



# MURI: Understanding and Controlling the Coupled Electrical, Chemical, & Mechanical Excitable Networks of Living Systems

*Wolfgang Losert, University of Maryland*

**GOAL:** Precise, noninvasive control of the behavior of cells and tissues

**APPROACH:** Targeted application of AC and DC electric fields to control cell signals and mechanics

**SCIENTIFIC FOUNDATION:** Cell Signals, mechanics, and electrical activity operate as coupled excitable systems

## **POTENTIAL BENEFITS of Precise Cellular Control:**

➤ **Accelerated Wound Healing**

Dermatology Expert

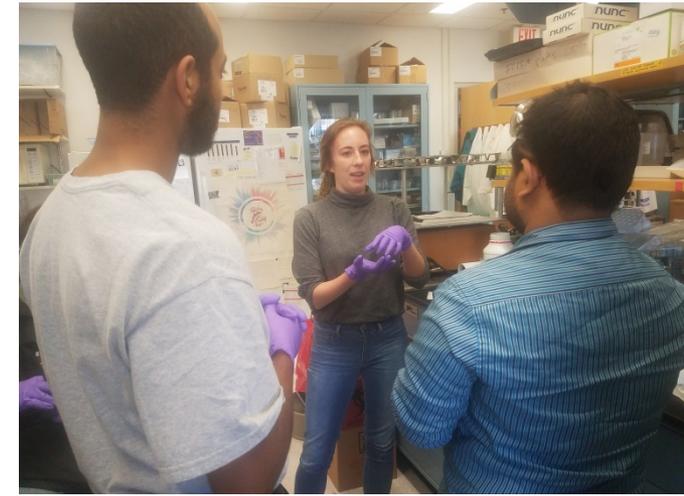
➤ **Control of Cell Signaling Pathways**

Cell Signaling Expert

➤ **Enhanced Cognition and Memory**

Neuroscience Expert

# MURI Research Activities



## **Research Interactions:**

Bi-Weekly Calls of TEAM

Regular Interaction of “Breakout Groups”

Image Analysis “Bootcamp”

Week-long Research Visits

## **Exchanging Biology and Technology:**

Unified Approach to EF Generation

Common Analysis Approach

Shared Cell Lines

***START: April 1, 2016***

**[33 Publications](#)**

**1 Patent Application**

## **Awards:**

Abby Bull, NSF Fellowship

Wolfgang Losert, APS Fellowship

Yuchuan Miao, Michael A. Shanoff Award

**Proposed Focus Session at Biomedical Engineering Society Annual Meeting 2018**



# Collaborations

- **Evan Miller** (UC Berkeley) – BerST voltage sensitive dye
- **Adam Cohen** (Harvard) - Model Cells for Electrical Activity
- **Vladislav Yakovlev** (Texas A&M) - New nonlinear optical imaging approaches

## **National Labs:**

- **Dr. Marc Cicerone and Dr. Charles Camp** (National Institute of Standards and Technology, Gaithersburg) Broadband CARS system for label-free imaging of intracellular dynamics. (DURIP Award)
- **Dr. Morgan Trexler** (The Johns Hopkins University, Applied Physics Laboratory). Electrogenic Biomaterials for severe battle-field cornea wounds (Army Award: W81XWH-14-1-0542).
- **Dr. Ed Giniger** (National Institutes for Neurological Disorders and Stroke) actin dynamics in neuronal processes.

## **International:**

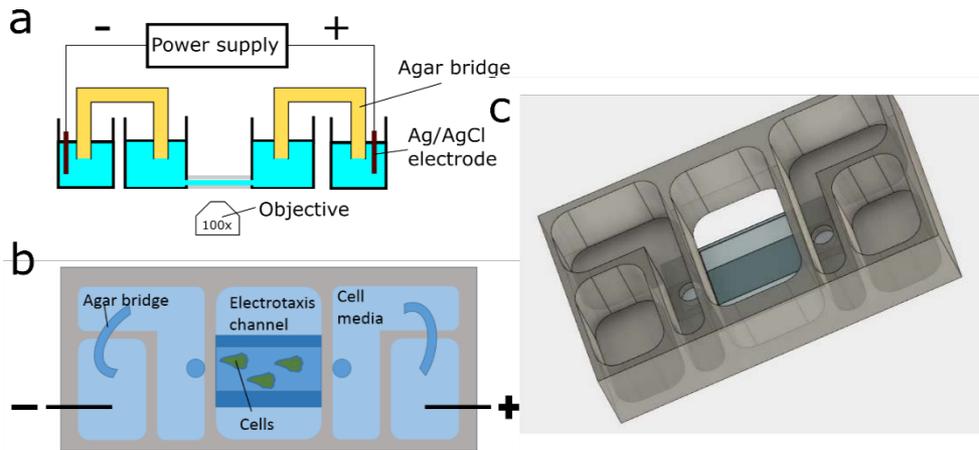
- **Dr. Valentina Benfanti**, (National Research Council of Italy) Measurement and Control of Excitable Dynamics in Astrocytes and Synapses
- **Dr. Roberto Mayor** (University College London, England) Comparative investigation of collective Electrotaxis and Chemotaxis.

## **Industry:**

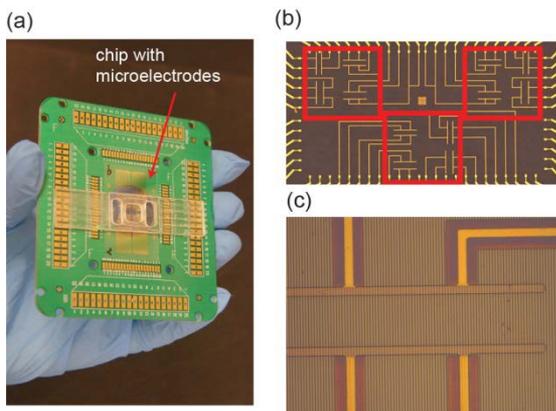
- **Dr. Michael Russell** (Aaken Laboratories, Inc., Davis, CA) Developing electrical brain stimulation targeting stem cells.
- **Dr. John Peterson** (Peterson Advanced Lithography) Custom nanotextures.

# Technology Exchange

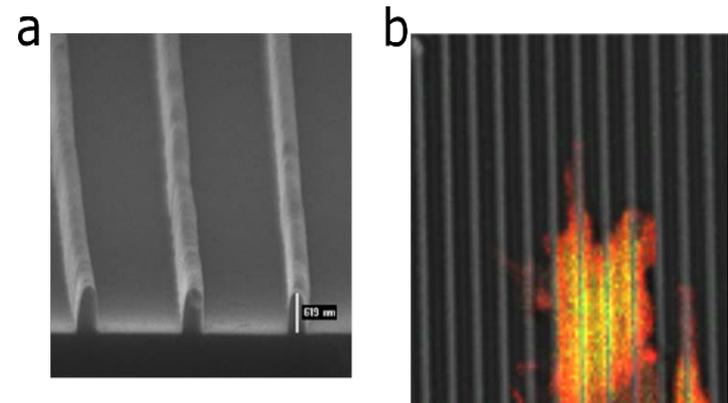
- DC field **ZHAO**



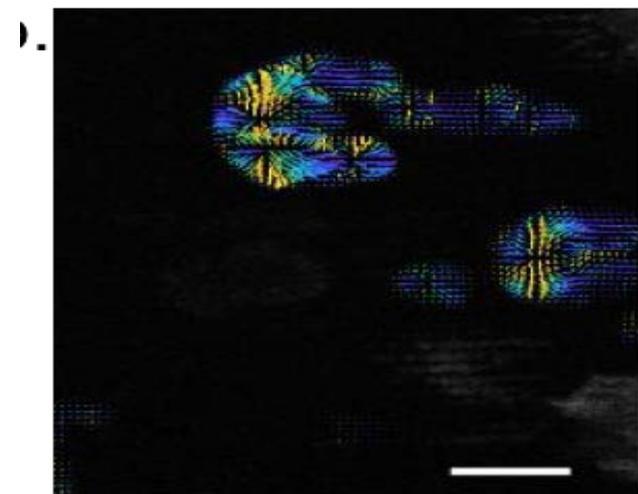
- AC field **QING**



- Nanotextured surfaces **FOURKAS**

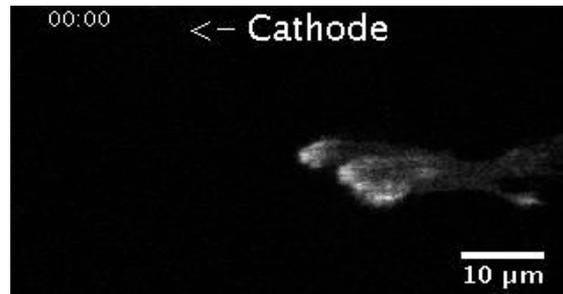


- Optical Flow Analysis **LOSERT**

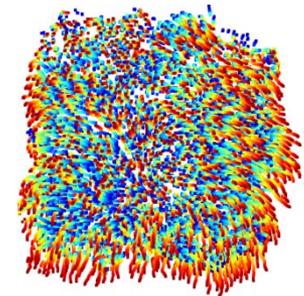
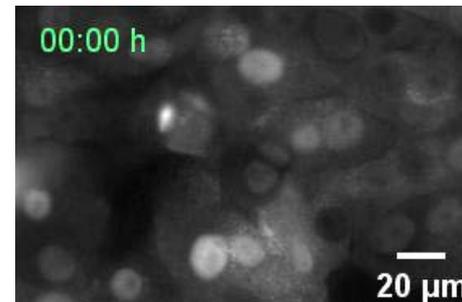


# Biological Systems

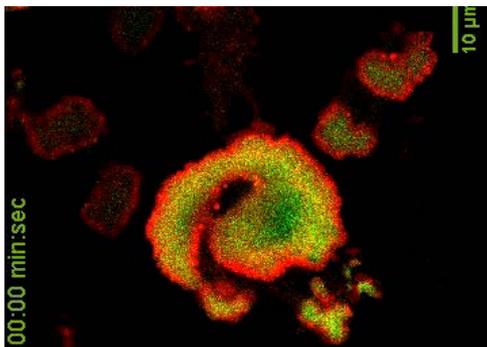
- Neutrophil-like HL60
  - Zhao, Devreotes, Losert, Fourkas



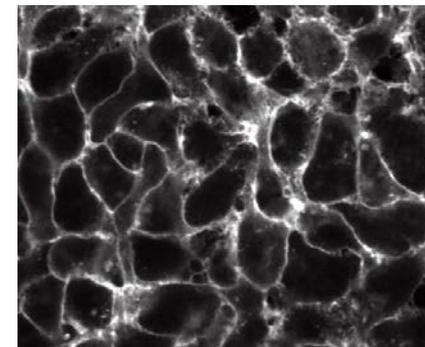
- Epithelial Cells (MCF10A, MDA231)
  - Devreotes, Zhao, Losert



- *Giant Dictyostelium discoideum*
  - Devreotes, Losert, Fourkas, Qing



- Electrically Active Cells (HEK, Neurons)
  - Losert, Kanold



**Common Biochemical Perturbations: Latrunculin, Rapamycin,...**



# MURI: Understanding and Controlling the Coupled Electrical, Chemical, & Mechanical Excitable Networks of Living Systems

Wolfgang Losert, John Fourkas, Patrick Kanold, *University of Maryland*

Min Zhao, *UC Davis*

Peter Devreotes, *Johns Hopkins University*

Quan Qing, *Arizona State University*



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### POTENTIAL BENEFITS of Precise Cellular Control:

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- Control of Cell Signaling Pathways
- Enhanced Cognition and Memory

Dermatology Expert

Cell Signaling Expert

Neuroscience Expert

# Publications

- [1] Ken-ichi Nakajima, Kan Zhu, Yao-Hui Sun, Bence Hegyi, Qunli Zeng, Christopher J. Murphy, J. Victor Small, Ye Chen-Izu, Yoshihiro Izumiya, Josef M. Penninger, et al. Kcnj15/kir4. 2 couples with polyamines to sense weak extracellular electric elds in galvanotaxis. *Nature communications*, 6:8532, 2015.
- [2] Ken Ichi Nakajima and Min Zhao. Concerted action of KCNJ15/Kir4.2 and intracellular polyamines in sensing physiological electric elds for galvanotaxis. 10(4):264{266, 2016.
- [3] Yulia Artemenko, Lucas Axiotakis, Jane Borleis, Pablo A Iglesias, and Peter N. Devreotes. Chemical and mechanical stimuli act on common signal transduction and cytoskeletal networks. *Proceedings of the National Academy of Sciences*, 113(47):E7500{E7509, 2016.
- [4] Fernando Ferreira, Guillaume Luxardi, Brian Reid, and Min Zhao. Early bioelectric activities mediate redox-modulated regeneration. *Development*, pages dev{142034, 2016.
- [5] Ken-ichi Nakajima and Min Zhao. Concerted action of kcnj15/kir4. 2 and intracellular polyamines in sensing physiological electric elds for galvanotaxis. *Channels*, 10(4):264{266, 2016.
- [6] Yunyun Shen, Trisha Puger, Fernando Ferreira, Jiebing Liang, Manuel F. Navedo, Qunli Zeng, Brian Reid, and Min Zhao. Diabetic cornea wounds produce significantly weaker electric signals that may contribute to impaired healing. *Scientific Reports*, 6:26525, 2016.
- [7] Yao-Hui Sun, Yuxin Sun, Kan Zhu, Bruce W. Draper, Qunli Zeng, Alex Mogilner, and Min Zhao. An Experimental Model for Simultaneous Study of Migration of Cell Fragments, Single Cells, and Cell Sheets, pages 251{272. Springer New York, New York, NY, 2016.
- [8] Rachel M. Lee, Haicen Yue, Wouter-Jan Rappel, and Wolfgang Losert. Inferring single-cell behaviour from large-scale epithelial sheet migration patterns. *Journal of the Royal Society, Interface*, 14(130), May 2017.
- [9] Xiangbing Jiao, Yuan Wang, and Quan Qing. Scalable fabrication framework of implantable ultrathin and exible probes with biodegradable sacrificial layers. *Nano Letters*, 17(12):7315{7322, 2017.
- [10] Li Li, Kejun Zhang, Conghua Lu, Qin Sun, Sanjun Zhao, Lin Jiao, Rui Han, Caiyu Lin, Jianxin Jiang, Min Zhao, et al. Caveolin-1-mediated stat3 activation determines electrotoxis of human lung cancer cells. *Oncotarget*, 8(56):95741, 2017.
- [11] Yuchuan Miao, Sayak Bhattacharya, Marc Edwards, Huaqing Cai, Takanari Inoue, Pablo A. Iglesias, and Peter N. Devreotes. Altering the threshold of an excitable signal transduction network changes cell migratory modes. *Nature cell biology*, 19(4):329, 2017.
- [12] Peter N. Devreotes, Sayak Bhattacharya, Marc Edwards, Pablo A. Iglesias, Thomas Lampert, and Yuchuan Miao. Excitable signal transduction networks in directed cell migration. *Annual review of cell and developmental biology*, 33:103{125, 2017.
- [13] Jun-Feng Feng, Jing Liu, Lei Zhang, Ji-Yao Jiang, Michael Russell, Bruce G. Lyeth, Jan A. Nolte, and Min Zhao. Electrical guidance of human stem cells in the rat brain. *Stem cell reports*, 9(1):177{ 189, 2017.
- [14] Thomas J. Lampert, Nadine Kamprad, Marc Edwards, Jane Borleis, Ayende J. Watson, Marco Tarantola, and Peter N. Devreotes. Shear force-based genetic screen reveals negative regulators of cell adhesion and protrusive activity. *Proceedings of the National Academy of Sciences*, 114(37):E7727-E7736, 2017.
- [15] Rachel M. Lee, Haicen Yue, Wouter-Jan Rappel, and Wolfgang Losert. Inferring single-cell behaviour from large-scale epithelial sheet migration patterns. *Journal of The Royal Society Interface*, 14(130), 2017.
- [16] Xiangbing Jiao, Yuan Wang, and Quan Qing. Scalable fabrication framework of implantable ultrathin and exible probes with biodegradable sacrificial layers. *Nano Letters*, 17(12):7315{7322, 2017.
- [17] Yan Zhang, Guoqing Xu, Rachel M. Lee, Zijie Zhu, Jiandong Wu, Simon Liao, Gong Zhang, Yaohui Sun, Alex Mogilner, Wolfgang Losert, Tingrui Pan, Francis Lin, Zhengping Xu, and Min Zhao. Collective cell migration has distinct directionality and speed dynamics. *Cellular and Molecular Life Sciences*, 74(20):3841{3850, 2017.
- [18] Rachel M. Lee, Haicen Yue, Wouter-Jan Rappel, and Wolfgang Losert. Inferring single-cell behaviour from large-scale epithelial sheet migration patterns. *Journal of The Royal Society Interface*, 14(130):20170147, 2017.
- [19] Xiaoyu Sun, Matt J. Hourwitz, Eleni M. Baker, B. U. Sebastian Schmidt, Wolfgang Losert, and John T. Fourkas. Replication of biocompatible, nanotopographic surfaces. *Scientific Reports*, 8(1), 2018.
- [20] Xiaoyan Sun, Hongsheng Qi, Xiuzhen Zhang, Li Li, Jiaping Zhang, Qunli Zeng, George S. Laszlo, Bo Wei, Tianhong Li, Jianxin Jiang, Alex Mogilner, Xiaobing Fu, and Min Zhao. Src activation decouples cell division orientation from cell geometry in mammalian cells. *Biomaterials*, 170:82{94, 2018.
- [21] Christina H. Stuelten, Rachel M. Lee, Wolfgang Losert, and Carole A. Parent. Lysophosphatidic acid regulates the motility of mcf10ca1a breast cancer cell sheets via two opposing signaling pathways. *Cellular Signalling*, 45:1{11, 2018.
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- [24] Fernando Ferreira, Vijay Krishna Raghunathan, Guillaume Luxardi, K. Zhu, and Min Zhao. Early redox activities modulate vertebrate regeneration. In *revisions*, 2018.
- [25] A. Li, J.H. Cho, B. Reid, C.C. Tseng, L. He, P. Tan, C.Y. Yeh, P. Wu, Y. Li, R.B. Widelitz, Y. Zhou, M. Zhao, R.H. Chow, and C.M. Chuong. Coupling of biochemical-bioelectric signals mediates collective dermal cell migration. In *revisions*, 2018.
- [26] Liang Guo, John Albeck, and Min Zhao. Direct current electric elds modulate frequency and amplitude of erk activation in electrotaxing cells. In *revisions*, 2018.
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- [28] R.B. Widelitz, T.X. Jiang, A. Li, C.M. Lin, C. Chiu, J.H. Cho, B. Reid, M. Zhao, R.H. Chow, and C.M. Chuong. Global feather orientation changed by electric current. In *preparation*, 2018.
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