

HARVARD

John A. Paulson
School of Engineering
and Applied Sciences

Tissue-wide interrogation and intervention of cellular electrophysiology with cell-type specificity

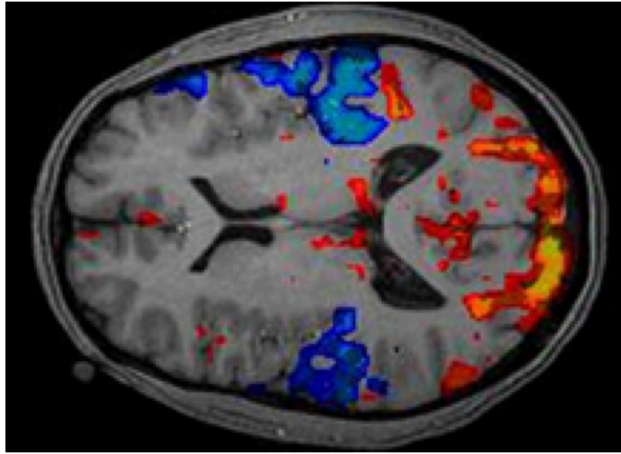
Jia Liu, Ph.D.

Assistant Professor of Bioengineering

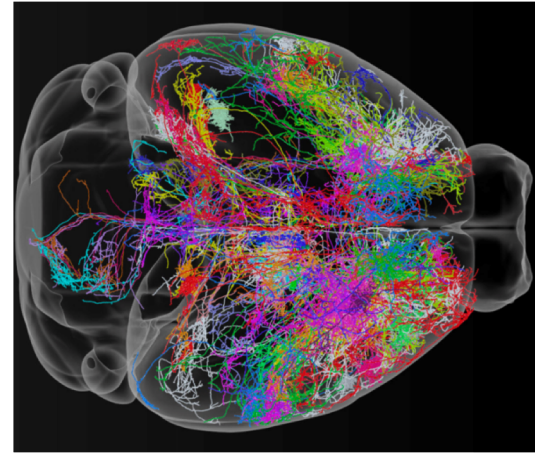
Harvard Bioelectronics Groups
School of Engineering and Applied Sciences
Harvard University

What are challenges?

Single-neuron activities across entire organ



Functionality



Connectivity

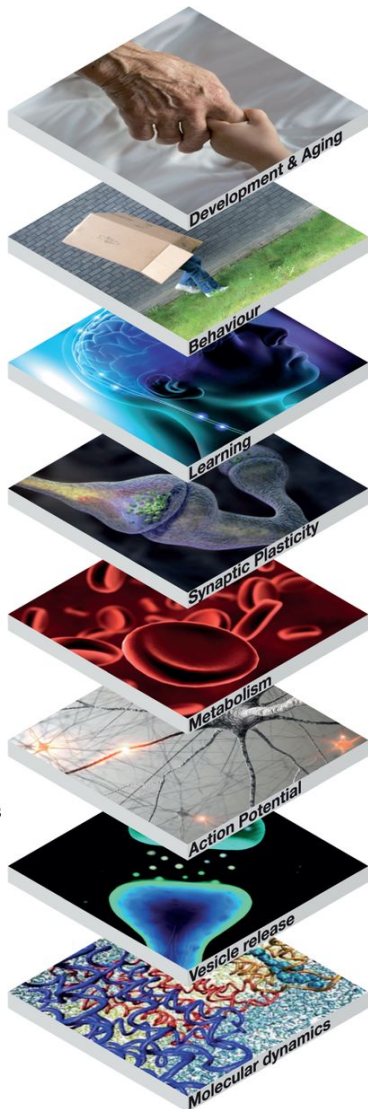
- **Brain functions are mostly associated with activities of neurons from multiple, deep brain regions.**
- **Different brain regions are highly innervated together through neural projections. Many connections are based on single neuron.**

What are challenges?

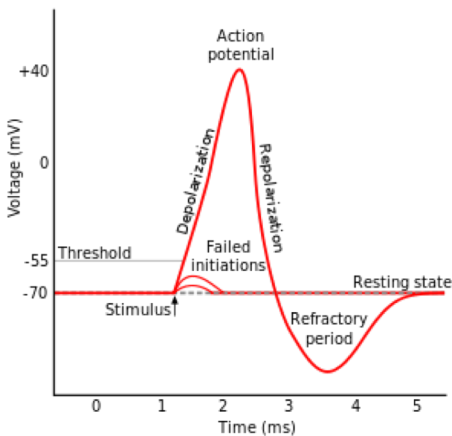
Spatiotemporal dilemma

Time Scale

Years
(10^7 s)

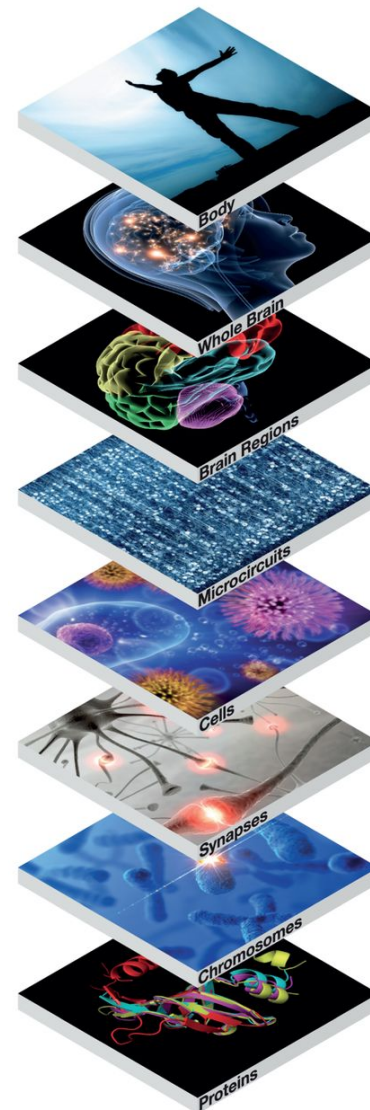


function



Spatial Scale

Metres
(10^0 m)



structure

Micrometres
(10^{-6} m)

Milliseconds
(10^{-3} s)

What are challenges?

Different types of cells interweave together

Morphology

HTR3A⁺
Sparse neurogliaform cell



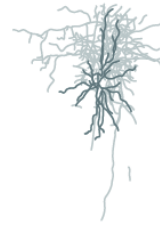
VIP⁺
Bipolar cell



SST⁺
Deep Martinotti cell



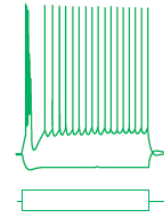
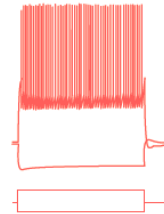
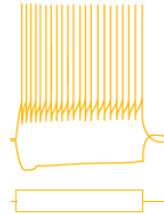
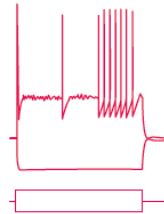
PVALB⁺
Basket cell



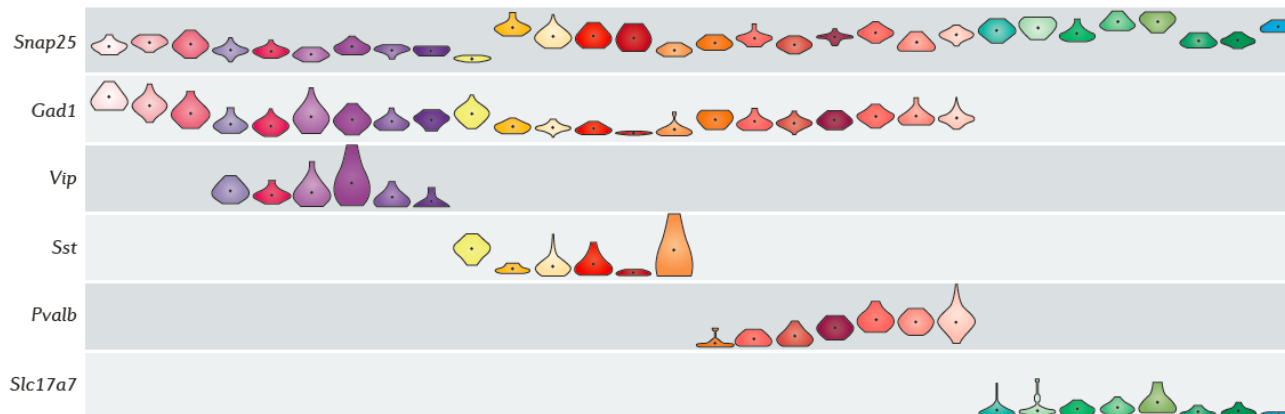
RBP4⁺
Thick-tufted cell



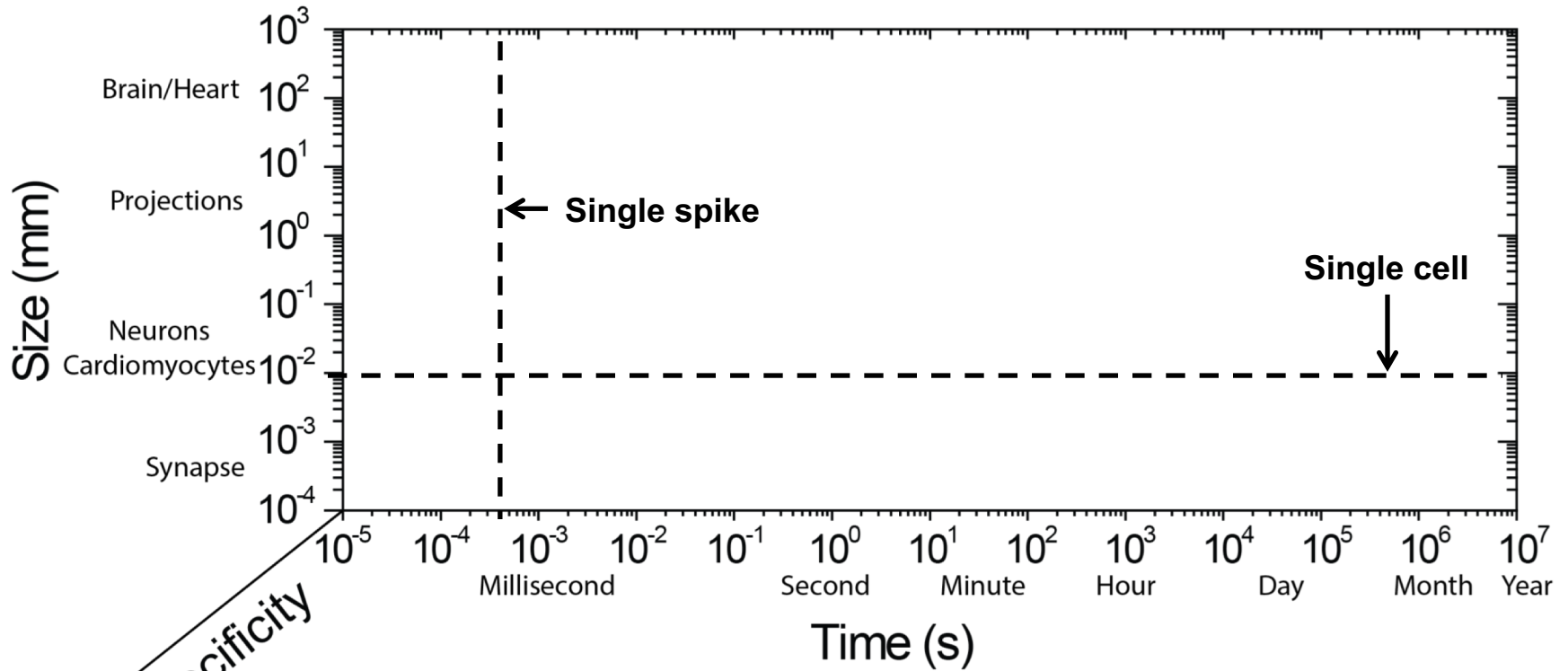
Physiology



Molecular signature

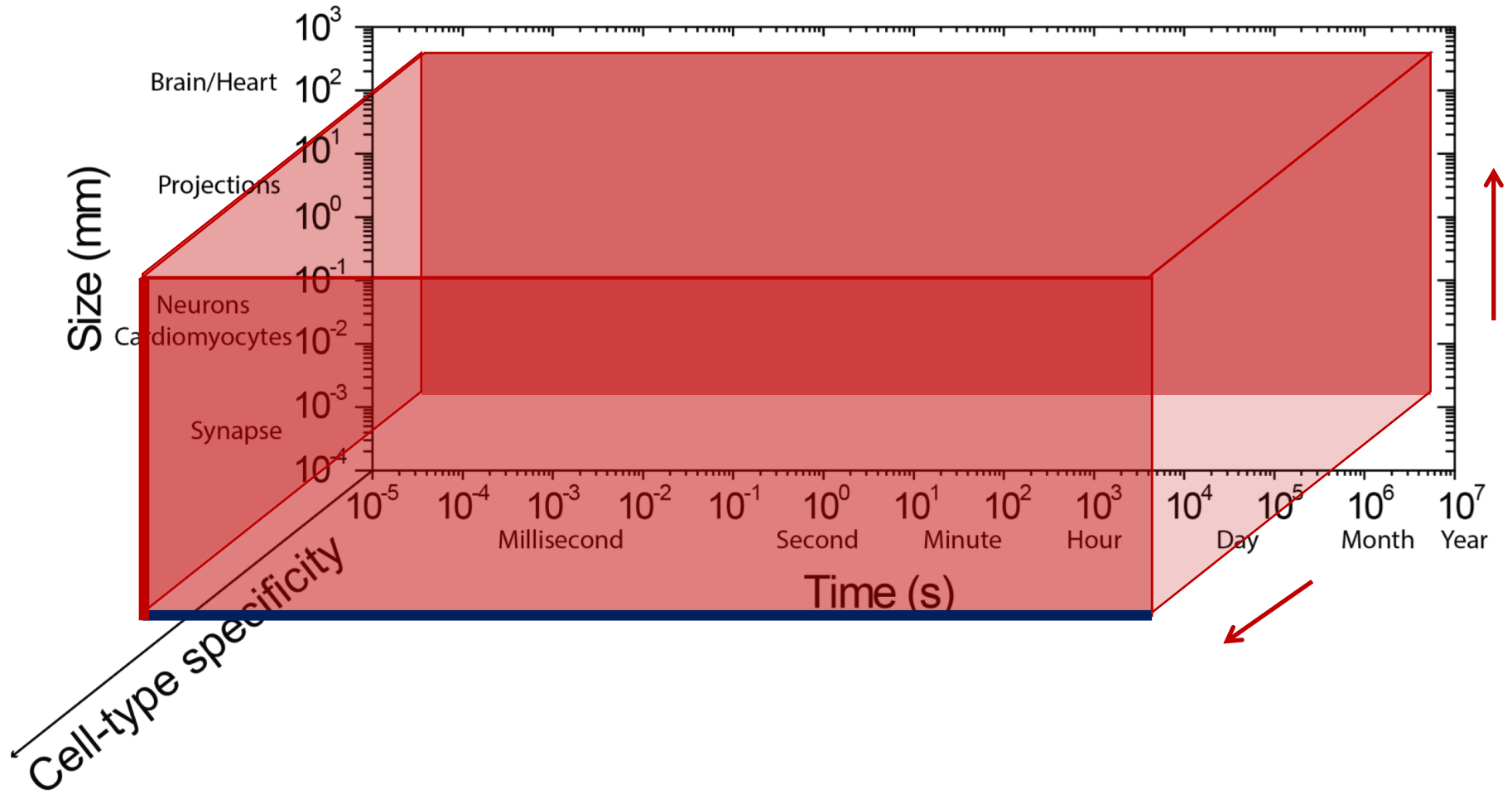


Scalable technologies for tissue interface

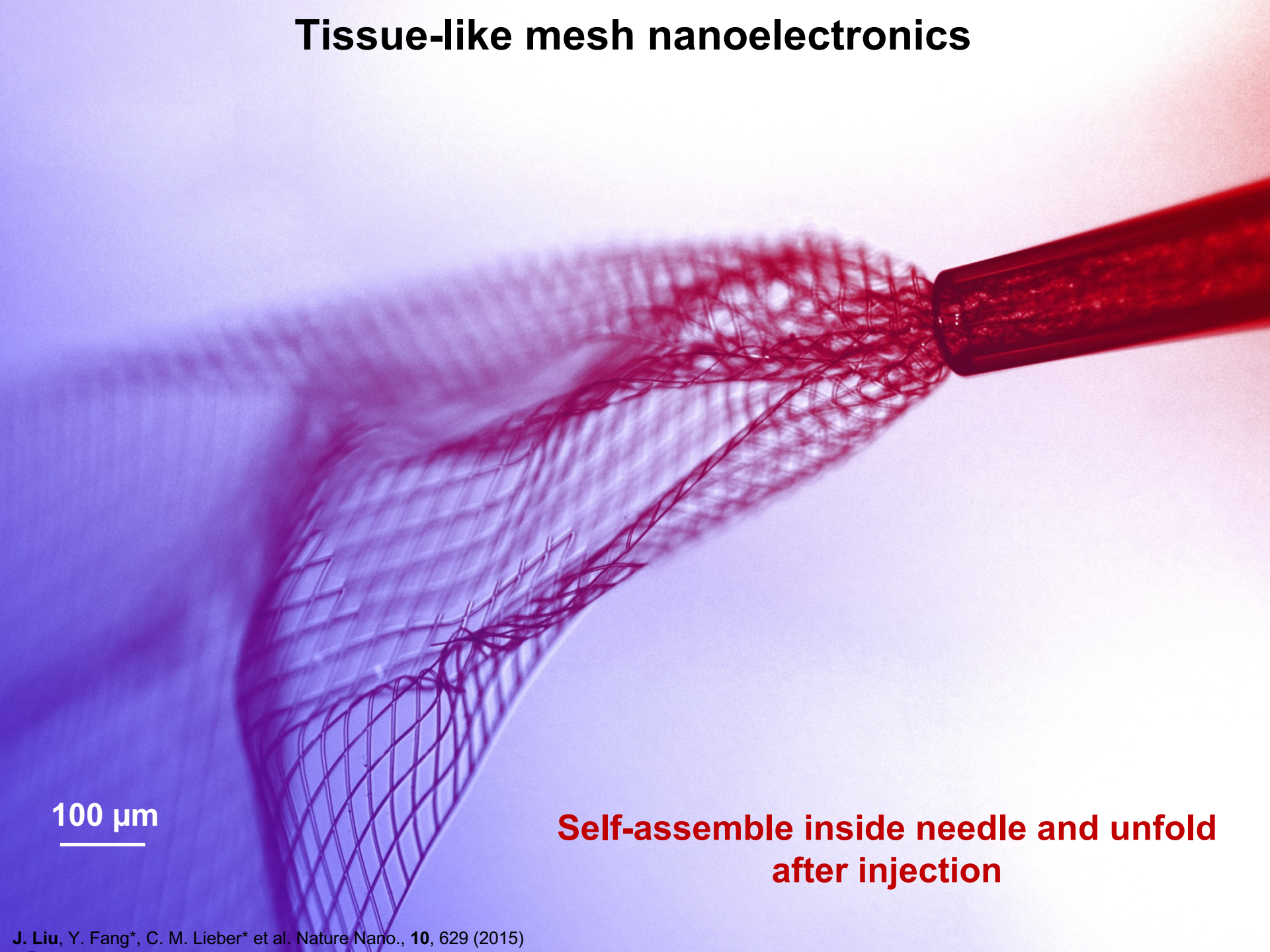


Cell-type specificity

Scalable technologies for tissue interface



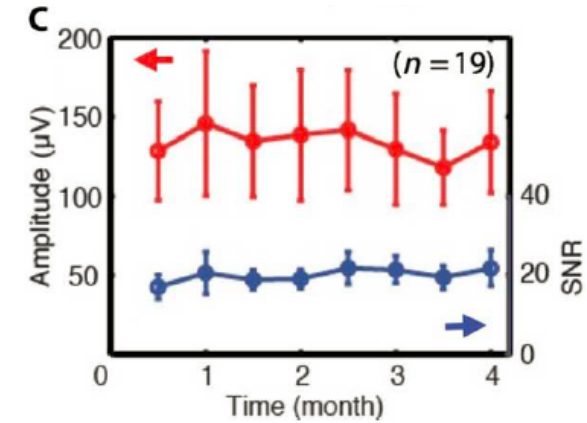
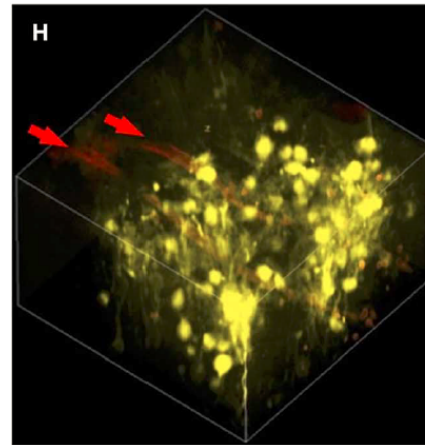
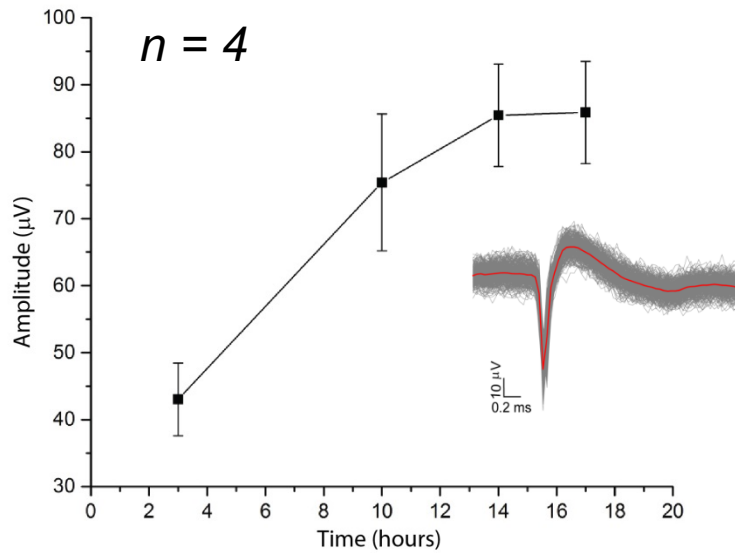
Tissue-like mesh nanoelectronics



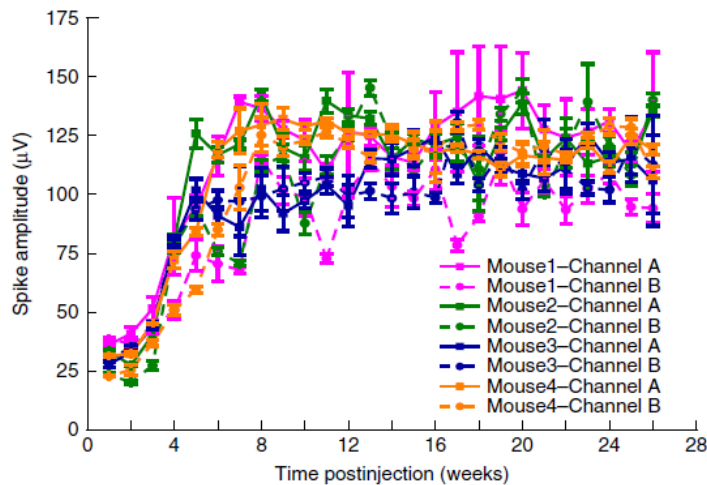
100 μm

Self-assemble inside needle and unfold after injection

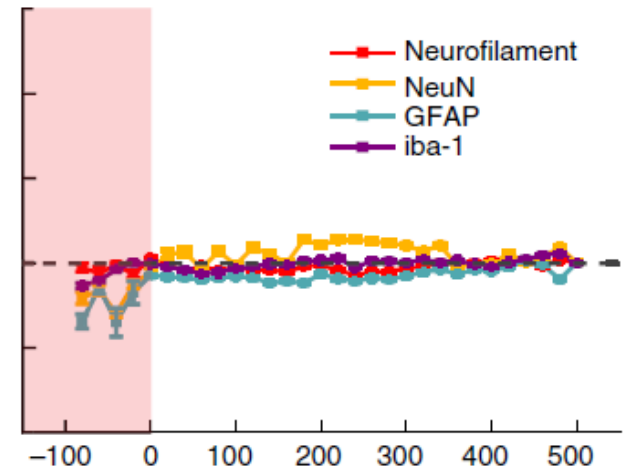
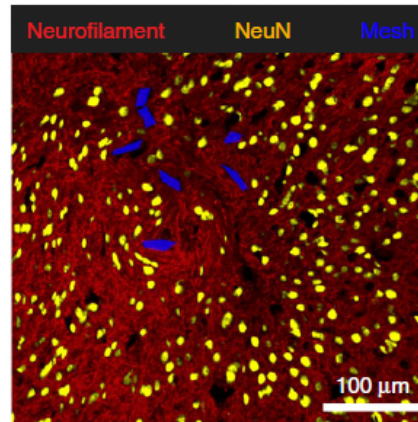
Long-term single-cell electrophysiology in behaving animal



Sci. Adv., 3, e1601966 (2017)

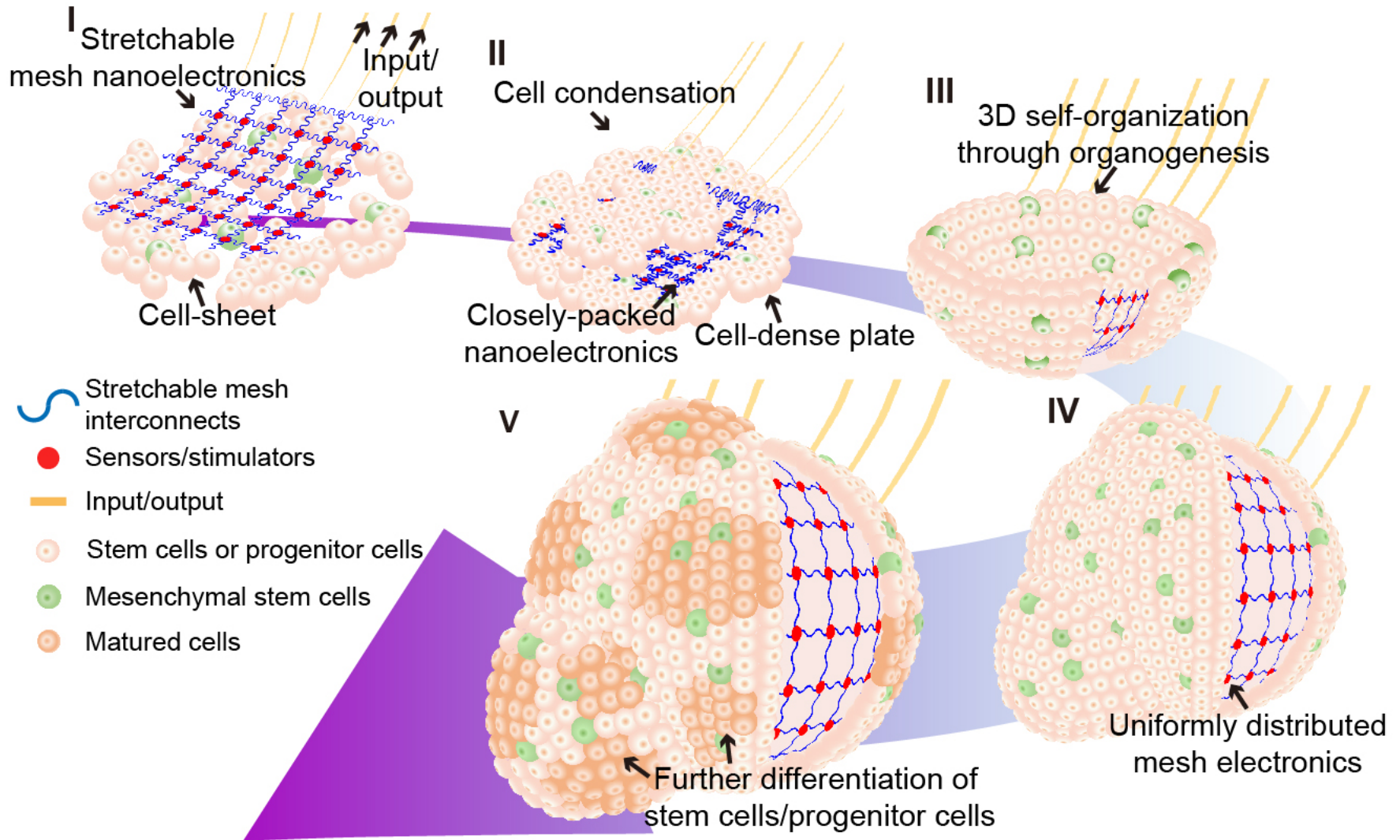


Nat. Methods 13, 875 (2016)

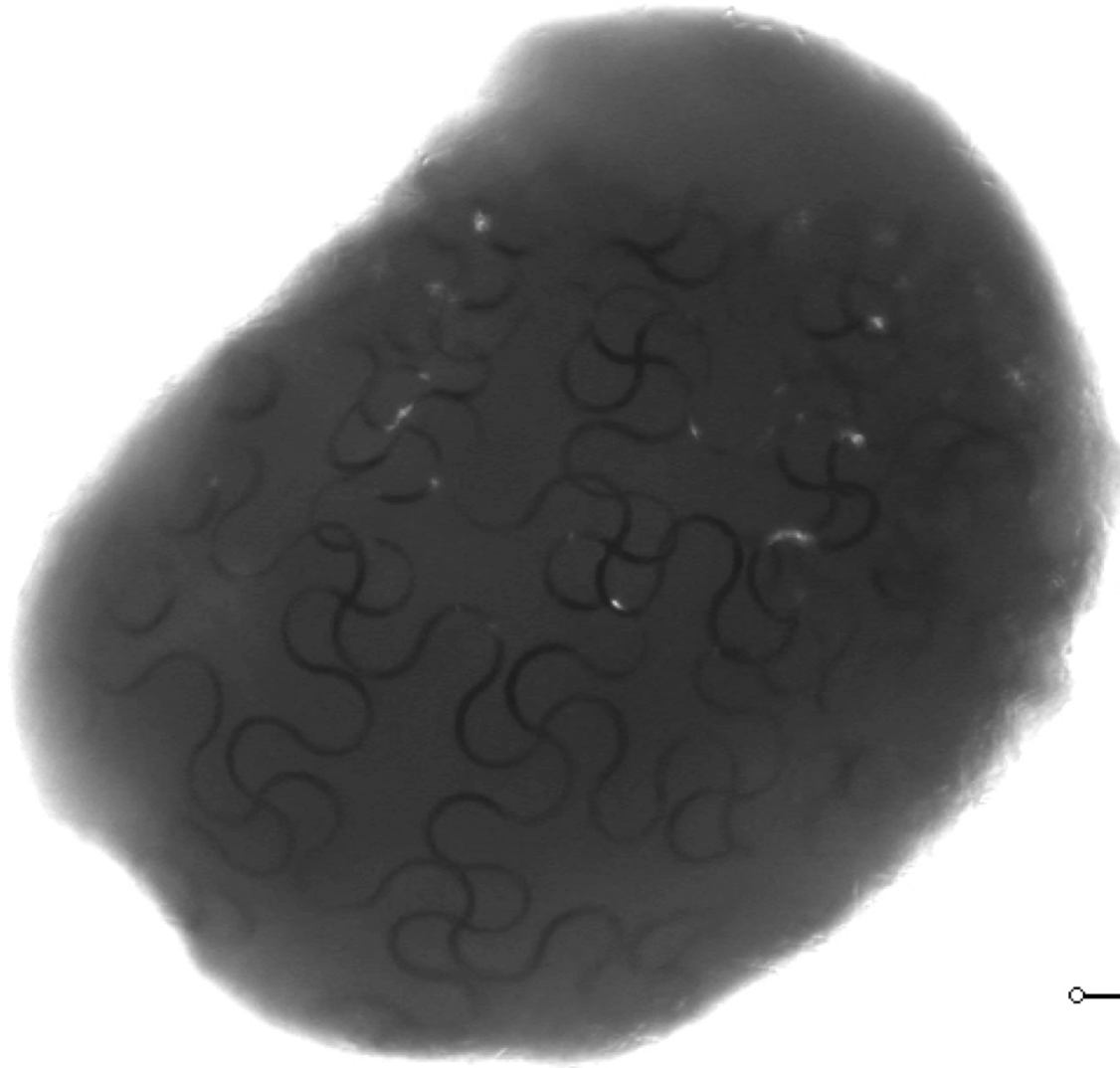


Proc. Natl. Acad. Sci. USA 114, 5894 (2017)

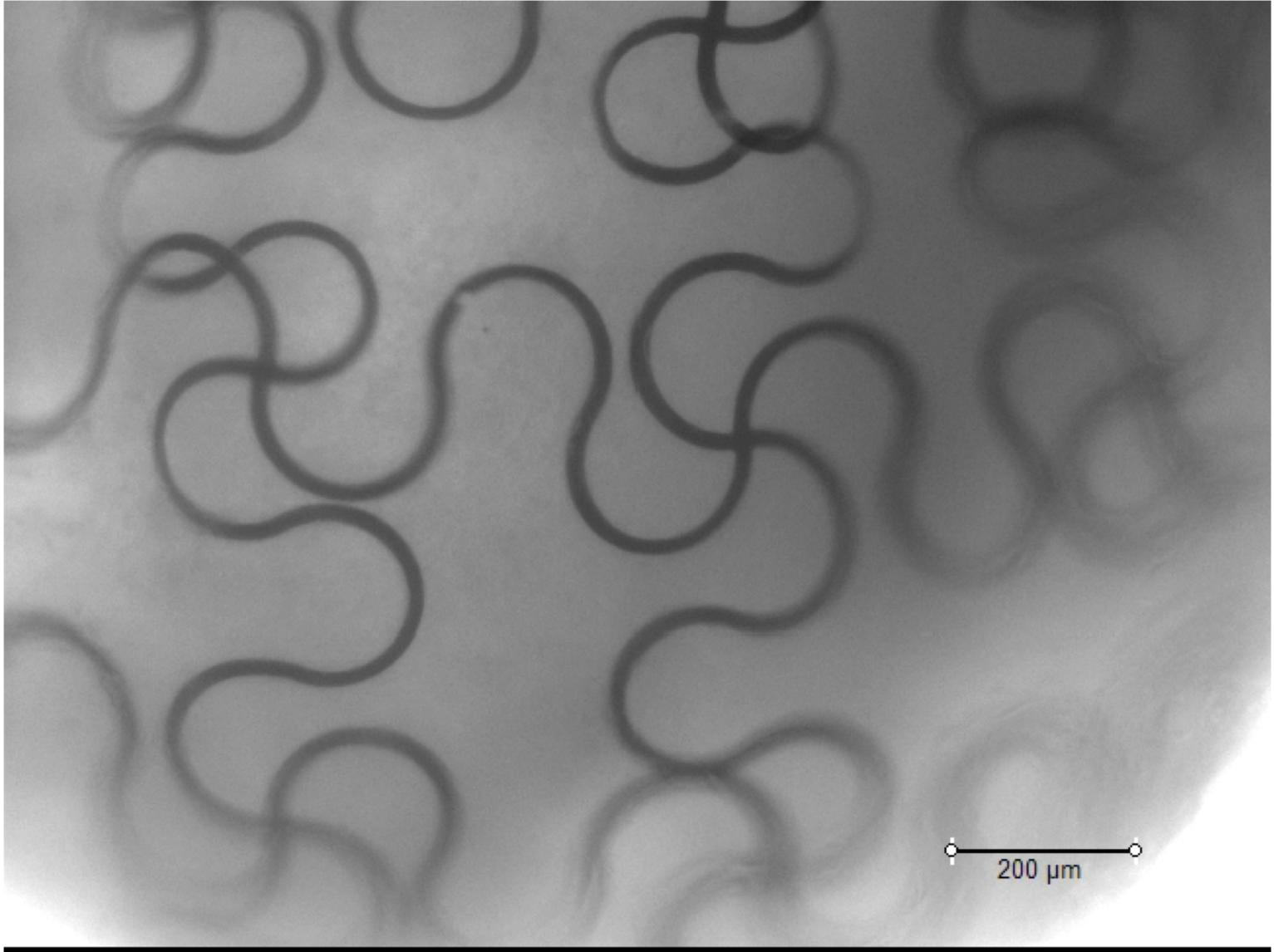
Cyborg organoid model



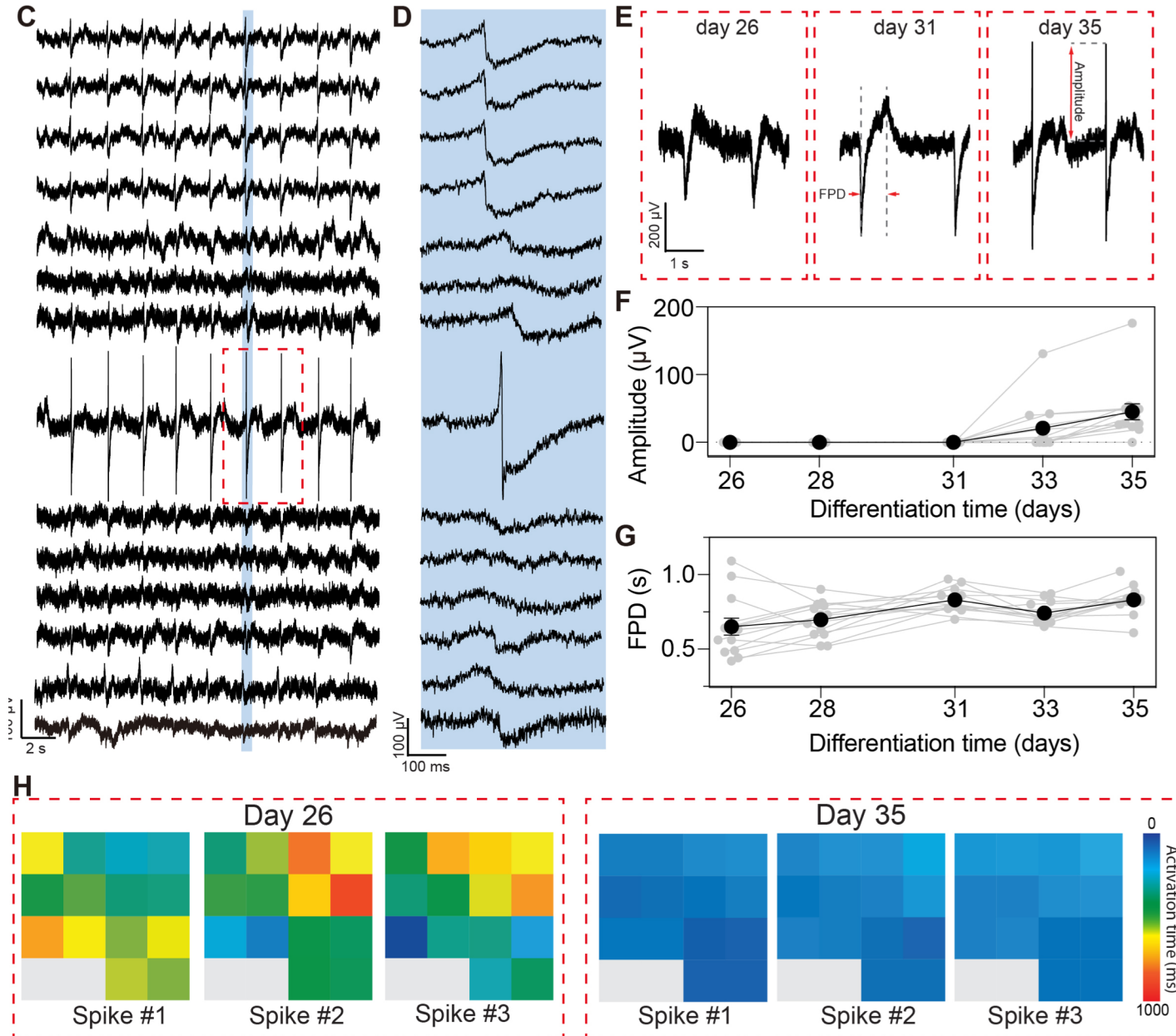
Cyborg organoids



Cyborg organoids



Tissue-wide burst dynamics during tissue development



Acknowledgements

Jia Liu Group



Paul, Le Floch (ME)

Dr. Qiang Li (BioE)

Dr. Kewang Nan (MSE)

Hao Sheng (ME)

Zuwan Lin (Chem)

Dr. Shiqi Guo (ECE)

Thomas Blum (BioE)

Tianyu Shao (Physics)

Vivi Song (Medicine)

Qinyi Chen (CS)

Xin Tang (EECS)

Gaël Ancel (CS)

Charlene de Guitaut (CS)

Collaborators:

Prof. Karl Deisseroth (Stanford, Bioengineering and Psychiatry and Behavioral Sciences)

Prof. Zhenan Bao (Stanford, Chemical Engineering)

Prof. Charles M. Lieber (Harvard, Chemistry and Chemical Biology)

Prof. Zhigang Suo (Harvard, Mechanical Engineering)

Prof. Lihua Jin (UCLA, Mechanical Engineering)

Prof. Seigiu Pasca (Stanford, Stem Cell Center, Psychiatry and Behavioral Sciences)

Prof. Kang Shen (Stanford, Biology, HHMI)