The ARC Centre of Excellence for Integrative Brain Function (CIBF)

Annual Report 2014
Collaborating organisations

MONASH University

THE UNIVERSITY OF QUEENSLAND

THE UNIVERSITY OF MELBOURNE

THE UNIVERSITY OF SYDNEY

Australian National University

UNSW

Partner organisations

Queensland Institute of Medical Research

Cold Spring Harbor Laboratory

Weill Cornell Medical College

MRC

National Institute for Medical Research

Duke University

SISSA

National Institute of Mental Health

NEW YORK UNIVERSITY

HBP

International Neuroinformatics Coordinating Facility

Institut de Neurosciences des Systèmes

RIKEN
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The ARC Centre of Excellence for Integrative Brain Function (CIBF) has been established to address one of the greatest scientific challenges of the 21st century – understanding how the brain interacts with the world. Led by Monash University, CIBF includes researchers from The University of Queensland, The University of Melbourne, The University of Sydney, Australian National University and The University of New South Wales. CIBF investigators are also based at the Queensland Institute of Medical Research and 11 other partnering institutions in Europe, Japan and the US. These researchers provide key research equipment and expertise and collaborate with CIBF researchers.

One key feature of the seven-year funded program (2014 – 2020) is a move to multidisciplinary collaborations involving neurobiologists, cognitive scientists, engineers and physicists. These collaborations are vital for Australia’s global competitiveness. They will better enable CIBF experts in cellular, systems and computational neuroscience, and neural engineering to answer complex questions in neuroscience.

**Mission**

CIBF research will lead to major social and economic advances through the development of new brain-based technologies. Specifically, we seek to understand how the brain integrates information at multiple scales, from nerve cell electrical and biochemical activity through patterns of activity in large scale circuit networks to yield complex behaviour in the three key integrative daily-life functions of attention, prediction, and decision.

We are developing predictive models of brain processes for the development of novel neural technologies for patentable devices and software. We are fostering a community of scholars by mentoring future research leaders skilled in multi-disciplinary approaches that are melding neuroscience, physics, and engineering. Through this process we will remain at the forefront of international research as well as engage with international neuroscience initiatives, including the European Human Brain Project and the US BRAIN initiative.

Multi-pronged, multi-disciplinary approaches have the ability to capture the enormous scientific impact of understanding the integrative functions of the brain, and ensure that Australians benefit from the rapid advances being made in neurotechnologies. The ambitious aims of the Centre cannot be achieved by shorter duration discovery-type project grants. By playing a key role in the international quest for understanding brain function, we are also able to communicate the ethical, social and economic impact of brain research to the wider community.

**Vision**

To address the greatest scientific challenge of the 21st century – understanding how the brain interacts with the world, by focusing on the complex brain functions that underlie attention, prediction and decision-making.

About
Aims

The Centre for Integrative Brain Function is an Australian focus of the international quest to understand how the activity of brain cells mediates the way we interact with the world. We are studying how electrical and biochemical activity is coordinated across brain regions, and across time, to enable adaptive behaviour. We are studying three key integrative functions: attention, prediction, and decision. These functions are familiar to everyone: for example, when crossing a street, your attention may be drawn to an oncoming car, your brain works to predict the car’s path, and you decide whether to continue crossing or to retreat to the kerb. These integrative functions depend on collecting accurate sensory information, and weighing this up based on experience and memory. We are probing these functions non-invasively in humans and, in parallel, through experimental studies of other mammals.

The Centre is complementing (not duplicating) current international programs. Our focus on integrative brain function is specifically chosen so we can cooperate with these groups to maximal mutual benefit. As a tangible sign of collaboration, our international Partner Investigators and Advisory Board members include leaders of the EU Human Brain Project and the USA Human Connectome and BRAIN Projects among others.

Objectives

To achieve the aims of the Centre we are focussing on:

• Revealing how the brain integrates information in large-scale networks to yield complex behaviour.
• Developing neural technologies and translating them into patentable devices and software.
• Maximising dissemination and exploitation of our findings, and public engagement, through a knowledge-sharing program.
• Mentoring a new generation of future research leaders at the interfaces between neuroscience, physics, and engineering, to foster an international competitive culture of combined theoretical and experimental neuroscience.
• Serving as an Australian focal point for interactions with leading international neuroscience initiatives, including the Human Brain Project and the BRAIN initiative.
Highlights from 2014

The Brain Dialogue twitter wall, August 2014

Monash University announces the funding of the CIBF, December 2013

Aidan Byrne (ARC CEO) looking at brain data at the CAVE2 (Monash University), August 2014

The CIBF Chief Investigators scientific meeting at the University of Queensland, December 2014

First journal article acknowledging the CIBF, March 2014

Public event “Neuroethics down under”, Melbourne Convention and Exhibition Centre, December 2014
HIGHLIGHTS

Inaugural Art Prize Winners, Anna Provost and Julian Matthews with their winning art work, August 2014

The first meeting of CIBF Chief Investigators following the announcement of funding, February 2014

CIBF Board visit to the University of Melbourne node, October 2014

Our first public event: “Who is in charge, you or your brain?” State Library of Victoria, August 2014

The Australian College of Optometry announce the funding of CIBF, March 2014

Rory Townsend – in front of his poster at the Society for Neuroscience meeting, Washington DC, November 2014

Inaugural Art Prize Winners, Anna Provost and Julian Matthews with their winning art work, August 2014
When I first heard of the CIBF proposal and was asked to Chair the Advisory Board, almost two years ago now, I was honoured by the invitation and impressed by the ambitious program.

I was delighted when we heard the good news that the application had succeeded, especially as the funding environment was so competitive. The news has heralded one of Australia’s largest research endeavours: to understand how the brain interacts with the world.

I applaud Professor Egan and the team of national and international researchers on their vision, and commend the Australian Research Council for its support.

Since funding was announced in late 2013 it has been a whirlwind effort to bring together the partners, more than 15 across Australia and internationally, and initiate the research program. The teams at Monash University and across all nodes have set up CIBF for success, both for research outcomes and to capture the public imagination.

All members have already demonstrated their commitment to CIBF. Our international members attended the first meeting by teleconference despite the time zone challenges across three continents. For the second meeting it was wonderful that all three international members travelled to Australia and during their visit undertook tours of the facilities in our two Melbourne nodes – Monash University and the University of Melbourne.

At the second meeting, the Advisory Board provided timely advice and recommendations for optimal collaboration across such a large and multi-organisation team. Ways were suggested to boost our research activities, as well as enhance our outreach and organisational aspects.

I am excited by CIBF’s potential and encouraged by its progress to date. I cherish my involvement and hope you enjoy reading about CIBF’s achievements to date and plans for the future.

Professor Lyn Beazley
Chair Advisory Board

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Professor Lyn Beazley
Chair Advisory Board
It has been a pleasure and unique challenge directing the Australian Research Council Centre of Excellence for Integrative Brain Function (CIBF) over the past 12 months.

As a researcher who has primarily led geographically co-located teams, being Director of the CIBF has been a new and interesting opportunity. I have certainly felt the weight of expectation that comes with bringing such an internationally competitive group of researchers together — each with a significant track record in their own right — and aiming to address a major challenge of the 21st century — how the brain interacts with the world.

The research program — comprising four themes, focused on three brain functions — has already made significant progress. We are excited about what new and interesting discoveries will be made in the near future.

There are also a number of projects — initiated in 2014 — whose completion will give the CIBF a competitive advantage in the field of brain research. These include the acquisition of a TMS compatible MR head coil, that will allow fMRI and TMS approaches to be combined in a single experiment.

We are also developing an implantable device that will allow the simultaneous recording and stimulation of a local brain region.

We are also enhancing existing brain atlases by combining them with data from new and higher resolution imaging techniques.

The Advisory Board has been very supportive and provided excellent advice in the establishment phase of the centre. Comprising members with stellar careers in brain research, government and industry, the Board has been heavily engaged in developing the centre’s activities and research ideas and developments.

The centre would not be operational without the hard work of the CIBF staff. They have worked tirelessly to bring together the (more than) 15 organisations that comprise the CIBF. They have also been instrumental in establishing a unique (and highly effective) program for sharing knowledge and information within and outside the CIBF — The Brain Dialogue.

During the establishment year of the CIBF, the Brain Dialogue has been one of the highlights. Other highlights included the official launch of the CIBF and our first public event. However, most significant to me has been the passion with which the researchers are approaching their role in making the CIBF a success, and working towards some truly remarkable advances. I hope you enjoy reading about the activities of 2014.

Professor Gary Egan
Director, CIBF

CIBF Advisory Board. Left to right: Ulf Eysel, David Van Essen, Allan Jones, Gary Egan, Lyn Beazley, Amanda Caples, Richard Huysmans, John Funder.
Monash University is the Administrating Organisation of the CIBF and has signed a collaboration agreement with five other Australian Universities to deliver the aims and objectives of the CIBF. There are a further 11 organisations from across Australia and the world, referred to as Partner Organisations, who are also involved in the CIBF — providing expert researchers or collaborative opportunities.

### CIBF participating organisations

- **Funding Organisation**
  - Australian Research Council

- **Administering Organisation**
  - Monash University

- **Collaborating Organisations**
  - University of Queensland
  - University of New South Wales
  - University of Sydney
  - Australian National University
  - University of Melbourne

- **Partner Organisations**
  - Human Brain Project (Switzerland)
  - Cold Spring Harbour (USA)
  - Weill Cornell (USA)
  - International Neuroscience Coordinating Facility (Sweden)
  - National Institute of Medical Research (UK)
  - National Institute of Mental Health (USA)
  - Queensland Institute of Medical Research
  - National Institute of Health and Medical Research (France)
  - New York University (USA)
  - National Institute of Health and Medical Research (France)
  - Riken (Japan)
  - International School of Advanced Studies (Italy)
  - Duke (USA)
The Advisory Board oversees the operations of the CIBF. It comprises local (Australian) and international members of the neuroscience and broader scientific research community. The Executive Committee (comprising centre researchers and senior administrators) provides management of the CIBF, and actions are implemented and overseen by the CIBF Administrative Team and Centre Coordinators.

**Advisory Board**

The Advisory Board provides strategic advice to the Director, regarding the research and non-research activities of the CIBF. It meets twice per year – once in person and a second time via video or teleconference. Members have significant experience in large multi-organisation collaborations as well as international neuroscience activities, industry and government engagement.
Executive Committee

The Executive Committee oversees the specific operations of the CIBF. In 2014, the Executive Committee met fortnightly to help ensure early establishment of the CIBF progressed as smooth as possible. The Executive Committee comprises representatives from each of the thematic areas of research, each node and the senior personnel of the CIBF. In 2014, the Executive Committee comprised:

- Professor Gary Egan (CIBF Director, Monash University)
- Professor Marcello Rosa (CIBF Deputy Director, Monash University)
- Dr Lisa Hutton (CIBF Manager)
- Dr Richard Huysmans (CIBF Acting Manager)
- Ms Vicki McAuliffe (CIBF Administrator, Committee Secretary)
- Professor Jason Mattingley (Brain Systems, University of Queensland)
- Professor Pankaj Sah (Neural Circuits, University of Queensland)
- Professor Greg Stuart (Cells and Synapses, Australian National University)
- Professor Peter Robinson (Models and Technologies, University of Sydney)
- Professor Michael Ibbotson (University of Melbourne)
- Professor George Paxinos (University of New South Wales)

Administrative Team and Research Coordinators

The Director and the Executive Committee are supported by the Administrative Team to conduct and communicate the day-to-day research, non-research and administrative activities of the CIBF. In 2014 the administrative team were:

- Dr Lisa Hutton (Manager)
- Dr Richard Huysmans (Acting Manager, May–Dec)
- Ms Janelle Giling (CIBF Administrator)
- Ms Samantha Goode (CIBF Administrator)
- Ms Priscilla Gross (University of Melbourne, Node Administrator (from November))
- Ms Cindy Guy (University of Sydney, Node Administrator)
- Ms Roxanne Jemison (University of Queensland, Node Administrator)
- Ms Danielle Khalidi (ANU Node Administrator)
- Ms Henrietta Leyonhjelm (University of Melbourne, Node Administrator (to November))
- Ms Vicki McAuliffe (CIBF Administrator)
- Dr Elizabeth Paton (Brain Dialogue and Education Administrator)
- Dr Emma Schofield (UNSW, Node Administrator)

There are also coordinators responsible for a number of non-research activities, including:

- Professor Sarah Dunlop (Equity and Diversity)
- Dr Wojtek James Goscinski (Computation)
- Professor Jakob Hohwy (Neurophilosophy)
- Dr Rachel Nowak (Brain Dialogue)
- Dr Jeanette Pritchard (Industry Engagement)
- Professor Ramesh Rajan (Education)
Brain systems

Chief investigators
Jason Mattingley – Theme Leader
Gary Egan
George Paxinos
Marta Garrido

About
Historically, brain science has focused on how distinct brain regions carry out specialised functions such as sensation, motor control and cognition. This approach has led to a “compartmentalised” map of the brain, whereby nerve cells (neurons) with shared morphology and function, located in the same area, correspond to discrete information processing modules. For example, the visual system is often described as comprising over 50 distinct areas, each processing a different aspect of the external world (e.g., colour, orientation, motion). However, it is now recognised that the next challenge is to understand how activity is coordinated across brain areas, in real time. Such coordination is crucial for virtually all brain functions. For example, when you cross the street, the sight and sound of an oncoming car are coordinated to yield a coherent, multisensory perception. Brain centres for movement planning are coordinated with the ones that produce goal-directed actions (initiating movements to ensure safe crossing). At the same time, sensory feedback from the environment is used to refine ongoing movement. These principles also apply to high-level functions such as language, where activity in many areas is coordinated to extract meaning and generate speech. In sum, the brain needs to be understood in terms of the interaction of its parts, not by considering each part in isolation.

Recent developments in brain imaging and brain stimulation allow functional studies of the living human brain. Despite this advance, there are still only tenuous connections between the results of human studies and those of experimental studies in other mammals, which can provide the most detailed information about the cellular processes and neural circuits of the brain. The Brain Systems research theme addresses this problem by conducting parallel investigations in monkeys and humans. A key strategy will be to develop measures of simple behaviours (e.g. shifting of visual attention, prediction of movement trajectories, and perceptual decisions on discrete sensory events).

Research aims

• To take maximum advantage of new analytic measures of human brain function, and apply these to human and non-human mammalian brains in order to understand the integration of brain systems.

• Adopt and develop analytical methods that are able to investigate physiological functions of brain networks

• Develop decoding techniques to reveal patterns of activity that might be obscured by noise

• Use recordings from connected nerve-cell groups and Magnetic Resonance Imaging (MRI) to reveal how networks of neurons communicate within the brain.

Case study – Mismatched brains

Your brain is very good at picking out odd noises from a series, a skill related to its ability to shift attention to what matters most, which it does continuously, subconsciously, and at lightning speed. Just consider what happens if your smoke detector chirps, or you hear the faint screech of brakes in the distance.

In a study conducted by CIBF researcher Marta Garrido (and colleagues), they found that the brain of an older person is less adept at picking up those odd-ball events. The ability to spot the unusual is called (somewhat clumsily) “mismatch negativity” or MMN. It is easy to measure as changes in brain electrical activity, and is most often studied using visual and sound cues, although it also happens with smell and touch.

“It’s a really well understood network in the brain, and a good place to start when investigating how the healthy ageing brain changes over time”, says Marta Garrido.

When a sound is played, Electroencephalogram (EEG) recordings pick up crosstalk between the auditory cortex (which receives sound inputs from the ears), the temporal lobes (which process sounds) and the frontal lobes (responsible for complex thought such as decision making). Odd-ball sounds in a sequence of identical tones, change the pattern and frequency of this crosstalk.
The research team, asked men and women aged either 70 to 78 years or 20 to 35 years to press a button when they heard an odd-ball sound. At the same time, the volunteers’ brain responses were measured via EEG.

Older people had far less change in activity in the frontal lobe in response to tone changes. Similar patterns are seen in people with memory disease such as dementia.

Nonetheless, in this study, the reaction times for the older people, as measured by how fast they pressed the button, was the same as for young ‘uns. One explanation is that the brains of older people process the information as efficiently as young people, albeit it differently.

Another explanation, favoured by the body of evidence, is that the brain recordings are picking up an age-related impairment that would lead to slower reaction times to more complex surprise events.

**Future directions**

In 2015, the theme aims to establish a method for tracking the transmission of brain signals across and through different regions of the brain. The intention is for this method to be used across CIBF nodes and in different animal models to ensure future research can be directly compared and correlated regardless of the location or animal model used.

Researchers will also purchase a transcranial magnetic stimulation (TMS) compatible magnetic resonance (MR) head coil to allow the conduct of novel behavioural experiments with functional brain imaging (fMRI and EEG) and neural stimulation (TMS and tDCS) to determine the neural circuits responsible for attention, decision-making and prediction in healthy human participants.

**Reference**

Neural circuits

Chief investigators
Pankaj Sah – Theme Leader
Marcello Rosa
Michael Ibbotson
Paul Martin
Ehsan Arabzadeh

About
The mammalian brain is assembled from local neural circuits that are connected into networks, in which signals are encoded as brief voltage spikes. This spiking activity is used to communicate information between neurons, and is the basis of the computations performed in the brain. Spiking rates in different neurons, and their change over time, are thought to encode diverse features such as the properties of sensory stimuli, the location of an important object in the environment, movements to be made, or memories of events. Ultimately, our ability to attend to particular aspects of the world, to predict events, and to make decisions results from activity in neuronal circuits. However, our understanding of how these circuits are organised, and how they are formed into large-scale networks, remains rudimentary.

From studies in the last 50 years we understand the initial processing of sensory stimuli. Moreover, physiological studies in animals and human imaging studies have revealed the brain regions that are involved in simple behavioural tasks, while anatomical tracing has shown the broad principles of how brain areas are connected. However, the functional nature of connections – i.e. how particular circuits determine activity and behaviour, and how circuits adapt to changing circumstances – remains poorly understood. Moreover, how information is encoded in these circuits remains a mystery. This understanding is essential to develop specific models of brain function.

The Neural Circuits research theme will achieve these aims through the use of well established behavioural paradigms for which the brain regions involved are well understood. For example, simple stimulus-response (Pavlovian conditioning) behavioural experiments are being employed in the contexts of attention, prediction and decision. To understand the circuits that underpin this behaviour we are studying the anatomy and connectivity of neurons in the brain regions involved using in vitro recordings and anatomical analysis. To study activity in the underlying neural circuits we record from multiple brain sites in awake behaving animals. Together, these recordings will lead to a model of how different brain centres drive the relevant behaviour. The new method of optogenetic modulation allows activation or silencing of neurons with millisecond precision, and can be engaged to activate the source (cell bodies) or destination (cell terminals) of functional paths. The anatomy and physiology of these connections can then be determined. These studies provide information on the activity of neural networks in rodents and non-human primates. A key part of our Centre strategy is to then test the relevance of these networks to human brain function, by implementing analogous behavioural tasks in non-invasive imaging studies.

Research aims
• To understand neural circuits
• To determine how neuronal circuit function(s) are encoded in neural networks.

Case study – Working out the brain connections that help us move
Marcello Rosa and his team have traced the actual nerve cell connections from the brain’s cognitive (thinking) centres to its motor (moving or doing) centres, from one end of the brain to the other.

By tracing these fine connections in a small primate, the marmoset, the Rosa team infer the likely function of two regions of the premotor cortex (a region in the front part of the brain). The findings are also a good illustration of how the brain “chunks” tasks, with different regions responsible for different parts of a process.
They found that one region — called 6DR — connects to the visual system via the prefrontal cortex, which is responsible for complex thoughts such as decision making. 6DR also connected to regions that are suspected to relay information about internal states and motivations.

The other — called 6DC — has numerous connections to the primary motor cortex. The primary motor cortex controls voluntary movement. It’s the part of the brain that is represented as the iconic homunculus (the distorted human-like figure that illustrates the relationship of different parts of the cortex to body parts).

Finally, the Rosa team also found plenty of connections between the 6DR and 6DC, suggesting that those regions are working closely together.

The high resolution physical evidence supports Rosa’s working hypothesis that 6DR and 6DC form a communication bridge, carrying information from the brain’s sensory and cognitive centres to its motor centres.

So, first the brain, or more specifically 6DR, considers the sensory inputs and internal motivations — I am thirsty. The drink is in the glass over there. I want to pick up the glass and drink.

Then, the rough plan of action is forwarded to 6DC, which works out the precise movements needed, and sends instructions to the primary motor cortex to implement them.

“It’s a cascade of events and information,” says Rosa. “And it all happens in a split second.”

Reference

Future directions
We will use electrophysiology techniques to record from single cells and networks in order to map the neural connections of specific brain regions. In particular we will use functional brain imaging (fMRI and EEG) and neural stimulation (TMS and tDCS) to determine the neural circuits responsible for attention, decision-making and prediction in healthy human participants.

We will make use of CLARITY and other imaging techniques to identify the visual and auditory pathways linking sensory thalamus to limbic centres.
**Cells and synapses**

**Researchers**
- Greg Stuart – Theme Leader
- Steve Petrou
- Ulrike Grünert

**About**

Brain function relies on spiking activity under control of sensory inputs and stored brain states (memories). However, spiking activity also depends on the biophysical properties of neurons and their connections (synapses), as well as whole brain (behavioural and hormonal) states. Ultimately, the generation of spikes requires the movement of charged ions. Thus, short- and long-term changes in neural properties and connections can arise via changes in spiking behaviour (e.g. via biophysical changes in ionic pores through cell membranes), or by dynamic changes in synapses. It is thus critical to determine how the biophysical properties of neurons and their connections govern network activity to understand brain function.

In 2014, researchers, led by CIBF CI Steve Petrou, designed and began prototyping an **optopatch** – a device that allows researchers to observe and control the firing of individual neurons using an all light interface. The device incorporates high power lasers deployed either in wide field or narrow field modes and a support system for cultured neurons. When combined under the correct conditions, the neurons light up as they integrate synaptic input and then transmit their signal by firing action potentials.

CIBF researchers are using another new imaging technique to visualise and subsequently map various **highways** of the brain (such as between the olfactory bulbs, barrel cortex and hippocampus – all used in processing what we see). The technique – called Glass brain imaging was first introduced almost 100 years ago but recent improvements – called Scale, Clarity and SeeDB – together with new microscope designs have accelerated development and use of this approach. This system will be used extensively by the cells and synapses theme.

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**Electric Field squared, incident and transmitted beams**

Diagram showing the design features of shallow angle fluorescence mode prism for illumination of neurons expressing Quasar genetically encoded voltage sensors. Image shows modeling of a Gaussian beam incident upon a glass-water interface, just below the critical angle and is refracted to a narrower shallow angle beam within the water where the neurons will eventually reside.
Research aims

- To establish how neurons combine their inputs and produce an output signal for communication with other brain regions.
- To review the functional (electrophysiological) properties of neurons and their projections via axons (membrane specialisations that provide the physical "wiring" of the brain) at critical sites of brain networks underlying attention, prediction and decision.
- To determine the distribution of different membrane channels within neurons.
- To characterise different membrane channels.
- To establish regions specific rules that govern how neurons combine their inputs to produce an output (spike train) for communication to other brain regions.

Case Study – Turns out red is faster!

The subcortical region of the visual system is divided into three parts – koniocellular (KC), parvocelluar (PC) and magnocellular (MC). Generally speaking, the PC and KC pathways are considered responsible for detecting colour and fine detail (red/green and blue/yellow respectively), whereas the MC pathway is considered responsible for detecting movement and edges.

The best-studied regions of the (subcortical) visual system in primates are the PC and MC pathways and it is known that the MC pathway processes and transmits information faster. Thus, visual signals passing along the MC pathway are assumed to reach the cerebral cortices before the signals from PC pathways do – essentially we notice movement before we notice colour.

However, less is known about response timing of the KC pathway.

In a recent study Paul Martin and his colleagues from the Save Sight Institute investigated the response timing of specialised KC cells (“blue-on/yellow-off” and “blue-off/yellow on”) cells in comparison to PC cells.

Essentially they found a hierarchy with MC as the fastest processor, followed by PC then KC.

Martin noted we have known for a while that “human reaction times are longer for blue colours than for others”. Here, his team has identified why: “nerve signals for seeing red and green colours travel more rapidly from the eye to the brain than those for blue.” That is – red is faster!

Reference


Future directions

Work on CLARITY and optopatch will continue. As with other themes, the intent is to develop standard methodological procedures that can scale across nodes, animal models and cell types to ensure all research in the CIBF can be appropriately compared and correlated.

In an image, an OpenSPIM microscope is shown developed to enable light sheet imaging of CLARITY processed tissues. The system is currently being optimised for dual illumination and multi-view deconvolution that will enable imaging of 10 x 7 x 7 mm blocks of tissue at 300 nm isotropic resolution.
Models and technologies

Chief investigators
Peter Robinson – Theme Leader
Arthur Lowery
Stan Skafidas

About
Until recently, data collection in neuroscience has outpaced developments in theory and computation. As a result the field has lacked the simple concepts needed to unify results of huge numbers of experiments. As the power of theoretical approaches has increased, we are now starting to see the formulation of models that are linked tightly to brain physiology and anatomy. At the same time, physics and engineering have advanced our understanding of complex systems and networks, and advances in digital computing hardware and software have made it feasible to test these models in detail. Finally, massive databases detailing brain structure and function are becoming available, covering scales from neuronal microcircuitry up to whole brain connectivity.

In 2014 the group carried out a wide range of research on neural field theory and its applications, cortical pattern formation and evolution, brain networks and modes, determination of brain connectivity from activity (the inverse problem), plasticity and TMS, arousal/alertness dynamics, and the hemodynamics underlying functional MRI. Development of the group’s neural field simulation and brain-state tracking software was also undertaken. The findings of this research will impact all aspects of the CIBF – Brain Functions and Research Themes – by providing software for future experiments to build on.

The design of a stimulating and recording electronic implant was initiated, and its key performance metrics workedhoff with the chief investigators of the centre. This implant will draw upon the skills and experiences of the Monash Vision Group’s cortical implant to restore bionic vision.

At the University of Melbourne, researchers have been focusing on the development of in vitro models of the brain in three dimensions (3D). In particular they are trying to identify the best combination of cell and growth scaffold to mimic the brain. There is a long history of using 2-dimensional cell cultures to model and test various tissue types and associated therapeutics, but the move towards 3D cultures provides for models that more closely mimic the cellular environment within the body. The focus has been on identifying a combination of cell and scaffold type that fosters cell growth and differentiation, allows recording of neuronal activity and are reflective of the real brain. Early successes include – what is believed to be – the first maintenance and growth of human neuronal cells in 3D culture. Derived from embryonic stem cells, (SH-SY5Y neuroblastoma cell lines and neurons) were grown in an off-the-shelf scaffold that is proving to be a good match (in terms of cellular properties and ability to record activity).

Research aims
• To institute the same kind of theory-experiment interaction that has proven fruitful in the physical sciences and engineering.
• To use our expertise in data analysis, data fusion, and control engineering to monitor, stimulate, and (potentially) control brain activity.
• To develop quantitative, testable theories of integrated brain function, and to test the predictions against experimental data that span multiple spatial and temporal scales.
• To develop electronic implants that can simulate and record from multiple sites on the cortex.

Case Study – Video (essence of brain)
Use a QR code reader on your phone to access this video of Peter Robinson talking about mathematically modelling the brain.
Functional magnetic resonance imaging (fMRI) is a powerful and broadly used tool for mapping human brain activity. Importantly it is non-invasive and does not rely on ionising radiation – making it relative safe to use.

However, fMRI is an indirect measure of brain activity. Specifically it makes a correlation between the amount of oxygen in the blood in a region of the brain and the likely brain activity (where more oxygen means more activity).

In order to make that correlation, a haemodynamic model (i.e. a model that estimates blood oxygen levels based on an MRI signal) is required. Thus, the quality of the information received about brain activity is directly related to the quality of the haemodynamic model.

Recently, researches have found that the haemodynamic response – essentially how blood flow is regulated in the brain to support brain activity – has unique dynamics (in both space and time) that are not captured in many fMRI haemodynamic models. Thus, many fMRI experiments may be inaccurate as a result.

CIBF researchers – Peter Robinson and Michael Breakspear – along with colleagues from the Universities of Sydney and Wollongong have developed a new haemodynamic model that appears to resolve this issue. Specifically, their model (published in NeuroImage in July 2014) uses a physiologically-based spatiotemporal hemodynamic response function (stHRF), which improved the estimated neuronal response relative to unphysical space–time separable forms (essentially it made better predictions of human brain activity when compared to real or simulated experiments).

Ultimately, their model can avoid ghost neuronal responses that can otherwise be falsely inferred (i.e. avoiding inferring brain activity when no activity is present). Applying the spatiotemporal deconvolution to high resolution fMRI data allows the prediction of neuronal responses that are consistent with independent electrophysiological measures.

Into the future, Robinson and Breakspear noted their model could be used in concert with neural field models of brain activity and enable new (model-driven) inferences of neuronal activity within and between brain regions.

References

Future directions
The CIBF will build on the expertise generated through the Monash Vision Group to make electrodes capable of both measurement and stimulation. These devices will be paired with wireless interfacing and data fusion algorithms and techniques to develop new research tools that can be applied across the CIBF.
**Attention**

**Function Leader**
Michael Ibbotson

**About**
In a complex environment, we prioritise certain objects and actions at the expense of others. Likewise, sudden or unexpected stimuli (e.g. an approaching car) can capture attention during an ongoing task (crossing the street). Attention therefore has two main aspects: an experience and state dependent (“top-down”) component for filtering complex information, and a stimulus driven (“bottom-up”) component that captures attention when there is an unexpected or salient change in the environment. Understanding the brain mechanisms underlying attention is of obvious importance, with implications for many areas including education, driving, surveillance and workplace safety. We know that when attention is focused on part of the visual world (e.g. when reading this text) there is increased activity in visual centres, where cells show enhanced electrical and biochemical activity, and responses synchronize. We also know that these changes depend on neural commands interchanged between brain areas with “executive” functions (in the parietal and frontal lobes), and those involved in sensory processing and motor control.

The most influential and detailed models of attention have come from behavioural and brain imaging studies in humans. Thus, human experiments will guide animal studies at the level of neurons and microcircuits. They will use functional MRI (fMRI) and scalp-recorded EEG to track the location and time course of neural activity associated with attention control and capture. These approaches will be complemented by TMS to modulate activity in specific brain areas, and provide causal evidence of involvement of specific areas in attention.

**Research aims**
- To develop models of attention from behavioural and brain imaging studies in human subjects.
- To map the connections of the attention networks in rodents and non-human primates.
- To understanding the synaptic and ion channel mechanisms underpinning attention.
- To reconstruct synaptic structures and neurotransmitter systems identified with attention.
- Use focal brain stimulation (TMS) to provide causal evidence for the involvement of specific cortical areas in attention.

**Case study – Lopsided brains**
People who have had a stroke can end up with a condition called “spatial neglect” – their brain ignores objects and sounds on one side of the body. This can make everyday tasks like dressing or eating next to impossible.

Curiously, spatial neglect is far more common and severe following damage to the right side of the brain. Why the brain behaves in this lopsided way has puzzled neuroscientists for decades.

According to one theory, the left side of the brain gets sight and sound inputs from the right side of the body, while the right side gets inputs from both sides. Because the right side is carrying more of the brain’s processing load, when it’s damaged, the outcome is worse.

To test whether this theory was correct, Marta Garrido and her colleagues recorded brain activity in 12 healthy people as they responded to sounds from their left and right sides. They used EEG – a way of monitoring rapid changes in electrical activity across the scalp.
Their observations strongly suggested that the theory was correct. “The right hemisphere seems to be interested in sounds coming from the left and the right, whereas the left hemisphere seems to be just interested in things coming from the right side of space,” says Garrido.

But EEG recordings only give a rough idea of where brain activity is occurring. So Garrido and her colleagues also used mathematical modelling to map the EEG activity onto discrete parts of the brain, confirming the finding.

“With modelling, we can tap into the networks and the mechanisms. We can really look at how information travels through different areas of the brain,” explains Garrido.

Studies like this are groundwork for investigating how the brain changes after injury and with recovery, which could lead to better treatments.

**Reference**


**Future directions**

We will investigate the causal role of cortical areas involved in visual searching using focal brain stimulation (TMS in humans; microelectrode stimulation in animals). We will determine the networks involved in coordinating visual search using network-based approaches, such as dynamic causal modelling (DCM) and network-based statistics (NBS), to uncover physiological interactions between functionally related areas during attention tasks.
Prediction

Function leader
Michael Breakspear

About
Recent research shows the brain does not simply respond to external events, but rather compares sensory information against predictions based on internal representations (models). The difference between predictions and external inputs (prediction errors) are used to initiate adaptive behaviours and update the internal models. For example, when you are crossing the street, the observed trajectory of an oncoming car (sensory input) allows your brain to predict your movement relative to that of the car, based on past experience (memories) of trajectories of moving vehicles. Appropriate movements are then initiated to avoid collision. The computational load on the brain is thus reduced, from all-encompassing sensory perception to the more tractable problem of comparing sensory inputs to internally stored predictions. This predictive error framework can be used to unify apparently diverse behavioural data, from low-level functions such as control of eye movements, through to attention and high-level functions such as decision.

Some of our physiologically based studies of prediction employ the well-established fear conditioning paradigm in rodents. This paradigm is being adapted to test predictive coding models by manipulating statistical regularities in the properties or timing of conditioned and unconditioned stimuli. For example, the probabilities will be changed so that only 50% of the tones (conditioned stimuli) are paired with the shocks (unconditioned stimuli). Thus animals can modify their expectation of a shock and respond adaptively. In other studies, we will use eye movement-based prediction tasks in non-human primates trained to “intercept” visual targets based on their prior history of movement, with or without concurrent multisensory cues (e.g. an auditory stimulus that predicts stimulus acceleration or deceleration with different probabilities). This same paradigm can be adapted to human studies once we have learned more about the physiological signatures of prediction errors. The new approach that the Centre research brings is to undertake multiscale experiments based on these paradigms, and analyse and interpret the data acquired from the scale of the single neuron, through neural circuits, up to the whole brain.

Research aims
- Integrate theoretical models of prediction at a multi-scale level: from single cells to whole brain.
- Use behavioural and electrophysiological responses to infer how “prediction errors” update models and change predictions.
- Build population-based models of the brain to generate cell- and circuit-level prediction experiments.

Case study – Can you tickle yourself if you swap bodies with someone else?
The body transfer illusion is as simple as it sounds – being tricked into thinking part or all of someone else’s body is yours. The most frequently used example is the rubber hand illusion. Making use of this technique, Jakob Hohwy and colleagues set out to test if it is possible to tickle yourself. Of course, if you have ever tried to tickle yourself you will know it is impossible.

The explanation of this fact has often been that the brain uses the motor command underlying a given action to make a prediction of the likely sensory consequences of that action. When incoming sensory information matches the prediction, it’s recognised as self-generated and cancelled. Using a form of the body transfer illusion established using a series of cameras and video goggles, participants were tricked into thinking they had swapped bodies with the experimenter. Although the illusion was
successful, the participants were still not able to tickle themselves. The result has now given more weight to an alternate theory of active interference. This theory states that self-generated movements cause non-specific suppression of sensory input, regardless of whether predictions of the consequences of one’s own movement are accurate or not.

Reference

Future directions
We will investigate the causal role of cortical areas involved in visual searching using focal brain stimulation (TMS in humans; microelectrode stimulation in animals). We will determine the networks involved in coordinating visual search using network-based approaches, such as dynamic causal modelling (DCM) and network-based statistics (NBS), to uncover physiological interactions between functionally related areas during attention tasks.
Decision

Function leader
Ehsan Arabzadeh

About
Every day we make decisions based on our internal goals and information captured by our senses. For example, when crossing the road we need to decide how to coordinate our movements to reach the destination safely and at the right time. To achieve this goal we make a guess about where cars are likely to be while we cross the road, given what we see and the sounds produced. Our estimate of a car’s future location is inevitably imperfect, and is combined with our experience of how fast cars encountered in the past have been travelling. For example, we may know that the car is likely to slow down if we are at a pedestrian crossing. This uncertainty places the problem of estimating the future position of the car and how and when we should move to cross the road in a statistical setting. A practical way to conceive of the problem is that the brain uses “rules of thumb” that approximate statistical methods of incorporating prior knowledge and uncertainty (Bayesian theory). The aim of Centre research is to determine these rules of thumb and how they can be implemented in neural circuitry.

Research aims
• To develop rodent models of decision-making with congruent and conflicting audio, visual and somatosensory stimulation.
• Use rodent models to identify neurons activated in decision-making.
• Use non-human primates to identify cortical networks activated during decision-making.
• To map networks engaged in decision-making tasks.
• Use various neural stimulation approaches to bias decision-making in relevant rodent, non-human primate and human models.

Case study – A single nerve cell can be better at distinguishing touch stimuli than an entire person
The somatosensory system (our sense of touch) offers the opportunity to monitor the performance of intact individual neurons (nerve cells) in live volunteers, while also being able to ask them about what they are feeling. Thus, it is possible to determine that a neuron has detected a stimulus (e.g. a vibration) and ask the person if they felt the vibration too.

Ehsan Arabzadeh and colleagues from across Australia did just that — they compared the sensitivity of single neurons (innervating the hand) to the ability of a person to distinguish between certain types of vibrating stimuli. They found that each individual nerve cell responded to a limited range of vibrations. But the cell was highly sensitive in discriminating vibrations that fell within its dynamic range. To discriminate between such vibrations, the individual cell was often more sensitive than the whole person. More specifically, when two vibrations with a subtle difference were applied to the fingertip, the single neuron could respond differentially to them, even when the person reported that the vibrations felt the same.

Although the exact reason for this differential sensitivity is not clear, the researchers postulate that pooling responses from a range of nerve cells results in reduced sensitivity — a reasonable conclusion given it is known that different neurons are sensitive to different stimuli.
It is also possible that noise could be introduced between the wrist (where nerve response was measured) and the brain. Regardless, this work suggests our ability to attend to stimuli is dependent on our brain’s ability to accurately process information that is collected by our senses.

Reference

Future directions

Sensory encoding
Establish neuronal response characteristics in anaesthetised animals while a precisely controlled sensory stimulus is delivered. In vivo electrophysiology or imaging techniques identify the neuronal representation of stimulus properties and investigate how these representations are modified with learning. These experiments could be formulated as computations within single cells (e.g. whole-cell recordings), neuronal ensembles (e.g. two-photon Ca imaging, multi-electrode array recordings), or brain regions (e.g. fMRI experiments).

Behavioural experiments
Psychophysical experiments in various subjects as they perform various forms of sensory decision.

Neuronal decoding and the cellular mechanisms underlying sensory decision
Neuronal activity is recorded in awake subjects as they perform a task that involves sensory decision-making. Projects will explore how neuronal activity relates to various aspects of the task (sensory representation, “read out” of neuronal data to generate a decision, execution by motor system) and how they differ in correct and incorrect trials. Altering neuronal activity (TMS, electrical stimulation, optogenetics) allows us to draw causal links between the identified neuronal mechanisms and the decision.
The success of the CIBF and the investigators who work within it relies on a number of pieces of equipment, technologies and standardised methodologies. Indeed, a number of CIBF investigators have contributed equipment to become available as part of the national research infrastructure. A number of investigators are also developing and refining their technologies and methodologies in order for them to become standards that can be used across the CIBF.

Brain atlases

Like cartographers of the 18th and 19th century, neuroscientists are developing maps of the brain – brain atlases – to guide other investigators as they go about their research. Like early geographical maps, the early brain atlases were paper-based, with researchers having to overlay their image with the atlas image to specify the region of the brain being investigated.

Now, with advances in brain imaging – such as high-field MRI – and enhanced computational power – such as MASSIVE (see Computation section) – neurocartographers can electronically build 3D maps of the brain, showing areas of interest identified using the imaging modality of interest. These maps can then be overlayed, electronically, to confirm similarities or highlight differences.

The CIBF has two world-renown neurocartographers in Professors Charles Watson and George Paxinos. Together, they developed and published a rat brain atlas (1982), including a more recent revision (2013).

With the resources available across CIBF (including advanced imaging and computational power of MASSIVE) this brain atlas will be further updated and a fully online 3D version built and made available to any person with an internet connection. Over the duration of the Centre, the CIBF will also develop atlases for other animals including the marmoset and macaque. These new-generation atlases will go beyond just showing brain anatomy: they will incorporate information about patterns of gene expression, detailed cellular connectivity and electrophysiological characteristics at different stages of an individual’s life, allowing analyses and simulations of brain function.

Case study – Using brain atlases to navigate neuroanatomy

The human cerebral cortex (the outer highly folded part of the brain) undergoes an extended and region specific development well into young adulthood. Areas that expand the most during human development are also those that showed greatest expansion in human evolution, when compared to non-human primates (e.g. macaque monkeys).

It is unclear if these differences are evolutionary adaptations, or a product of applying the same developmental “program” to brains of different sizes. According to the first interpretation, our brains grew specifically in these regions due to a process of natural selection, which favoured “smarter” individuals. According to the second, humans became “smarter” as a by-product of having these areas growing disproportionately, as the head and brain expanded as a whole.

Using existing and publicly available brain maps of cortical expansion between the macaque monkey and humans (published by CIBF collaborator and Board Member Professor David Van Essen) Marcello Rosa and colleagues compared the human cerebral cortex to those of various species of monkey, from the tiny marmoset to the macaque.
Using the existing maps and data they collected from research volunteers, Rosa and his colleagues were able to show the differences in brain configuration that we observe today could be explained simply as the result of the same developmental program, which governs brain growth across all primates, rather than specific evolutionary adaptations of humans.

Reference


Imaging

Magnetic Resonance Imaging (MRI) is a powerful tool that allows research or investigation of soft-tissues (e.g. organs or muscles as opposed to bones). It is considered quite safe and does not require the use of toxic materials, chemicals or radiation for the production of high quality images or results. Importantly, it is non-invasive. These factors have made MRI a highly-used tool in the area of brain research.

At CIBF, MRI machines at Monash University and the University of Queensland are already part of the National Imaging Facility – NIF. In an example of how MRI can be used, Marcello Rosa and colleagues compared brain regions from different species and ruled out one of the theories behind Alzheimer’s disease.

Case study – How imaging is helping us understand Alzheimer’s disease

Alzheimer’s disease is the most common form of dementia. As the disease progresses, more and more areas of the brain become damaged and begin to shrink. But what makes some parts of the brain succumb to Alzheimer’s disease sooner than others remains a mystery.

“We don’t know exactly what is the cellular or molecular fingerprint that says the brain is going to start to degenerate in one particular area,” says Marcello Rosa, one of the study authors.

Because Alzheimer’s disease is almost exclusively seen in humans, one theory is that the condition targets areas of the brain that are uniquely human as judged by their size relative to other species. The assumption is that those brain regions that have become bigger over the course of evolution play a critical role in human brain function.

To investigate that theory, Rosa and his colleagues compared MRI brain scans of people with and without Alzheimer’s disease with those of other primates – capuchin monkeys, macaques and marmosets.

The theory was wrong: while some brain regions that are larger in humans were more vulnerable to Alzheimer’s disease, other areas did not fit this trend.

One region that is particularly susceptible to Alzheimer’s was a primitive part of the brain called the medial temporal lobe, which is not among the areas that expanded in human evolution.

The medial temporal lobe is involved in forming new memories.

The team also discovered that this and other regions affected by Alzheimer’s were the very same regions that are vulnerable to breakdown in normal ageing.

Rosa now suspects that the vulnerability to Alzheimer’s may have something to do with how active an area of the brain is. “Those areas that have to work the hardest are the ones that are more likely to fail first,” he suggests.

In the medial temporal lobe, for example, memory formation means that neurons must continuously make and break connections.

Reference

Neural recordings

CIBF investigators at Melbourne, Monash and Sydney nodes have invested in the ‘Blackrock’ array electrode recording system and are developing common platforms for stimulus presentation and data analysis. This resource allows recordings of nerve cell action potentials as well as slower “field” potentials and interfaces with developments in Neural Technologies.

Case study – Your brain is working hard, even if you’re unconscious

Brain states such as sleep and anaesthesia are characterised by slow changes in brain electrical activity. These slow waves were thought to indicate low levels of activity, like the slow rise and fall of the ocean on a calm day.

CIBF investigators Pulin Gong and Paul Martin, and their colleagues at University of Sydney and University College London, have shown that even unconscious brains may be very active indeed.

When they used multi-electrode array recordings and measured the fine detail of electrical activity of the brain’s visual centres in anaesthetised monkeys, they found the slow waves actually hide a previously unidentified class of brain electrical activity: a rich variety of micro-patterns, just 4 mm across, that evolve continuously in space and time.

“These micro-patterns were not at all like a calm sea,” says Martin. “In fact the pictures we get were more like a series of tropical storms.” According to Martin, the micro-patterns morph and move rapidly, at rates similar to those seen in electrical activity associated with conscious processing of vision, touch and hearing, and physical activity, not with anaesthesia or sleep.

To make sense of the patterns, physicists in the team applied methods for analysing turbulent flow in gas and fluids. When you experience air turbulence on a bumpy flight it can feel that the bumps are random. In fact, there are hidden patterns in turbulence, and physics has special mathematical tools to analyse them.

“We modified the equations and applied them to the micro-patterns, and the fit was excellent,” says lead author Rory Townsend, a CIBF graduate student.

The team speculate that information may be encoded in the micro-patterns, communicated by their movement, and processed when they interact. Next, the team will investigate what influence the micro-patterns have on “spiking activity” in nerve cells, which is already known to encode information for communication between brain regions, and to control physical movement and other functions.

Reference

Computation

MRI and other equipment used in brain research generate vast amounts of digital data, resulting in data storage and analysis issues. Traditionally, researchers have purchased larger and larger desktop storage and associated computer power. In many cases, this has forced the researchers to develop their computer knowledge as well as their neuroscience knowledge.

Recognising that, the CIBF has partnered with the Multi-modal Australian Science$ Imaging and Visualization Environment (MASSIVE), to allow CIBF researchers to store, access and analyse their research data via the cloud. Thus, researchers can spend less time (and money) on developing their computing expertise and more on data acquisition and analysis.
A grant of $1M for data storage space has been successfully funded through the Research Data Storage Infrastructure (RDSI) program and will be dedicated to Characterisation researchers, including a specific data space allocation to CIBF. Called the Australian Coordinated Characterisation Data Space, the proposal requested approximately 4.8PB (peta bytes) (composed of 1.6PB, plus 3.2PB growth in 2014) to underpin national-scale research programs, including the CIBF. The capability developed through this grant will be made available to researchers in 2015 onward.

In addition to this, a plan has been developed to dedicate three full-time roles, through the Research Data Service, to underpin data management support for Characterisation, including specific tools for Neuroinformatics data management.

**Informatics infrastructure and expertise**

In coordination with a range of participants from Australian imaging facilities, MASSIVE has developed a proposal for a coordinated Informatics Capability across imaging facilities for the benefit of Australian imaging scientists. The proposal is for the development of a network model for informatics support across instrument facilities and will leverage state and federal eResearch infrastructure.

**Building future projects and other support**

In 2015 and beyond, the computational program will continue its meetings with the Human Brain Project (HBP) to discuss neuroscience visualisation projects. Early successes include a Visualisation in Neurosciences workshop, presentations at the INCF Congress, and a planned visit by a HBP visualisation expert to Australia. The computational program has also been the major link between CIBF, the Australian Neuroinformatics Community and INCF (international Neuroscience Coordinating Facility).

Dr Wojtek James Goscinski is overseeing this collaboration and is both the CIBF Computation Coordinator and the MASSIVE Coordinator.

**Case study – On-line gaming gives brain research a leg-up**

Industries from marketing to financial services are amassing vast quantities of digital data. With ever more powerful brain imaging, neuroscience is no exception. Take Computed Tomography. A single CT scan captures over 2000 images in under a minute – equivalent to tens of thousands of smart phone photos – requiring tens of gigabytes storage. Multiply that by the hundreds of scans that go into the typical brain study, and it is easy to see why processing the data is beyond the capacity of most computers. This is where facilities like MASSIVE come in.

MASSIVE is one of a growing number of neuro-computing facilities around the globe. Indeed, the success of The European Union’s Human Brain Project and the US-based BRAIN Initiative will depend in large part on the development of supercomputing technologies and novel neuroinformatics.

MASSIVE gets brain image data directly from MRI machines, electron microscopes, CT scanners, and other imagers from around Melbourne, and increasingly across Australia, including from the Australian Synchrotron. Two powerful computers at its heart provide a combined 170 teraflops of processing power – almost 2000 times the speed of a desktop computer. A desktop interface and cloud computing means that neuroscientists can use MASSIVE from their offices.

Facilities like MASSIVE owe much of their prowess to online gamers, whose demands for ever more immersive virtual environments have driven innovation in visualisation technology. For example, MASSIVE has 148 Graphics Processing Units (GPUs) – standard computers have just one.

Those speeds are a game-changer for brain research. Neuroscientists can collect and examine information about the living brain in near real time, and even watch changes in the brain of a person lying in an MRI scanner as they complete different tasks, tasks that can be modified according to what appears on the scan.

Next steps: In the near future, neuroscientists will be able to visualise their data even more effectively. MASSIVE, along with similar facilities, will connect directly to virtual environments that allows researchers to view 3D projections of their brain images.

**Reference**

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Centre scholars

Iris Zhu – Monash University
The goal of CIBF’s education and training portfolio is to bring together neuroscientists and students, engaging them in active learning and providing world-class resources such as ebooks and simulations on cells and synapses, neural circuits and brain systems, models and neurotechnologies.

In 2014, our major focus was on consulting with stakeholders in the community (teachers, policymakers) to create partnerships and align CIBF with the current school curriculum and regulations, and within the centre (investigators, early career researchers, students) to understand the full depth and breadth of knowledge across CIBF and to ensure programs are driven by Early Career Researcher (ECR) and student needs.

This consultation process has resulted in a strategic focus on years 9 and 10 in the secondary education system, where CIBF is best placed to create resources and programs that capture students’ interest in the brain and encourage the adoption of neuroscience as a profession.

It has also resulted in the creation of an ECR network, with resources and programs that support ECRs and their developing careers and encourage collaboration across CIBF’s nodes to be rolled out in 2015.

Profile of an ECR - Marta Garrido and the oracle brain

Your brain has to be ahead of the game, predicting what will happen next and combining its predictions with information from the environment. This allows you to respond rapidly to a threat or opportunity – an incoming tennis ball, say.

The idea that the brain is a prediction machine – the so-called “Bayesian brain hypothesis” – is at the forefront of brain research. But the details are still being worked out. This is what Marta Garrido, a CIBF chief investigator and ECR, researches at the University of Queensland.

“I look at pattern recognition, and what happens in the brain when we encounter a surprising event,” she says. One of her lines of enquiry is working out how distraction – performing an intellectually demanding task, say – changes the brain’s ability to learn and predict.

Previously, Garrido studied electrical activity in the brains of people in coma.

She was one of a team that used maths to extract signatures of brain activity in people in vegetative states, who are thought not to feel pain or have any cognitive function. The team also looked at people in minimally conscious states, who may speak a few words, and feel pain.

The signatures suggested that communication between the planning part of the cortex, and the part where sounds and words are processed, is disrupted in people in a vegetative state.

At the moment, doctors work out levels of consciousness by watching patients’ behaviour – how well a patient tracks an object with their eyes, for example. But these diagnoses are notoriously inaccurate. Combining Garrido’s signatures with behavioural observations could lead to better diagnoses.

When Garrido is not examining EEG records, she can be found playing her guitar, or at a contemporary dance class.
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Events

Centre launch

The Centre for Integrative Brain Function was officially launched on 20 August by the Honourable Josh Frydenberg, Parliamentary Secretary to the Prime Minister and Member for Kooyong.

It also included a speech from Monash University Vice Chancellor Ed Byrne, who said the support from the Australian Research Council was vital and would help researchers collaborate on important research.

“This Centre will help unite researchers from a number of institutions, across a number of fields, and help build the University’s strengths in medicine and health sciences, engineering and neurotechnologies”. The official launch and work of CIBF featured in a number of news outlets including the Herald Sun and Adelaide Advertiser.

CIBF Board tour of Melbourne facilities

As part of their face-to-face meeting in October, the CIBF Board did a tour of the facilities at Monash University and the University of Melbourne.

Neuroanatomy workshop

The CIBF’s world-class expertise in neuroanatomy was made available in two workshops offered by Charles Watson (one in each of Melbourne and Perth). Drawing on Watson’s world-renown brain anatomy atlases, the workshops were attended by over 30 postgraduate students, researchers and clinicians. Feedback from the event was overwhelmingly positive, with participants pleased with the detailed content and the opportunity to receive one-on-one instruction from Professor Watson.

Similar workshops will be held in Brisbane and Sydney in 2015.

CIBF science meetings

Each year the CIBF funds two science meetings comprising all investigators.

In 2014, science meetings bookended the year – with one held in January at the Melbourne airport and another in December at the University of Queensland.

The first meeting allowed the Chief Investigators and Coordinators to get together as the CIBF for the first time. Researchers were able to plan, in more detail, their intended voyage of discovery research and coordinators took the opportunity to establish their respective areas.

In December, the science meeting focused on the research activities of 2014 and put in place a research plan for the next three years.
CIBF/The Brain Dialogue sponsored the second annual Neuroethics Down-Under conference, organised by CIBF associate investigator Dr Adrian Carter as a two-day event.

The event also included a symposium of leading neuroscientists, legal and healthcare practitioners, policy makers, ethicists, philosophers, and other stakeholders, who considered how neuroscience will, and is, changing current practices in their respective professions.

To coincide with Neuroethics Down-Under 2014, CIBF director Gary Egan, and The Brain Dialogue director Rachel Nowak, co-authored an article in The Australian “Getting our heads around brain research”, calling for more rigorous public discussion about brain research and where it should take us.

Audiences were clearly engaged at this and other Brain Dialogue events (see later), with each running long due to audience interaction. Positive survey feedback from attendees, including calls for more events, and suggestions. Social and traditional media coverage, particularly for Neuroethics Down-Under 2014, but also for “Manipulating Morality” and “Who’s in charge – you or your brain?”

One of the challenges is to ensure that CIBF-organised events go beyond simply raising awareness about CIBF, ARC and brain research, to also explore the potential of brain research, and the cultural, societal and ethical implications, both positive and negative.

We are expanding the range and number of CIBF end-users attending. Coordination of social media discussion with CIBF investigators. Further expert-opinion articles authored by CIBF for the mainstream press.

Art competition and show

The Scream, Guemica, The Kiss. Emotions inspire great art. But when it comes to the physical crucible of those emotions – the brain – you’d be hard-pressed to think of any art at all.

To find out how the brain might inspire artists in our community, The Brain Dialogue ran an art competition. The rules were simple: the artwork should be inspired by the brain. The competition was open to neuroscientists and the general public. There were three categories: multimedia/animation; digital/2D; and textiles.

We had 17 entries. Most, but not all, from non-professional scientist-artists. CIBF exhibited the entries at its opening, and on The Brain Dialogue website.

Our judges were Dr Ella Finkel, Editor-in-Chief of Cosmos magazine, which makes science imaging and science art its trademark; Geraldine Barlow, Senior Curator and Collections manager at Monash University Museum of Art; and Professor Marian Simms, Australian Research Council Executive Director for Social, Behavioural and Economic Sciences.

They named The Thinking Cap AKA The Brain Beanie by Julian Matthews and Anna Provost overall winner.

For the future we are exploring collaboration with professional artists to create works that will engage broad audiences with emerging issues in neuroscience.
A new ARC Centre of Excellence has been established to explore integrative brain function, with a focus on attention, prediction and decision. Have you heard?

The Centre is a collaboration of multiple universities and partner organisations conducting multi-scale and multi-disciplinary investigations beyond the reach of any single laboratory. The Centre will integrate with large scale international brain research initiatives, leading to the development of educational tools, software and technologies to benefit society.

Visit us online cibf.edu.au

Sponsored events

International Conference on Cognitive Neuroscience 2014

The International Conference on Cognitive Neuroscience (ICON) was held in Brisbane in 2014 and the CIBF took it as an opportunity to build awareness amongst the wider (international) neuroscience community. The event also included a Key Note from Professor Jason Mattingley (CIBF Chief Investigator) and presentations from several CIBF researchers including Dr Marta Garrido, Professor Jakob Hohwy and Dr Naotsugu Tsuchiya.

Marmoset Social

The marmoset is increasingly becoming an animal model of choice for brain researchers, with features such as size, temperament and similar human morphology all contributing to use. As part of the annual Society for Neuroscience (SIN) 2014 annual meeting, CIBF supported Associate Professor James Bourne to conduct a marmoset social. The marmoset social held at the 2014 Society for Neuroscience annual conference was an open social mixer aimed at fostering closer relationship between the international community of marmoset researchers. This year’s programme featured short talks from three researchers with an interest in marmosets, each research in a different stage of their career. Leon Teo described current in vitro applications in marmoset research; Jude Mitchell discussed contemporary and future trends in marmoset behavioural experiments; and Hideyuki Okano provided a comprehensive overview of the BRAIN/MINDS project. In addition, Professor Jon Kaas provided an overview on the history of marmoset research and initiated a discussion on the future of marmoset research. The event was attended by 140 international marmoset researchers, providing excellent networking opportunities in addition to the large SIN conference. The attendees agreed to the inclusion of their email addresses on a mailing list to help facilitate future communication between marmoset researchers internationally.

CIBF support enabled a reduction in the registration fee for researchers as well as sharing the marmoset expertise at CIBF with a wider neuroscience audience.

Students of Brain Research 2014 Symposium

Students of Brain Research (SOBR) was established in 2011 to connect graduate students and early career researchers in the fields of neuroscience and brain research from across Melbourne. Each year their activities have grown, and in 2014 they held a student symposium at the Melbourne Brain Centre. Over 150 students registered from 14 organisations, covering bachelors, honours, masters and PhD students as well as Postdoctoral researchers. Presentations covered behavioural, cellular, molecular and computational neurosciences, as well as neurodevelopment, brain injury, psychology and psychiatry. Contribution from the CIBF helped ensure the event was low cost (free) for students to attend, while also making them aware of the excellent brain research taking place across Australia.
The Brain Dialogue goals

Dissemination and exploitation of CIBF results – for industry linkage, cultural enrichment, convergence, collaboration, and responsible innovation

Foster discussion of emerging issues – for responsible innovation

Encourage participation in brain research – for cultural impact, and responsible innovation, aligning research with society’s needs and aspirations

Listen to end-users – for responsible innovation, align research with society’s needs

Smoothing the path to impact

A century ago, reports in the best scientific journals were as easy to read as the New York Times (“Scientific Literacy: as clear as mud. J Knight. Nature, Vol 423, page 376-378”). In other words, new findings and knowledge were accessible to all.

But neuroscience, like other sciences, has been a victim of its own success. An ever-expanding knowledge base, and increasing specialisation, means that today’s research papers are usually only accessible to other neuroscientists working in closely-related areas.

Other traditional ways of sharing research findings – conferences, personal contacts, university industry-engagement services, and media offices – though critically important have limited reach. This is due to the communication barriers that are part and parcel of specialisation, and the cultural differences that exist between professions.

CIBF decided that to maximise the ability of its research to lead to social, economic, or cultural good, and to speed scientific progress, other mechanisms were needed to reach CIBF end-users both in and outside of academia.

This is where The Brain Dialogue comes in. Through this program, CIBF is implementing a range of activities designed to meet four goals that will smooth the path to impact.

The Brain Dialogue activities

1. A novel use of plain-English summaries

To ensure CIBF discoveries are disseminated widely, a plain English summary of every CIBF-auspiced journal article is published in the Discovery section of The Brain Dialogue website. Some of these summaries are presented in this report as Case Studies.

The Brain Dialogue shares the plain English summaries on social media (Twitter and Facebook), targeting key end-users, including leading journals, industry, media, and other researchers.

Occasional “Ideas” papers – discussions of emerging issues in neuroscience – are also published in the Discovery section, for example “Who’s to blame when medicine triggers criminal behaviour?” by neurobiologist and ethicist Adrian Carter.
Early indicators of success: Our approach to knowledge dissemination has received external interest, including from news media (Herald Sun, Brigid O’Connell, “Brain to be unlocked” 21st August, 2014). Other research organisations are replicating our approach. One unsolicited comment from a communications expert was that “[CIBF] have really raised the bar with [The Brain Dialogue website]. It is very exciting to see”.

2. Building a community of interest

One barrier to impact is the black-box effect. End-users – industry, say – don’t know the nuts and bolts of a research entity’s interests and capabilities. Investigators don’t know much about end-user needs and aspirations. A way to lower this barrier is to foster communities where people from different sectors come together over a shared interest.

The Brain Dialogue is working to build such a community through several mechanisms. These include “Who’s Dialoguing” – a section on the website designed to introduce diverse parties interested in brain research to one another.

“Who’s Dialoguing” currently features David Van Essen, leader of the US Human Connectome Project, advertising guru Jane Caro, and magician Nicholas Johnson. In the pipeline are profiles of educators, people working in industry, artists, and other researchers with an interest in brain research.

Other mechanisms for building a community of interest include explicit messaging about CIBF’s interest in working with end-users; CIBF designated end-user representatives; and social media, talks, and events targeted at specific end-users, such as those working in industry.

Early indicators of success: Our policy of encouraging end-users to approach CIBF has led to an informal proposal to collaborate with Stanford University neuroscientists on a science-based art project.
3. Twitter, with a twist

Twitter is gaining increasing prominence as a mechanism for disseminating new findings within research communities and to end-users. But publishing a high-quality, evidence-based Twitter feed is time-consuming, and requires deep subject-matter expertise. For these reasons, CIBF felt it could not ask a single investigator, or a communications officer, to run its Twitter feed.

To solve the problem, The Brain Dialogue set up its Twitter Wall. This novel use of social media enables investigators, end-users, and communications professionals to contribute to the same feed, simply by including #braindialogue in their tweets.

Besides sharing the work load, and ensuring high-quality science tweets, the Twitter Wall also enables CIBF to showcase the diversity of expertise within the neuroscience community, and to host live Twitter discussion between neuroscientists and other experts and end-users.

The Twitter Wall is also fed by The Brain Dialogue’s own Twitter account (@BrainDialogue). This account is also used to promote neuroscience events, research papers in top journals, and popular neuroscience of interest to neuroscientists and others.

**Early indicators of success:** By the end of 2014, and after only 3 months in operation, CIBF’s Twitter feed had 129 followers from across the globe, including PLoS Neuro Community (a PloS-hosted community for discussion of neuroscience), AusScienceWeek (Australian National Science week), INCForg (the International Neuroscience Coordinating Facility), journalists, and – importantly – many world-renowned neuroscientists.

4. Events

In 2014, The Brain Dialogue, organised or co-organised/sponsored three events, each designed to meet at least one of CIBF’s knowledge-sharing goals.

1. **Who’s in charge, you or your brain?**

Held at the State Library of Victoria, *Who’s in charge, you or your brain?* celebrated the official opening of CIBF with a panel discussion focusing on the three brain functions at the centre of CIBF research – attention, prediction and decision.

The ‘Q and A’ style event was chaired by Jane Caro of ABC’s *Gruen Transfer*, and included a panel chosen for its breadth of experience and knowledge about neuroscience. They were:

- Nicholas J Johnson, a professional magician, adept at manipulating attention
- Jason Mattingley, CIBF Centre Investigator, and ARC Laureate Fellow, University of Queensland.
- Lilach Avitan, computational neuroscientist, University of Queensland.
- Ehsan Arabzadeh, CIBF Centre Investigator, and neuroscientist, Australian National University.
- Jakob Hohwy, CIBF Coordinator for Society and Ethics, philosopher and ARC Future Fellow, Monash University.
- Marian Simms, Australian Research Council Executive Director for Social, Behavioural and Economic Sciences.

The event was preceded by refreshments and the opportunity for the audience to get up close and personal with CIBF neuroscientists and magician Nicholas J Johnson. “Who’s in charge, you or your brain?” was followed on Twitter, and on blogs.

This public lecture by Oxford University’s Professor Julian Savulescu attracted more than 400 people to the Melbourne Conference and Exhibition Centre on 10 December 2014. Professor Savulescu discussed the moral case for using artificial means to improve human decision-making in the face of the complex social challenges of the 21st century.

The event received widespread media coverage.

Professor Savulescu and Ingmar Persson, also of Oxford University, published an article on the topic on The Brain Dialogue website Discovery section.

The event was hosted by ABC online editor, Religion and Ethics, Scott Stephens, and recorded for broadcast on Radio National’s Big Ideas program on the 11 March 2015.

This event was conceived of, planned and co-organised by, CIBF associate investigator Dr Adrian Carter of Monash University.

Future plans for The Brain Dialogue

Citizen science

Also known as crowd, civic or networked science, citizen science is research conducted in partnership with amateur or non-professional scientists. Globally, researchers – including neuroscientists see http://www.thegreatbrainexperiment.com/ – are using citizen science to access large and representative sample populations; deal with data deluge; and for pattern recognition and data collection that machines can’t do. It also directly engages the publics, and helps address their appetite for scientific discovery.

CIBF is exploring the possibility of using citizen science in its program.

Social Research

Responsible innovation depends on a research enterprise engaging early with end-users, including the general public, to understand their concerns and aspirations, and to incorporate those views into the research program. CIBF is exploring different mechanisms to understand and reflect on end-user views of its research.
### CIBF Focus Area: Cells and Synapses
- Model organism known and agreed to by end of 2015

### Research Theme: Neural Circuits
- At least two relevant brain atlases built (human and animal model) – end 2015
- Behavioural tasks defined and agreed to by all theme participants – end 2015
- Tracer systems defined and agreed to by all theme participants – end 2015

### Research Theme: Brain Systems
- Established method for tracking transmission of brain signals across and through different brain regions – end 2015

### Research Theme: Models and Technologies
- Advances made in the bionic eye project are translated into the CIBF – end 2015

### Attention
- Animal and human models of attention and attention control established within the CIBF (including training of rodents and non-human primates) – end 2015.
- fMRI, EEG and TMS protocols established for the measurement of attention and attention control – end 2015

### Prediction
- Brain region recording systems and processes established, including training of animals and non-human primates – end 2015 for systems and process, training sufficiently developed by end 2016.
- Techniques for labelling and mapping brain regions involved in prediction established – end 2015.

### Decision
- Research methods involving stimulation (TMS or micro-stimulation) are established for each model – end 2015

### Industry Partnerships
- Engagement of industry partners – ongoing
- Industry engagement plan – early 2015
- Industry engagement advisory group – early 2015

### Brain Dialogue
- Social research baseline by Q3 2015

### Education and Training
- The CIBF works with schools to promote its research and neuroscience in general – from 2015 onwards
- A range of Education and Training activities are offered by the CIBF including but not limited to:
  - School student or teacher camps – from 2015 onwards
  - Early Career Researcher support – from late 2015 onwards
  - Seminars – 2015 onwards
  - Workshops – 2015 onwards

### Neurophilosophy
- CIBF research outputs include consideration of appropriate philosophical, societal and ethically central questions – end 2015 and beyond.

### Governance
- Two advisory board meetings
- Monthly Executive Committee Meetings
- Monthly virtual CIBF laboratory meetings
- Monthly administrators meeting
- Weekly management team meetings
Papers


Presentations


Book chapters


## Selected CIBF KPIs

<table>
<thead>
<tr>
<th>Measure</th>
<th>Target 2014</th>
<th>Actual 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of research outputs (including journal articles)</td>
<td>26 (13)</td>
<td>49 (24)</td>
</tr>
<tr>
<td>Quality of research outputs – % articles in A* or A Journals</td>
<td>75%</td>
<td>58%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(71% if B journals included)</td>
</tr>
<tr>
<td>Number of professional training courses for staff and postgraduate students attended. Includes CIs, post doctoral researchers and postgraduate students</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Number of Centre attendees at all professional training/development courses offered by the Centre (include courses offered for external stakeholders and clients)</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>Number of postdoctoral researchers recruited to the Centre working on core Centre research</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Number of Early Career Researchers (within five years of completing PhD) working on core Centre research. Also included in number of postdoctoral researchers.</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Number of students mentored (all levels)</td>
<td>16</td>
<td>22</td>
</tr>
<tr>
<td>Number of mentoring programs offered by the Centre (include programs for students, new staff, external stakeholders and clients)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Number of international visitors and visiting fellows (Includes partner investigators)</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Number of national and international workshops held/organised by the Centre</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Number of visits to overseas laboratories and facilities</td>
<td>8</td>
<td>17</td>
</tr>
<tr>
<td>Number of government, industry and business community briefings</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Number and nature of public awareness/outreach programs. (Total, breakdown provided below)</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Number of website hits</td>
<td>2,500</td>
<td>12,423</td>
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<tr>
<td>Number of talks given by Centre staff open to the public</td>
<td>8</td>
<td>4</td>
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<tr>
<td>Number of new organisations collaborating with, or involved in, the Centre</td>
<td>1</td>
<td>1</td>
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Statement of Income and Expenditure for the year ended 31 December 2014

<table>
<thead>
<tr>
<th>Income</th>
<th>2014 Reporting Period</th>
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<tbody>
<tr>
<td>ARC Indexed Income</td>
<td>$1,308,750</td>
</tr>
<tr>
<td>Node Contribution</td>
<td>$948,954</td>
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<tr>
<td>Other</td>
<td>$4,955</td>
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<tr>
<td><strong>Total Income</strong></td>
<td><strong>$2,262,659</strong></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Expenditure</th>
<th>2014 Reporting Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salaries</td>
<td>$506,979</td>
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<tr>
<td>Goods, Services and Advice</td>
<td>$144,126</td>
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<tr>
<td>Partner payments</td>
<td>$94,686</td>
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<tr>
<td>Travel, Accommodation and Conferences</td>
<td>$44,384</td>
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<tr>
<td>Outreach and Promotions</td>
<td>$10,494</td>
</tr>
<tr>
<td><strong>Total Expenditure</strong></td>
<td><strong>$800,667</strong></td>
</tr>
</tbody>
</table>

**Balance** $1,461,992

In-Kind report

<table>
<thead>
<tr>
<th>2014 Reporting Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monash University</td>
</tr>
<tr>
<td>University of Queensland</td>
</tr>
<tr>
<td>University of Sydney</td>
</tr>
<tr>
<td>Australian National University</td>
</tr>
<tr>
<td>University of New South Wales</td>
</tr>
<tr>
<td>Queensland Institute of Medical Research</td>
</tr>
<tr>
<td>Swiss Federal Institute of Technology, Lausanne</td>
</tr>
<tr>
<td>Brain Science Institute, Riken</td>
</tr>
<tr>
<td>International School for Advanced Studies</td>
</tr>
<tr>
<td>Karolinska Institute</td>
</tr>
<tr>
<td>National Institute for Health and Medical Research</td>
</tr>
<tr>
<td>Cold Spring Harbor Laboratory</td>
</tr>
<tr>
<td>Duke University</td>
</tr>
<tr>
<td>National Institute for Medical Research</td>
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<tr>
<td>National Institute of Mental Health</td>
</tr>
<tr>
<td>New York University</td>
</tr>
<tr>
<td>Weill Cornell Medical College</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>