BINF sights.

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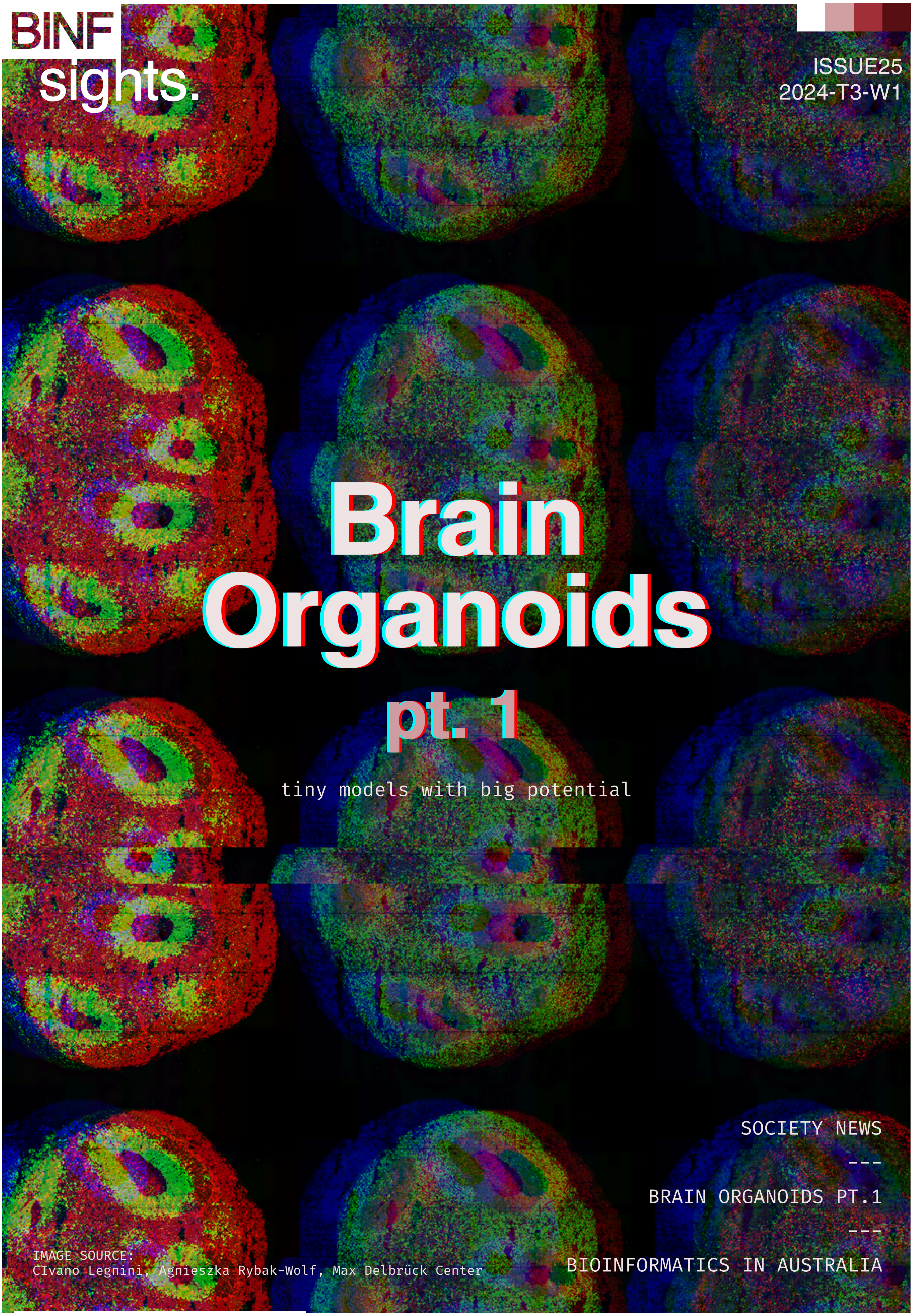


Brain Organoids

pt. 1

tiny models with big potential

SOCIETY NEWS

BRAIN ORGANOIDS PT.1

BIOINFORMATICS IN AUSTRALIA

IMAGE SOURCE:
CIvano Legnini, Agnieszka Rybak-Wolf, Max Delbrück Center

Society News

BINFSOC

Recent Events.

-- BINFSOC x CPMSOC Graph Theory Seminar

-- BINF3010 Revision Workshop

Upcoming Events.

-- Meet Your Cohort	T3W2 Friday 20th Sep
-- BINFSOC AGM	T3W3 Monday 23rd Sep
-- COMBINE Conference	T3W9 Monday 4th Jul

B GRAPH THEORY SEMINAR

On Friday 19th July, UNSW Bioinformatics society teamed up with UNSW Competitive Programming and Mathematics Society to host the BINFSOC x CPMSOC Graph Theory Seminar. This seminar aimed to bridge the gap between classroom learning and practical problem-solving, allowing students to extend beyond their theoretical knowledge developed in courses like COMP2521 Data Structures and Algorithms. During the event, students delved into unique real-world applications of graph theory techniques, such as protein and gene networks analysis, Sydney train/metro networks and student class records. The learning experience was complemented by the addition of delicious pizzas. Overall, the seminar was simultaneously an enriching and enjoyable experience, providing students both valuable insights into graph theory applications and an opportunity to connect with peers.

B REVISION WORKSHOP

On Saturday 10th August, BINFSOC hosted a revision workshop for the level 3 bioinformatics course BINF3010 Applied Bioinformatics. The workshop was delivered by the BINF3010 tutor, Gavin Li, who is also a subcommittee member of BINFSOC. The revision seminar proved to be a highly productive session, offering students a valuable opportunity to consolidate their understanding of the course content. Lasting for three hours, key concepts and topics were covered in a concise and coherent manner, ensuring that both in-person and online participants could easily follow along. Additionally, the highly conceptual and complex topics were broken down into simpler successive steps to aid clarity and understanding, thereby providing students with a solid foundation for their upcoming assessments. Overall, the seminar served as an excellent review, reinforcing the main points of the course and boosting students' confidence.

tiny models *with* big potential

***Author**: Gavin Li* ***Compiled**: Yvonne Huang* ***Edit:** Yvonne Huang*

brain organoids pt. 1

> brain organoid reservoir computing - Brainoware

Cultivating your brain in the lab?

Brain organoids, or “mini-brains”, are 3D structures grown from human stem cells that resemble certain aspects of the human brain. They are developed from **pluripotent stem cells** - special stem cells that can differentiate into any cell type in the body. Under specific conditions, these stem cells can be guided to form brain-like structures that replicate the cellular architecture and some functional aspects of the human brain. These remarkable creations have transformed neuroscience by providing a novel way to study brain development, disease, and even brain-inspired computing.

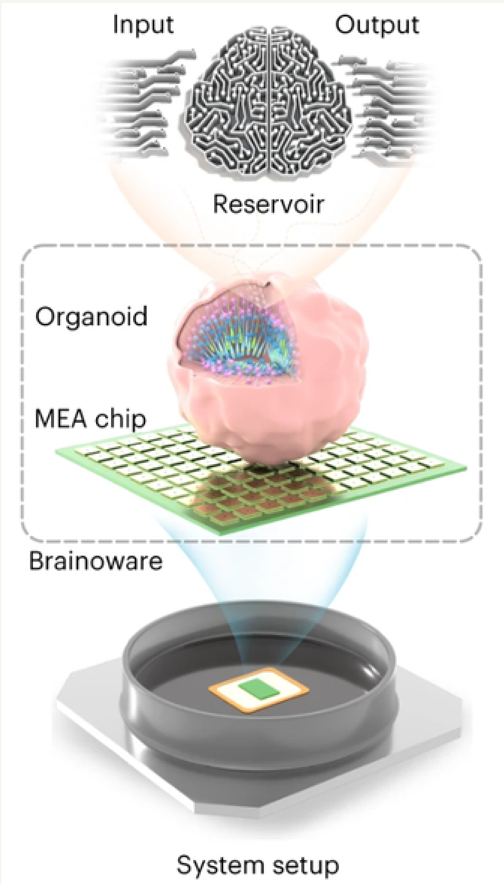
“Brain-Inspired Breakthrough”: AI Revolutionised with Energy-Efficient Brain Organoids

The human brain is a marvel of biological engineering with about 200 billion cells interconnected by trillions of synapses. Unlike current AI systems, the brain naturally consumes 20 watts while efficiently processing and learning from noisy data through **neuronal plasticity** and **neurogenesis**. This impressive feat has inspired researchers to develop **neuromorphic chips**, chips, like **memristors**, which aim to replicate the brain’s storage and processing capabilities. Despite their promise, a key limitation in designing these chips stems from the drawbacks of advancements in **artificial neural networks (ANNs)** - that is, the energy-intensive and time-consuming nature of training ANNs. Neuromorphic chips fall short of fully mimicking brain functions and require improvements in processing capabilities and energy efficiency.

This is where brain organoids offer a potential solution. These mini-brains recapitulate aspects of a developing brain's structure and function. In a groundbreaking approach termed **Brainoware**, researchers have harnessed the reservoir computation and unsupervised learning abilities of **organoid neural networks (ONNs)**. By leveraging the neuroplasticity of brain organoids, Brainoware processes spatiotemporal information with low energy consumption and rapid learning, potentially outperforming current two-dimensional neuronal cultures and neuromorphic chips. The brain organoid, characterised by various brain cell identities and early development of brain-like structures, forms the core of Brainoware - an advanced AI computing framework that integrates human brain organoids with high-density **multielectrode arrays (MEAs)** to leverage the computational capabilities of ONNs. This setup enables the processing of inputs via external electrical stimulation and the generation of outputs through evoked neural activity, laying the foundation for AI computing. All in all, this brain-inspired breakthrough could revolu-tionise AI, bringing us closer to creating systems that learn and adapt as efficiently as the human brain all the while mitigating the persistent problems surrounding ANNs.

Brainoware: Introducing Unsupervised Learning for Advanced AI Computing

Brainoware operates within a reservoir computing framework, a model where input signals are mapped into higher-dimensional computational spaces through a reservoir - a dynamic physical system. Conventional reservoir computing uses fixed *physical* reservoirs, but Brainoware's use of a brain organoid as an *adaptive living* reservoir enables unsupervised learning. In such systems, inputs are converted into spatiotemporal sequences of electrical stimulation, which are then projected into ONNs for processing. The resulting neural activities are utilised to perform various tasks with the help of a readout function that interprets the signals measured. The adaptive living reservoir allows Brainoware to improve its computing performance through training with electrical stimulation sequences, which reshapes the functional connectivity of the organoids, allowing for unsupervised learning. Studies have shown that blocking synaptic plasticity with K252A protein kinase inhibitor halts the unsupervised learning process but maintains computing performance, highlighting the role of neuroplasticity in Brainoware's adaptive capabilities.



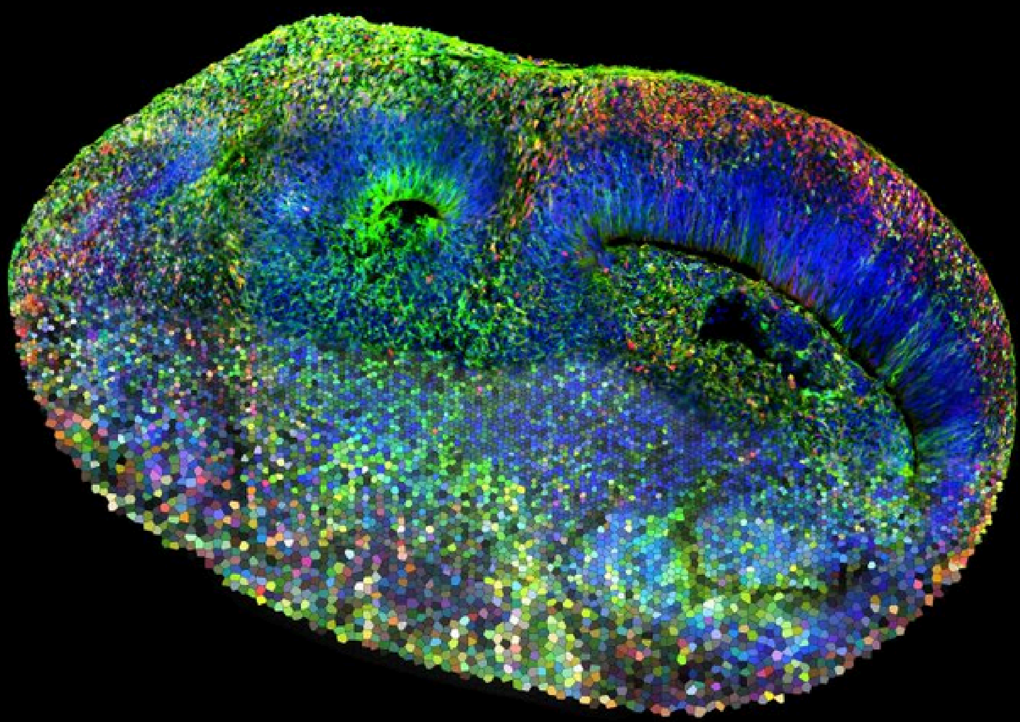
Schematic of Brainoware setup that mounts a single brain organoid onto a high-density MEA for receiving inputs and sending outputs. Image: Cai H. et al., 2023, Nature.

However, it is worth noting that prior to applying Brainoware to specific tasks, its properties as a physical reservoir need to be characterised. Key properties such as nonlinear dynamics, short-term memory, and spatial information processing were tested using bipolar voltage pulse stimulations. Results revealed behaviours similar to those seen in ANNs and memristor-based reservoir computing systems.

AI - Enroute to cognitive behaviour

As an explicit connection between AI and neuroscience, a real-world application that Bainoware has to offer is *speech recognition*. Using a Japanese vowel database, Brainoware was able to distinguish between vowels pronounced by different speakers. The audio clips were converted into spatiotemporal sequences of stimulation pulses and applied to Brainoware. The resulting ONN activity was fed into a logistic regression function for classification. Training Brainoware over multiple time intervals significantly improved its speech recognition accuracy from 51% to 78%, demonstrating the system's ability to learn and improve performance through training. The reshaping of functional connectivity in the organoid during training facilitated this improvement, highlighting Brainoware's unsupervised learning capabilities.

Brainoware was also applied to predict a **Hénon map** - a nonlinear dynamic system with chaotic behaviour. The task involved



Confocal image of a CHOOSE (CRISPR-human organoids-scRNA-seq) human brain organoid mosaic system.
Image: Knoblich Lab / IMBA-IMP Graphics.

dimensionally reducing the 2D Hénon map into a 1D decomposition, encoding it into spatiotemporal sequences of voltage pulses, and stimulating Brainoware. A simple readout linear regression algorithm was able to decode the neural activity of the organoid to predict the Hénon map. Training Brainoware with the Hénon map dataset over multiple epochs improved its regression score from 0.356 to 0.812, demonstrating effective learning. Furthermore, blocking synaptic plasticity reduced the learning improvement, confirming the dependence on neural plasticity. Comparisons with other machine learning algorithms showed that Brainoware outperformed traditional ANNs without **long short-term memory (LSTM)** units, achieving comparable accuracy with significantly reduced training times.

Current Challenges

The current Brainoware approach faces several challenges. For example, the generation and maintenance of brain organoids suffer from high variability, low throughput, and limited viability. Engineering efforts are being made to optimise and standardise production. Power consumption of peripheral equipment (e.g., CO_2 incubator, computer) is another concern that needs to be addressed. Additionally, more advanced interfacing methods are being developed to replace the rigid electrodes currently in use, which limit stimulation and recording capabilities. Lastly, data extraction, management, analysis and interpretation represent another area that is essential in maximising Brainoware's potential. Bioinformatics techniques and algorithms could potentially be useful in encoding and decoding the huge volumes of data delivered to and collected from Brainoware.

References and further reading:

- Cai, H., Ao, Z., Tian, C. et al. Brain organoid reservoir computing for artificial intelligence. Nat Electron 6, 1032–1039 (2023). https://doi.org/10.1038/s41928-023-01069-w

Opportunities

In this issue, the BINFSOC team is pleased to introduce ABACBS and COMBINE, Australia's leading organizations for bioinformatics and computational biology. BINFSOC will be organising an event to the COMBINE National Student Symposium in November.

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AUSTRALIAN BIOINFORMATICS AND COMPUTATIONAL BIOLOGY SOCIETY

Australia's leading body for bioinformatics and computational biology is the **Australian Bioinformatics and Computational Biology Society (ABACBS)**. The society aims at fostering bioinformatics in Australia by supporting students, providing representation as well as promoting interaction and awareness. ABACBS assists in establishing career opportunities in the field of bioinformatics and computational biology by providing a platform for companies to advertise job openings on their jobs board.

Furthermore, the society strives to promote the importance of their field of science to the general public. ABACBS runs many regional and national events (e.g., seminars and workshops), with their annual national conference being their flagship event. They also offer memberships if you are seeking to help contribute towards achieving their aims. Membership benefits include discounted attendance fees for ABACBS events and access to travel bursaries, prizes and awards.

ABACBS National Conference

The **ABACBS national conference** brings together students, academics, researchers and professionals, representing an excellent opportunity to network with professionals and learn about the latest cross-discipline research and cutting-edge technologies. The 2024 conference will be held at the **University of Sydney** on **4-6 November**, featuring both national and international keynote speakers as well as contributed oral and poster presentations. A few key themes that will be covered include AI in biology and medicine, single-cell and spatial technologies, genomics and the application of bioinformatics in cancer and immunology research. The conference will run in conjunction with the **COMBINE student symposium**, **Symposium on Bioinformatics Excellence and Innovation**, **BiocAsia**, and **EMCR Hackathon**.

COMBINE is the student subcommittee of ABACBS and the **International Society for Computational Biology (ISCB)** Regional Student Group for Australia. They are a student-run society setup for students in computational biology, bioinformatics and related fields. COMBINE facilitates professional development, collaboration and networking for students and early-career researchers. They provide a platform for university students all across Australia to come together to discover the different kinds of research occurring at various institutes through seminars, workshops and social events. COMBINE also hosts an annual student symposium which will be in conjunction with the ABACBS national conference this year.

Participating in COMBINE's free webinars and hackathons is a fantastic way to learn, meet new people and collaborate with bioinformatics students from various institutions. Their bioinformatics workshops can also help you in sharpening your research skills and ability to use different bioinformatics tools. If you are currently studying bioinformatics, computer biology or a related field, be assured that there are opportunities for you. Check out ABACBS and COMBINE's websites for more information regarding job opportunities and upcoming events.

For more information:

`ABACBS website_` www.abacbs.org

`COMBINE website_` www.combine.org.au

Contact us

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

TO VIEW PAST AND PRESENT issues of BINFsights, check out our website at unswbinfsoc.com/binfsights
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-- The BINFSOC Team