

BIOGRAPHICAL SKETCH

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NAME: Litt, Brian

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

POSITION TITLE: Professor with Tenure, Neurology and Bioengineering

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)	END DATE MM/YYYY	FIELD OF STUDY
Harvard University	AB	05/1982	Engineering & Applied Science
Johns Hopkins, Medicine	MD	05/1986	Medicine
Johns Hopkins Hospital	Other training	06/1987	Intern, Internal Medicine
JHU Appl Physics Lab	Fellow	06/1988	Dana Research Fellow
Johns Hopkins Hospital	Resident	06/1991	Chief Neurology Resident
Johns Hopkins Hospital	Resident	06/1991	Neurology Residency
Johns Hopkins Hospital	Fellow	06/1993	Fellowship, Epilepsy&Clinical Neurophys

A. Personal Statement

This proposal is an excellent fit for my expertise in collaborative, multidisciplinary research bridging engineering, neuroscience and clinical medicine. My lab focuses on applying new engineering technology to map and modulate functional networks in brain to understand and treat human disease. As PI and co-Investigator on government, institutional, and privately funded grants, I engage and innovate in the areas of hardware design, machine learning, cloud-based informatics/ signal processing and brain-computer interfaces. Clinical translation is an important goal of my work, in addition to mentoring clinicians and scientists across fields. My work is both individual and collaborative. It often involves multiple institutions and fields, so I have broad experience in handling all aspects of grants administration for large and small projects. An important focus of my efforts is publication in high quality peer-reviewed journals, in addition to patents and building open-source tools to share with the scientific community. My collaborative group is composed of clinical and basic scientists and engineers; our activities been enhanced by the creation of the Penn Center for Neuroengineering and Therapeutics where I serve as director. My lab emphasizes training in research, hosting 11 doctoral candidates and 13 post-doctoral researchers, including 6 residents and fellows, during the past five years. As PI of a recently awarded T32 serving both MDs and PhDs, "Training Program in Neuroengineering and Medicine," I look forward to training more individuals in successful translational research.

B. Positions and Honors**Positions and Employment**

1979 -	Research Intern, Non-Newtonian Fluid Mechanics, U.S.Gov.AberdeenProvingGrounds
1980 -	Systems Applications Programmer Intern, JHU Applied Physics Lab
1981 -	SystemsDesign, Programming, SignalProcessing Intern, Biomed. Eng., JHU Medicine
1982 -	Systems Analysis Engineer Intern, U.S. Gov. Aberdeen Proving Grounds
1987 - 1988	Dana Foundation Fellow, Magnetoencephalography, JHU Appl.Phys.&Schl Medicine
1990 - 1991	Chief Resident in Neurology, Johns Hopkins Hospital
1991 - 1996	Attending Neurologist, Johns Hopkins Hospital & Sinai Hospital, Balt. (Director EEG)
1993 - 1994	Instructor in Neurology, Johns Hopkins University School of Medicine
1994 - 1996	Assistant Professor, Neurology and Medicine, Johns Hopkins Univ. School Medicine
1996 - 1999	Director, EEG Lab, Assistant Professor of Neurology, Emory Univ. Schl of Medicine
1999 - 2004	Assistant Professor of Neurology and Bioengineering, University of Pennsylvania
2000 - 2007	Director, EEG Lab, Hospital of the University of Pennsylvania

2001 - 2002 Acting Director, Intraoperative Monitoring, Hospital of University of Pennsylvania
 2004 - 2008 Associate Professor of Neurology and Bioengineering, University of Pennsylvania
 2008 - 2012 Associate Professor with Tenure, Neurology and Bioengineering, UPenn
 2012 - Director, Epilepsy Center, University of Pennsylvania
 2012 - Professor with Tenure, Neurology and Bioengineering, University of Pennsylvania
 2014 - Professor of Neurosurgery (secondary appointment), University of Pennsylvania
 2014 - Director, Center for Neuroengineering and Therapeutics, University of Pennsylvania
 2017 - Co-Director, Penn Center for Health, Devices and Technology

Other Experience and Professional Memberships

2001 - Grant Reviewer, National Science Foundation, multiple European and US agencies
 2001 - 2014 NIH Benchmarks Epilepsy Research Advisory Board, Director of the NIH, NINDS
 2004 - Presidential Symposium Lecturer, American Epilepsy Society National Meeting
 2004 - 2012 Member/late Co-Chair of ANIE, NIH Study Sections (multiple, eg. SBIRs, SE Panels)
 2005 - Elected to, American Neurological Association
 2009 - Elected Senior Member, Institute of Electrical and Electronic Engineers (IEEE)
 2010 - Member, Society for Neuroscience
 2010 - Invited Platform Speaker, Brown University's Brain Science Inst. 10th Anniversary
 2011 - Invited for nomination, DARPA Defense Science Research Council, U.S. Govt
 2013 - Invited Advisor for Neurotechnology, President Obama's BRAIN Initiative
 2013 - Elected Fellow, American Neurological Association
 2014 - Editorial Board, Science Translational Medicine

Honors

1982 Scholarship Award for Medical Training (4 years), March of Dimes
 1986 Postdoc Research Fellowship Award: Magnetoencephalography, Dana Foundation
 1991 "Resident Teacher of the Year" Award, Johns Hopkins Hospital
 1991 Fellowship (3 yrs), Merritt-Putnam then William Gowers Scholar, Epilepsy Foundation
 1996 Junior Investigator Research Award, Epilepsy Foundation
 2000 Biomedical Engineering Research Grant (3 years), Whitaker Foundation
 2001 Award for Innovative Research, American Epilepsy Society
 2001 Research Award, Brain-Cardiac Interface (2 years), Dana Foundation
 2003 Dreifuss-Penry Award for Epilepsy Research, American Academy of Neurology
 2004 Fellowship Award in the Neurosciences, Klingenstein Fund
 2004 Bioengineering Transitional Award (3 years), Whitaker Foundation
 2011 Hans Berger Award for Contribution to EEG Research, Virginia Commonwealth Univ.
 2012 Brain and Behavior Foundation Distinguished Investigator Award, NARSAD
 2013 Scientific Innovations Award, Brain Research Foundation
 2013 Luigi Mastroianni Clinical Innovator Award, Perelman School of Medicine, UPenn
 2015 Research Recognition Award for Clinical Science , AES
 2016 Medical Professional of the Year, Epilepsy Foundation Eastern PA

C. Contribution to Science

1. A central theme of my work is that I blend engineering with translational medical research to develop new therapies for neurological disease. This leverages my experience as both a clinician and engineer. I build diverse teams across disciplines and institutions, and mentor young faculty in Neuroengineering. Populating this space with strong clinician-scientist-engineers, collaborating across fields and translating basic science into therapy for patients are main missions. The passion that drives my career is the search for better ways to treat epilepsy. 1/3 of over 60 million people with epilepsy worldwide have seizures despite medication. Seizure-free outcomes after surgery for epilepsy are modest. I lead a long-term effort to define biomarkers of epileptic networks and seizure generation, such as High Frequency Oscillations

(HFOs) and Microseizures, to enable more effective surgery and antiepileptic device therapy. My group has helped establish HFOs as a biomarker, established that seizures evolve in a cascade of neurophysiologic events over time, and built algorithms and open source tools to advance human treatment.

- a. Bink H, Sedigh-Sarvestani M, Fernandez-Lamo I, Kini L, Ung H, Kuzum D, Vitale F, Litt B, Contreras D. Spatiotemporal evolution of focal epileptiform activity from surface and laminar field recordings in cat neocortex. *J Neurophysiol.* 2018 Jun 1;119(6):2068-2081. PubMed PMID: [29488838](#); PubMed Central PMCID: [PMC6032123](#).
 - b. Pearce A, Wulsin D, Blanco JA, Krieger A, Litt B, Stacey WC. Temporal changes of neocortical high-frequency oscillations in epilepsy. *J Neurophysiol.* 2013 Sep;110(5):1167-79. PubMed PMID: [23761699](#); PubMed Central PMCID: [PMC3763087](#).
 - c. Stead M, Bower M, Brinkmann BH, Lee K, Marsh WR, Meyer FB, Litt B, Van Gompel J, Worrell GA. Microseizures and the spatiotemporal scales of human partial epilepsy. *Brain.* 2010 Sep;133(9):2789-97. PubMed PMID: [20685804](#); PubMed Central PMCID: [PMC2929333](#).
 - d. Litt B, Esteller R, Echaz J, D'Alessandro M, Shor R, Henry T, Pennell P, Epstein C, Bakay R, Dichter M, Vachtsevanos G. Epileptic seizures may begin hours in advance of clinical onset: a report of five patients. *Neuron.* 2001 Apr;30(1):51-64. PubMed PMID: [11343644](#).
2. The resolution of cm-scale electrodes used in clinical care may degrade clinical outcome from functional neurosurgery. We and others have found biomarkers of epileptic networks at the submillimeter scale that are not recorded clinically and may impact patient care. My lab pushes the boundaries of brain implants to make less invasive, thin, flexible, transparent and dissolving devices to define brain networks down to the cellular and cortical column scales. I assemble teams including talented materials scientists/ engineers to define optimal spatial and temporal resolution for brain recording.
- a. Yu KJ, Kuzum D, Hwang SW, Kim BH, Juul H, Kim NH, Won SM, Chiang K, Trumpis M, Richardson AG, Cheng H, Fang H, Thomson M, Bink H, Talos D, Seo KJ, Lee HN, Kang SK, Kim JH, Lee JY, Huang Y, Jensen FE, Dichter MA, Lucas TH, Viventi J, Litt B, Rogers JA. Bioresorbable silicon electronics for transient spatiotemporal mapping of electrical activity from the cerebral cortex. *Nat Mater.* 2016 Jul;15(7):782-791. PubMed PMID: [27088236](#); PubMed Central PMCID: [PMC4919903](#).
 - b. Kuzum D, Takano H, Shim E, Reed JC, Juul H, Richardson AG, de Vries J, Bink H, Dichter MA, Lucas TH, Coulter DA, Cubukcu E, Litt B. Transparent and flexible low noise graphene electrodes for simultaneous electrophysiology and neuroimaging. *Nat Commun.* 2014 Oct 20;5:5259. PubMed PMID: [25327632](#); PubMed Central PMCID: [PMC4331185](#).
 - c. Viventi J, Kim DH, Vigeland L, Frechette ES, Blanco JA, Kim YS, Avrin AE, Tiruvadi VR, Hwang SW, Vanleer AC, Wulsin DF, Davis K, Gelber CE, Palmer L, Van der Spiegel J, Wu J, Xiao J, Huang Y, Contreras D, Rogers JA, Litt B. Flexible, foldable, actively multiplexed, high-density electrode array for mapping brain activity in vivo. *Nat Neurosci.* 2011 Nov 13;14(12):1599-605. PubMed PMID: [22081157](#); PubMed Central PMCID: [PMC3235709](#).
 - d. Kim DH, Viventi J, Amsden JJ, Xiao J, Vigeland L, Kim YS, Blanco JA, Panilaitis B, Frechette ES, Contreras D, Kaplan DL, Omenetto FG, Huang Y, Hwang KC, Zakin MR, Litt B, Rogers JA. Dissolvable films of silk fibroin for ultrathin conformal bio-integrated electronics. *Nat Mater.* 2010 Jun;9(6):511-7. PubMed PMID: [20400953](#); PubMed Central PMCID: [PMC3034223](#).
3. Innovative devices require new approaches to define brain networks and mine huge high-resolution data sets to power diagnostic and therapeutic applications. I lead efforts to define new algorithms to detect and predict seizures, define brain states, localize pathologic signals and steer neural stimulation. This work includes a portfolio of more than 15 patents, in addition to standard publications. My work in this area has contributed substantially to new implantable devices, some FDA approved, including the NeuroPace responsive neurostimulator, the NeuroVista seizure prediction device, the Medtronic closed loop brain stimulation devices (PC+S), and methods for deploying and controlling them.
- a. Kremen V, Brinkmann B, Kim I, Gurgain H, Nasserli M, Magee A, Attia TP, Nejedly P, Sladky V, Nelsson N, Chang, S, Herron J, Adams T, Baldassano S, Cimbalnik J, Vasoli V, Fehrmann E,

- Chouinard T, Patterson E, Litt B, Stead M, Gompel J, Sturges B, Crowe C, Denison T, Worrell G. Integrating Brain Implants with Local and distributed Computing Devices: A Next Generation Epilepsy Management System. IEEE Journal of Translational Engineering in Health and Medicine. Accepted August 16, 2018. *In press*. DOI: 10:1109/ JTEHM.2018.2869398. PMC Pending.
- b. Khambhati AN, Bassett DS, Oommen BS, Chen SH, Lucas TH, Davis KA, Litt B. Recurring Functional Interactions Predict Network Architecture of Interictal and Ictal States in Neocortical Epilepsy. eNeuro. 2017 Jan-Feb;4(1)PubMed PMID: [28303256](#); PubMed Central PMCID: [PMC5343278](#).
 - c. Khambhati AN, Davis KA, Lucas TH, Litt B, Bassett DS. Virtual Cortical Resection Reveals Push-Pull Network Control Preceding Seizure Evolution. Neuron. 2016 Sep 7;91(5):1170-1182. PubMed PMID: [27568515](#); PubMed Central PMCID: [PMC5017915](#).
 - d. Wulsin D, Jensen S, Litt B. Nonparametric Multi-level Clustering of Human Epileptic Seizures. The Annals of Applied Statistics. 2016; 10(2):667-689.
4. A major thrust of my lab is on collaborative science, sharing data, algorithms, open-source tools and big neuro data. I lead an effort to accelerate science through data sharing using our U24 funded platform <http://ieeg.org>, which we hope to make the “go-to” repository for sharing neurophysiologic data, algorithms and collaborative research. With ~1,000 users worldwide and ~2,000 data sets, IEEG is growing rapidly.
- a. Baldassano SN, Brinkmann BH, Ung H, Blevins T, Conrad EC, Leyde K, Cook MJ, Khambhati AN, Wagenaar JB, Worrell GA, Litt B. Crowdsourcing seizure detection: algorithm development and validation on human implanted device recordings. Brain. 2017 Jun 1;140(6):1680-1691. PubMed PMID: [28459961](#); PubMed Central PMCID: [PMC6075622](#).
 - b. Brinkmann BH, Wagenaar J, Abbot D, Adkins P, Bosshard SC, Chen M, Tieng QM, He J, Muñoz-Almaraz FJ, Botella-Rocamora P, Pardo J, Zamora-Martinez F, Hills M, Wu W, Korshunova I, Cukierski W, Vite C, Patterson EE, Litt B, Worrell GA. Crowdsourcing reproducible seizure forecasting in human and canine epilepsy. Brain. 2016 Jun;139(Pt 6):1713-22. PubMed PMID: [27034258](#); PubMed Central PMCID: [PMC5022671](#).
 - c. Davis KA, Ung H, Wulsin D, Wagenaar J, Fox E, Patterson N, Vite C, Worrell G, Litt B. Mining continuous intracranial EEG in focal canine epilepsy: Relating interictal bursts to seizure onsets. Epilepsia. 2016 Jan;57(1):89-98. PubMed PMID: [26608448](#); PubMed Central PMCID: [PMC4770560](#).
 - d. Wagenaar JB, Worrell GA, Ives Z, Dümpelmann M, Litt B, Schulze-Bonhage A. Collaborating and sharing data in epilepsy research. J Clin Neurophysiol. 2015 Jun;32(3):235-9. PubMed PMID: [26035676](#); PubMed Central PMCID: [PMC4455031](#).

Complete List of Published Work in My Bibliography: <http://bit.ly/1N8Msfo>

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

R01 NS099348-01, NIH	Litt (PI)	09/01/16-08/30/20
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Virtual Resection to Treat Epilepsy

The goal is to develop a new method to localize epileptic networks from intracranial EEG with: (1) automated, objective method; (2) no need to precipitate acute seizures during evaluation; (3) simulate effects of different brain surgeries or device placements for individual patients.

Role: PI

T32 NS091006-01	Litt (PI)	07/01/15-06/30/20
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Training Program in Neuroengineering and Medicine

The goal is to train pre-doctoral Engineering students, and post-doctoral MD/MD-PhD fellows in Neuroengineering and its translation to clinical care.

Role: PI

Mirowski Family Foundation, Grant	Litt (PI)	12/31/11-12/30/18
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