BIOGRAPHICAL SKETCH

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NAME: Hong, Guosong

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

POSITION TITLE: Postdoctoral Fellow

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
Peking University, Beijing, China	B.S.	07/2008	Chemistry
Stanford University, Stanford, CA	Ph.D.	06/2014	Chemistry
Harvard University, Cambridge, MA	Postdoctoral	08/2018	Chemistry and Chemical Biology

A. Personal Statement

Originally trained as a chemist, I have expanded my research interests far beyond chemistry to the fields of biology, medicine and neuroscience. Both my doctoral and postdoctoral research have demonstrated successful translation of new breakthroughs made in physical sciences and engineering (chemistry, nanoscience, optics and electronics) to pressing biological questions and real-world medical challenges, ranging from inquiries in neuroscience to cardiovascular and cerebrovascular diseases.

- As an undergraduate student at Peking University, I developed nanoscale biosensors for detection of blood-borne biomarkers using the photonic bandgap shift, a fascinating phenomenon found in periodic nanostructures upon surface binding of specific analyte molecules.
- As a graduate student at Stanford University, I invented and developed a new noninvasive biomedical imaging technique, termed second near-infrared fluorescence imaging (NIR-II imaging, using fluorescence in the 1,000-1,700 nm spectrum), for deep-tissue real-time imaging of cancer, cardiovascular disease (such as lower limb ischemia and cardiac infarction) and cerebrovascular disease (such as stroke and cerebral hypoperfusion), under the co-advice of Prof. Hongjie Dai (chemistry), Prof. John P. Cooke (cardiology), Prof. Calvin J. Kuo (hematology/neurology) and Prof. Ngan F. Huang (cardiology/regenerative medicine).
- As an American Heart Association (AHA) Postdoctoral Fellow and a recipient of the NIH K99 Pathway to Independence Award at Harvard University under the advice of Prof. Charles M. Lieber, I developed and demonstrated syringe-injectable mesh electronics as a powerful tool for chronically stable single-neuron electrophysiology in rodent brains for ≥8 months, a feat unattainable with other brain interrogation techniques and therefore ideally suited for the proposed study of neural circuit evolution during aging at the single-neuron level. I have also led projects using mesh electronics for minimally invasive electrophysiology on live rodent retina (under co-advice of Prof. Joshua R. Sanes, Dept. Molecular and Cellular Biology), in live primate brain (under co-advice of Prof. Margaret S. Livingstone, Harvard Medical School) and for neurological diseases (under co-advice of Profs. Emad N. Eskandar and Sydney Cash, Massachusetts General Hospital).

The research projects above have given me highly interdisciplinary training and background in chemistry, nanotechnology, optics, electronics, neuroscience and biomedicine, with a focus on chronic rodent and primate experiments, and have led to 26 first-author publications in journals including *Science, Nature Medicine*, *Nature Photonics*, *Nature Methods, Nature Biomedical Engineering* and *Nature Communications*, and 34 other publications in journals including *Nature Materials* and *Nature Nanotechnology*.

During my postdoctoral training, in particular during the tenure of the NIH K99 award, I have accomplished successful transition from a mentored postdoctoral fellow to an independent research group leader, by securing a tenure-track position as an assistant professor in the Department of Materials Science and Engineering at

Stanford University, effective September 2018. In addition, my postdoctoral training supported by the K99 award is not only a transition to independence, but also a transition from a research focus on physical sciences to neuroscience and medical research with clinical relevance and an impact on global health. To this end, with the support of K99 award, I have published a review article on the potential neuroscience and neurological applications of mesh electronic neural probes developed in our lab in *Current Opinion in Neurobiology*, one of the leading journals in neuroscience. Additionally, in collaboration with one of my K99 Advisory Committee members and the director of Harvard Center for Brain Science, Prof. Joshua Sanes, I have demonstrated the first chronic in-vivo recording of individual retinal ganglion cells in awake mice in a first-author publication in *Science*. Besides, during the K99 phase of this award, I have made solid progress in accomplishing the aims specified at the outset of this project, and believe that I am in a uniquely qualified position to carry out the proposed research for the R00 phase of the award, particularly, applying the latest advances in mesh electronic neural probes for understanding the single-neuron basis of cognitive decline during brain aging. Furthermore, the proposed research and career plan during the R00 phase of this award will allow me to continue receiving mentoring support from my career mentoring committee (see **Plan and Timeline for Independent Grant Applications**), as well as carry out professional development activities including academic networking, public speaking, grant/paper writing, mentoring and lab management as an independent group leader at Stanford University.

a. Hong G, Lee JC, Robinson JT, Raaz U, Xie L, Huang NF, Cooke JP, Dai H (2012). Multi-functional in vivo vascular imaging using near-infrared II fluorescence. *Nat Med* 18*:*1841-6. PMCID: PMC3595196
b. Hong G, Diao S, Chang J, Antaris AL, Chen C, Zhang B, Zhao S, Atochin DN, Huang PL, Andreasson KI, Kuo CJ, Dai H (2014). Through-skull fluorescence imaging of the brain in a new near-infrared window. *Nat Photonics* 8:723-30. PMCID: PMC5026222
c. Fu TM,* Hong G,* Zhou T,* Schuhmann TG, Viveros RD, Lieber CM (2016). Stable long-term chronic brain mapping at the single-neuron level. *Nat Methods* 13:875-82. *(co-first author) PMID: 27571550
d. Hong G,* Fu TM,* Qiao M,* Viveros RD, Yang X, Zhou T, Lee JM, Park HG, Sanes JR, Lieber CM (2018). A method for single-neuron chronic recording from the retina in awake mice. *Science* 360:1447-1451. PMID: 29954976

B. Positions and Honors

Positions and Employment

2018- Assistant Professor, Department of Materials Science and Engineering, Stanford University, Stanford, CA
2014-2018 Postdoctoral Fellow, Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA

Other Experience and Professional Memberships

2010- Member, American Chemical Society
2012- Member, American Heart Association
2014- Member, Materials Research Society
2015- Member, Biomedical Engineering Society

Honors

2010 Abbott Laboratories Stanford Graduate Fellowship, Stanford University, Stanford, CA
2013 William S. Johnson Graduate Fellowship, Stanford University, Stanford, CA
2014 Silver Award, Materials Research Society Graduate Student Awards
2015 The International Union of Pure and Applied Chemistry (IUPAC) International Award for Young Chemists, Honorable Mention Award
2016 Postdoctoral Fellowship, American Heart Association
2017 Pathway to Independence Award (Parent K99/R00), National Institutes of Health (NIH)

C. Contributions to Science

1. NonInvasive Deep-Tissue Imaging Modality Based on Second-Near-Infrared (NIR-II) Fluorescence: Existing biomedical imaging modalities widely used in research labs and hospitals either lack sufficient tissue penetration depth (e.g., fluorescence-based confocal, two-photon and wide-field imagers) or adequate spatiotemporal resolution (e.g., X-ray radiography, CT, fMRI and ultrasonography) for real-time imaging at cellular or subcellular scale in a 3D volume. To address this longstanding challenge, in my graduate research at Stanford I invented a

new optical imaging modality by employing fluorescence in an unexplored electromagnetic spectrum, the second near-infrared (NIR-II) window with wavelengths in the range of 1,000-1,700 nm. Photons in the NIR-II spectral window have the highest penetration depths in the optical spectrum while maintaining high imaging resolution of optical imaging.

In the 2012 *Nature Medicine* paper that debuted this non-invasive imaging technique, I demonstrated deep-tissue imaging of normal and pathological vasculature and hemodynamics in a rodent model of peripheral arterial disease (lower limb ischemia), with spatial resolution well exceeding that of microCT, and temporal resolution comparable to that of Doppler blood flowmetry with clear differentiation of arterial and venous vessels based on real-time video-rate imaging. In the 2014 *Nature Photonics* paper that applies this advantageous NIR-II fluorescence imaging modality in a rodent mouse of stroke, I demonstrated through-scalp/skull imaging of microvasculature in the brain with sub-10 μm resolution without the need for craniotomy, cranial window, skull thinning or any invasive removal of scalp skin.

My invention of in-vivo NIR-II fluorescence imaging has led to a worldwide adaptation of the technique in many research and clinical labs for imaging deep organs in a number of diseases ranging from cancer to vascular and neurological diseases, with minimum or no surgical intervention.

a. Hong G, Lee JC, Robinson JT, Raaz U, Xie L, Huang NF, Cooke JP, Dai H (2012). Multi-functional in vivo vascular imaging using near-infrared II fluorescence. *Nat Med* 18*:*1841-6. PMCID: PMC3595196
b. Hong G, Diao S, Chang J, Antaris AL, Chen C, Zhang B, Zhao S, Atochin DN, Huang PL, Andreasson KI, Kuo CJ, Dai H (2014). Through-skull fluorescence imaging of the brain in a new near-infrared window. *Nat Photonics* 8:723-30. PMCID: PMC5026222
c. Hong G, Lee JC, Jha A, Diao S, Nakayama KH, Hou L, Doyle TC, Robinson JT, Antaris AL, Dai H, Cooke JP, Huang NF (2014). Near-infrared II fluorescence for imaging hindlimb vessel regeneration with dynamic tissue perfusion measurement. *Circ Cardiovasc Imaging* 7:517-25. PMCID: PMC4079035
d. Hong G, Antaris AL, Dai H (2017). Near-infrared fluorophores for biomedical imaging. *Nat Biomed Eng* 1:0010.

2. Surface-Plasmon-Based Fluorescence-Enhancing Microarray for Ultrasensitive Detection of Biomarkers: Sensitive detection of biomarkers indicative of a certain disease is critical to accurate diagnosis, precise medicine and optimum prognosis. Existing techniques (e.g., ELISA and radioimmunoassay) for detection of biomarkers such as cytokines, tumor-specific antigens and autoantibodies associated with type 1 diabetes lack sufficient sensitivity, multiplexity and throughput for detection of trace biomarkers in the blood at an early stage of the disease onset. During my graduate study at Stanford, my colleagues and I developed a plasmonic gold substrate-based microarray assay for ultrasensitive detection of disease-specific biomarkers with a femtomolar detection limit, many orders of magnitude lower than existing methods with high detection specificity between different biomarkers. Besides my publications on this topic listed below, I also hold a patent on the invention of this fluorescence-enhancing microarray that has been licensed to a handful of biotechnology companies commercializing the products for ex-vivo use in worldwide clinical laboratories.

a. Hong G, Tabakman SM, Welsher K, Wang H, Wang X, Dai H (2010). Metal-enhanced fluorescence of carbon nanotubes. *J Am Chem Soc* 132:15920-3. PMID: 20979398
b. Hong G, Tabakman SM, Welsher K, Chen Z, Robinson JT, Wang H, Zhang B, Dai H (2011). Near-infrared-fluorescence-enhanced molecular imaging of live cells on gold substrates. *Angew Chem Int Ed* 50:4644-8. PMID: 21506225
c. Hong G, Wu JZ, Robinson JT, Wang H, Zhang B, Dai H (2012). Three-dimensional imaging of single nanotube molecule endocytosis on plasmonic substrates. *Nat Commun* 3:700. PMID: 22426221
d. Zhang B, Price J, Hong G, Tabakman SM, Wang H, Jarrell JA, Feng J, Utz PJ, Dai, H (2013). Multiplexed cytokine detection on plasmonic gold substrates with enhanced near-infrared fluorescence. *Nano Res* 6*:*113-20.

3. Syringe-Injectable Mesh Electronics for Chronically Stable Brain and Retina Mapping at Single-Neuron Level: Our understanding of the brain comes mainly from longitudinal studies with low spatiotemporal resolution (e.g., fMRI on human patients over years), and cross-sectional studies comparing different subject populations, due to chronic instability (e.g., single-neuron electrophysiology with invasive brain electrodes). However, many functions and processes in the brain (such as aging) occur over years and centimeter-scale regions of the brain, but involve cellular electrophysiological changes that have to be quantified at the millisecond and micrometer scales of individual neurons. To address this scale discrepancy in current neural interrogation techniques, in my postdoctoral research I have contributed as first and co-first author to the invention of a new form of flexible nanoelectronics, termed ‘syringe-injectable electronics’, for chronically stable, large-scale mapping of the brain and the retina by tracking the firing activities of the same individual neurons for >8 months. This capability, which

is not possible with other neurotechnologies, is due to the unique mechanical and structural design of the mesh-like electronics. Specifically, a flexibility comparable to that of brain tissue, feature sizes on order of axons/soma, and a macroporous structure that allows interpenetration of neurons through the electronics eliminate movement of the probe relative to neurons during chronic experiments, minimizing the glial scarring that would otherwise insulate neurons from the probe. Since publication of our groundbreaking technique, many neuroscientists and neurologists around the world have started using our mesh electronics in their own work, to chronically interrogate the neural circuits and neurons of interest over extended time periods in live subjects.

a. Hong G,* Fu TM,* Qiao M,* Viveros RD, Yang X, Zhou T, Lee JM, Park HG, Sanes JR, Lieber CM (2018). A method for single-neuron chronic recording from the retina in awake mice. *Science* 360:1447-1451. PMID: 29954976
b. Fu TM,* Hong G,* Viveros RD, Zhou T, Lieber CM (2017). Highly scalable multichannel mesh electronics for stable chronic brain electrophysiology. *Proc Natl Acad Sci USA* 114:E10046-55. *(co-first author) PMID: 29109247
c. Fu TM,* Hong G,* Zhou T,* Schuhmann TG, Viveros RD, Lieber CM (2016). Stable long-term chronic brain mapping at the single-neuron level. *Nat Methods* 13:875-82. *(co-first author) PMID: 27571550
d. Hong G,* Fu TM,* Zhou T, Schuhmann TG, Huang J, Lieber CM (2015). Syringe injectable electronics: Precise targeted delivery with quantitative input/output connectivity. *Nano Lett* 15:6979-84. PMID: 26317328

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

5K99AG056636-02 National Institutes of Health (NIH) Hong, Guosong (PI) 07/15/17-08/31/18
Brain Aging Studies with Single-Neuron Resolution Using Syringe-Injectable Electronics
The goal of this study is two-fold: 1) Applying tissue-like mesh electronics neural probes for elucidation of the single-neuron basis of age-related cognitive decline by tracking the same individual neurons and the neural circuits they comprise in longitudinal single-neuron studies spanning the entire aging process; 2) using mesh electronics as an ‘electroceutical’ that can be delivered into the brain via syringe to modulate brain activity and ameliorate deleterious cognitive changes in brain circuitry due to aging.
Role: PI