INTERNATIONAL HELLENIC UNIVERSITY

Organoid Intelligence (OI)

The notion and evolution

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Agenda

1. *Introduction*
2. *Organoid Intelligence vs. Neuromorphic Computation*
3. *Progress in Organoid Intelligence*
4. *Potential ethical concerns related to OI*
5. *The potential of OI and conclusion*

Introduction

Introduction

- The use of brain cell cultures for robotics and learning tasks has been explored for over 20 years.
- Shahaf and Marom (2001) showed that rodent primary cortical neurons can learn by responding to low-frequency stimuli, resulting in distinct post-learning electrophysiological patterns.
- The human brain differs significantly from rodents in terms of size, complexity, and architecture (Qian et al., 2019).

Introduction

- Shinya Yamanaka's Discovery (2006): Introduced induced pluripotent stem cells (iPSCs), marking a pivotal moment in stem cell research.
- Significance: Revitalized the field of stem cell research, garnering excitement among scientists and bioethicists.
- Mechanism: iPSCs are created by genetically reprogramming somatic cells to a pluripotent state through specific transcription factors.
- Advancement in Neural Research (2013): Lancaster et al. developed a method for creating cerebral organoids from iPSCs.
- Enabled the study of human neurodevelopmental processes in vitro.

Introduction

01

Organoids are miniaturized, self-organizing versions of organs or tissues that replicate their in vivo counterparts (Yang et al., 2023).

02

Brain organoids are 3D structures derived from human stem cells that resemble the organization and features of a developing human brain (Trujillo & Muotri, 2018).

03

Cerebral organoid cultures allow for the replication of multiple brain regions within a single structure (Nowakowski & Salama, 2022).

Use cases of Brain Organoids

01

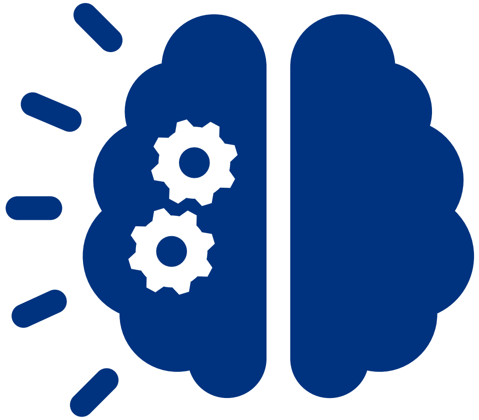
Disease modeling

Brain organoids can be used to model various neurological and psychiatric diseases

02

Drug testing

brain organoids offer a more accurate and physiologically relevant model of the human brain than 2D cell cultures



03

Understanding human brain development

Brain organoids can be used to study the processes of human brain development

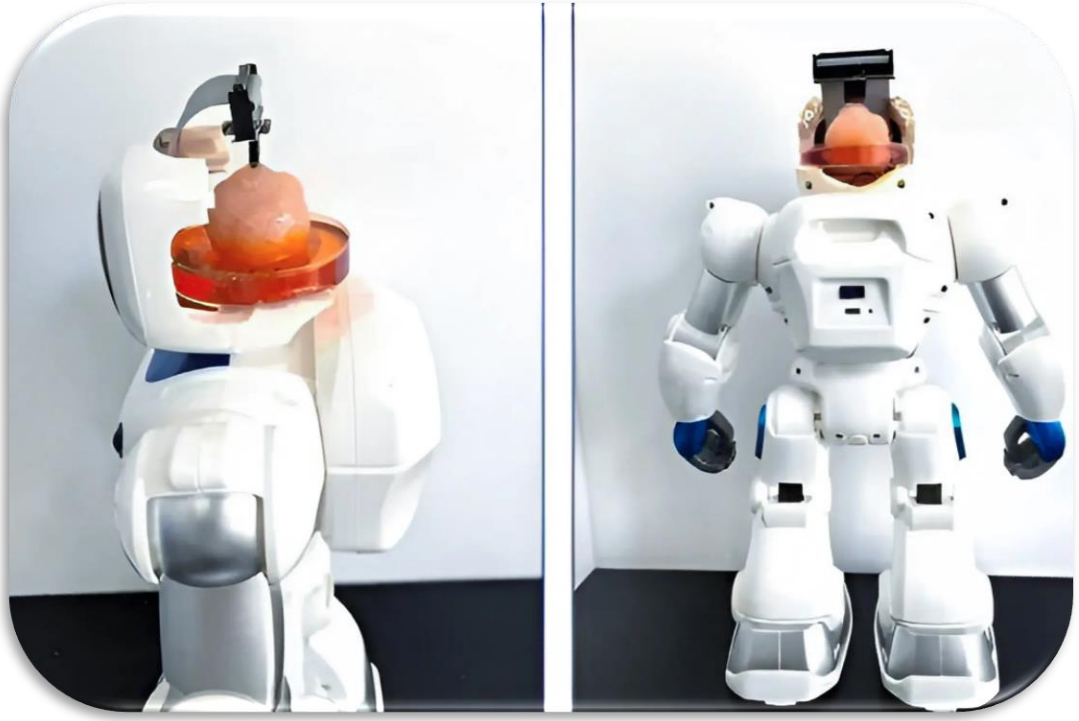
04

Neurodegeneration

Brain organoids have become a promising resource for researching neurodegenerative diseases such as Alzheimer’s, Parkinson’s, Huntington’s, and amyotrophic lateral sclerosis (ALS).

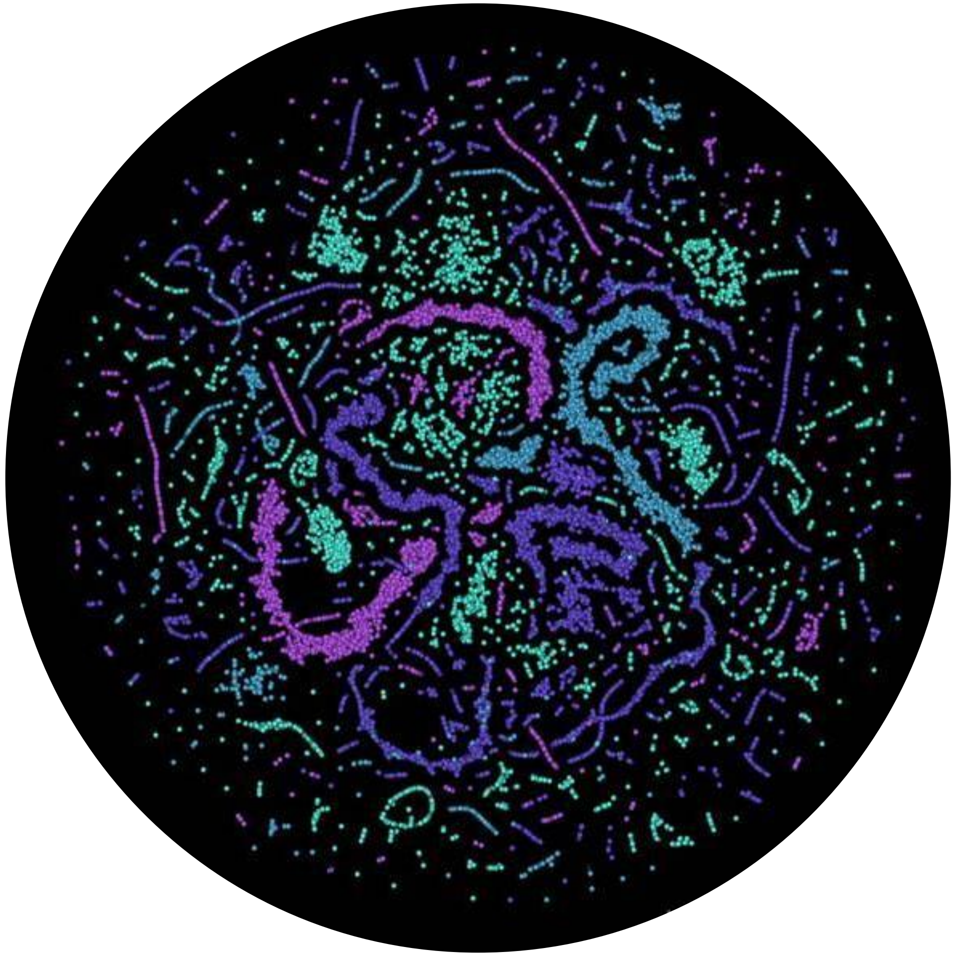
Brain Organoids for Biocomputing

the overarching aim of OI is to harness the computational power of biological neural networks to create novel forms of intelligence and biocomputing (Hartung et al., 2023).



Human brain organoids wired into computer chips can now learn to drive robots thanks to a new biocomputing interface! Tianjin University

What is Organoid Intelligence?



What is Organoid Intelligence?

- "Organoid Intelligence" aims to integrate brain organoids with computer technology for biocomputing and synthetic intelligence (Ballav et al., 2024) and seeks to harness the biological functions of organoids to enhance biocomputing capabilities.
- The term “OI” is used for this approach to stress its complementarity to AI, where computers aim to perform tasks done by brains, often by modeling our understanding of learning.

What is Organoid Intelligence?

- The term **"organoid intelligence"** was first coined in early 2022 during the first Organoid Intelligence Workshop held at Johns Hopkins University in February 2022. This workshop aimed to establish a community around the concept and lay the groundwork for organoid intelligence as a new scientific discipline.
- The term describes a research approach that seeks to harness the capabilities of brain organoids, which are three-dimensional structures derived from stem cells that mimic certain functionalities of the human brain, for applications in biocomputing and synthetic intelligence.

The drivers for Organoid Intelligence

The drivers for Organoid Intelligence

OI is recognized as a key investment area, leading the National Science Foundation (NSF) in the U.S. to launch the Emerging Frontiers in Research and Innovation (EFRI) program through its Directorate for Engineering (ENG).

The EFRI solicitation for Biocomputing through EnGINeering Organoid Intelligence (BEGIN OI) is designed to support foundational and transformative research aimed at enhancing the design, engineering, and fabrication of organoid systems that can dynamically process information and interact with non-living systems.

The program allocates ca **USD 15 million** each fiscal year for FY24 and FY25.

The drivers for Organoid Intelligence

To understand human brain capabilities, we compare it to supercomputers, which require significant space and power.

Example: The Frontier supercomputer processes over one quintillion operations per second, occupies **680 square meters**, and needs **22.7 megawatts of power**.

In contrast, the human brain operates with only **20 watts** and weighs **1.3–1.4 kg**, achieving a similar operations rate.

Neuromorphic computing aims to explore the brain's efficiency, potentially through OI or a blend of Human Brain Organoids and AI.

https://theconversation.com/a-new-supercomputer-aims-to-closely-mimic-the-human-brain-it-could-help-unlock-the-secrets-of-the-mind-and-advance-ai-220044

Neuromorphic Computing

Neuromorphic Computing

Neuromorphic computers are built on two types of neural networks: formal neural networks, known as **Artificial Neural Networks (ANNs)** which are a series of algorithms run on conventional computers to simulate the logic of human brain function, and event-driven networks, called **Spiking Neural Networks (SNNs)** which attempt to replicate the functional principles of the human brain and communicate through spikes.

ANNs have been a focus of study since the early days of machine learning, whereas SNNs are a more recent development (Bouvier et al., 2019).

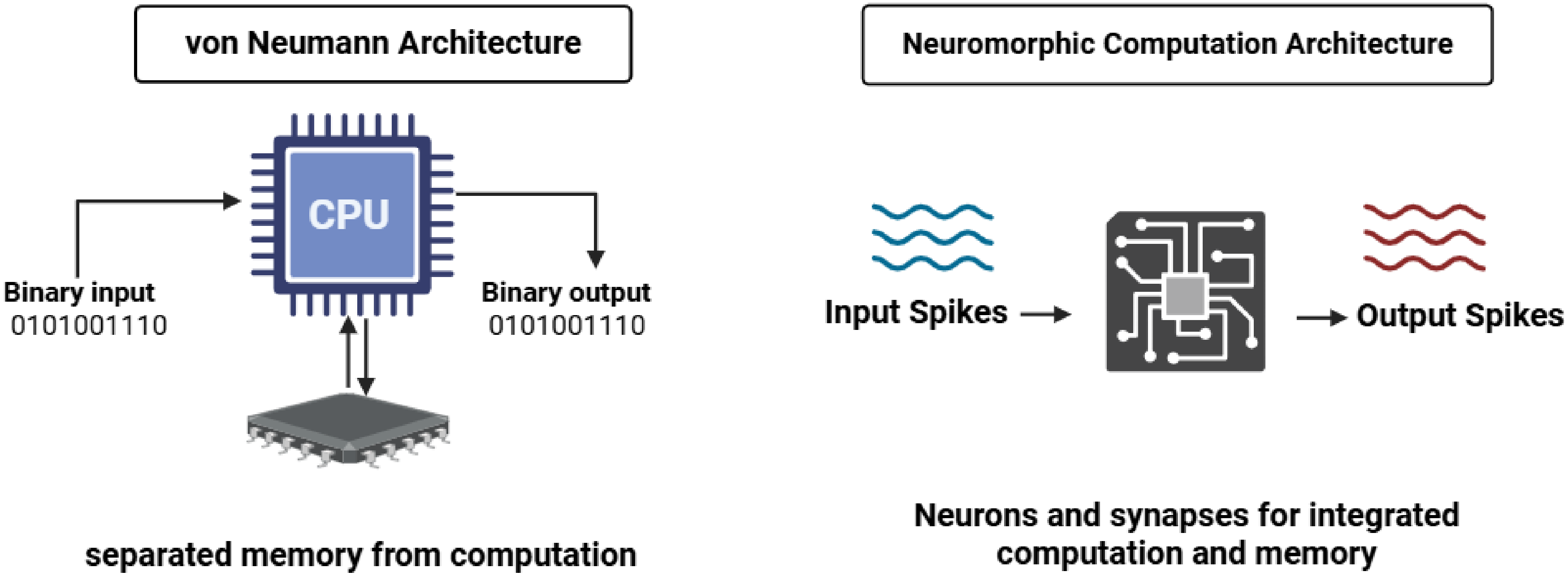
Neuromorphic Computing

The cutting-edge methods for developing a human brain-like system on an artificial basis primarily involve quantum computing and neuromorphic computing.

Neuromorphic Computing, which refers to non-von Neumann computers—unlike conventional computers—that are designed to mimic the structure and function of the brain, consisting of neurons and synapses

von Neumann computers, which have separate CPUs and memory units for storing data and instructions, neuromorphic computers integrate processing and memory within neurons and synapses (Schuman et al., 2022).

Neuromorphic Computing

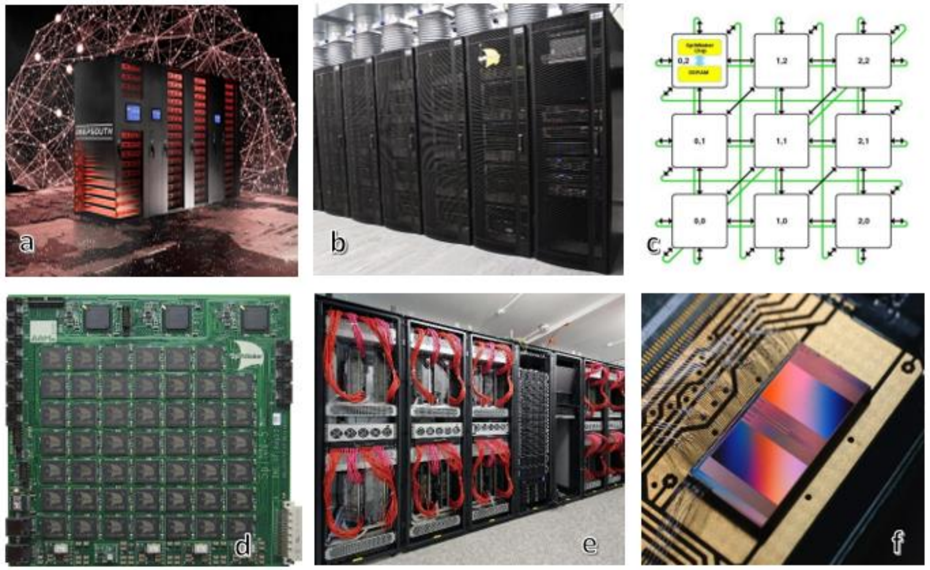


difference between von Neumann architecture and neuromorphic computation architecture - Created with BioRender.com

Neuromorphic Computing

DeepSouth, developed by researchers at the International Centre for Neuromorphic Systems at Western Sydney University, is proposed as the world's first supercomputer capable of simulating networks at the scale of the human brain. It uses a neuromorphic system that mimics biological processes, achieving 228 trillion synaptic operations per second, similar to the operational rate of the human brain.

The Human Brain Project (HBP), funded by the EU from 2013 to 2023, resulted in the creation of **BrainScaleS**, a machine in Heidelberg, Germany, designed to emulate the functions of neurons and synapses.



These images show (a) DeepSouth system hardware at ICNS[5] (b) SpiNNaker system hardware (c) SpiNNaker system structure, (d) SpiNNaker Standalone 4- and 48-chip boards for real-time robotics[6], (e) BrainScaleS system hardware (f) BrainScaleS-2 single chip (Heidelberg University)[7]

https://www.humanbrainproject.eu/en/science-development/focus-areas/neuromorphic-computing/hardware/
Image downloaded from: https://www.deepsouth.org.au/
image downloaded from: https://www.humanbrainproject.eu/en/science-development/focus-areas/neuromorphic-computing/
image downloaded from; https://wiki.ebrains.eu/bin/view/Collabs/neuromorphic/SpiNNaker/

Where do neuromorphic computers fall short?

- Neuromorphic computation has made significant strides but still falls short of fully emulating the human brain. While spiking neural networks (SNNs) reduce hardware demands, challenges remain. Techniques like weight quantization can decrease memory and computation needs for embedded systems, but if not applied carefully, they may compromise network accuracy.
- Backpropagation-based training is heavily emphasized in deep learning, but accessible software and hardware for the broader computational community remain limited.
- Neuromorphic systems often depend on conventional machines for their software architecture, which can reduce their advantages.
- Furthermore, the development of neuromorphic algorithms faces challenges due to a lack of clear benchmarks and metrics, as well as insufficient programming abstractions for non-machine learning algorithms suited for neuromorphic applications (Schuman et al., 2022).

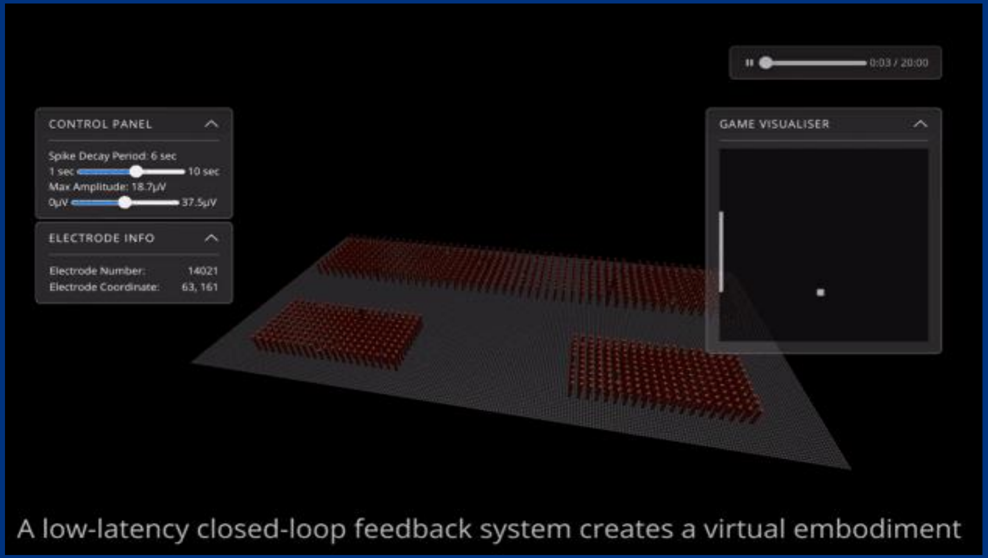
Progress in Organoid Intelligence

Progress in Organoid Intelligence

In early 2023, Smirnova et al. published an article proposing that biocomputing might surpass silicon-based computing and AI in speed, efficiency, and power while consuming only a fraction of the energy.

Recent breakthroughs in human stem cell-derived brain organoids suggest the potential to replicate key molecular and cellular aspects of learning, memory, and possibly cognition *in vitro*.

Progress in Organoid Intelligence



DishBrain

Developed by: Monash University, Australia; spun off to CorticalLabs.

Purpose: Harness the adaptive computation of neurons in a structured environment.

Integration: Combines in vitro neural networks (from human or rodent origins) with in silico computing using a high-density multielectrode array.

Method: Employs electrophysiological stimulation and recording.

Game Simulation: Cultures are embedded in a simulated version of the arcade game "Pong."

Learning Mechanism: Based on the theory of active inference and the free energy principle.

Findings: Apparent learning observed within five minutes of gameplay, which was not seen in control conditions (Kagan et al., 2022).

***Source**: Kagan, B. J., Kitchen, A. C., Tran, N. T., Habibollahi, F., Khajehnejad, M., Parker, B. J., Bhat, A., Rollo, B., Razi, A., & Friston, K. J. (2022). In vitro neurons learn and exhibit sentience when embodied in a simulated game-world. Neuron, 110(23), 3952-3969.e8. https://doi.org/10.1016/j.neuron.2022.09.001*

Progress in Organoid Intelligence

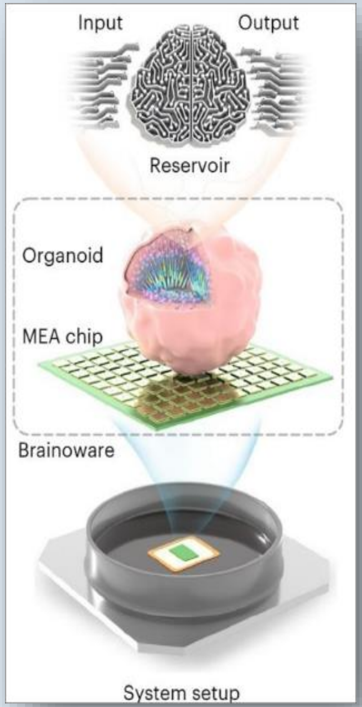
Brainoware

- Indiana University developed a brain organoid less than a nanometer in diameter, integrated onto a silicon chip with a high-density multielectrode array (MEA) for electrical signal exchange.
- AI Hardware Development: Researchers created Organoid Neural Networks (ONNs) that utilize reservoir computation and unsupervised learning capabilities.
- Functionality: ONNs process inputs via external electrical stimulation and produce outputs through evoked neural activity, forming a functional basis for AI computing, termed Brainoware.
- Learning Mechanism: Brainoware processes spatiotemporal information and exhibits unsupervised learning due to the neuroplasticity of the brain organoid.

Source: *Cai, H., Ao, Z., Tian, C., Wu, Z., Liu, H., Tchieu, J., Gu, M., Mackie, K., & Guo, F. (2023). Brain organoid reservoir computing for artificial intelligence. Nature Electronics, 6(12), 1032–1039. https://doi.org/10.1038/s41928-023-01069-w*

Progress in Organoid Intelligence

Brainoware



Advantages:

Flexible adaptation to electrical stimulation, enhancing reservoir computing.

Potential reduction in time, energy consumption, and heat generation compared to traditional AI hardware.

Successful applications in speech recognition and nonlinear equation prediction.

Limitations:

High heterogeneity and low production throughput of organoids.

Issues with necrosis/hypoxia and variable organoid viability.

Necessity for proper maintenance and support to optimize computational power.

Despite low power consumption of Brainoware, peripheral equipment (e.g., CO_2 incubators, computers) consumes significant power.

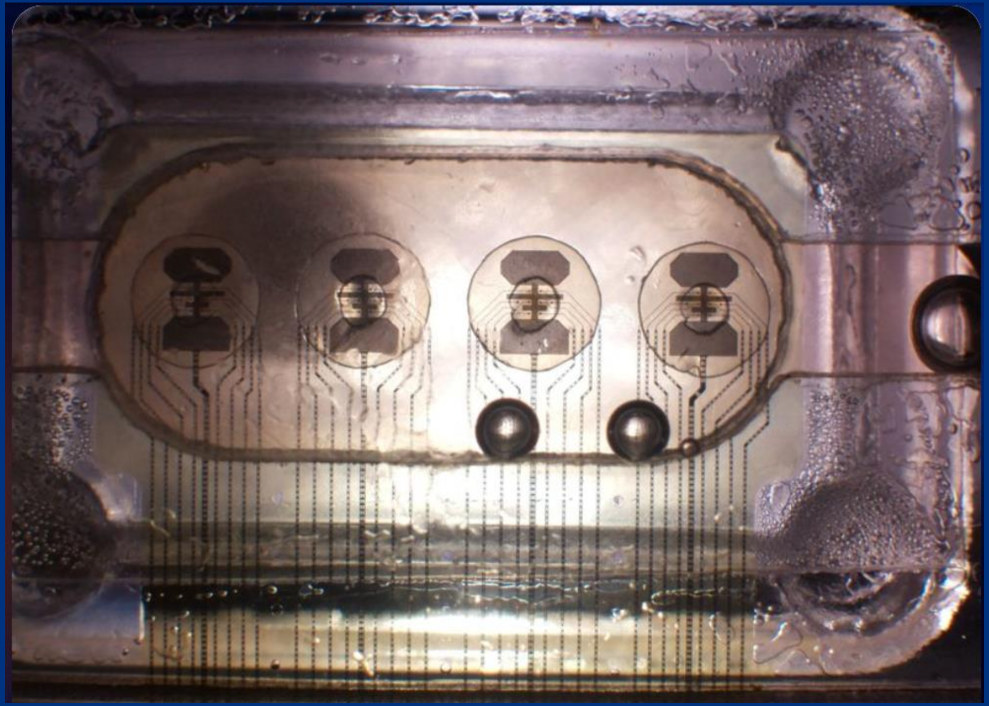
Source: *Cai, H., Ao, Z., Tian, C., Wu, Z., Liu, H., Tchieu, J., Gu, M., Mackie, K., & Guo, F. (2023). Brain organoid reservoir computing for artificial intelligence. Nature Electronics, 6(12), 1032–1039. https://doi.org/10.1038/s41928-023-01069-w*

Progress in Organoid Intelligence

FinalSpark

Swiss startup FinalSpark has developed living brain-cell cyborg biocomputers trained with dopamine.

Their neuroplatform allows for experimentation on neural organoids with lifespans exceeding 100 days.

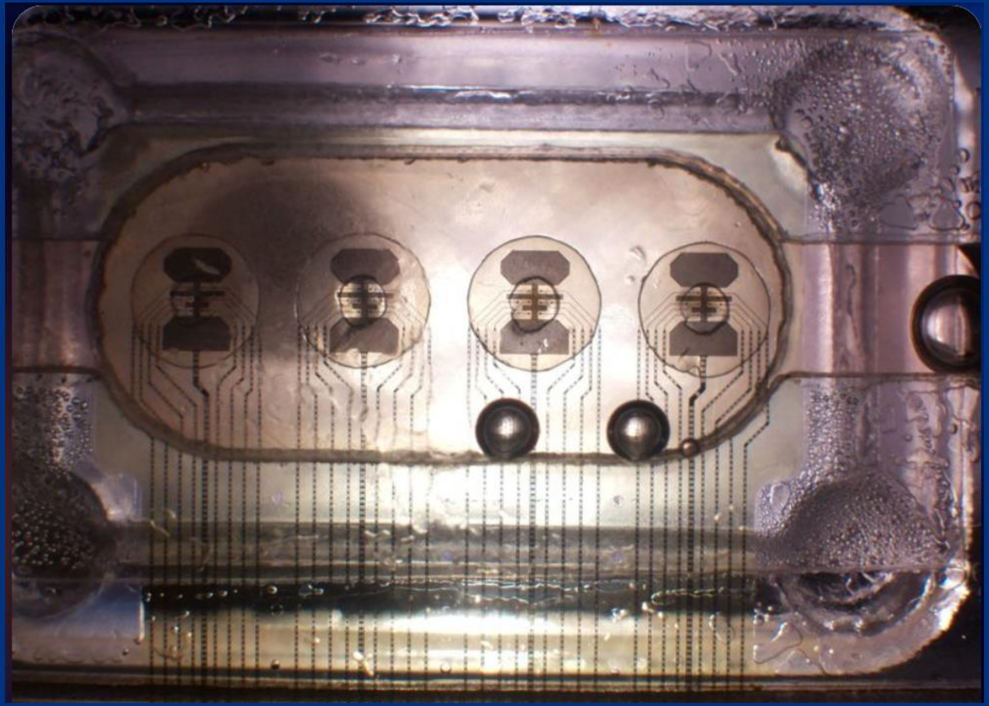


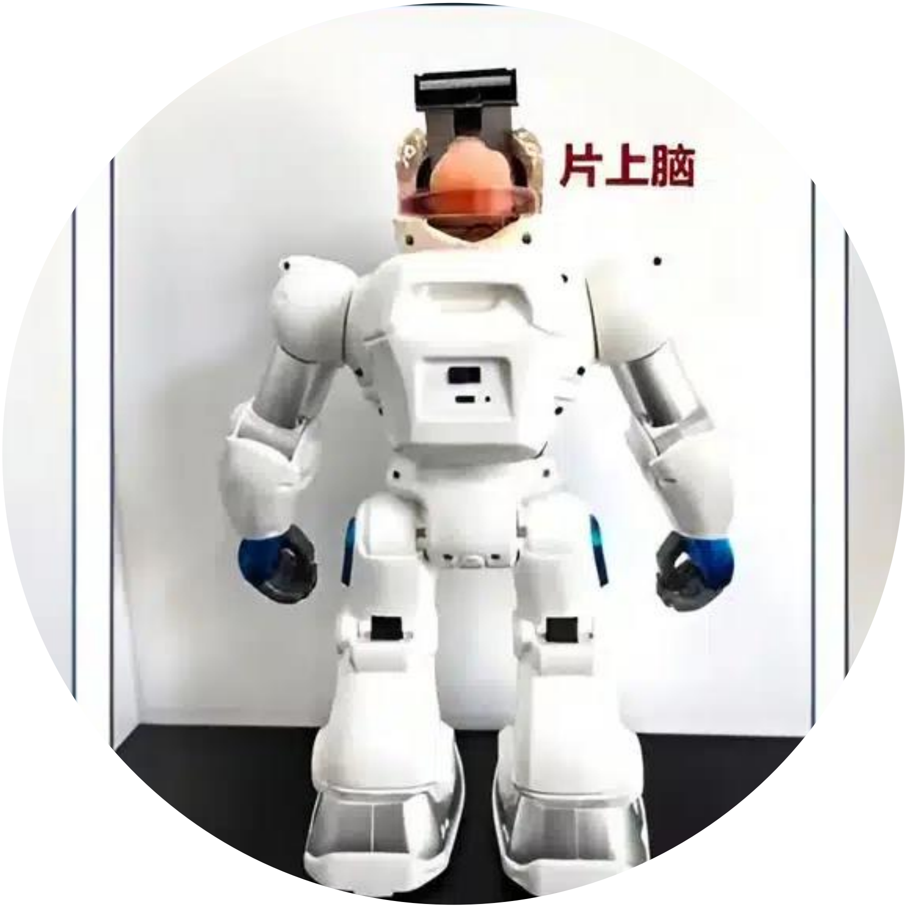
Progress in Organoid Intelligence

Brain Spheroids: Uses "forebrain organoids" (FOs) placed on four Multi-Electrode Arrays (MEAs).

Dopamine was used as a reward to increase elicited neural spikes; a general increase in spikes was observed.

Causality between closed-loop stimulation and spike increase could not be conclusively established.





Progress in Organoid Intelligence

MetaBOC

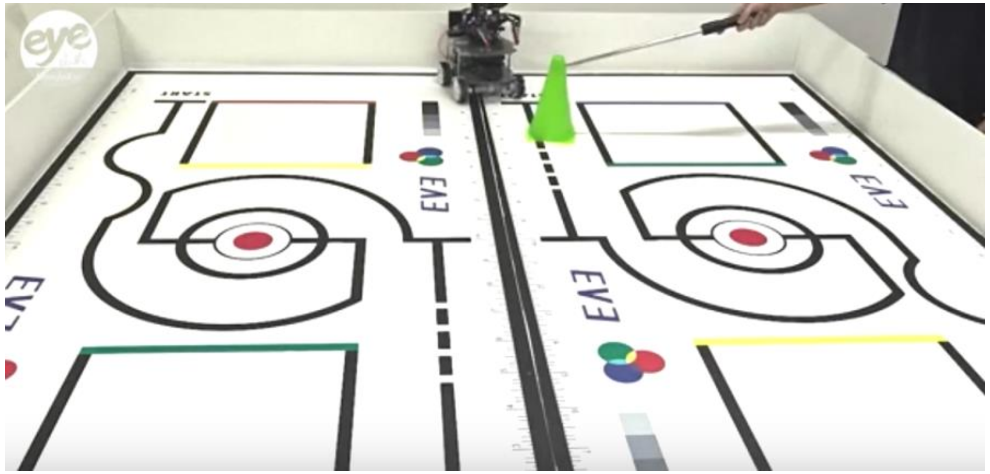
- It is an open-source intelligent interaction system developed by researchers from Tianjin University's Haihe Laboratory and the Southern University of Science and Technology.
- The Tianjin team utilizes spherical organoids, similar to those used by the Indiana University Brainoware team, due to their 3D structure that fosters intricate neural connections like those in human brains.
- Organoids are cultivated using Low-Intensity Focused Ultrasound Stimulation (LIUS), believed to enhance the foundation for intelligence development.

Progress in Organoid Intelligence

MetaBOC

The system, MetaBOC, enables a brain organoid to autonomously control robots for tasks such as obstacle avoidance, tracking and grasping, completing inspired work of various brain-like computing.

The brain-on-a-chip consists of two components: the electrode chip and the in vitro-cultured brain tissue. This brain organoid is created through stem cell culture technology and possesses some of the intelligent functions of a biological brain.



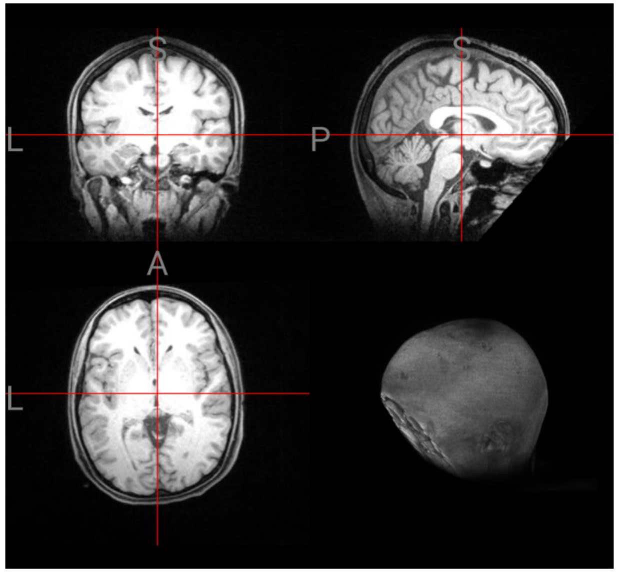
https://www.youtube.com/watch?v=o_zsjINNHBE

__Source:__ Li, X.-H., Guo, D., Chen, L.-Q., Chang, Z.-H., Shi, J.-X., Hu, N., Chen, C., Zhang, X.-W., Bao, S.-Q., Chen, M.-M., & Ming, D. (2024). Low-intensity ultrasound ameliorates brain organoid integration and rescues microcephaly deficits. Brain. https://doi.org/10.1093/brain/awae150

Progress in Organoid Intelligence

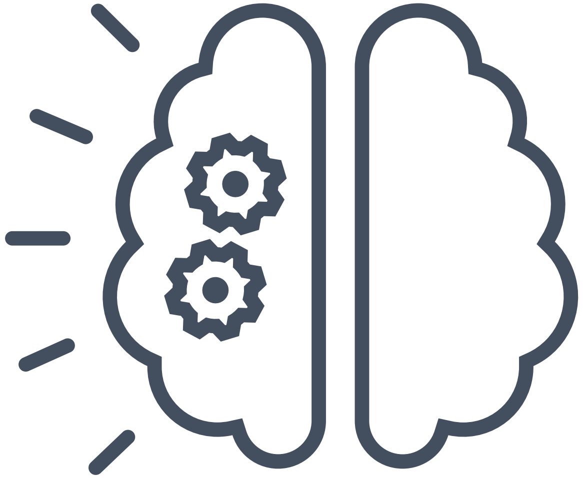
PyOrganoid

- The mechanisms behind music-induced cognitive changes are largely unknown (Szelogowski, D. 2024).
- Organoid intelligence and deep learning models can help simulate and analyze neural responses to classical music.
- Introduction of the PyOrganoid library for simulating organoid learning models with machine learning techniques.
- Development of the Pianoid model, a "deep organoid learning" model using Bidirectional LSTM (Bidirectional Long Short-Term Memory) (Bi-LSTM) networks.
- Pianoid predicts EEG responses based on audio features from classical music.
- Demonstrates the feasibility of computational methods replicating complex neural processes.
- Provides insights into music perception and cognition and highlights the value of synthetic models in neuroscience research.



Szelogowski, D. (2024). Simulation of Neural Responses to Classical Music Using Organoid Intelligence Methods.

Ethical concerns related to Organoid Intelligence



Ethical concerns related to Organoid Intelligence

Ethical and legal issues of using BO

- Informed Consent
- Moral Status and Consciousness
- Human-Animal Chimeras
- Commercialization and Intellectual Property

Potential ethical issues of using AI

- Privacy Concerns
- Environmental Impact
- Autonomy and Control
- accountability for AI errors

*AI enabled Organoids**

One area of research that is of particular interest is the intersection of organoids and AI. For example, AI algorithms can be used to analyze large amounts of data generated by organoids experiments.

Milestones in AI development

include AlphaGo, AlphaFold, and Generative Pretrained Transformers like ChatGPT. Furthermore, the emergence of big data has enabled the training of AI algorithms on extensive datasets, resulting in enhanced performance across various tasks.

**Bai, L., Wu, Y., Li, G., Zhang, W., Zhang, H., & Su, J. (2024). AI-enabled organoids: Construction, analysis, and application. Bioactive Materials, 31, 525–548. https://doi.org/10.1016/j.bioactmat.2023.09.005*

Ethical concerns related to Organoid Intelligence

Use cases of AI in AI-enabled Organoid

Through Machine learning-guided

- *guided spatial structure* ***discerning of matrix gel***
- *guided fine-tuning of* ***cell culture conditions***
- *guided* ***identification of active inducing factors***
- *guided assessment of* ***external stimuli***
- *guided image analysis of in* ***morphology scale***
- *guided image analysis in* ***organoids scale***
- *guided image analysis in* ***tissue scale***

Bai, L., Wu, Y., Li, G., Zhang, W., Zhang, H., & Su, J. (2024). AI-enabled organoids: Construction, analysis, and application. Bioactive Materials, 31, 525–548. https://doi.org/10.1016/j.bioactmat.2023.09.005

Ethical concerns related to Organoid Intelligence

Accountability and Liability: *Identifying responsibility when an AI system errs or causes harm can be challenging. It is crucial to establish clear lines of accountability and liability to effectively address issues related to AI.*

Privacy*: AI systems typically need access to large amounts of data, including sensitive personal information. The ethical challenge is in how this data is collected, utilized, and safeguarded to avoid privacy violations*

Environmental Impact: *The computational resources needed to train and operate AI models can greatly affect the environment. Ethical considerations involve reducing AI's carbon footprint and fostering sustainable development practices in the field.*

MIT Technology Review reported that training just one AI model can emit more than ***626,00 pounds of carbon dioxide*** *equivalent – which is nearly five times the lifetime emissions of an average* ***car****.*

https://annenberg.usc.edu/research/center-public-relations/usc-annenberg-relevance-report/ethical-dilemmas-ai

Conclusion

Potential and Rapid Advancements

OI: research approach that seeks to harness the capabilities of brain organoids, which are three-dimensional structures derived from stem cells that mimic certain functionalities of the human brain, for applications in biocomputing and synthetic intelligence.

Neuromorphic computation has made significant strides but still falls short of fully emulating the human brain.

biocomputing might surpass silicon-based computing and AI in speed, efficiency**, and power while consuming only a fraction of the energy.**

Potential and Rapid Advancements

01

Engineered brain organoids are advancing quickly, enhancing their functions. With significant potential across neuroscience, medicine, computing, robotics, and brain-machine interfaces.

02

While these organoids can mimic specific brain regions, they fall short of achieving whole-brain organization and connectivity.

03

Ethical and regulatory challenges, such as accountability for AI errors and data privacy, add another layer of complexity

Thank you

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