National Institutes of Health
The BRAIN Initiative®

Towards Convergence Intelligence – neuromorphic engineering and engineered organoids for intelligent systems

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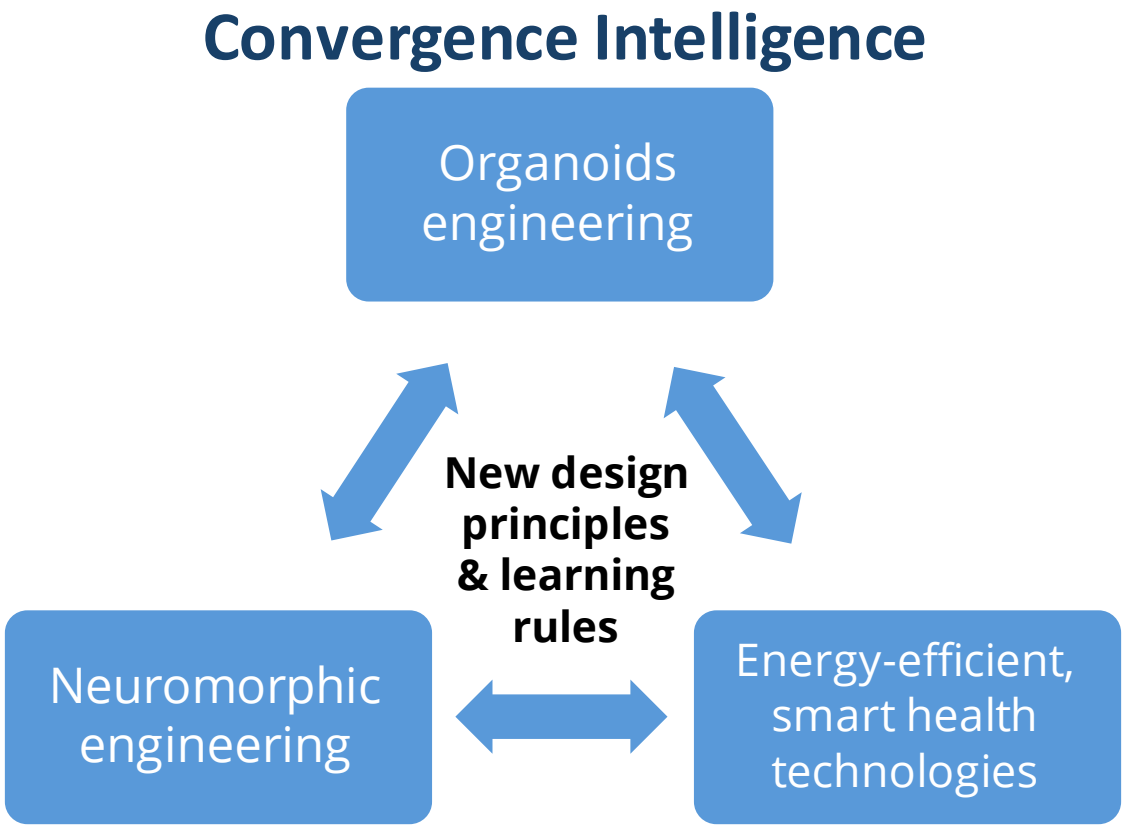
Disclaimers

- The opinions expressed in this presentation do not reflect the views of the National Institutes of Health, the Department of Health and Human Services, or the United States Government.

- Financial disclosure: none

Talk Outline



- **Funding Opportunities**
  - NSF Emerging Frontiers in Research & Innovation (EFRI): Biocomputing through EnGINeering Organoid Intelligence (BEGIN OI) – NSF 24-508
  - NIH Brain-Behavior Quantification and Synchronization (BBQS)
  - NIH Complement Animal Research and Experimentation (Complement-ARIE)
  - NIH Engineering Next-Generation Human Nervous System Microphysiological Systems – R01 & R21
  - NIH BRAIN New Technologies and Novel Approaches for Recording and Modulation in the Nervous System (R01)
  - NIH BRAIN New Concepts and Early-Stage Research for Large-Scale Recording and Modulation in the Nervous System (R21)
  - NIH BRAIN Theories, Models and Methods for Analysis of Complex Data from the Brain (TMM)
  - NSF Collaborative Research in Computational Neuroscience (CRCNS)
- **Meetings of interest**

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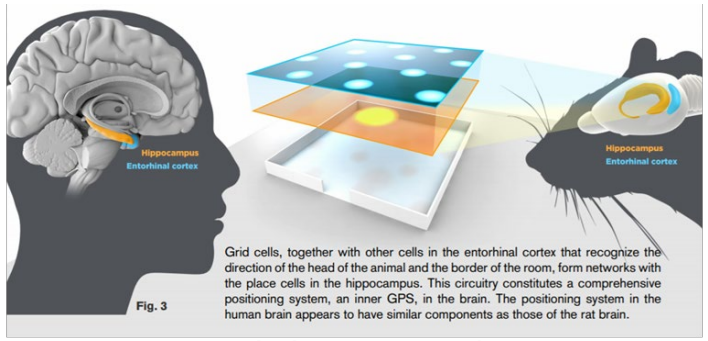
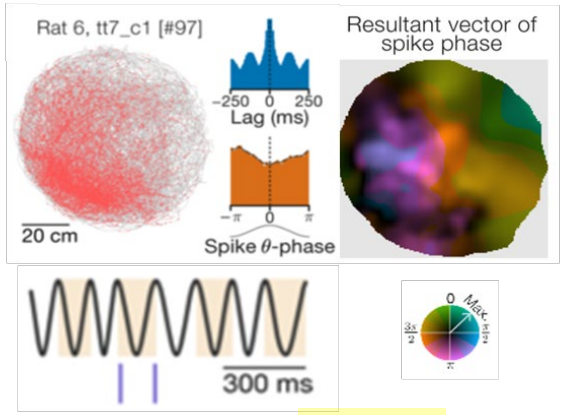
Spatial intelligence for swarms based on hippocampal dynamics (NCS FO 1835279)

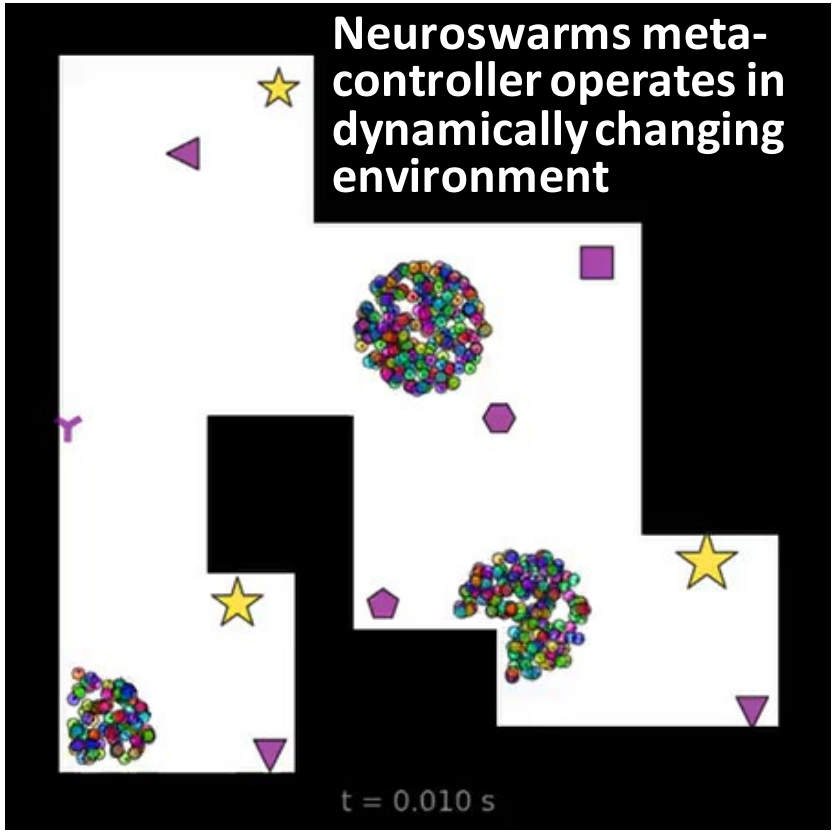


2014 Nobel Prize in Medicine –
inner GPS of the brain based on rate code



Phaser cells apply temporal code

Monaco .. Zhang (2019)
PLOS Computational Biology 15 (1) e1006741



There is no training involved

Monaco, Hwang .. (2020)
Biological Cybernetics 114, 269-284
Code: https://github.com/jdmonaco/neuroswarms
Hadzic, Hwang .. (2022) Array 15:100218
Monaco & Hwang (2022) Cognitive Computation

Rewards
Landmarks
Robotic agent
color represents phase;
dot represents place field
preferred location

Swarming is Learning

- SW reward activated: 0-20s, 80-90s
- NW reward activated: 20-40s, 60-80s
- SE reward activated: 40-60s

- Emergent self organization of phase-based spatiotemporal sequences from interagent phase-coupled attraction /repulsion dynamics

Johns Hopkins U. School of Medicine
Kavli Neuroscience Discovery Institute
Johns Hopkins Applied Physics Lab

Brain-inspired Funding Activities

2008 DARPA SyNAPSE ~102M

2013 EU 607M Euro

2014 BRAIN Initiative >3B

2015 MICrONS 100M

2018 SRC 150M

IARPA's MICrONS produced large neuroscience dataset suitable for AI

2022-23 NSF

2024-25 NSF

Emerging Frontiers in Research & Innovation (EFRI) Programs

BRAID: Brain-Inspired Dynamics for Engineering Energy-Efficient Circuits and Artificial Intelligence (~30M, 4-year)

BEGIN OI: Biocomputing through EnGINeering Organoid Intelligence (~30M, 4-year)

IBM TrueNorth (28nm)

Intel Loihi (14nm)

(G60脑智科创基地) Tianjic Chip (28nm)

1997 NSF sponsored Telluride Neuromorphic Workshop 2025

NSF funded efforts

2004 CELEST: A Center for Learning in Education, Science, and Technology (~40M, 10-year)

Boston University
Brandeis University
MIT
U. Pennsylvania

2006-2020 Temporal Dynamics of Learning Center – TDLC (~30M, >10-year)

U. California San Diego

2014 NSF ERC for Sensorimotor Neural Engineering (~40M, 6-year+)

U. Washington

2019 Present & Future Frameworks Theoretical Neuroscience Workshop

U. Texas at San Antonio

2021 NSF Expedition Award *In Vitro* Computing (15M, 7-year)

U Illinois Urban-a Champaign

2023 NSF AI Institute for Artificial and Natural Intelligence (20M, 5-year)

Columbia U.
Tuskegee U.
City U. of New York
Baylor College of Medicine
UT Health Houston…

The time is now to move this convergence intelligence field forward

NSF FY22/23 EFRI BRAID Awardees

Award #	Abbreviated Title	Principal Investigator
2223495	Optical Neural Co-Processors for Predictive and Adaptive Brain Restoration and Augmentation	Arka Majumdar [1]
2223725	Using Proto-Object Based Saliency Inspired By Cortical Local Circuits to Limit the Hypothesis Space for Deep Learning Models	Ralph Etienne-Cummings [1]
2223793	Unsupervised Continual Learning with Hierarchical Timescales and Plasticity Mechanisms	Gianfranco Doretto [1]
2223811	Rapid contextual learning in resilient autonomous systems	Thomas Cleland [1]
2223822	Neurally Inspired, Resilient Closed Loop Feedback Control of Learned Motor Dynamics	Vikash Gilja [1]
2223827	DenPro3D—Dendritic Processing of Spike Sequences in Biological and Artificial Brains	Kwabena Boahen [1]
2223839	Principles of sleep-dependent memory consolidation for adaptive and continual learning in artificial intelligence	Maksim Bazhenov [1]
2317706	Efficient Learning of Spatiotemporal Regularities in Humans and Machines through Temporal Scaffolding	Dhireesha Kudithipudi [2]
2317974	Emulating Cerebellar Temporally Coherent Signaling for Ultraefficient Emergent Prediction	Mark Hersam [2]
2318065	Brain-inspired Algorithms for Autonomous Robots (BAAR)	Junmin Wang [2]
2318081	Resilient autonomous navigation inspired by the insect central complex and sensorimotor control motifs	Floris van Breugel [2]
2318101	Neuroscience Inspired Visual Analytics	Vijaykrishnan Narayanan [2]
2318139	Fractional-order neuronal dynamics for next generation memcapacitive computing networks	Fidel Santamaria [2]
2318152	Scalable-Learning Neuromorphics	Dmitri Strukov [2]

[1] Fiscal Year 2022. [2] Fiscal Year 2023.

Neuroscience inspirations

- Predictive coding – stroke rehab
- Attention

- Electric fish inspired robotics
- Olfaction inspired sensing
- Manifold theory – motor rehab
- Dendrites – sequence detection
- Sleep states of honeybees
- Temporal Scaffolding/replay
- Cerebellar neuronal coding

- Insect central complex
- Vision to aid persons with visual impairments
- Fractional-order neuronal dynamic

Table from Hwang (2024) Biosensors 14(2), 68

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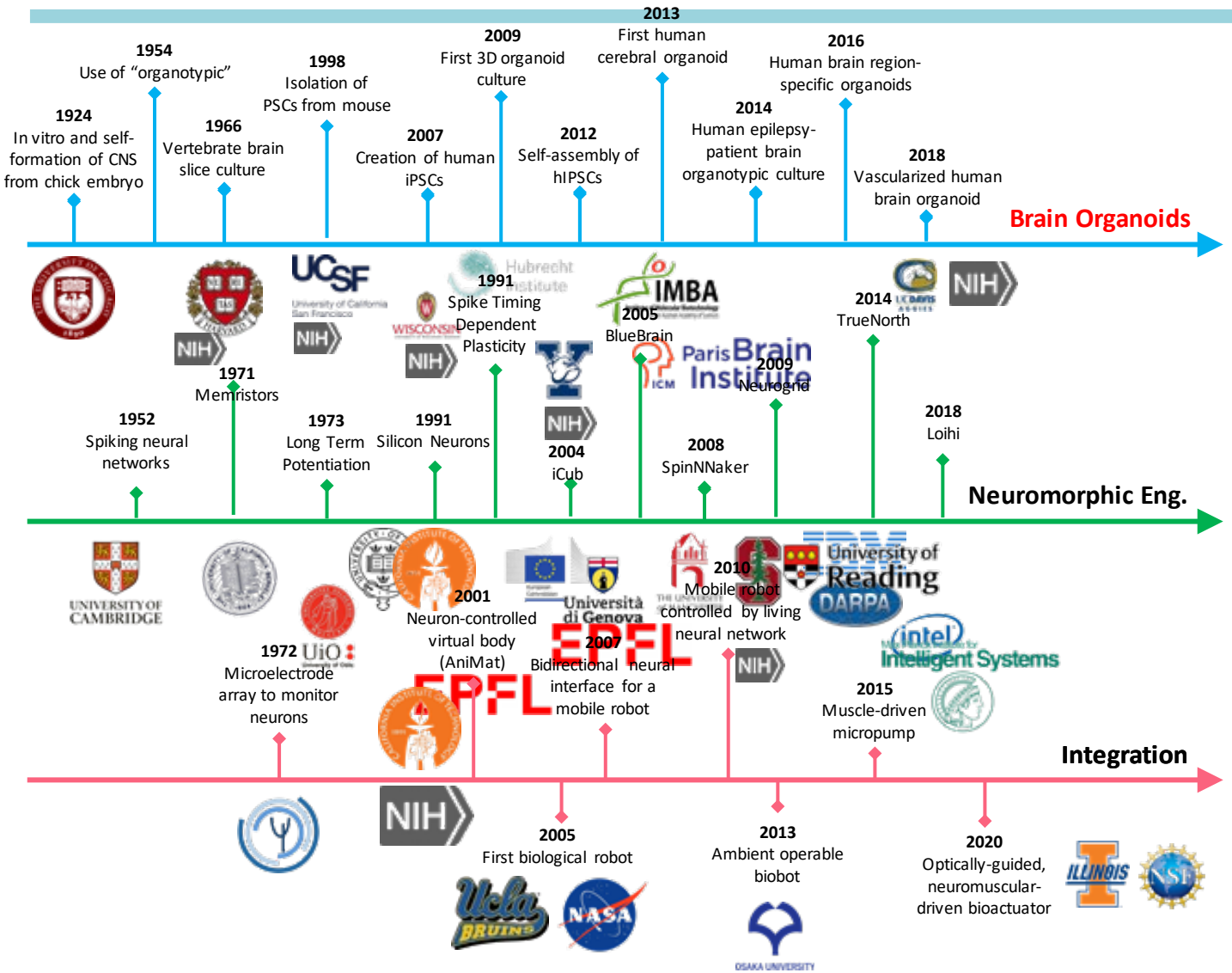
Convergence of neuromorphic engineering and engineered organoids for intelligence & health



Convergence Intelligence

Organoids engineering

[Organoids](#) are small organ-like structures usually derived from stem cells and are a complementary model system

New design principles & learning rules

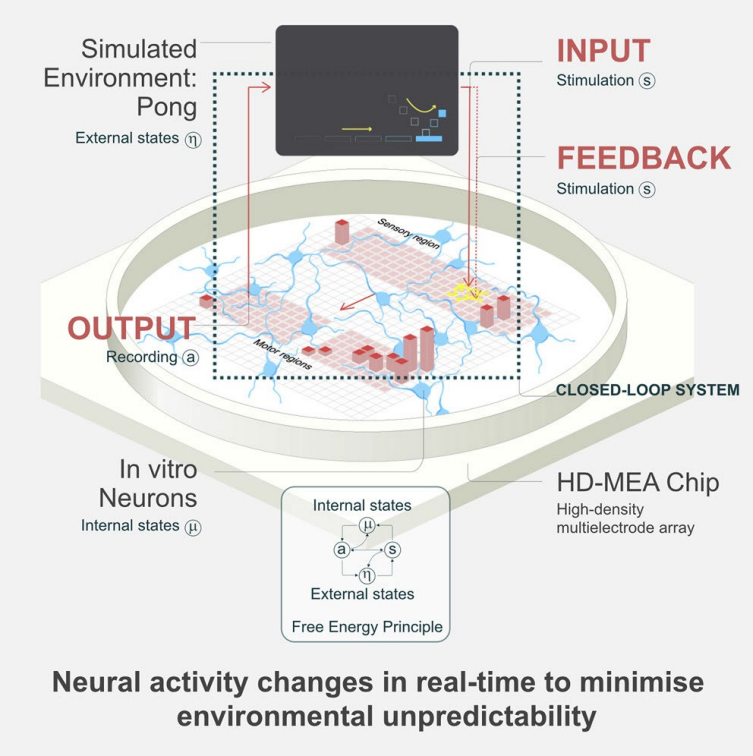
New neuromorphic algorithm, architecture

Energy-efficient, smart health technologies

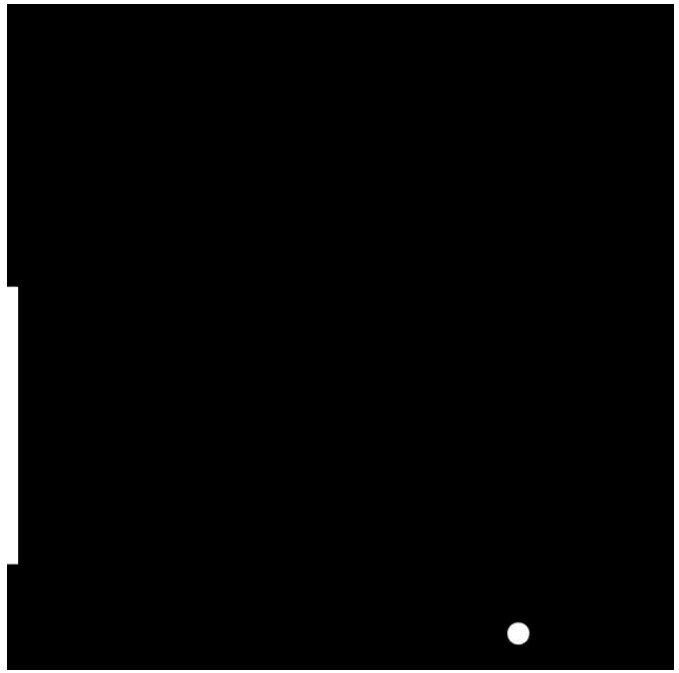
Organoids/assembloids can be a simplified model to deduce learning rules and/or a new substrate for computation

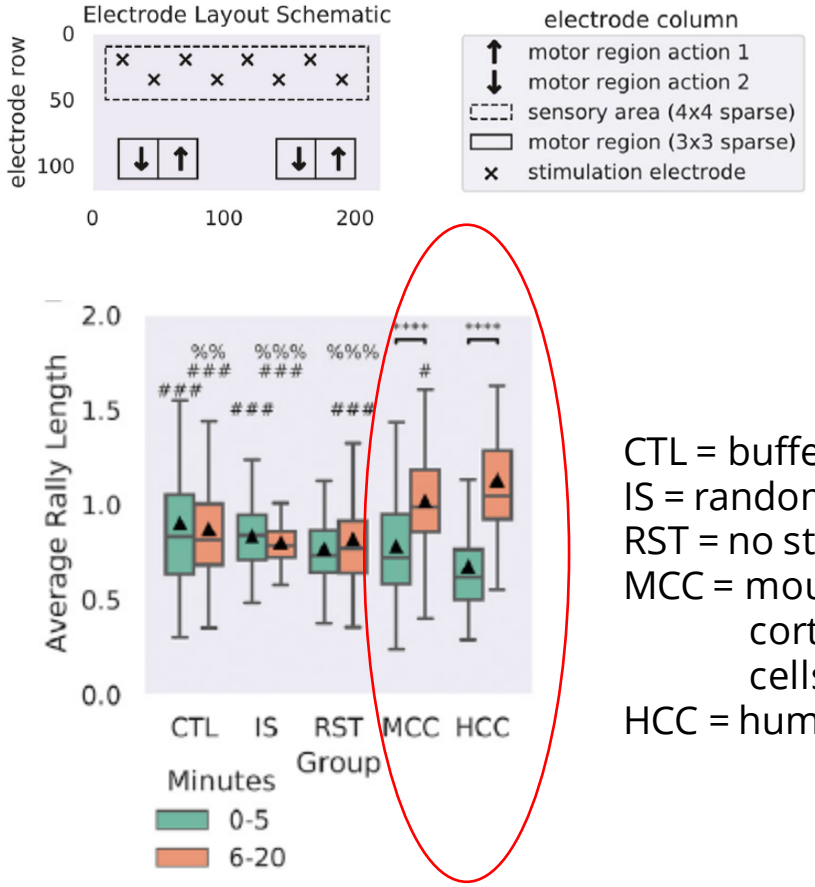
Graphics adapted from J. Kulwatno, AAAS ST&P Fellow with permission, NSF

Engineered cell culture from mice and human learn to play pong in 5 minutes



Neural activity changes in real-time to minimise environmental unpredictability





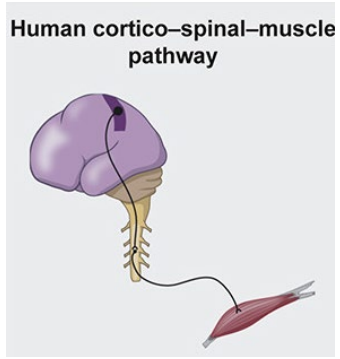
CTL = buffer only
IS = random stim
RST = no stim
MCC = mouse cortical cells
HCC = human CC

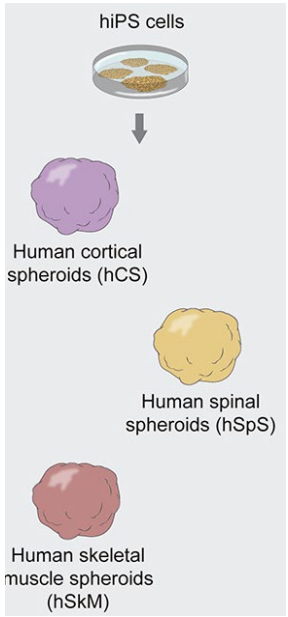
Cortical Lab
RMIT U.
Monash U.

U. Manchester
CIFAR

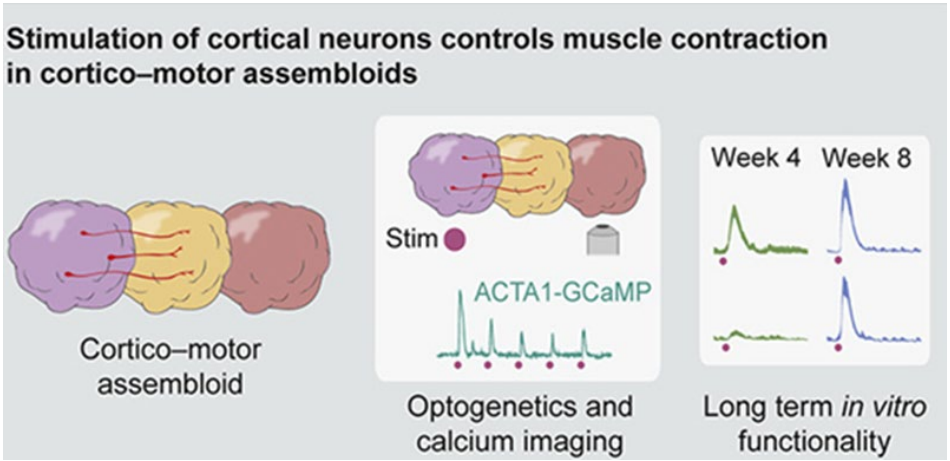
Figures from Kagan, B. J.,... & Friston, K. J. (2022) Neuron ***110(23)3952-3969***

Stimulation of cortical neurons control muscle contraction in cortico-motor assembloid





- Stimulation of cortical neurons controls skeletal muscle in three-part assembloid
- Cellular and functional changes in cortico-motor assembloids were maintained long term (10 weeks post fusion)
- Self-assembly of 3D assembloids can be used to understand development and disease



Sequence 1

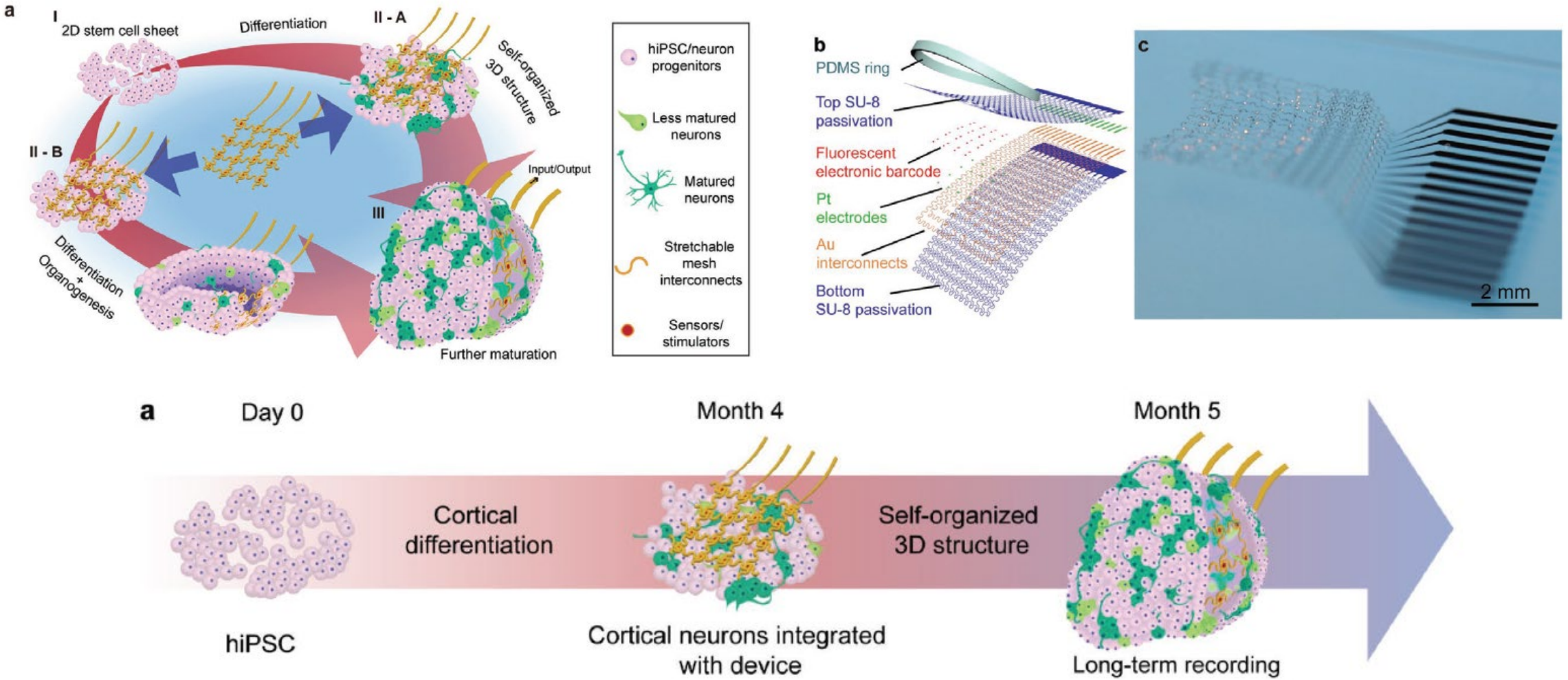
Figures adapted from Andersen … Pasca 2020 Cell 183 (7) 1913-1920

https://www.pascalab.org/

NIH BRAIN Award R01MH107800

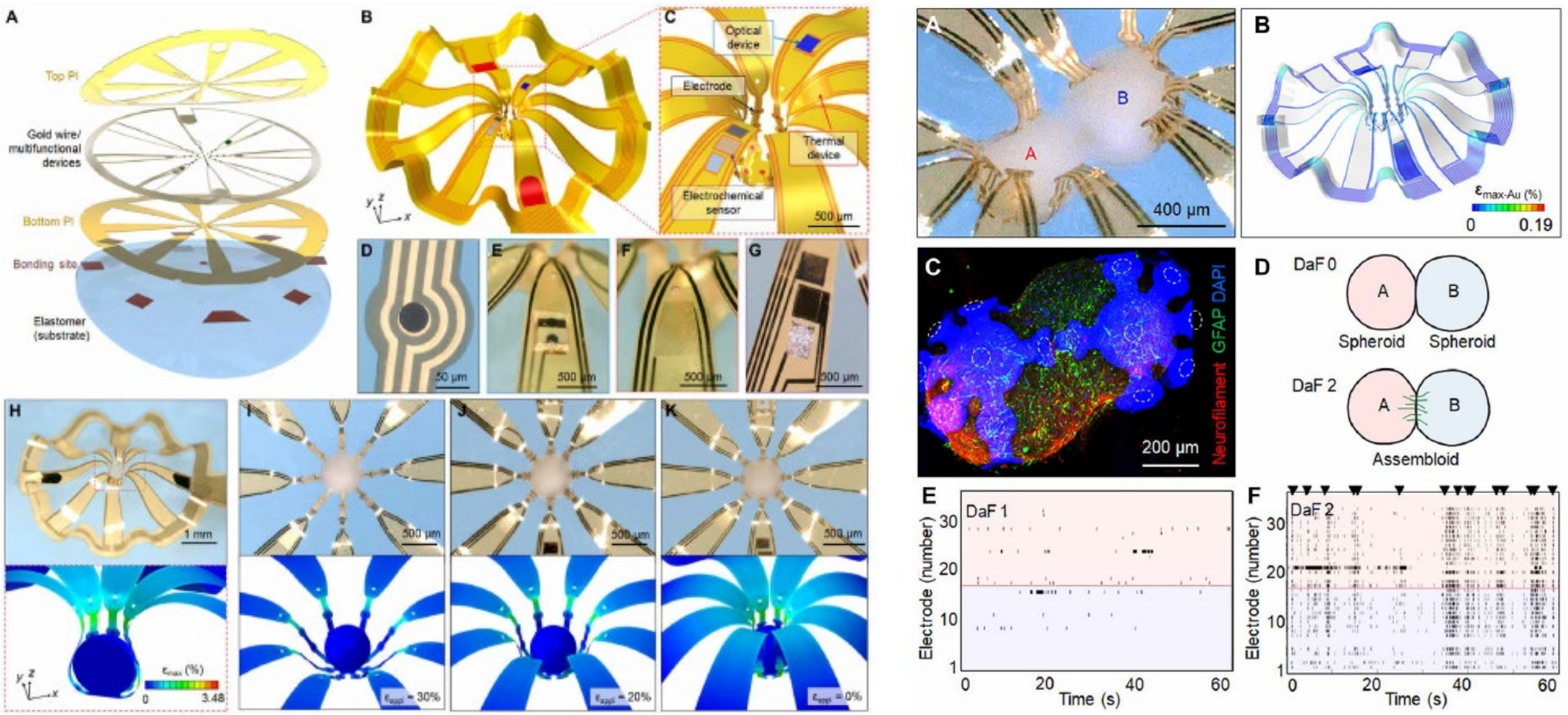
Stanford

Stretchable Mesh Nanoelectronics for 3D Single-Cell Chronic Electrophysiology from Developing Brain Organoids



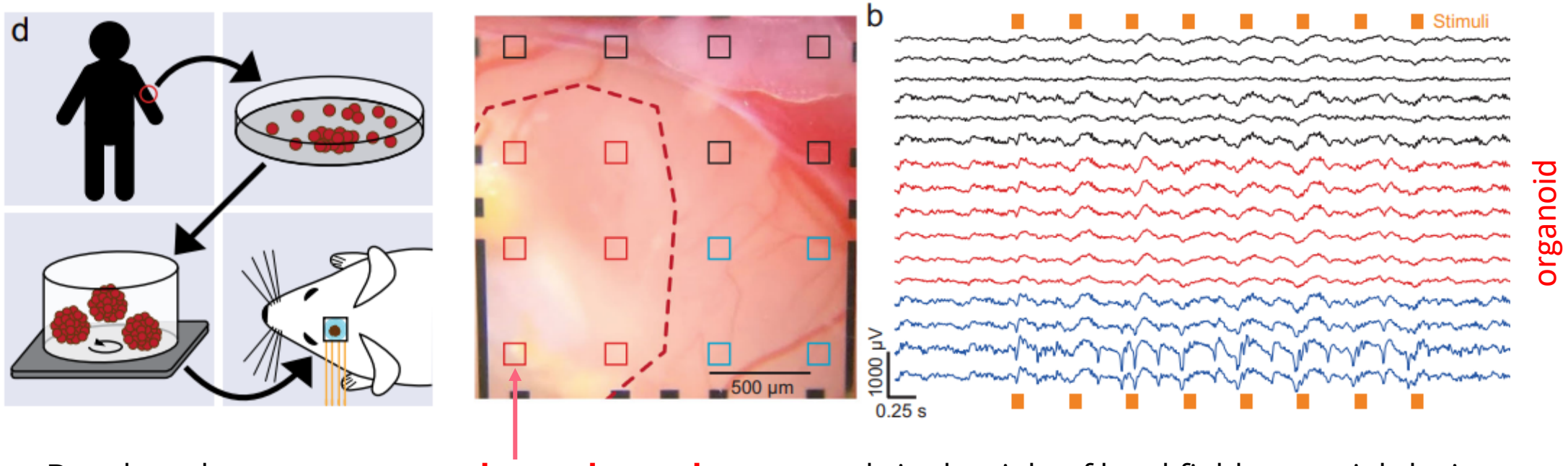
Le Floch … Jia Liu. 2022 Adv. Mater. 34. MH123948-01

Three-dimensional, multifunctional neural interfaces for cortical spheroids and engineered assembloids



Park *et al.*, *Sci. Adv.* 2021; **7** : eabf9153 17 March 2021

Human organoid implanted in mice reveal functional connection with visual cortex & organoid vascularization



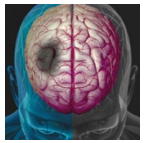
- Developed transparent **graphene electrode** to record single trials of local field potential during visual stimulation with white LED on contralateral eye
- Observed vascularization of the implanted organoid in the retrosplenial cortex
- Combination of stem cell and neurorecording technologies shows promise for modeling disease, personalized treatment, evaluation of organoid's potential to restore lost function …

Figures adapted from Wilson … Kuzum 2022 Nature Comm 13: 7945

NIH BRAIN Award R21EY03727,
R01MH111359, R01DA050159, DP2EB030992

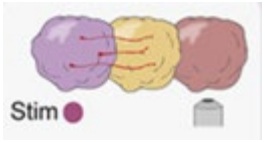
U. California
San Diego

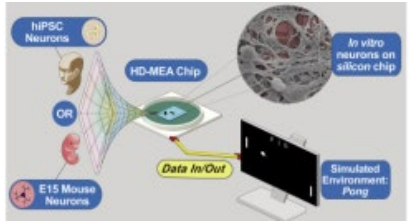
Convergence Intelligence is ripe for exploration



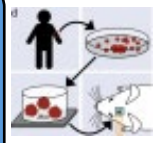
Do: organoid for neuro-restoration

Pasca: Motor contraction in cortico-motor assembloid





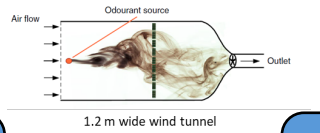
Assembloids engineering (musculoskeletal, brain)



Kuzum: Functional integration of human organoid in mice & vascularization

Monaco: Phaser cell based meta-controller for robotic swarms

Cleland: Olfaction-based chemical sensing

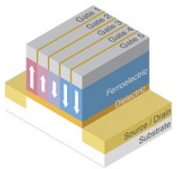


1.2 m wide wind tunnel

Adaptive robotics …

New neuromorphic algorithm, architecture, learning systems

Energy-efficient, smart health technologies for neural/biomedical engineering



Boahen: Dendrite-based nanoscale devices

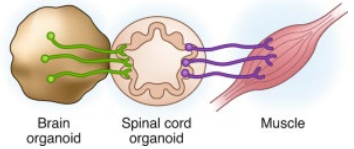
Opportunity: organoid-informed, nervous-system inspired neuromorphic technologies

- Neuromorphic engineering is showing promise **beyond** extreme power efficiency
- Organoids and assembloid are emerging as promising design platform (new substrate for computation) and model organism systems
- Yet, organoid/assembloid research, neuromorphic engineering, and neuromodulation are currently on **parallel independent** research paths
- Deliberate effort across government, industry, and research communities is poised to accelerate the promise of convergence intelligence

An envisioned future for convergence intelligence for energy efficient, resilient, health technologies







Assembloids engineering (visceral, musculoskeletal, brain) - personalized

New design principles & learning rules

New neuromorphic algorithm, architecture, learning systems - adaptive | efficient

Energy-efficient, smart health technologies for neural/ biomedical engineering and behavior to improve patient care

Many challenges ahead

- ❑ Replicability in organoid connectome & dynamics over connectome
- ❑ Integration of brain organoids with visceral and/or musculoskeletal organoids
- ❑ Long term memory
- ❑ Vascularization
- ❑ Infrastructure for on-demand assembloid factory for closed-loop design-driven integration

- Personalized brain-body interface technologies
- Personalized rehabilitation following stroke or other neurological disorders

FY24-25 Emerging Frontiers in Research & Innovation (EFRI): Biocomputing through EnGINeering Organoid Intelligence (BEGIN OI) NSF 24-508

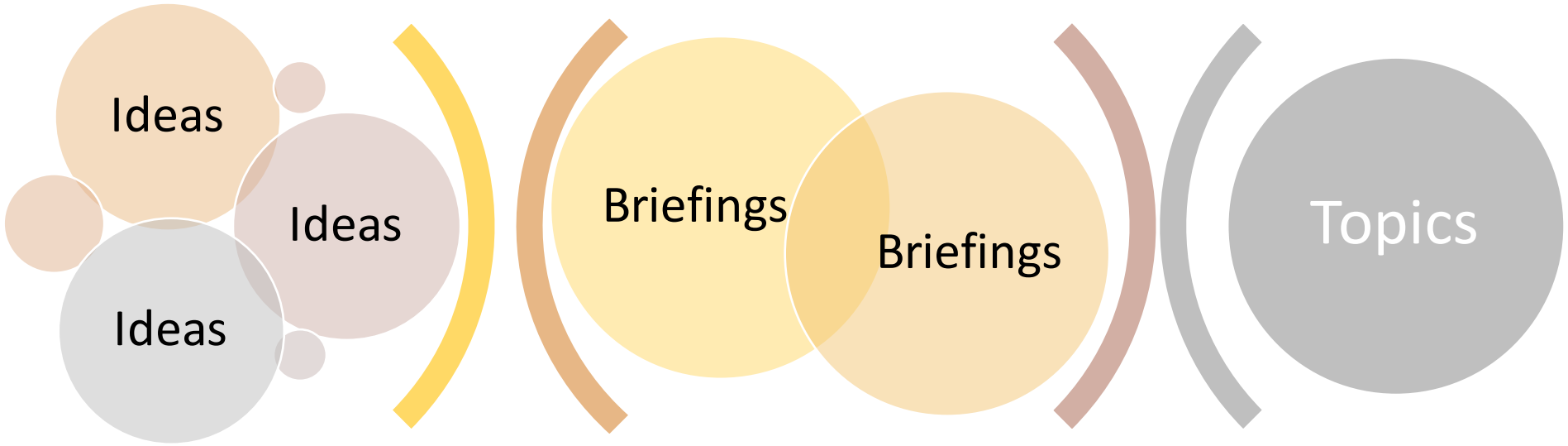
- Objective of BEGIN OI is to harness the novel discoveries and advances in biological sciences, engineering, material sciences, and computer sciences toward designing 3D in vitro biological systems that are capable of information processing and actuation
- BEGIN OI supports foundational and transformative research to advance the design, engineering, and fabrication of organoid systems that are capable of processing information dynamically while interfacing with non-living systems.
- Letter of intent required, due 9/12/2024
- Full proposal due 12/24/2024
- Team Proposals Only: 3-5 PIs/Co-PIs
- Up to 4 Years in duration and $2M over grant lifetime including direct and indirect
- Webinar: https://www.nsf.gov/attachments/308669/public/EFRI-BEGIN-OI-webinar-FY2024.pdf
- Questions: contact efri2024-2025@nsf.gov

https://new.nsf.gov/funding/opportunities/emerging-frontiers-research-innovation-efri

Topic selection for the Emerging Frontiers in Research Innovation (EFRI) Program – Biennial Global Competition

https://beta.nsf.gov/funding/opportunities/efri-topic-ideas-request

Next submission for FY26/27 topics likely due in Fall 2024



Historically, 30M per topic over two fiscal years.
Each project is 2 M over 4 years.

https://www.nsf.gov/eng/efma

NIH Funding Opportunities

Brain Behavior Quantification & Synchronization (BBQS)

Appropriate for low-power, data-efficient, neuromorphic approaches

Complement Animal Research and Experimentation (Complement-ARIE)

Appropriate for organoids / assembloids as complementary models systems

The Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN) Initiative

Appropriate for high-risk/high-reward neuromodulation, recording, and stimulation technologies

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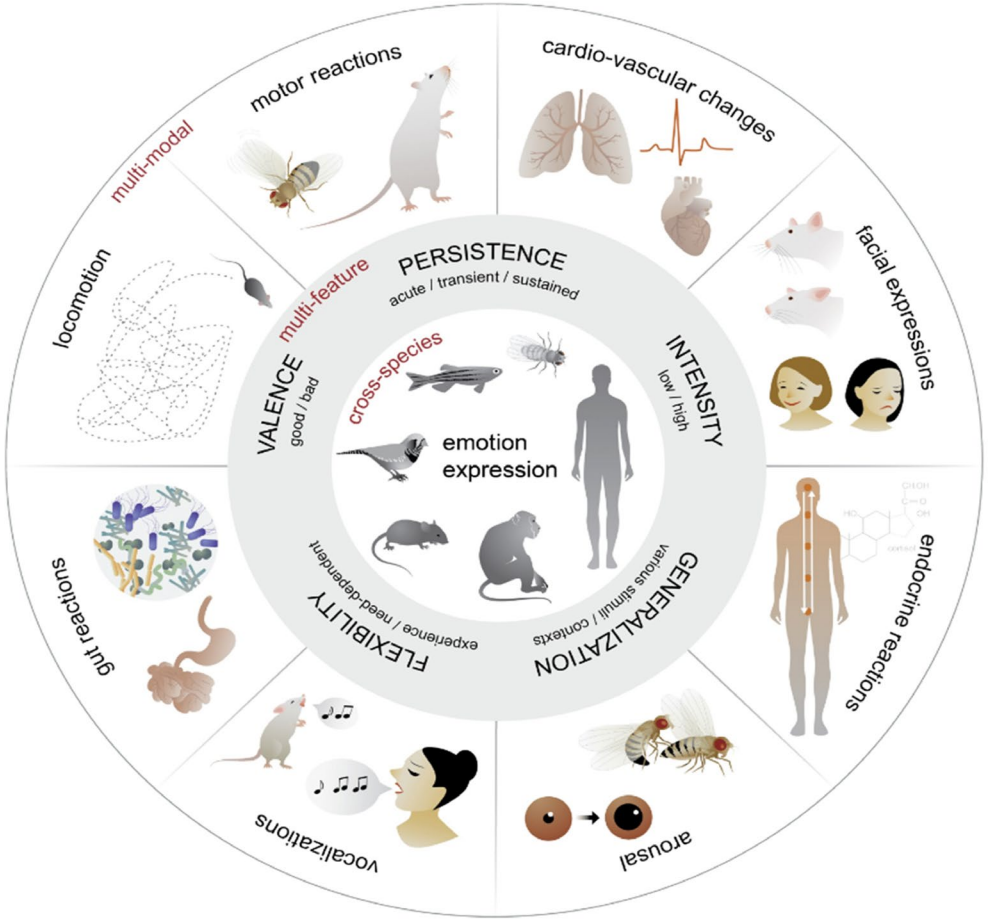
Brain Behavior Quantification and Synchronization (BBQS)

- A set of integrated funding opportunities with the goal of:
  - Measuring behavior through use of sensors & brain recordings
  - Development of computational models
  - Ultimately informing closed loop therapies
- Related NOFOs:
  - RFA-MH-23-270 and NOT-MH-23-115 Informatics tools
  - RFA-DA-24-042 Organismal Studies
  - RFA-MH-23-335 Human Studies



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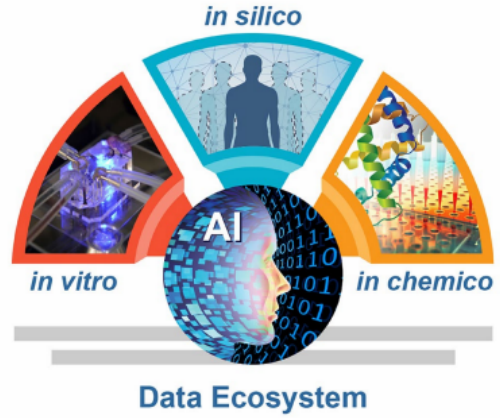
Complement Animal Research and Experimentation (Complement-ARIE)

Purpose: To catalyze the development, standardization, validation and use of **human-based new approach methodologies (NAMs)** that will transform the way we do basic, translational, and clinical sciences

Goals:

1. Better model and **understand human health and disease** outcomes **across diverse populations**.
2. Develop NAMs that **provide insight into specific biological processes** or disease states.
3. Validate mature NAMs to **support regulatory use** and standardization.
4. Complement traditional models and **make biomedical research more efficient and effective**.



- Scientific Needs: *Innovate and Transform*
  - ***Chronicity***
  - ***Neuroscience***
  - ***Personalized health***
  - ***Cross-disease pathogenesis***
  - ***Population diversity***

Projected Timeline and Budget:

2025	2026	2027	2028	2029	2030	2031	2032	2033	2034
$35M	$35M	$40M	$40M	$40M	$40M	$40M	$40M	$40M	$40M

NIH Funding Opportunities

- **Engineering Next-Generation Human Nervous System Microphysiological Systems (MPS)**
  PAR-23-046 – R01 Clinical Trial Not Allowed
  - Supports developing next-generation human cell-derived MPS and related assays that replicate complex nervous system architectures and physiology with improved fidelity over current capabilities. Supported projects will be expected to enable future studies of complex nervous system development, function, and aging in healthy and disease states.
  - **Application due dates**: June 5, 2024; October 5, 2024; February 5, 2025; June 5, 2025; October 5, 2025
- **Engineering Next-Generation Human Nervous System MPS**
  PAR-23-047 – R21 Clinical Trial Not Allowed
  - The R21 grant mechanism is intended to encourage exploratory/developmental research by providing support for the early and conceptual stages of project development. **High risk/high reward projects that lack preliminary data may be most appropriate for this FOA.**
  - **Application due dates**: June 16, 2024; October 16, 2024; February 16, 2025; June 16, 2025; October 16, 2025

BRAIN Funding Opportunities – Neuromodulation Technologies

- **New Technologies and Novel Approaches for Recording and Modulation in the Nervous System**

  RFA-NS-24-004 – R01 Clinical Trial Not Allowed

  - Proof-of-concept testing and development to enable transformative understanding of dynamic signaling in the nervous system. Proposed technologies should be compatible with experiments in behaving animals and should include advancements that enable or reduce major barriers to hypothesis-driven experiments.
  - **Application due dates:** October 1, 2024; June 02, 2025; January 20, 2026

- **New Concepts and Early-Stage Research for Large-Scale Recording and Modulation in the Nervous System**

  RFA-EY-21-001 – R21 Clinical Trial Not Allowed

  - Unique and innovative technologies including new and untested ideas that are in the initial stages of conceptualization
  - **Application due date:** October 27, 2023

Contact: BRAIN-FOAs@nih.gov or grace.hwang@nih.gov

BRAIN Funding Opportunities – Integrated Approaches

- **Theories, Models and Methods for Analysis of Complex Data from the Brain (TMM)**

  RFA-DA-23-039 – R01 Clinical Trial Not Allowed

  - Supports development of theories, computational models, and analytical tools to derive understanding of brain function from complex neuroscience data. Proposed projects could develop tools to integrate existing theories or formulate new theories; conceptual frameworks to organize or fuse data to infer general principles of brain function; multiscale/multiphysics models to generate new testable hypotheses to design/drive future experiments; new analytical methods to substantiate falsifiable hypotheses about brain function
  - **Application due dates:** September 12, 2024

Contact: BRAINTheoriesFOA@mail.nih.gov

Collaborative Research in Computational Neuroscience (CRCNS)

- Computational neuroscience, inclusively defined

  encompassing many approaches and goals; related to biological processes; disease and normal function; theory, modeling, and analysis; implications for biological and engineered systems

- ***Innovative, collaborative, and interdisciplinary***

  to make significant advances on important hard problems, and to develop new research capabilities

The program considers **Research Proposals** describing collaborative projects that bring together complementary expertise on interdisciplinary challenges; and **Data Sharing Proposals** to support preparation and deployment of data and other resources, in a manner that responds to the needs of a broad community. US domestic and international collaborations are welcome. Opportunities for ***parallel international funding*** (Germany, France, Israel, Japan, Spain, and multilateral).

Collaborative Research in Computational Neuroscience (CRCNS)

1. National Institute on Deafness and other Communication Disorders
2. National Institute of Biomedical Imaging and Bioengineering
3. National Center for Complementary and Integrative Health
4. National Institute of Child Health and Human Development
5. National Institute of Neurological Disorders and Stroke
6. National Institute on Alcohol Abuse and Alcoholism
7. National Institute of Mental Health
8. National Institute on Drug Abuse
9. National Institute of Aging
10. National Eye Institute

For more information about NIH participation, contact Dr. Siavash Vaziri at siavash.vaziri@nih.gov
For more information about DoE participation, contact Dr. Robinson Pino at Pino@science.doe.gov

Meetings of interest

- BRAIN Special Session: NeuroAI – June 18, 2024, Bethesda, MD
- SfN Symposium - Advancing Organoids – 5-9 Oct 2024, Chicago, IL
- Neuromorphic Neurotech/Biotech Workshop – 21-22 October 2024, DC Area (hybrid)
- BRAIN NeuroAI Workshop – mid-November 2024, Bethesda, MD
- Email me at grace.hwang@nih.gov and I can add you to mailing list.

Funding Opportunities

Brain Behavior Quantification & Synchronization (BBQS)

Complement Animal Research and Experimentation (Complement-ARIE)

The Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN) Initiative

Questions

Grace.Hwang@nih.gov

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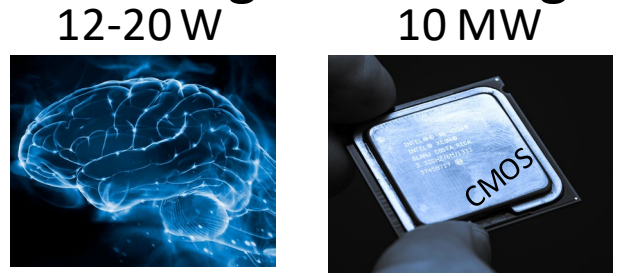
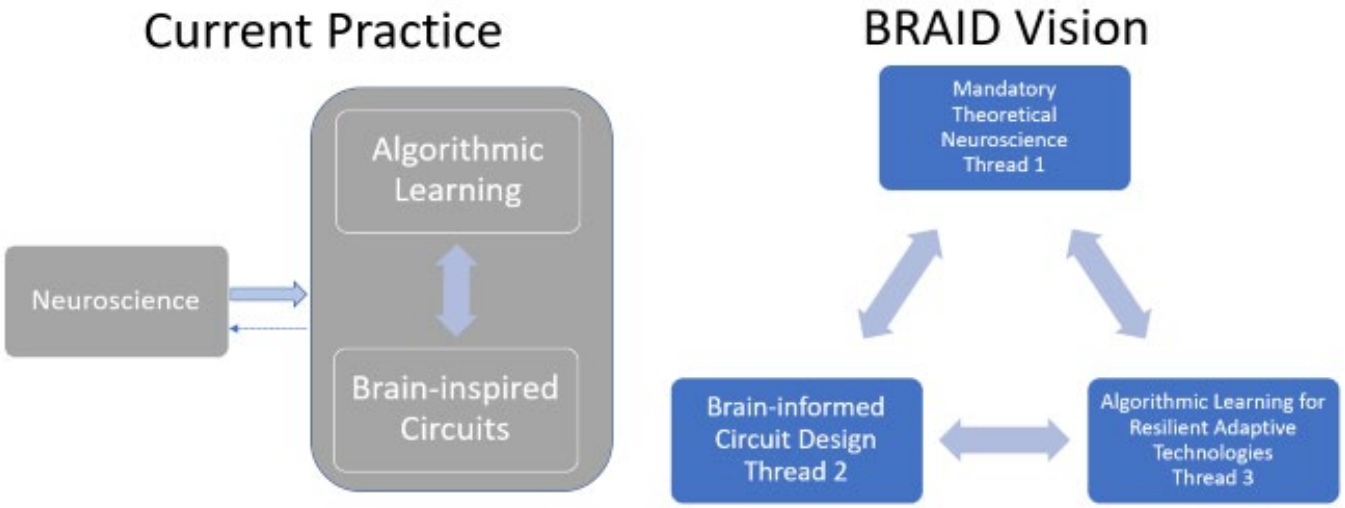
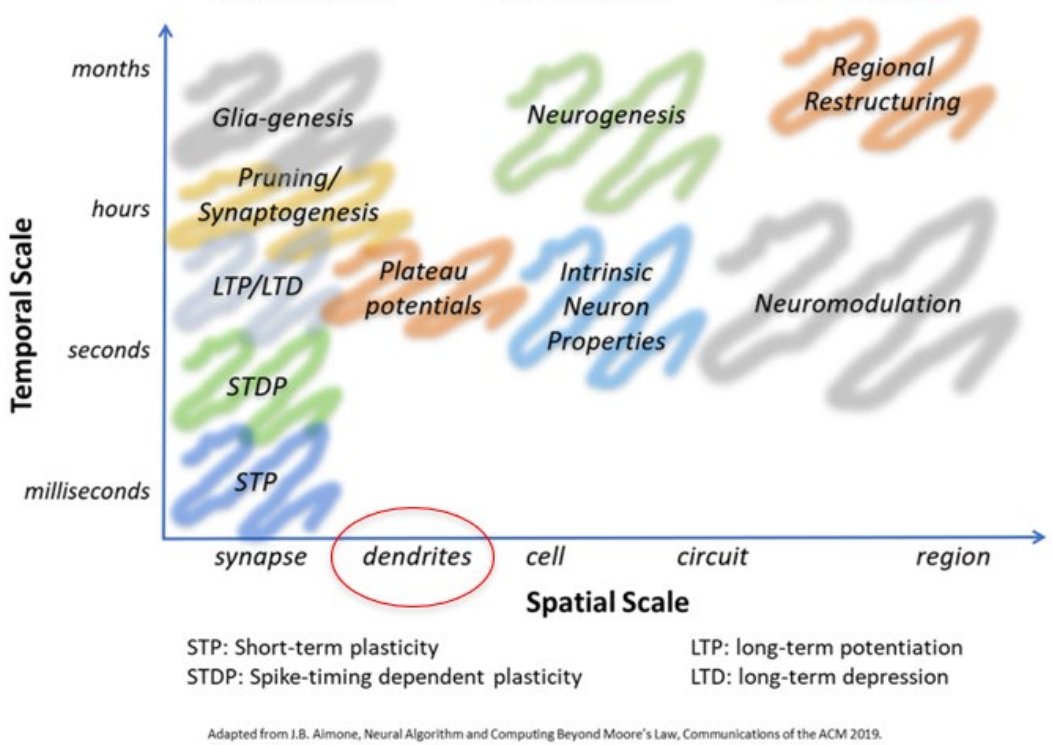
The BRAIN Initiative®

NSF EFRI FY22-23 Topic: Brain-Inspired Dynamics for Engineering Energy-Efficient Circuits and Artificial Intelligence (BRAID)

- BRAID supports fundamental research toward understanding and applying dynamical neuroscience to leverage the unique features of biological learning and decision-making for AI systems. 30 M. 2 M per award.
  - Energy-efficient
  - Data-efficient
  - Flexible
  - Continual learning from few examples

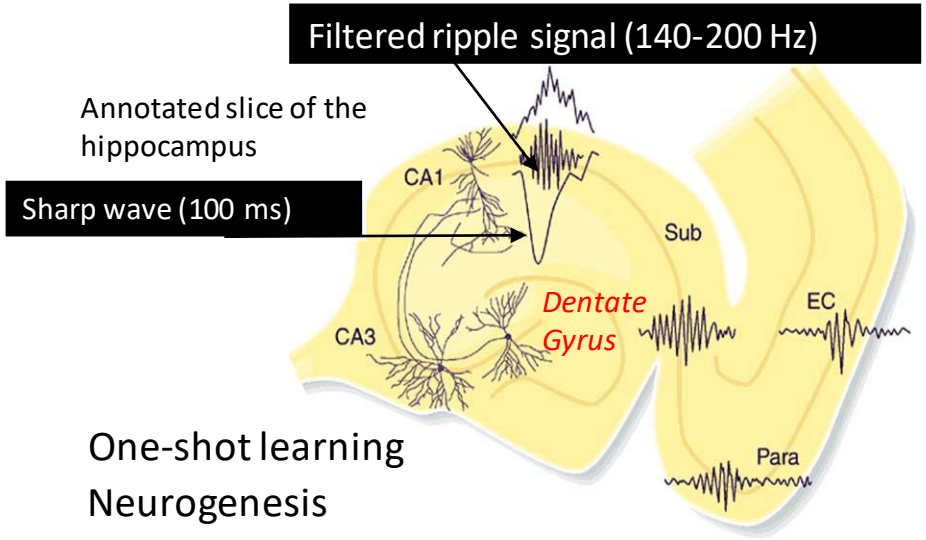




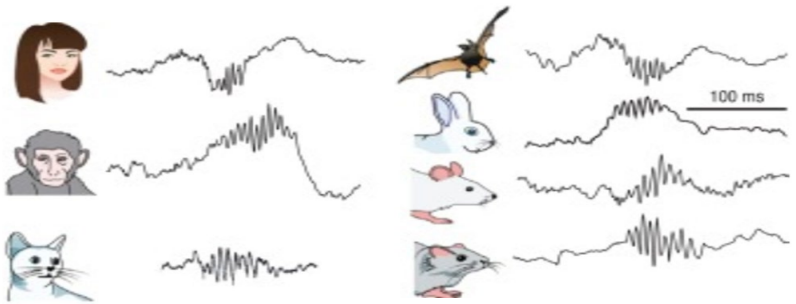


https://www.nsf.gov/pubs/2021/nsf21615/nsf21615.htm

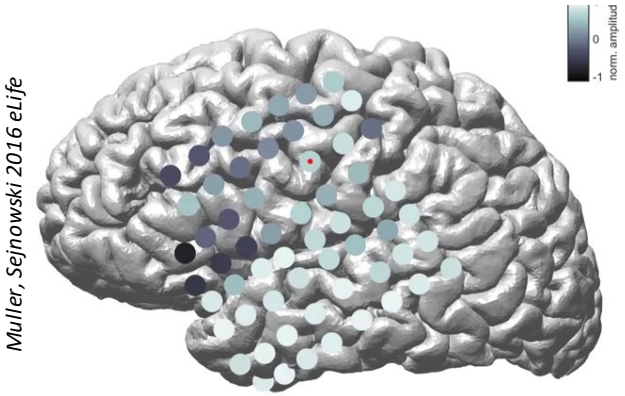
Recent insights from the US BRAIN Initiative can fuel new neuromorphic engineering, NeuroAI algorithms, and other brain-inspired technologies



One-shot learning
Neurogenesis



Dotson 2018; Pfeiffer & Foster 2013; Pfeiffer & Foster 2015 ; Pfeiffer 2020, Buzsáki G. 2015 Hippocampus



Muller, Sejnowski 2016 eLife

Conventional wisdom

New insight: Glia involved in plasticity

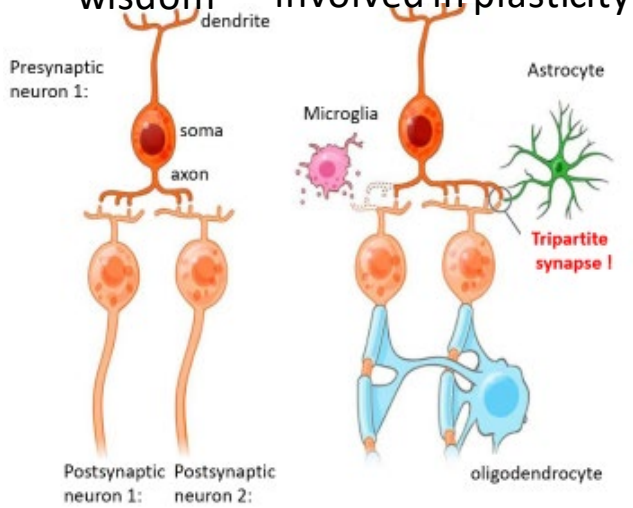


Fig modified from Pan and Monje (2020) J. Neuroscience

Dendrites within a neuron can apply different learning rules

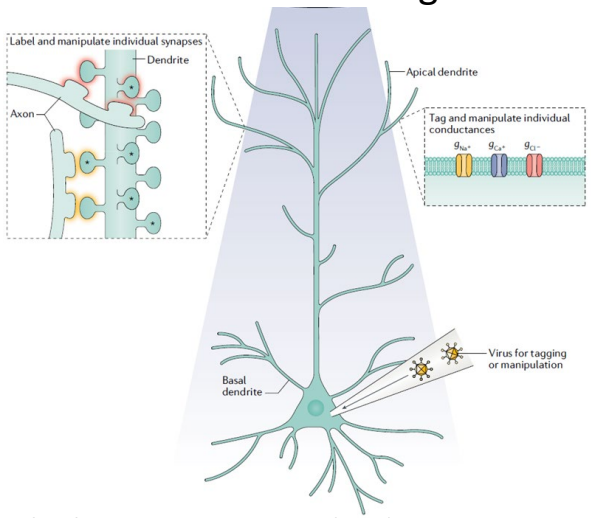
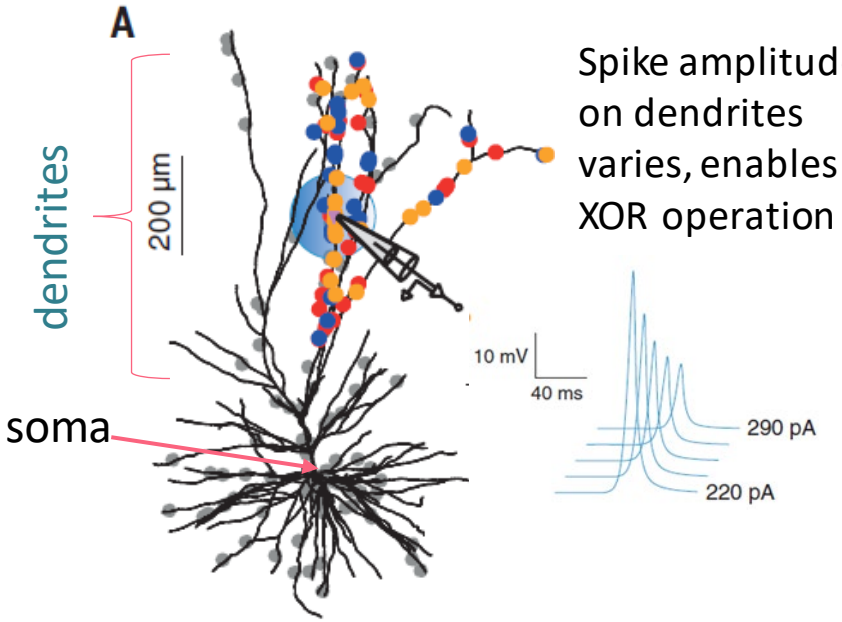


Fig modified from Poirazi and Papoutsi (2020) Nature Reviews Neuroscience



Spike amplitude on dendrites varies, enables XOR operation

Gidon (2020) Science 367