

Brain Organoids

pt. 2

tiny models with big potential

SOCIETY NEWS

BRAIN ORGANOID PT.2

OPPORTUNITIES

IMAGE SOURCE:

Ciavano Legnini, Agnieszka Rybak-Wolf, Max Delbrück Center

Society News

Recent Events.

- Meet Your Cohort
- 2024 AGM



BINF
SOC

Upcoming Events.

- | | |
|---------------------------------|------------------------|
| -- "What is Bioinformatics" Q&A | T3W5 Tuesday 8th Oct |
| -- Game Show | T3W5 Thursday 10th Oct |
| -- COMBINE Conference | T3W9 Monday 4th Nov |

B 2024 AGM



On Monday, 23rd October, we were pleased to host the 2024 BINFSOC Annual General Meeting. The AGM commenced with the president's and treasurer's reports, reflecting on BINFSOC's unprecedented success over the past eventful year. This was followed by the election of the 2025 BINFSOC executive board, concluding with a refreshing serving of pizza and drinks. Additionally, a raffle was held for all participants, offering a chance to win one of five exclusive BINFSOC-branded mugs. The winners will soon be announced on BINFSOC's social media. Congratulations to all the successful candidates of the 2025 BINFSOC team:

Sarina Chai	President
Yvonne Huang	Vice President
Alexander Chin	Treasurer
Lipda Chantayasakorn	General Secretary
Emaan Khurram	Marketing Executive
Jessica Le	Sponsorships Executive
Guru Venkateswaran	Events Executive
Jake Latchford	HR Executive
Stanley Hou	Education Executive
Hafsa Fahad	IT/Publications Executive

Building upon the work of this year's brilliant team, the 2025 team will continue striving to expand community outreach and offer diverse programs for the benefit of bioinformatics students and the wider STEM community.



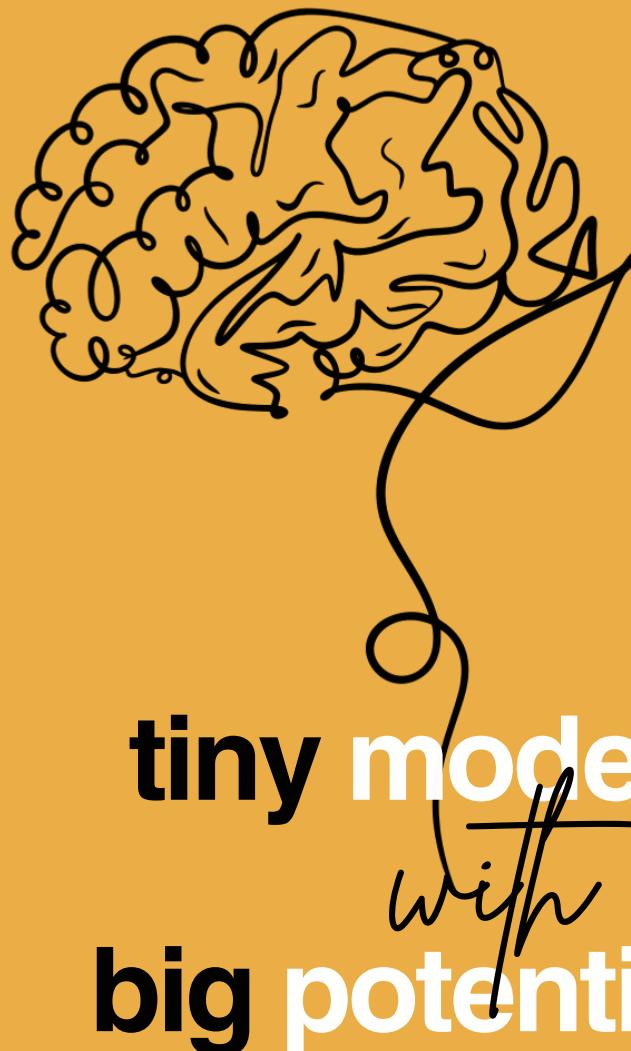
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MEET YOUR COHORT



On Friday, 20th September, BINFSOC hosted the second Meet Your Cohort event of the year at 9 Degrees Bouldering in Waterloo. Students had the opportunity to challenge themselves physically while getting acquainted with fellow peers who share a passion for bioinformatics. After our climbing adventures, the group concluded the adrenaline-filled day of fun, laughter, and bonding with a delicious dinner in the city.





tiny models
~~with~~
big potential

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brain organoids pt. 2

> brain organoids in neurology and medicine

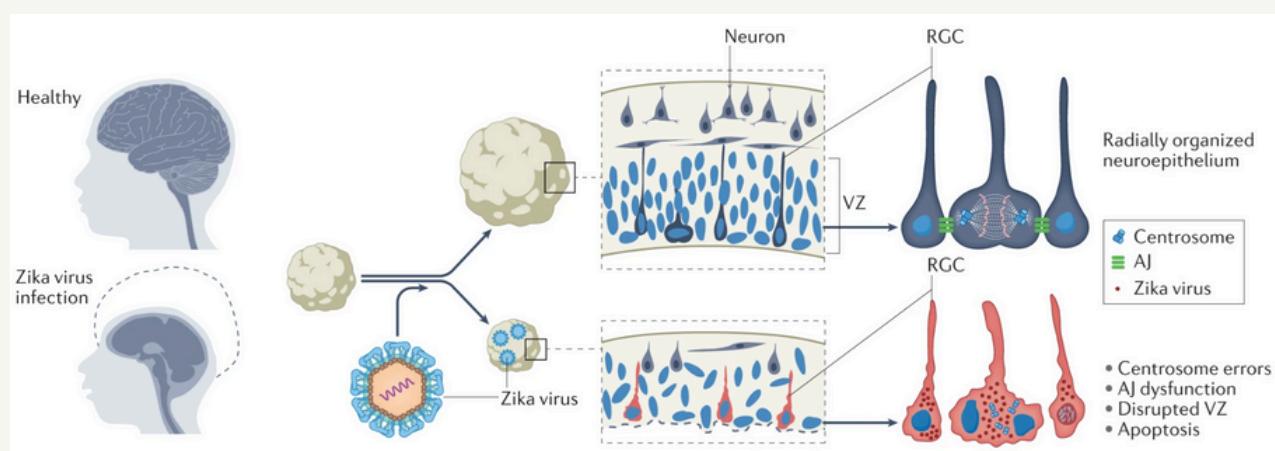
In the previous issue of BINFsights, we introduced a novel 3D stem cells derived model known as the brain organoid model, as well as its applications in computing: an approach termed brain organoid reservoir computing or Brainoware. In this article, we will explore the broader applications of brain organoids in neuroscience research, focusing on their potential for studying neurodevelopmental diseases and modelling complex brain functions.

A Novel Way to Study Neurodevelopmental Disorders

Traditionally, neuroscience research has primarily relied on animal models, post-mortem human tissues and direct analysis of patients to explore the mysteries of the

brain. While valuable, these methods are known to have significant limitations: animal models struggle to fully replicate human brain complexity and human-specific pathways; patient samples only provide snapshots of disease progression and usually fail to capture earlier stages of their development; post-mortem human tissues, on the other hand, is limited to offering a static view of the brain at the time of death.

This is where brain organoids come in. By cultivating **human induced pluripotent stem cells (hiPSCs)** into 3D structures that resemble parts of the human brain, researchers can observe cellular processes with unprecedented accuracy and depth,



Zika virus infection mechanism, discovered using brain organoid models.
Source: Eichmüller O., Knoblich J., 2022, Nature.

	2D culture	brain organoid	animal model
Cell types	homogeneous / heterogeneous	heterogeneous (limited)	heterogeneous (rodent-specific)
Cellular interactions	lost	conserved	conserved
Modelling cellular/mechanical communications	feasible	feasible	limited
Human specific genes	conserved	conserved	introduced by genetic tools in rodent context
Manipulation	feasible	feasible	limited
Biobanking	feasible	feasible	feasible (only at cellular level)
Reproducibility	moderate	low	high

Comparison of characteristics among 2D cell culture, 3D brain organoid models, and animal models.
Source: Castiglioni S. et al., 2023, International Journal of Molecular Sciences.

opening up new possibilities for understanding disorders like autism, Alzheimer's disease, Parkinson's disease, and even the impact of viral infections.

A notable example that highlights the potential of brain organoids is the Zika virus outbreak in 2016. The virus spread through Central and South America and was associated with foetal microcephaly - a reduction in infant brain size and head circumference. Early studies using 2D cultures revealed that **neural progenitor cells (NPCs)** were easily infected by the virus, but it was only through 3D organoid

models that microcephaly-like phenotypes could be fully replicated. Researchers found that the Zika virus specifically targets neural progenitor cells in key brain regions, disrupting brain architecture by affecting **radial glial cells (RGCs)**. This leads to reduced neuron production and increased cell death. Studies also identified the viral protein NS2A as a major factor in damaging the structure of these cells. Unlike other flaviviruses such as Dengue, only the Zika virus caused this specific damage, highlighting the precision of using organoids to study disease mechanisms.

Simulating Brain Networks: Modelling the Building Blocks of Thought

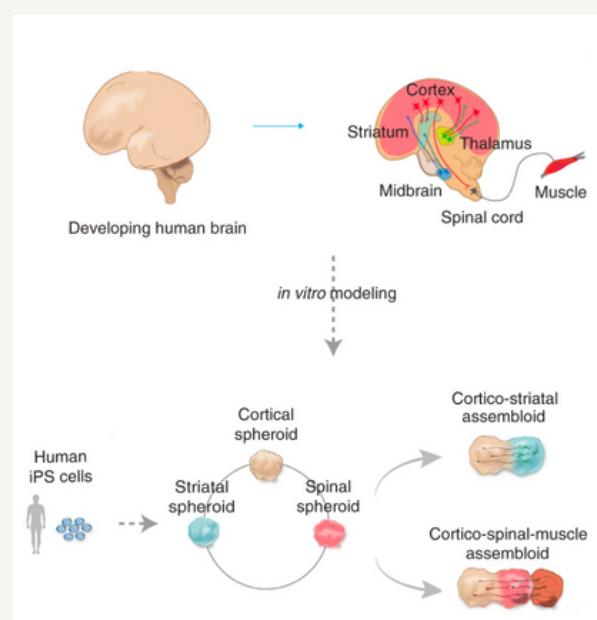
Another fascinating application of brain organoids is their use in modelling core brain functions. Specifically, modelling of long-range neural connections is essential for understanding how different regions of the brain communicate and function together. In the past, studying the human nervous system has been extremely difficult owing to the complexities involved in accessing human brain tissues and maintaining their functions *in vitro*. This challenge can be overcome through the development of brain assembloids: where organoids representing distinct brain regions - such as the cortex and striatum - are fused together to replicate the complex network of interactions that take place between these areas.

For instance, in a 2022 study by Miura et al., cortico-striatal assembloids were used to study the connections between the cortex (involved in decision-making and higher cognition) and the striatum (responsible for motor control and reward processing). These assembloids have shed light on the specific brain circuits that are disrupted in neuropsychiatric conditions such as schizophrenia, autism spectrum disorder, and obsessive-compulsive disorder. By using brain assembloids, researchers can now probe how genetic mutations or environmental factors impact the

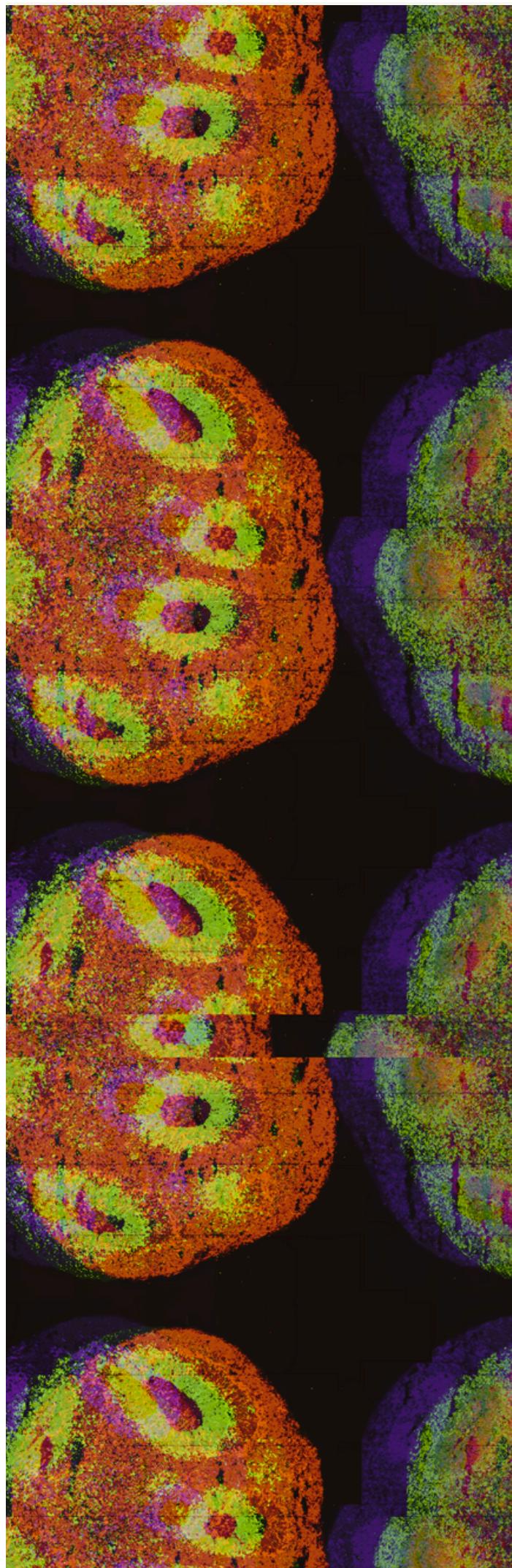
development and functioning of these neural circuits.

From Promise to Practice: Tackling the Limitations

Despite the potential of brain organoids, several challenges remain. One major limitation is their lack of full maturity. In comparison to real human brains, organoids lack important components like vascular systems and certain cell types (e.g., microglia which are the primary immune cells of the central nervous system), contributing to **hypoxia** (oxygen deficiency) and stress in organoids. Attempts have been made to overcome these hurdles by integrating vascular cells or microglia into organoid models through co-culture, induction and transplantation methods, creating vascularised brain organoids. However, existing techniques require further improvements in scalability



In vitro modelling of developing human brain using hiPSC-derived region-specific neural cultures and assembloids.
Source: Miura, Y. et al., 2022, Nature.



before they can be implemented to fully replace current organoid cultures.

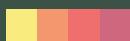
Conclusion

3D brain organoids surpass 2D cell cultures and animal studies in accurately modelling disease pathology and brain functions, providing a powerful platform for studying brain disorders in a way that traditional methods cannot replicate. Despite challenges, the opportunities that this novel technology can offer - combined with the analytical power of bioinformatics - make them a promising tool in the future of neuroscience.

References and further reading:

- Eichmüller, O.L., Knoblich, J.A. Human cerebral organoids - a new tool for clinical neurology research. *Nat Rev Neurol* 18, 661–680 (2022). <https://doi.org/10.1038/s41582-022-00723-9>
- Kim SH, Chang MY. Application of Human Brain Organoids—Opportunities and Challenges in Modeling Human Brain Development and Neurodevelopmental Diseases. *Int J Mol Sci.* 2023 Aug 7;24(15):12528. doi: 10.3390/ijms241512528. PMID: 37569905; PMCID: PMC10420018.
- Miura, Y., Li, M.Y., Revah, O. et al. Engineering brain assembloids to interrogate human neural circuits. *Nat Protoc* 17, 15–35 (2022). <https://doi.org/10.1038/s41596-021-00632-z>

Opportunities



In this issue, the BINFSOC team is pleased to introduce an upcoming opportunity at the Garvan Institute of Medical Research: the Summer Scholarship Program for the upcoming 2024/25 summer holidays.





Garvan Institute
of Medical Research

Garvan Institute



SCHOLARSHIP PROGRAM

SUMMER
2024/25

about Garvan

The Garvan Institute of Medical Research is an independent Medical Research Institute (MRI) based in Sydney, known for delivering scientific and clinical impact on a global scale in collaboration with organisations that share its vision. It stands as one of Australia's largest and most highly regarded MRIs.

Full-time

Sydney

\$625 per week

8 weeks

Mid-Nov 2024

about the program

The Summer Scholarship Program, provides an exceptional opportunity for currently enrolled undergraduate students to engage in research projects during the summer of 2024/2025.

This program is designed to immerse highly talented undergraduates, particularly those in Science or related disciplines, in the research process. It aims to enrich your educational journey and inspire a deeper interest in research or related fields.

how to apply

The position will remain open until filled. Positions are aimed to be filled by the end of October 2024. All applicants will be notified of the outcome of their application by the end of October 2024.

https://garvan.wd3.myworkdayjobs.com/en-US/garvan_institute/job/Garvan-Summer-Scholarship-Program-2024-25_PRF7378



PROJECTS

1

► **Pan-Cancer analysis of fetal-like cells in tumours at spatial resolution**

It has been discovered that fetal-like cells in liver cancer play an essential role in immune suppression and impact clinical outcomes. On this project you will specifically learn how to explore spatial transcriptomic data to identify fetal-like cells in the various tumour microenvironment.

Prerequisites: R, Python

2

► **Decoding the epigenetic principles of early embryonic development**

This project focuses on gene expression and next generation sequencing technology to investigate the fundamental epigenetic mechanisms driving the complex organization of tissues in a developing embryo. These findings will aid in exploring how aberrant changes to the epigenome drive congenital disorders associated with improper organ development and positioning.

Prerequisites: R, Unix shell

3

► **Evaluation and finetuning of phenotype concept recognition tools**

In this study, you will evaluate the performance of advanced phenotype concept recognition tools using a newly created gold corpus of HPO annotations from medical case reports, with potential for finetuning the tools if time permits.

Prerequisites: Python (required), familiarity with NLP and LLMs (helpful)

4

► **Building a polygenic risk prediction pipeline for whole genome sequence data**

The task is to build and validate a pipeline for calculating polygenic risk scores (PRS) from whole genome sequence data, facilitating clinical risk prediction across various diseases using diverse genomic datasets.

Prerequisites: Unix, Python/R

5

► **Developing a Novel Diagnostic Method for the Muscle Disease FSHD Using Long-Read Sequencing**

A streamlined diagnostic test for FSHD will be developed using Oxford Nanopore Technologies (ONT) long-read sequencing, combining genetic and epigenetic markers to improve diagnostic accuracy and speed.

Prerequisites: GitHub for hosting the comparison and automation with GitHub actions Bash, Python, and R for running tools and visualisation Enthusiasm for genomics data analysis

6

► **Understanding the heterogeneity of breast cancer**

You will apply and compare several omics-based subtyping methods to analyze breast cancer heterogeneity using bulk and single-cell data, aiming to resolve inconsistencies between different subtyping approaches.

Prerequisites: Experience in R is preferred



PROJECTS

7

► **Development of REDCap Integration for CTRL using Typescript and REST**

In this project, you will help develop a new REDCap integration for the CTRL platform using TypeScript and REST APIs, enabling better data sharing between the platform and electronic data collection software.

Prerequisites: Typescript, REST API

8

► **Harnessing single-cell multi-omics and population genetics to identify novel regulatory elements for autoimmune diseases**

By integrating large-scale single-cell multi-omics data, this project aims to identify novel regulatory elements associated with autoimmune diseases, shedding light on the genetic mechanisms driving these conditions.

Prerequisites: Basic skills in Unix are required. Experience in R/Python is preferred. Experience in C/C++ will be given priority.

9

► **Multi-omics single-cell data integration and gene regulatory network inference using deep learning**

Adopting deep learning techniques, you will integrate unpaired single-cell RNA and chromatin accessibility datasets to infer gene regulatory networks in different cell types.

Prerequisites: Basic skills in Unix are required. Experience in R/Python is preferred.

10

► **Identifying novel genetic markers for coronary artery disease by combining blood samples from both patients and healthy donors**

This investigation seeks to improve the detection of functionally relevant genes for coronary artery disease by utilizing patient gene expression data rather than relying solely on data from healthy donors.

Prerequisites: Basic skills in Unix are required. Experience in R/Python is preferred

11

► **Genomic Research Results Return in Australasia**

In this research, you will explore the potential for expanding the My Research Results (MyRR) program by conducting interviews, surveys, and literature reviews to develop strategies for improving return-of-results practices in genomic research.

Prerequisites: Microsoft Office/Google workspace; research methods subjects including literature reviews, annotated bibliographies and an introduction to qualitative and/or quantitative research

Contact us



IF YOU HAVE ANY COMMENTS or feedback regarding BINFsights, please write to us at binfo@unswbinfsoc.com

We also encourage anyone to share with us anything you'd like us to take a look at, be it a bioinformatics tool that you have made or find useful; or news in the bioinformatics world that you'd like to see written about in future issues.



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-- The BINFSOC Team

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