers (PECASE)
2003-04 Distinguished Lecturer, IEEE Circuits and Systems Society
2011 Fellow, IEEE

C. Selected Peer-reviewed Publications

1. R.J. Vogelstein, U. Mallik, J.T. Vogelstein and G. Cauwenberghs, "*Dynamically Reconfigurable Silicon Array of Spiking Neurons With Conductance-Based Synapses*," IEEE Trans. Neural Networks, vol. 18 (1), pp. 253-265, 2007.
2. M. Stanacevic, K. Murari, A. Rege, G. Cauwenberghs and N.V. Thakor, "VLSI Potentiostat Array With Oversampling Gain Modulation for Wide-Range Neurotransmitter Sensing," *IEEE Trans. Biomedical Circuits and Systems*, vol. 1 (1), pp. 63-72, 2007.
3. R. Karakiewicz, R. Genov, and G. Cauwenberghs. "480-GMACS/mW Resonant Adiabatic Mixed-Signal Processor Array for Charge-Based Pattern Recognition," *IEEE J. Solid-State Circuits*, vol. 42 (11), pp. 2573-2584, 2007.
4. M. Mollazadeh, K. Murari, G. Cauwenberghs, and N. Thakor. "Micropower CMOS Integrated Low-Noise Amplification, Filtering, and Digitization of Multimodal Neuropotentials," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 3 (1), pp. 1-10, 2009.
5. M. Mollazadeh, K. Murari, G. Cauwenberghs, and N. Thakor. "Wireless Micropower Instrumentation for Multimodal Acquisition of Electrical and Chemical Neural Activity," *IEEE Trans. Biomedical Circuits and Systems*, vol. 3 (6), pp. 388-397, 2010.
6. T. Yu and G. Cauwenberghs. "Analog VLSI Biophysical Neurons and Synapses with Programmable Membrane Channel Kinetics," *IEEE Trans. Biomedical Circuits and Systems*, vol. 4 (3), pp. 139-148, 2010.
7. Y.M Chi, T.P. Jung, and G. Cauwenberghs. "Dry-Contact and Noncontact Biopotential Electrodes: Methodological Review," *IEEE Reviews in Biomedical Engineering*, vol. 3, pp. 106-119, 2010.
8. T. Yu, T.J. Sejnowski, and G. Cauwenberghs. "Biophysical Neural Spiking, Bursting, and Excitability Dynamics in Reconfigurable Analog VLSI," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 5 (5), pp.420-429, 2011.
9. J.D. Driscoll, A.Y. Shih, S. Iyengar, J.J. Field, G.A. White, J.A. Squier, G. Cauwenberghs, and D. Kleinfeld. "Photon Counting, Censor Corrections, and Lifetime Imaging for Improved

Detection in Two-Photon Microscopy," *J. Neurophysiology*, vol. 105 (6), pp. 3106-3113, 2011.
10. G. Indiveri, B. Linares-Barranco, T.J. Hamilton, A. van Schaik, R. Etienne-Cummings, T. Delbruck, S.C. Liu, P. Dudek, P. H¨afliger, S. Renaud, J. Schemmel, G. Cauwenberghs, J. Arthur, K. Hynna, F. Folowosele, S. Saighi, T. Serrano-Gotarredona, J. Wijekoon, Y. Wang, K. Boahen. "Neuromorphic Silicon Neuron Circuits," *Front. Neuroscience*, vol. 5 (73), 2011.
11. Y.M. Chi, Y.-T. Wang, Y. Wang, C. Maier, T.-P. Jung, and G. Cauwenberghs, "Dry and Noncontact EEG Sensors for Mobile Brain-Computer Interfaces," *IEEE Trans. Neural Systems and Rehabilitation Engineering*, vol. 20 (2), pp. 228-235, 2012.
12. Y.M. Chi, P. Ng, and G. Cauwenberghs, "Wireless Noncontact ECG and EEG Biopotential Sensors," *ACM Trans. Embedd. Comput. Syst.*, vol. 12 (4), pp. 103:1-19, 2013.
13. E. Neftci, S. Das, B. Pedroni, K. Kreutz-Delgado, and G. Cauwenberghs, "Event-Driven Contrastive Divergence for Spiking Neuromorphic Systems," *Frontiers in Neuroscience*, doi: 10.3389/fnins.2013.00272, vol. 7, pp. 272:1-14, 2014.
14. S. Ha, C. Kim, Y.M. Chi, A. Akinin, C. Maier, A. Ueno, G. Cauwenberghs, "Integrated Circuits and Electrode Interfaces for Noninvasive Physiological Monitoring," *IEEE Trans. Biomedical Engineering*, vol. 61 (5), pp. 1522-1537, 2014.
15. F.D. Broccard, T. Mullen, Y.M. Chi, D. Peterson, J.R. Iversen, M. Arnold, K. Kreutz-Delgado, T.P. Jung, S. Makeig, H. Poizner, T. Sejnowski, and G. Cauwenberghs, "Closed-Loop Brain-Machine-Body Interfaces for Noninvasive Rehabilitation of Movement Disorders," *Annals of Biomedical Engineering*, vol. 42 (8), pp. 1573-1593, 2014.

D. Research Support

Ongoing Research Support

NSF ENG-1137279 (Cauwenberghs, PI) 9/11-9/15
EFRI-M3C: Distributed Brain Dynamics in Human Motor Control
Towards non-invasive remediation of Parkinson's through EEG-EMG force neurofeedback.

DARPA and SAIC (Cauwenberghs, UCSD PI) 10/11-9/15
Cognitive Radio Low Power Signal Analysis ICs
RF analog circuit design of adaptive beamforming and signal classification systems for cognitive radar.

Completed Research Support

NIH/NIA 1R01AG029681 (Cauwenberghs, PI) 9/06-6/10
CRCNS: Imaging and Modeling of Cortical Microvascular Dynamics
Development and application of high-resolution functional imaging techniques to study the interaction between bloodflow and neural activity in cortex at micrometer and millisecond resolution.

NSF SBE-0847752 (Cauwenberghs, PI) 10/08-9/10
SGER: Wireless EEG Brain Interface for Extended Interactive Learning
Design and implementation of a mobile EEG headset for monitoring and augmenting learning function.

DARPA and Evolved Machines (Cauwenberghs, UCSD PI) 6/10-12/11
Neovision2: Neuromorphic Modular and Evolvable Vision Systems
Large-scale neuromorphic silicon implementation of neocortical vision systems.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Silva, Gabriel A.	Professor of Bioengineering and Ophthalmology Vice Chair, Bioengineering
eRA COMMONS USER NAME (credential, e.g., agency login) gsilva	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Toronto, Ontario, Canada	Hon. B.Sc.	06/96	Human Physiology
University of Toronto, Ontario, Canada	B.Sc.	06/96	Biophysics
University of Toronto, Ontario, Canada	M.Sc.	06/98	Neuroscience
University of Illinois at Chicago, Illinois	Ph.D.	07/01	Bioengineering and Neuroscience
Northwestern University, Chicago, Illinois	Postdoctoral	10/03	Nanotechnology and Neuroscience

A. PERSONAL STATEMENT

We are interested in theoretical and computational neuroscience aimed at understanding how the structure and geometry of neurobiological networks constrain and determine network signaling, dynamics, and information flow in the brain. An emerging application of this work is the development of neuromimetic (i.e. neural imitating) algorithms based on a mathematical understanding of the rules by which the biological brain computes. We are also interested in neural engineering applications at the interface between nanotechnology and neuroscience, in particular nanoelectronic technologies for the stimulation and recording of neural activity and the restoration of neural function. To achieve this we operate at the interface between experiment, theory, and computation, integrating experimental molecular and cellular neurobiology and physiology with engineering, mathematics, and chemistry. Of particular note, our lab has been one of the leading groups on the development and use of nanotechnologies and nanoengineering for neuroscience applications, which is central to this project. We have published extensively on the subject, with a total of 28 primary research papers and invited reviews on the subject, including a textbook published in 2011.

B. POSITIONS AND HONORS

Positions and Employment

2004-2009 Assistant Professor, Departments of Bioengineering and Ophthalmology, UC San Diego
2008- Affiliated Faculty Member, Department of NanoEngineering, UC San Diego
2009- Associate Professor, Departments of Bioengineering and Ophthalmology, UC San Diego
2009- Co-Director, Retinal Engineering Center, Institute of Engineering in Medicine, UC San Diego
2009-2014 Jacobs Faculty Fellows Professor of Bioengineering, UC San Diego
2014-present Full Professor, Departments of Bioengineering and Ophthalmology, UC San Diego
2014-present Vice Chair, Department of Bioengineering, UC San Diego

Also active faculty member in the following at UC San Diego (years in parentheses indicate year joined): Neurosciences Graduate Program (2004); Bioengineering Graduate Program (2004); Materials Science and Engineering Graduate Program (2004); Computational Neurobiology

Graduate Program (2004); Stein Institute for Research on Aging (2004); Institute of Engineering in Medicine (2009), Institute for Neural Computation (2009); Biocircuits Institute (2009)

Selected Other Experience and Professional Memberships (Limited to professional memberships, peer reviewed journal editorial responsibilities, and national and international grant review panels)

Professional memberships

1997-present Member, Society for Neuroscience
1997-2004 Member, International Society for Clinical Electrophysiology of Vision
1998- resent Member, Association for Research in Vision and Ophthalmology
2006-present Member, Biomedical Engineering Society
2007-present Member, IEEE Engineering in Medicine and Biology Society
2007- resent Member, Society for Experimental Biology and Medicine
2008-present Member, American Mathematical Society
2009-present Scientific advisory board and Member, International Conference on Neuroprotective Agents

Grant review panels (national and international)

2004-2012 NIH Peer Review Committee: Neurotechnology, standing member
2004-2005 NSF Peer Review Committee: Nanoscale exploratory research, ad hoc reviewer
2006 NSF Peer Review Committee: Graduate research fellowship program, ad hoc member
2006 Air Force Office of Scientific Research, grant reviewer
2006 Science Foundation Ireland, grant reviewer
2006 NSF Peer Review Committee: Nanotechnology integrated research, ad hoc reviewer
2007 NIH Peer Review Committee: Nanotechnology, ad hoc reviewer
2007 NIH Peer Review Committee: Neurogenetics, ad hoc reviewer
2007 Citizens United for Research in Epilepsy, grant reviewer
2007-2008 US Army Medical Research and Material Command, grant reviewer
2008 Alberta Ingenuity Fund Canada, grant reviewer
2008 Grants Research Council of Hong Kong, grant reviewer
2009 Alzheimer's Association, grant reviewer
2009 National Institute for Nanotechnology, National Research Council of Canada, grant reviewer
2010 US-Israel Binational Science Foundation
2010 Fondazione Cassa di Risparmio di Pisa, Italy
2010 Biomedical Research Council (BMRC), Singapore
2010 Human Frontier Science Program, France
2010 Neurosciences Collaborative, American Association for the Advancement of Science (AAAS)
2012 National Institute for Health and Medical Research, Paris, France
2012 French National Alliance for Life and Health Sciences (AVIESAN), Paris, France
2012 French National Cancer Institute (INCa)
2012 Vision Research Program (VRP), US Army Medical Research and Materiel Command
2013 Wellcome Trust and India Alliance Fellowship

Editorial responsibilities and service

2004-present Associate editor, IEEE Transactions on Nanobioscience
2006-present Editorial board, Experimental Biology and Medicine
2007-present Associate editor, Journal of Biomedical Nanotechnology
2007-present Editorial board, Journal of Nanoneuroscience
2008-present Associate editor, Frontiers in Neuroengineering
2008-present Editorial board, International Journal of Nanotechnology and Molecular Computation
2009-present Editorial board, American Journal of Neuroprotection and Neuroregeneration
2009-present Editorial board, Stem Cell Letters
2009-present Editorial board, Current Nanoscience
2010-present Editorial board, Journal of Bioengineering and Biomedical Sciences

2011-present Editorial board, ISRN Nanotechnology
2011-present Editorial board, World Journal of Neurology
2011-present Editorial board, Journal of Tissue Science and Engineering
2011-present Editorial board, Frontiers in Fractal Physiology
2012-present Editorial board, Dataset Papers in Medicine, Ophthalmology Section
2012-present Editorial board, CNS Drug Target
2014-present Journal of Bioengineering and Biomedical Sciences

Awards and Honors

1998 University of Toronto Open Fellowship
1998 College of Engineering Dean's Fellowship, University of Illinois at Chicago
1999 American Society for Artificial Internal Organs (ASAIO) Biomedical Engineering Fellowship
1999-2001 Natural Sciences and Engineering Research Council (NSERC) Graduate Fellowship
2002 Retina Research Foundation Fellowship
2004-2006 Whitaker Foundation Leadership Award
2004 Stein Institute for Research on Aging (SIRA) Faculty Award
2004 University of California Academic Senate Faculty Award
2004 Ray Thomas Medical Foundation Young Investigator Recognition Award
2005 UC San Diego Faculty Career Development Award
2005 IEEE/EMBS Excellence in Neural Engineering Award
2005 Associated Students of UC San Diego Faculty Award for undergraduate education
2007 Coulter Foundation Young Investigator Award
2007 NSF/Science magazine Visualization Challenge entry semi-finalist
2008 American Society of Mechanical Engineers (ASME) Y.C. Fung Young Investigator Award
2009 National Academy of Engineering (NAE) Frontier's Conference selection
2009 Selection to "Nanoscience: The best of NATURE publications"
2009 Jacobs Faculty Fellows Endowed Chair in Bioengineering
2010 Beverley and Clarence Chandran Distinguished Lecture, Duke University
2012 'Faculty of the Year' award, undergraduate education; Tau Beta Pi Engineering Honors Society
2014 Biocom Cell Art Exhibit winning entry: "SEM of cortical neurons on optoelectronics nanowires"

C. SELECTED PEER-REVIEWED PUBLICATIONS (Selected from over 50 peer-reviewed publications)

1. J Blumling III and GA Silva (*in press*) Sulforhodamine B-loaded polyethyleneimine/silica hybrid nanoparticles. *Journal of Nanoneuroscience.*
2. S-J Kim, J Blumling, MC Davidson, H Saad, S-Y Eun, and GA Silva (2012) Calcium and EDTA induced folding and unfolding of calmodulin on functionalized quantum dot surfaces. *Journal of Nanoneuroscience* 2:75-81.
3. C Evans, M Fitzgerald, T Clemons, M House, B Padman, J Shaw, M Saunders, A Harvey, B Zdyrko, I Luzinov, GA Silva, S Dunlop, KS Iyer (2011) Multimodal analysis of PEI-mediated endocytosis of nanoparticles in neural cells. *ACS Nano* 5:8640-8648.
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D. RESEARCH SUPPORT

Ongoing Research Support

NIH NIBIB R21 EB017898 [Silva: Principal Investigator] 09/30/13-08/31/15
Experimental testing and validation of a quantum dot FRET calcium sensor
The goal of this study is to test in neural cells *in vitro* a novel quantum dot based FRET system for measuring dynamic calcium signaling.

Army Research Office (ARO), DoD [Silva: Principal Investigator] 09/01/13-06/01/14
Information flow and capacity in geometric networks
The goal of this work is to develop theoretical insights and mathematical theorems about how information propagates through geometric networks, with specific applications to signaling in biological neural networks.

National Health and Medical Research Council of Australia [Silva: Co-Investigator] 02/01/12-01/01/17
Targeting early cellular damage during secondary degeneration using nanosphere-based drug delivery
The PI is an Associate Investigator on this grant with our collaborators at the University of Perth in order to develop a nanoparticle drug delivery system.

Selected Completed Research Support (from a total of 13 different grants and awards)

TATRC, US Army [Silva: Co-Principal Investigator] 06/01/11-05/31/12
Ultra-high photosensitivity vertical nanowire arrays for retinal prosthesis
This grant was focused on fabrication and development aspects of the nanoengineered retinal prosthesis.

NIH NINDS R01 NS054736 [Silva: Principal Investigator] 04/01/06-03/31/11
High throughput mapping and the topology of neural networks
The goal of this study is to develop theoretical and computational methods, validated using experimental data, for identifying and mapping the unknown functional connectivity of cellular neural circuits and networks.

Samsung Group, South Korea [Silva: Principal Investigator] 01/01/09-12/31/11
Deciphering how the biological brain computes: Simulating and mapping multi-scale functional signaling
The goal of this study is to simulate and engineer neural mimetic networks that can perform complex computations and be morphometrically implemented on an integrated circuit chip.

High resolution, low power retinal prosthetic
William Freeman, MD (Ophthalmology)
Gabriel Silva, PhD (Bioengineering)
Gert Cauwenberghs, PhD (Bioengineering)

Damage to the photoreceptors of the retina, which occurs in conditions such as retinitis pigmentosa and age-related macular degeneration, results in irreversible loss of vision. Few treatment options are available for patients with advanced cases of these retinal diseases. The rate of photoreceptor degeneration can be slowed in some cases, but the damage cannot be repaired. Vision loss caused by these diseases can progress to a complete absence of light perception, resulting in significant emotional and socioeconomic burdens for these individuals.

Even in cases of severe photoreceptor degeneration, most of the cells in the inner retina remain alive and functional. Because photoreceptors are the only cells that can transduce light into neural activity, the spontaneous activity of the residual retinal neurons does not produce functional vision. However, electrical stimulation can be used to activate these neurons, generating signals that are transmitted to the brain and interpreted as visual information. Retinal prosthetics are devices that deliver electrical stimulation to the retina with the goal of producing functional artificial vision. These technologies have produced very limited success to date; small and transient improvements in the detection of light and movement are the most common outcomes.

Our group has developed a novel method of providing high-resolution electrical stimulation to the retina. We are actively working to develop this technology into a complete retinal prosthetic device suitable for implantation into humans. Our design consists of two major components – 1) silicon nanowires that serve as both photodetectors and electrodes for neural stimulation and 2) circuitry required to power and control the electrical stimulation delivered to the retina. In this project, Dr. Freeman, Dr. Silva, and Dr. Cauwenberghs will collaborate on the development of the electronic circuitry components required for this retinal prosthetic system.

This retinal prosthetic utilizes a 3×4 mm array of small silicon tiles coated in nanowires (Figure 1). This design provides maximal coverage of the visual field, allows the device to conform to the curvature of the eye, and facilitates the diffusion of oxygen and nutrients through the retina. The nanowire structures act as photodetector elements, producing a current when they are exposed to light. Small groups of nanowires are bundled together to form electrodes that funnel this current into the retina. We have demonstrated that visual sensations can be elicited by shining light on a silicon nanowire device implanted beneath the retina of a rabbit (Figure 2). In this case, no external power was applied to the device, and high intensity light was required to produce sufficient current to activate retinal neurons.

The photocurrent produced by the nanowire devices can be amplified through active circuits using an external power supply. Such current gain mechanism in the output of the nanowires enables less intense light stimuli to still produce sufficient current to recruit retinal neurons. Our preliminary animal and in vitro data shows that an external bias will be needed to achieve electrical stimulation of the human retina. By careful design of voltage bias pulse

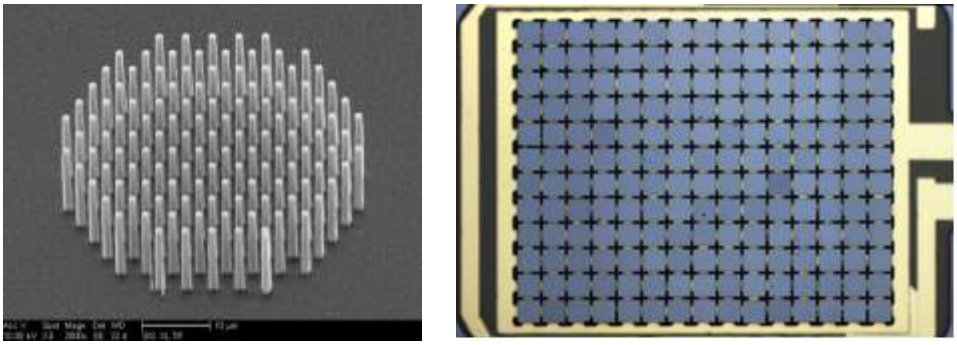

Figure 1: At left, a SEM image of a grouping of silicon nanowires during an intermediate step in the fabrication of the nanowire tiles. At right, an array of nanowire tiles affixed to a flexible, perforated substrate for implantation beneath the retina.

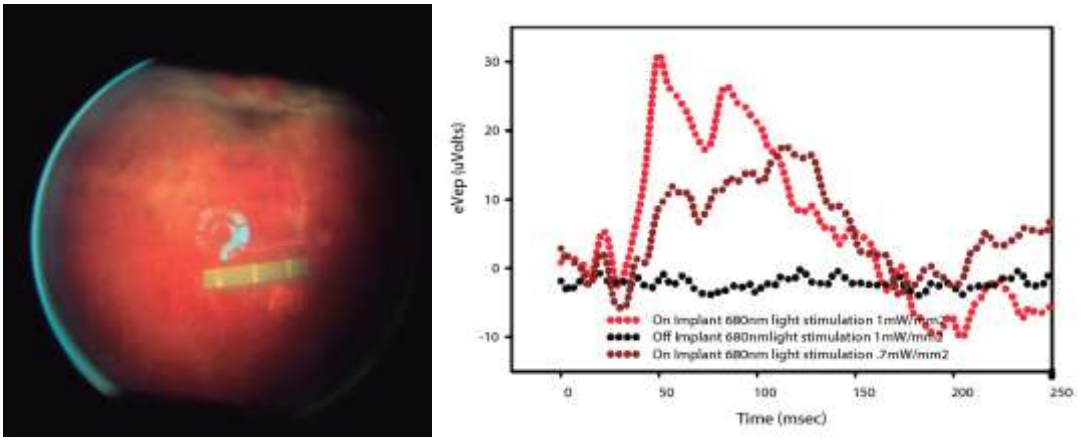

Figure 2: At left, a microscopic image of a nanowire device implanted under the rabbit retina. At right, visually evoked potentials recorded from the visual cortex of a rabbit implanted with a nanowire device (averaged response to 200 trials). Because the rabbit retina is not naturally responsive to 680 nm light, no response is observed when this light is focused on an area away from the implant. When the light was focused onto the nanowire device, strong neural responses were recorded.

waveforms along with peripheral support circuits for electrical stimulation across the entire array, the retinal prosthetic is expected to provide functional vision under normal lighting conditions. The added electrical controls will also enable a larger degree of adjustment over the lifetime of the device, ensuring that patients receive maximal benefit from this techology.

The addition of power and active circuits to the retinal prosthetic dramatically extends the functionality of the device, but it also adds significant challenges to the device design. Electronic components added to the device must be capable of storing and delivering power to the nanowire tiles. There is limited space within the orbital socket to accommodate these components, and they must not interfere with normal eye movement. Additionally, external controls of the frequency, amplitude, and duration of the bias stimulation pulses are desired in order to extend the flexibility of the implant. This information, and power to recharge the implanted battery, must be transmitted via telemetry. Although power and data telemetry circuits are standard in biomedical instrumentation, the specific form factor, energy efficiency, and functionality requirements of the nanowire prosthetic pose unique challenges in their implementation, requiring novel custom integrated circuit design.

The unique design of this retinal prosthetic system provides significant advantages over retinal prosthetic systems being developed by other research groups. No external cameras or signal processing units are required because the light sensing components of the device are implanted into the eye. This also allows the system to take advantage of natural saccadic eye movements, which prevents fading of the visual image. As all of our stimulation electrodes receive the same bias pulse and are not individually addressed, the complexity of the wiring required to interface with the device is dramatically reduced. This enables the device to cover a larger area of the retina with many more electrode contacts, which is expected to result in higher resolution vision, theoretically up to a visual acuity of 20/80.

Prof. William Freeman is a clinician scientist with extensive experience in the clinical management of retinal disease and vitreoretinal surgery. We are making great progress collaborating with Drs Yuhwa Lo and Yi Jing on the design and fabrication of our silicon nanowire devices and have excellent support with Prof. Gabe Silva's experience in electrophysiology to evaluate in vitro and in vivo tests of the retinal implant. In order for this project to evolve into a functioning human implant we require Gert Cauwenberghs' expertise in designing compact and energy efficient electronics for biomedical application. The combination of clinical and engineering experience within our team will lead to success in the completion of this novel retinal prosthetic device.