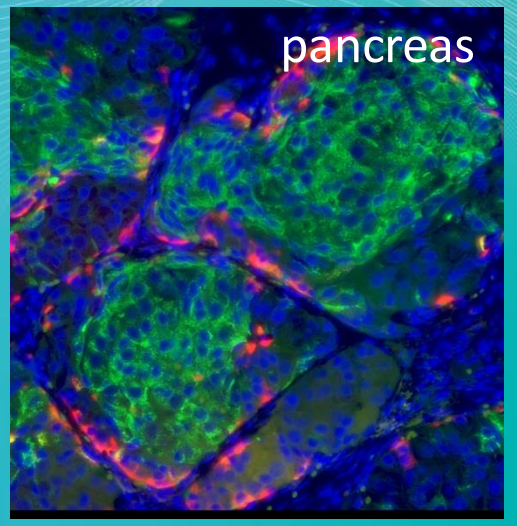
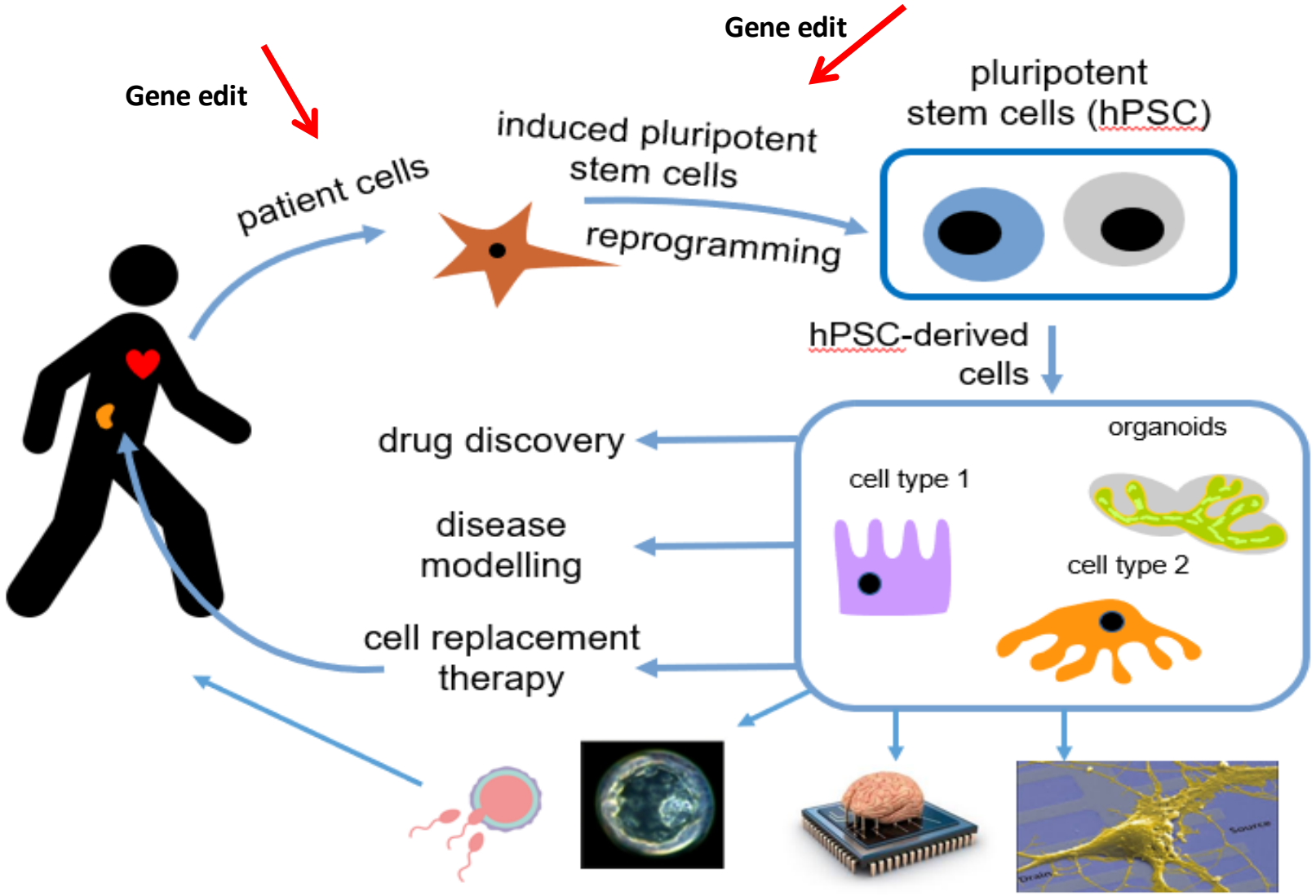
Challenges of Organoid Application



Outline for Today

1. Stem Cells as Individual Avatars
2. Brain Organoids – status and models
3. Embodyment of brain organoids
4. Chimeras

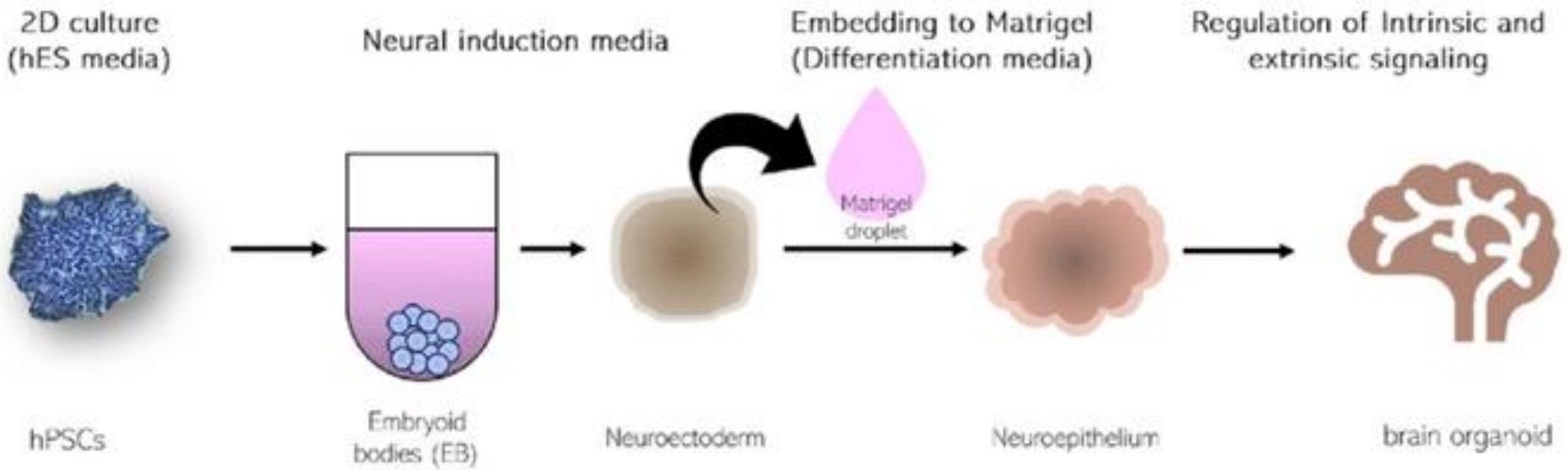
Digital cell identities



Modify genotype, enhance, dishenhance, add and delete phenotype features

Experiment with organoid to assess effects on donor tissue

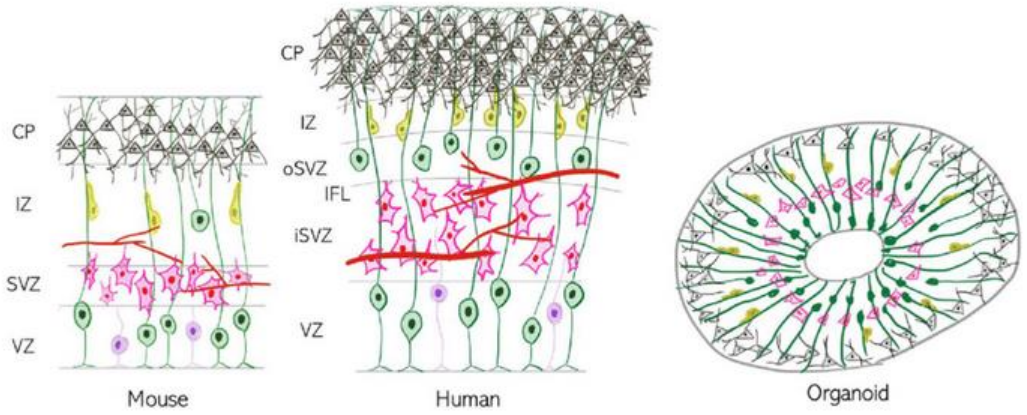
How to make a brain organoid



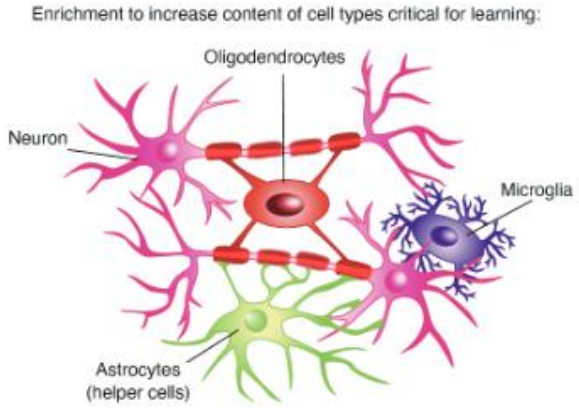
Jürgen Knoblich, IBMA

Jeong et al., 2020

How does a brain organoid compare



Jeong et al., 2020



	Frontier supercomputer (June 2020)	Human brain	Current laptop, e.g., Apple MacPro M1max 14"
Speed	1.102 exaFLOPS	~1 exaFLOPS (estimate)	10 teraFLOPS
Power requirements	21 MW	10-20 W	10-100 W
Dimensions	680 m^2 (7,300 sq ft)	1.3-1.4 kg (2.9-3.1 lb)	1.5 kg
Cost	$600 million	Not applicable	~$3,000
Cabling	145 km (90 miles)	850,000 km (528,000 miles) of axons and dendrites	Not known
Memory	75 TB/s read / 35 TB/s write / 15 billion IOPS flash storage system, along with the 700 PB Orion site-wide Lustre file system	2.5 PB (petabyte)	32 GB Upgradable 64 GB
Storage	58 billion transistors	125 trillion synapses, which can store 4.7 bits of information each	1 TB RAM Upgradable 8 TB

Smirnova et al., 2023

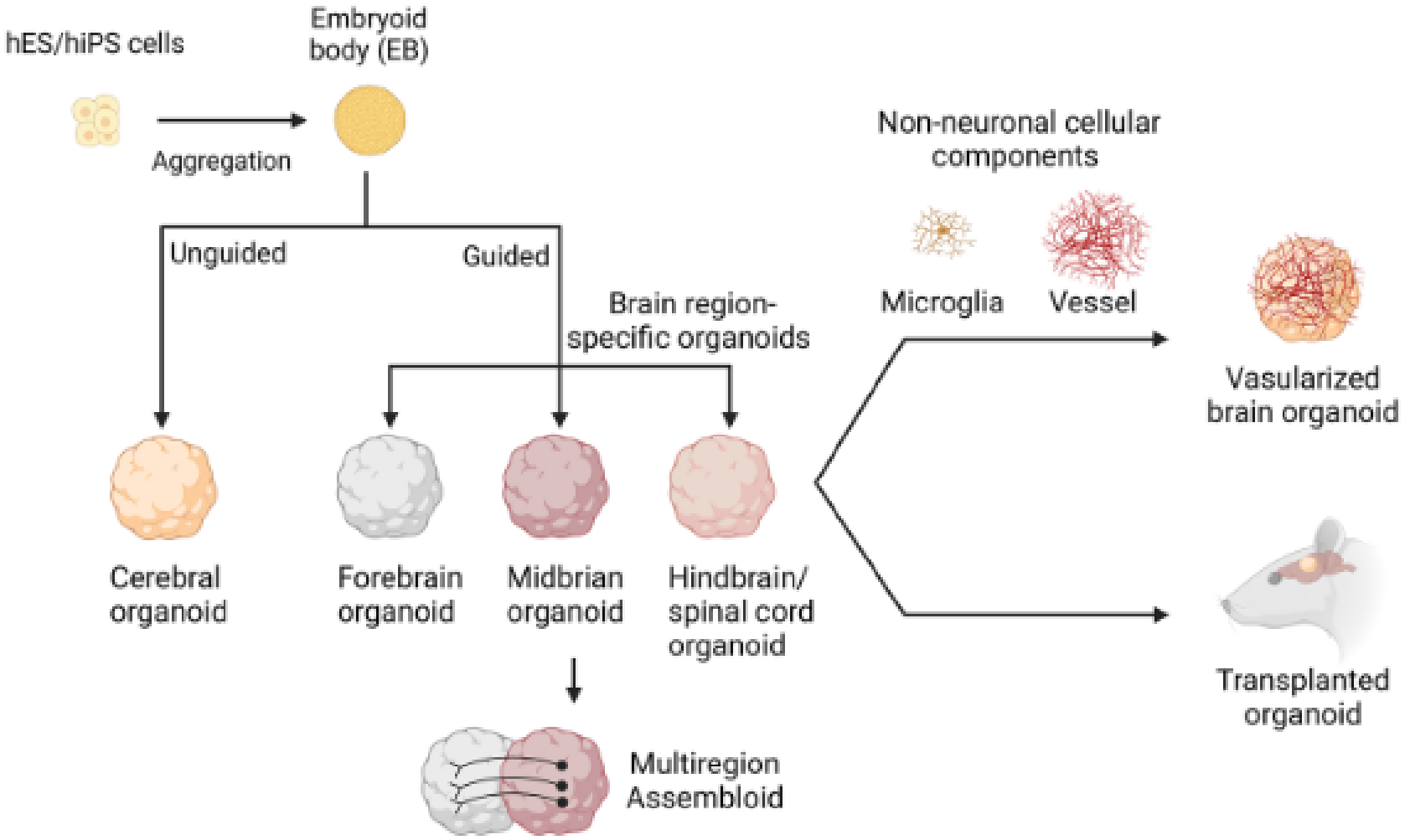
Increase cell number and diversity

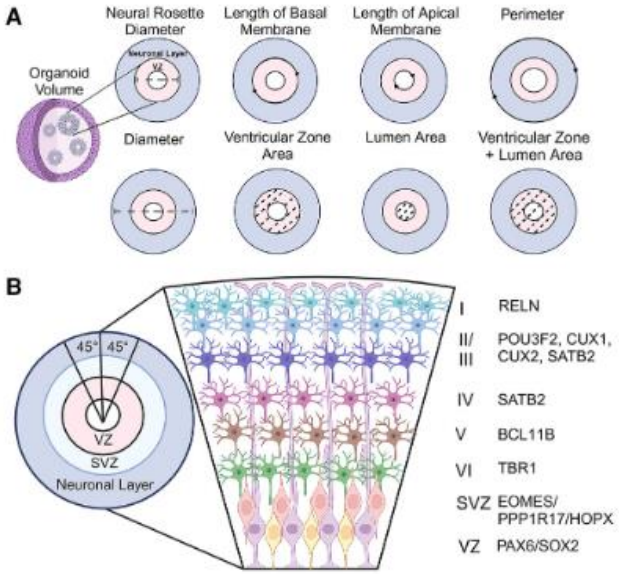
Induce synapticpruning and increase compexity

Increase conductivity by myelinazation

Microphysiological systems to modulate and measure activity

Improving complexity and reproducibility

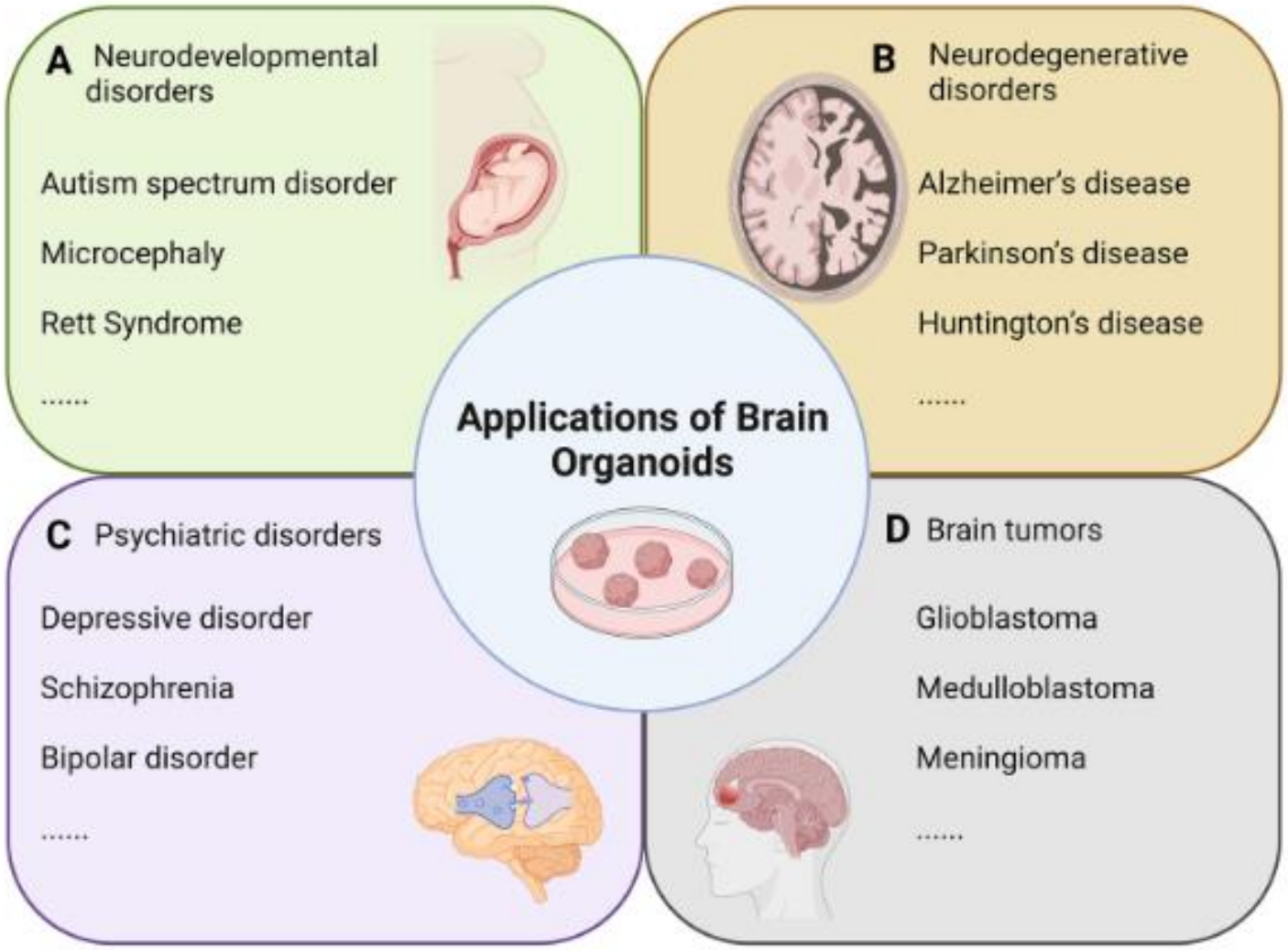




Measurements:
Morphology
Molecular
Metabolic
Functional

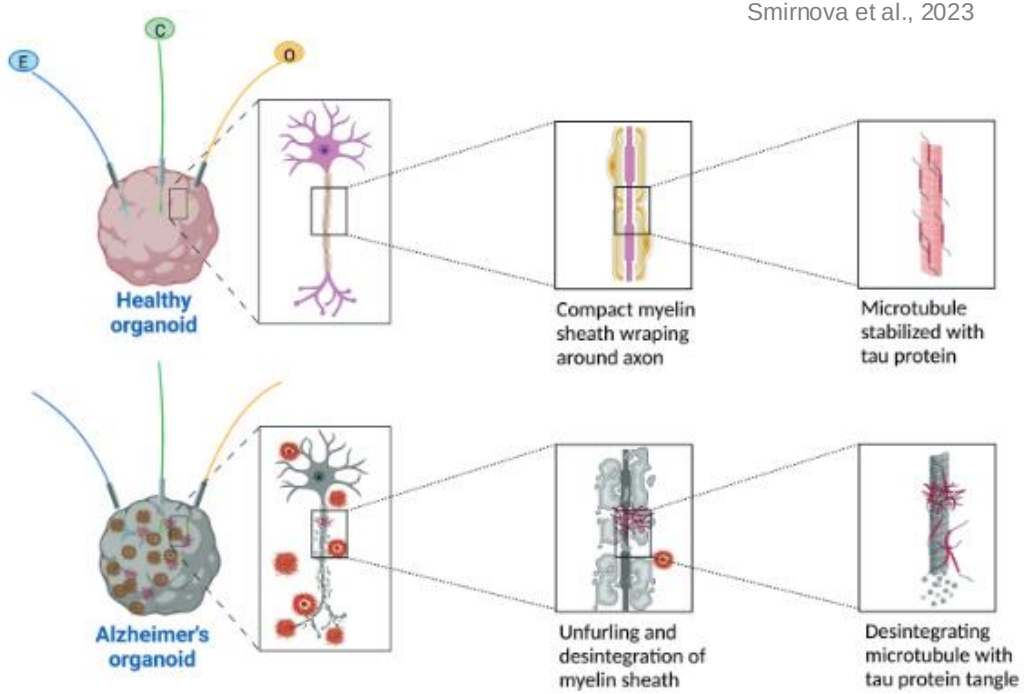
Li et al., 2023

Applicability: Disease modeling



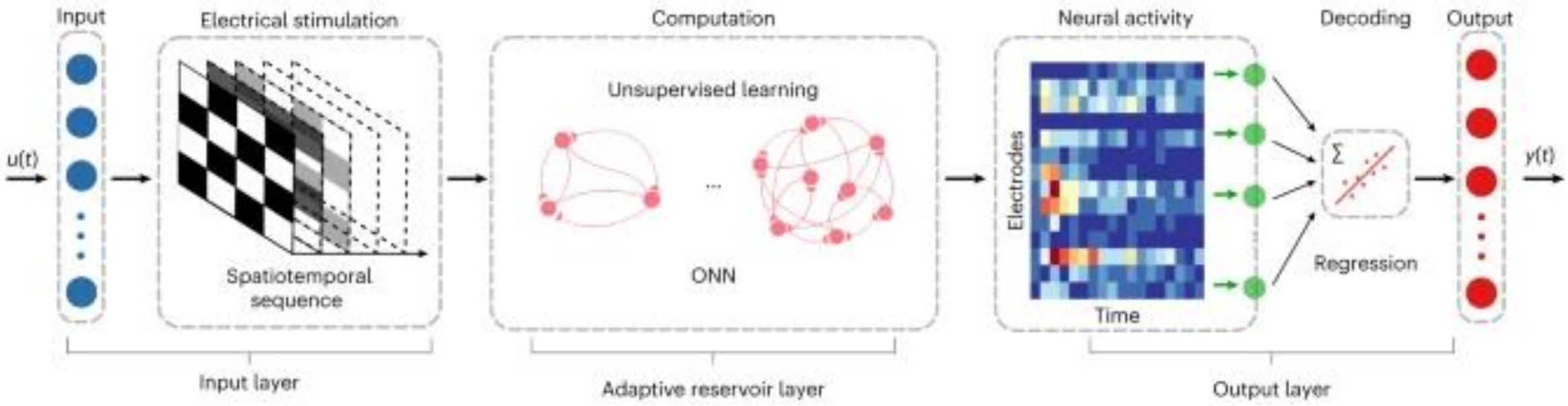
Li et al., 2023

Smirnova et al., 2023



Psychiatric and „standard“ phenotypes are adequately mimiced in organoids on cytological, molecular and functional levels

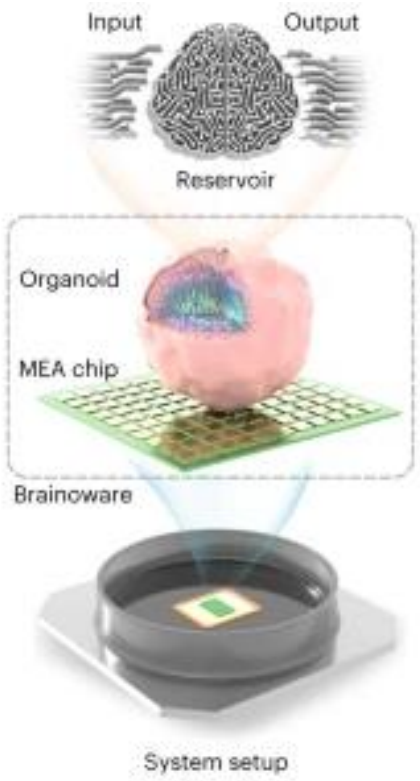
Applicability: Computing

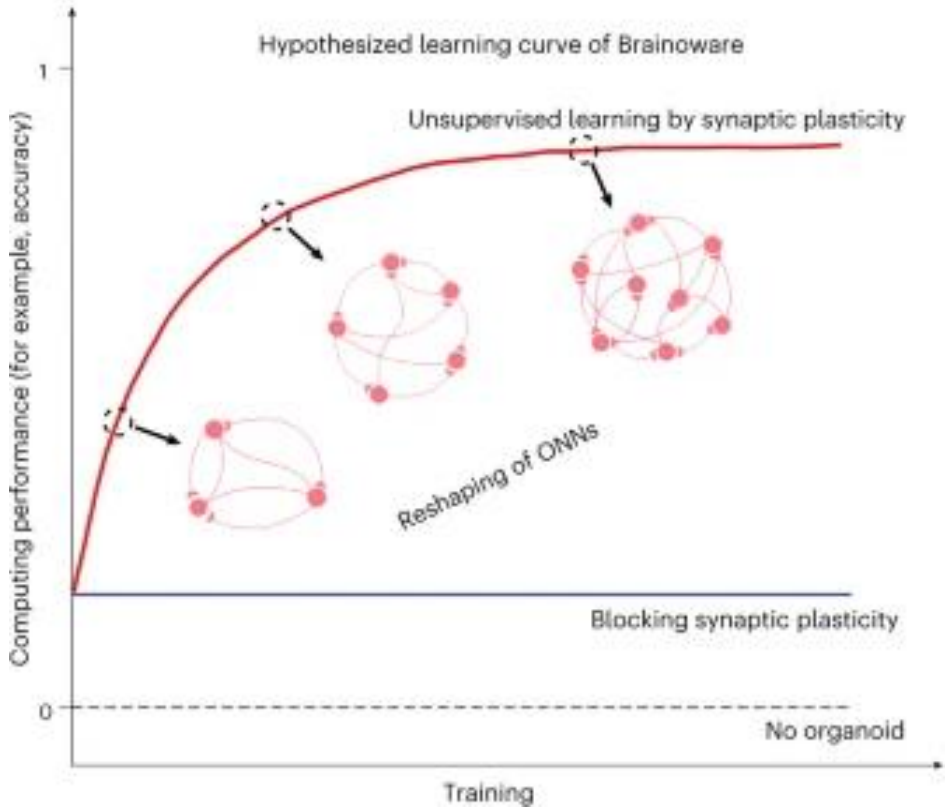


Using brain organoids for AI - computing

Cai et al., 2023

Applicability: Computing

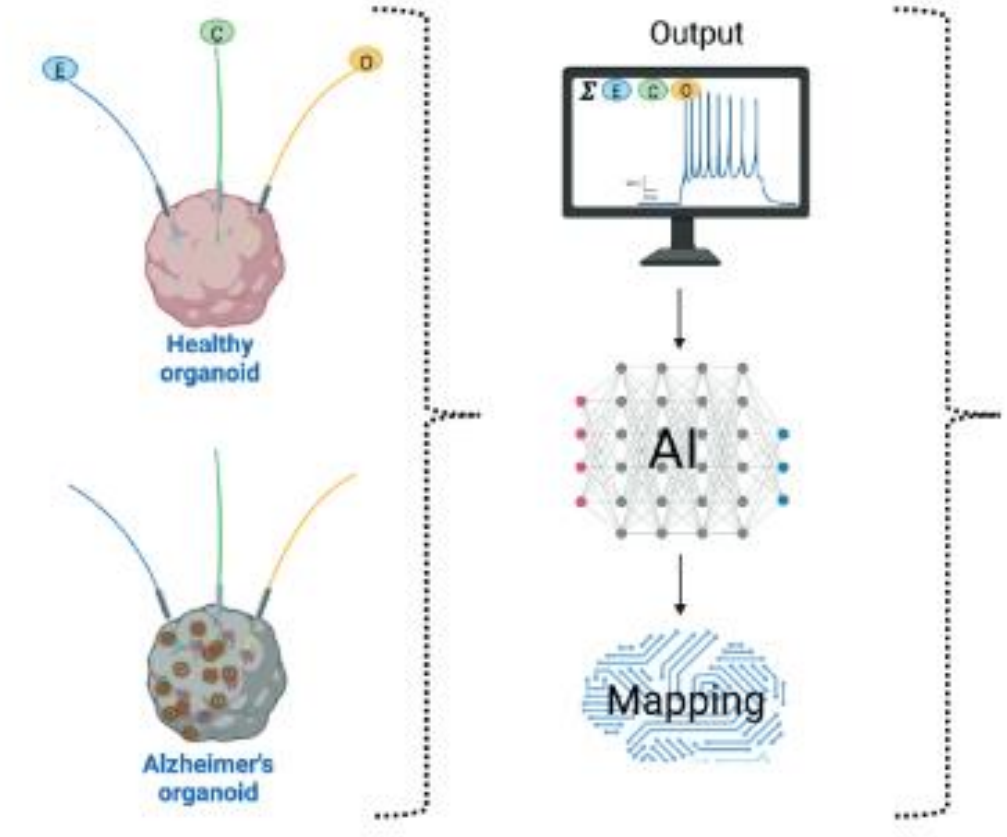




Using brain organoids instead of silicon chips to emulate brain-inspired computing (ONN = organoid neural network)

Cai et al., 2023

Determining input – output relationships (Organoid Intelligence)



Neuroplasticity and calcium signaling

- Strengthening of connections (LTP)
- Weakening connections (LTD)
- Creating new connections (synaptogenesis)
- Calcium signaling regulates crucial neuronal processes in synaptic plasticity responsible for learning and memory.

Characterization of neuroplasticity and calcium signaling under homeostasis and disease

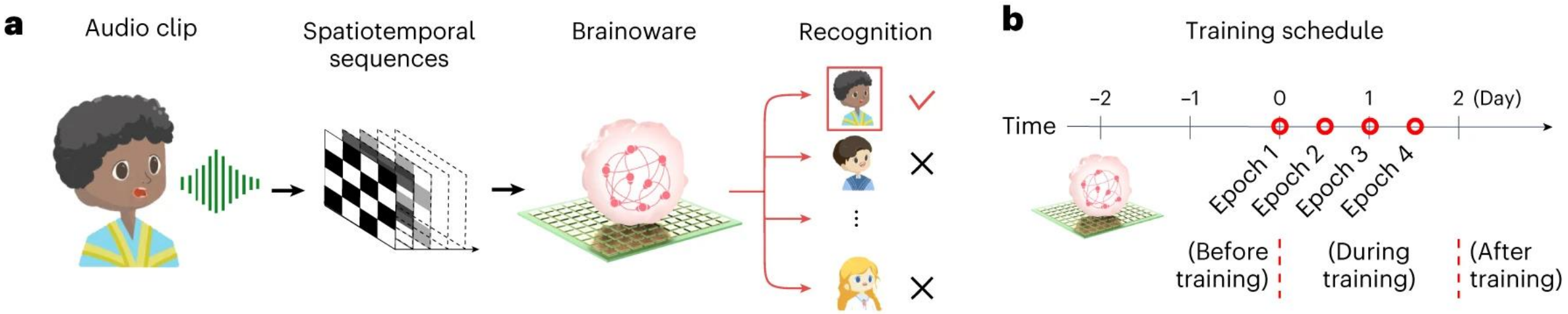
- Understand responses globally and regionally
  - Map function and connectivity

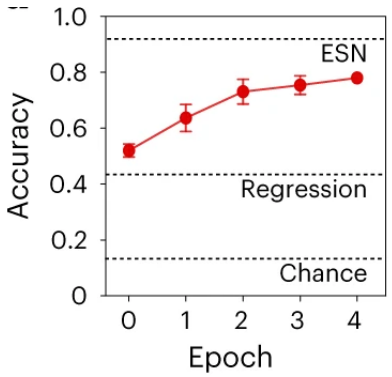
Drug screening to enhance/maintain cognition (AMPA modulators, (re)myelinating agents)

- Identify neuronal circuit
  - Baseline
  - Stimulate before and after drug testing
  - Quantify neuroplasticity

Smirnova et al., 2023

Modifying the input (Speech)





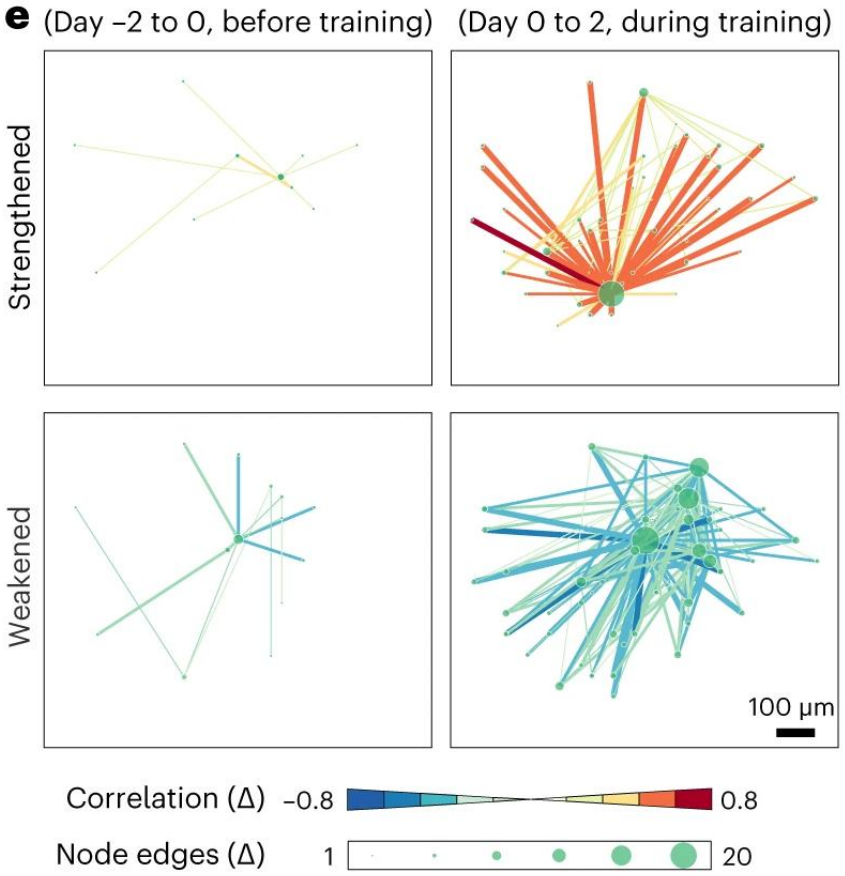
Japanese vowel traing for several days

Goal: Distinguish from other speakers

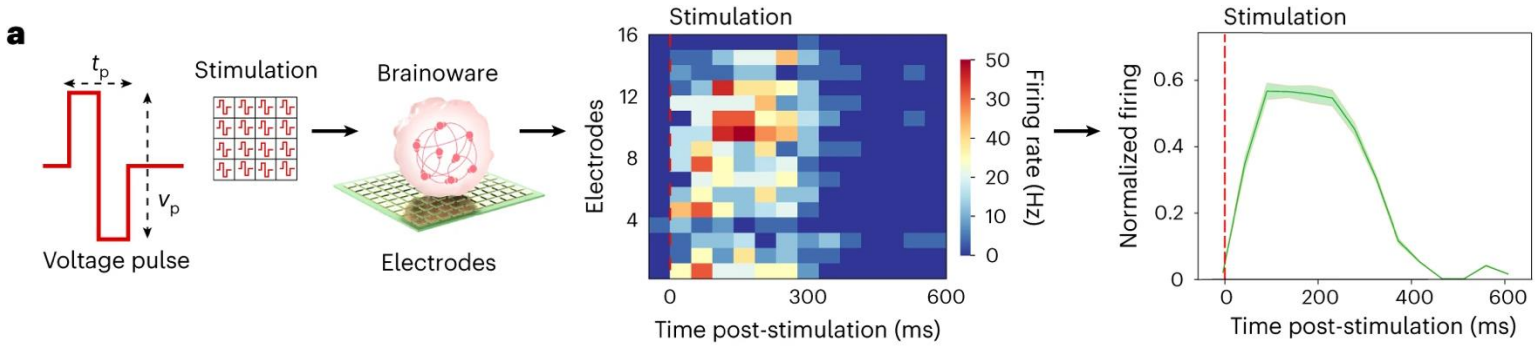
Increase in speech recognition accuracy over training epochs

Cai et al., 2023

Modifying the input (Speech)

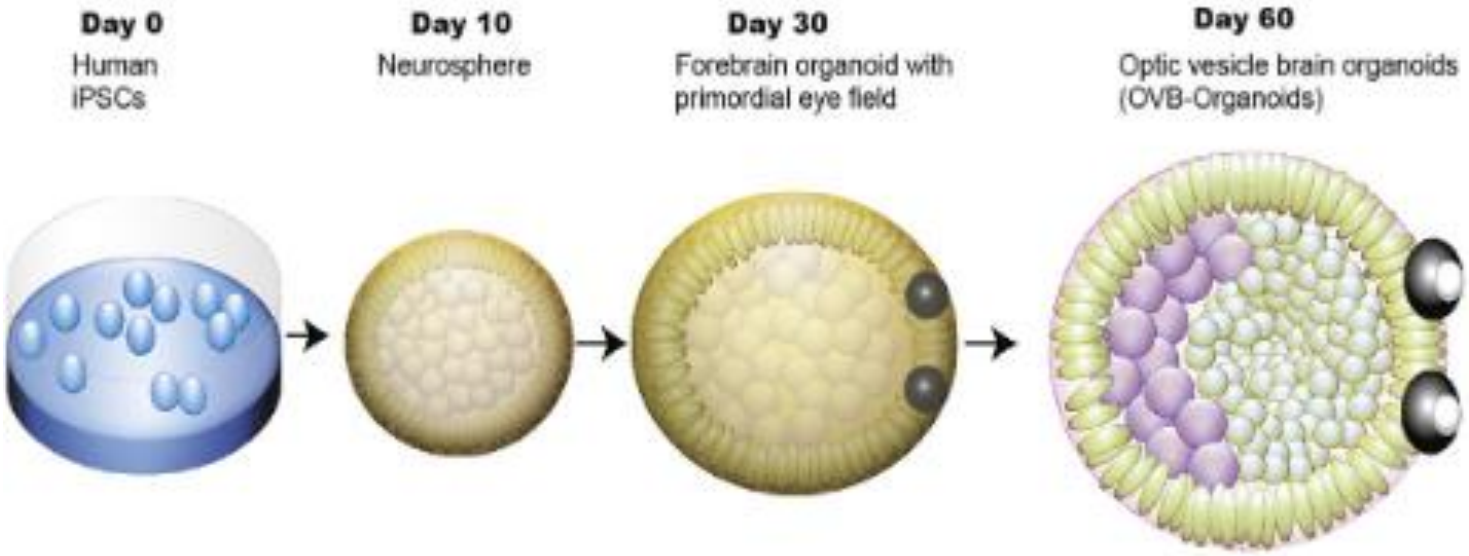


Quantification of connectivity changes (weakened, strengthened, new and pruned) before and during training

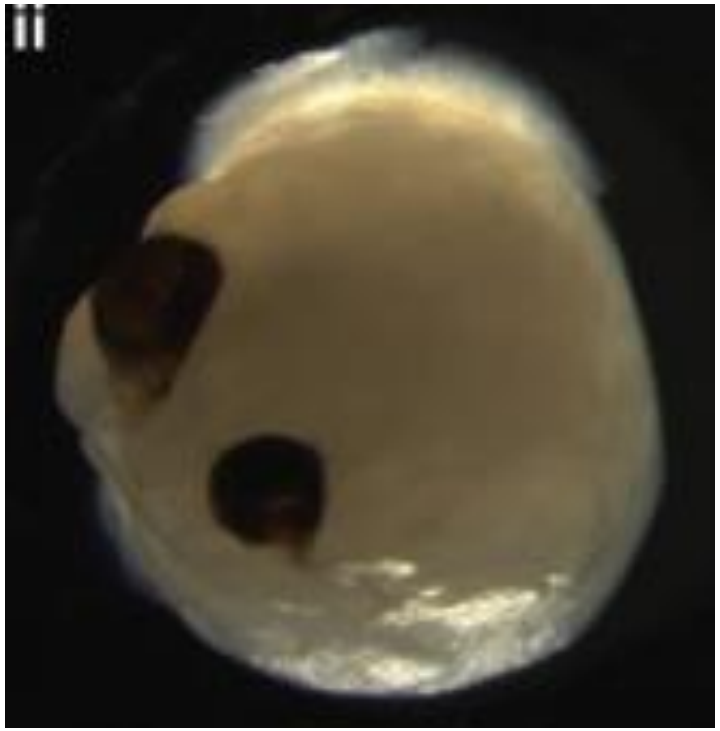


Cai et al., 2023

Modifying the input (Light)

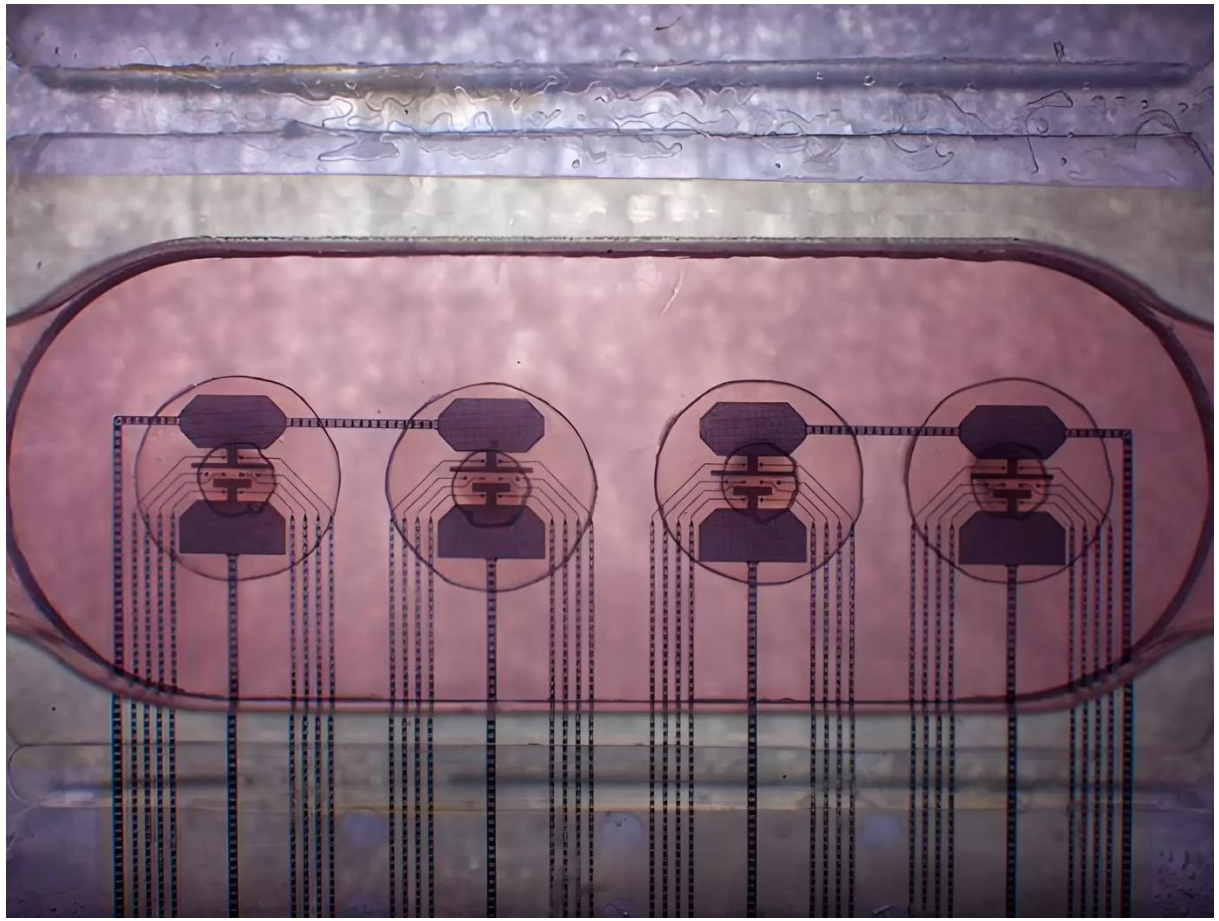


Optical and other sensory inputs trigger physiological responses



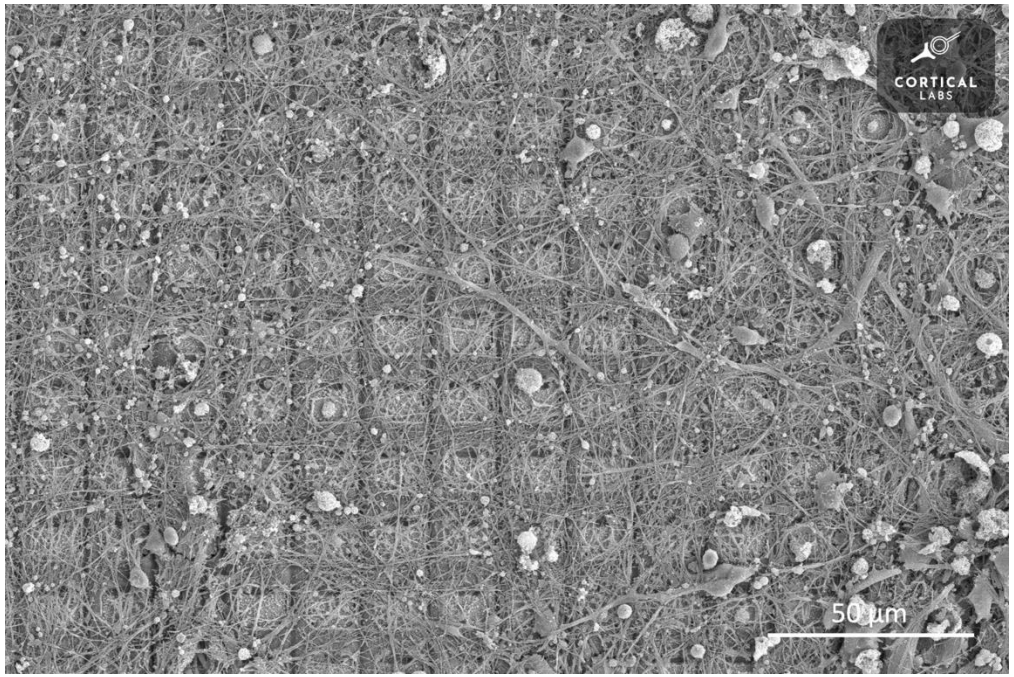
Gabriel et al., 2021

Utilizing the output



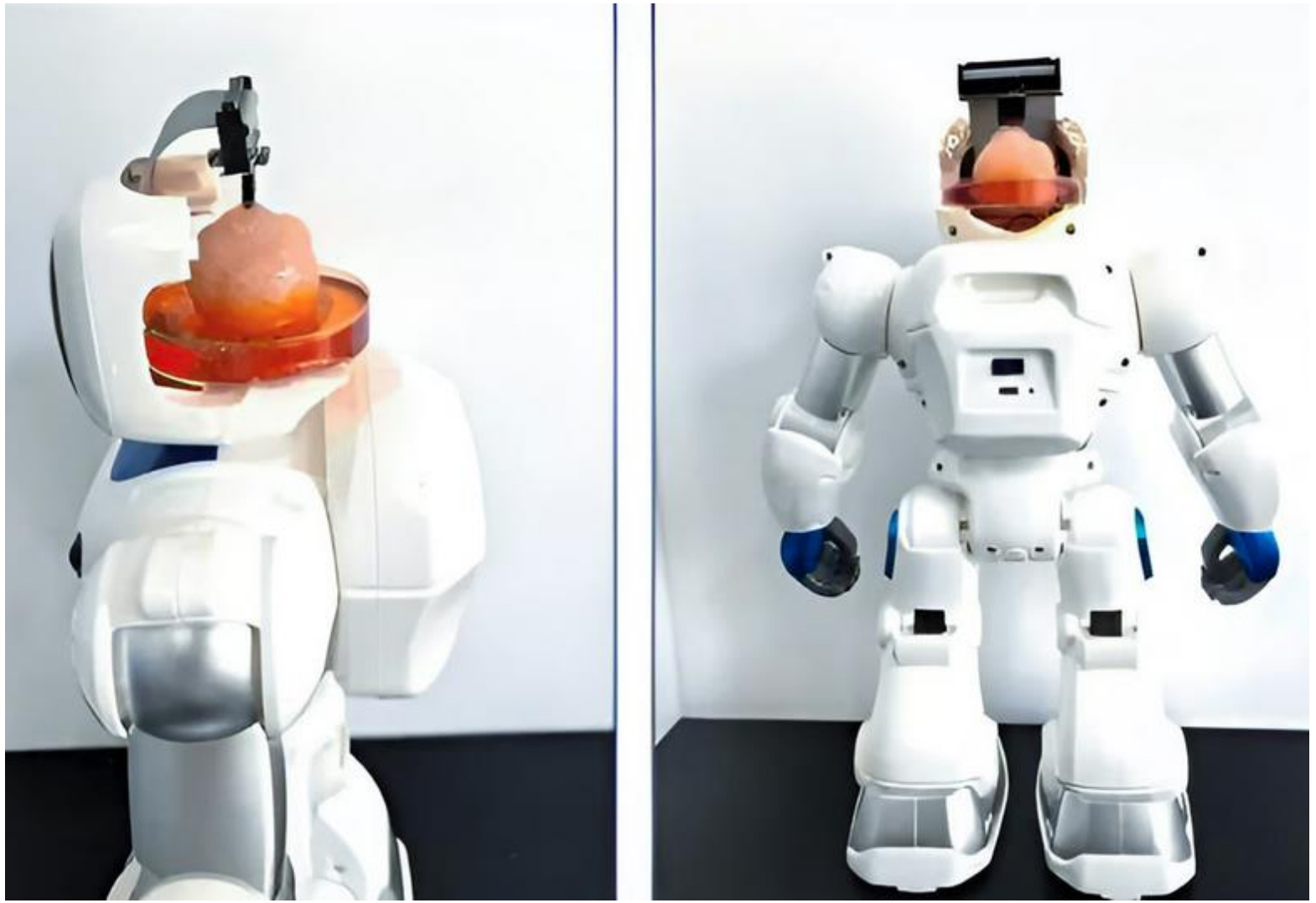
FinalSpark Neuroplatform

Four brain organoids (10.000 human cell each) are wired to a biocomputing array



Dishbrain neurons on electrode array (learned to play Pong)

Utilizing the output



A possible future scenario

If combined with self-awarding module, the organoid may be fully embodied

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