The BRAIN

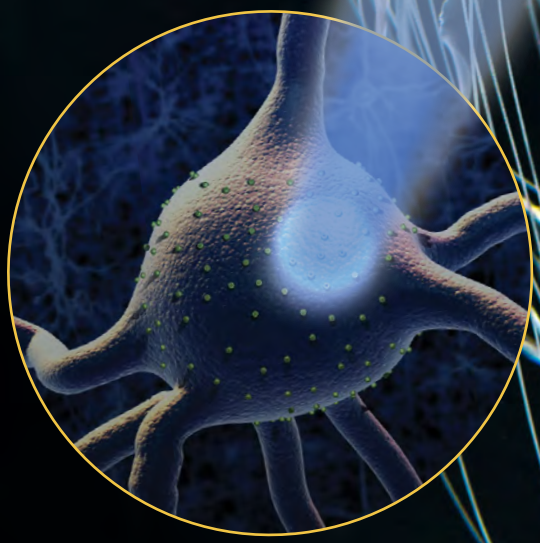
BROUGHT TO YOU BY UQ'S QUEENSLAND BRAIN INSTITUTE

Issue Five

THE NATURE OF DISCOVERY

HOW A JELLYFISH lights up the brain

THE BIG QUESTIONS in neuroscience



CONTROLLING THE BRAIN *with light*

What we learn from animal brains

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

Publisher
Professor Pankaj Sah

Editor
Carolyn Barry

Writers
Carolyn Barry
Dr Fiona McMillan
Dr Alan Woodruff

Scientific advisers
Associate Professor Tim Bredy
Professor Massimo Hilliard
Dr Dhanisha Jhaveri
Professor Justin Marshall
Professor Fred Meunier
Associate Professor Ethan Scott
Emeritus Professor Srini Srinivasan
Professor Stephen Williams
Dr Steven Zuryn

Designer
Katharine McKinnon

The Queensland Brain Institute
is located at
The University of Queensland,
St Lucia, QLD, 4072

communications@qbi.uq.edu.au

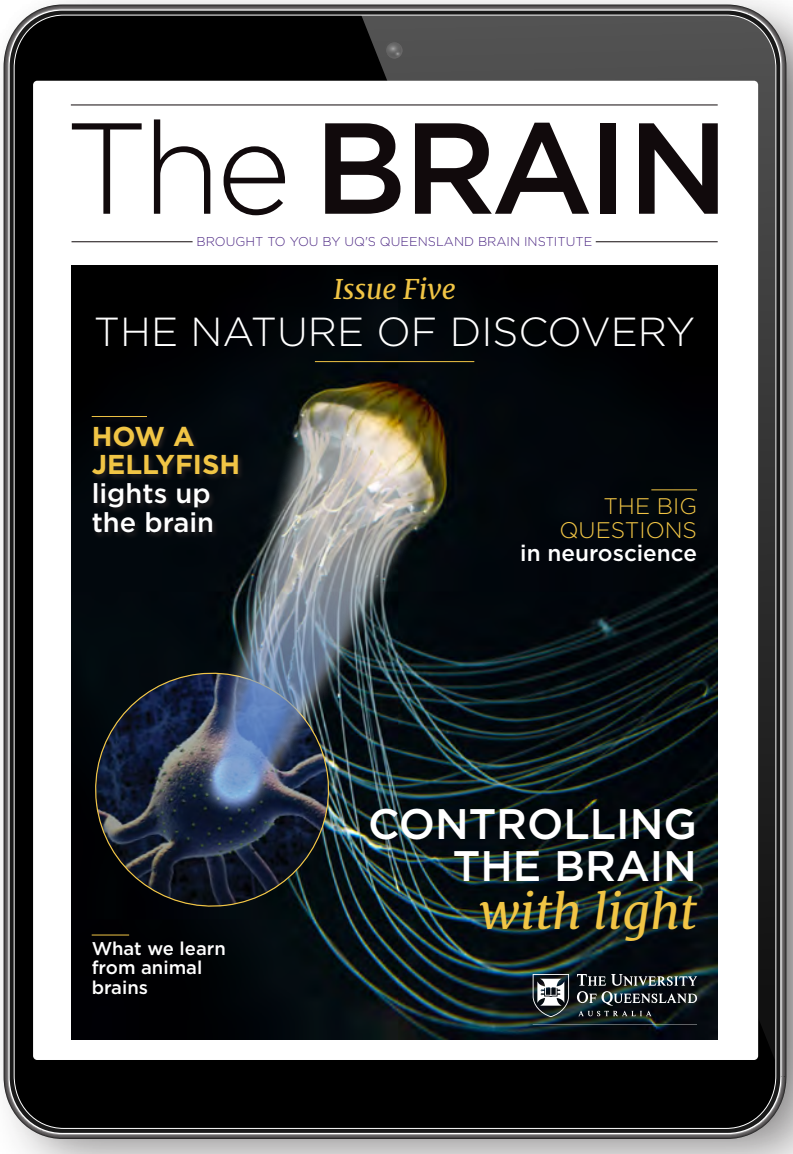
The Brain Series:
The Nature of Discovery
was produced by the Queensland Brain Institute, The University of Queensland, April 2020

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA
CREATE CHANGE

SPECIAL REPORT: THE NATURE OF DISCOVERY

DOWNLOAD, READ AND SHARE

qbi.uq.edu.au/nature-discovery



FACEBOOK
facebook.com/QldBrainInstitute

TWITTER
twitter.com/QldBrainInst

INSTAGRAM
instagram.com/QldBrainInstitute

CONTENTS

A MESSAGE FROM

PROFESSOR PANKAJ SAH

DIRECTOR, QUEENSLAND BRAIN INSTITUTE

Our brains are incredible. They allow us to interpret our sensory world, understand and create language, control movements, plan for the future, and so much more. They are complex machines that make us who we are.

Each human brain contains around 100 billion neurons with a trillion possible connections, and an even larger number of other support cells. Together, these cells and their connections interpret and move information across the brain according to a logic that, until recently, was unfathomable. Now, decades of research and some incredible discoveries have given us a deeper understanding of the brain. How did these discoveries come about, and what lessons do they hold for the future of brain research?

One important ingredient has been scientists' desire to understand the basic workings of the many diverse organisms that make up the natural world. First, as a product of evolution, the basic molecular and cellular workings of the brain have synergies with brains of smaller and simpler organisms that we can study in detail. By understanding them we understand ourselves. Second, evolution has led to organisms that thrive in diverse environments: jellyfish that glow, perhaps as a protection against predators; algae that sense light, controlling their movement to help in photosynthesis; or bacteria that protect themselves against viruses by quickly slicing up the invader's DNA. Scientists are using these developments from nature as tools to study the brain.

As you'll find throughout this magazine, these and many other natural innovations have had an enormous impact on what we know about the brain, and all of them have one thing in common: how they were discovered. In each case, researchers—driven by curiosity rather than pressure to develop a new therapy—simply wanted to understand 'how things work'. Later, others used their own creativity to adapt these discoveries to brain research, with some amazing and often unanticipated findings.

PATRICK HAMILTON

This is discovery science, and it has already given us incredible advances in neuroscience and beyond. A study of new medicines approved by the USA's Food and Drug Administration (FDA) found that every single one of the 210 new medicines approved from 2010-2016 was developed from discoveries in fundamental science. The benefits of discovery science are broader than new disease treatments. Discovery science will also provide insights into new architectures for information processing and storage, and deliver breakthroughs we can't even dream of right now. In this magazine, we celebrate scientific innovations inspired by nature. Brains are such complex machines—curiosity-driven research into their inner workings is sure to lead to new knowledge in health, technology and other fields that don't yet exist.

I hope you enjoy our latest issue.

CHAPTER 1

WHY STUDY THE BRAIN?

The brain is the complex and mysterious core of who we are: it determines our personalities and preferences—why we prefer chocolate over vanilla, or ballet over football—and how we think, act, move and remember.

There is no question we have made some major advancements, particularly in the last 40 years. But when it comes to understanding how the brain processes information and produces outcomes, there is much still to learn and many exciting discoveries to come.

Definitive answers to so many questions remain: Why do we sleep and dream? Why does dementia only affect certain people as they age? How do our brains store some memories, but discard others? What are the critical elements that affect the brain in the earliest stages of life, and can brain diseases and disorders be delayed or treated? How can we repair injured brains and nerves?

What we hope to achieve by unravelling the brain's secrets can be broadly broken down into three areas:

1 To understand what it is to be human

You are your brain. Your brain is the very essence of your personality, individuality and abilities. Unravelling how the brain works will help us understand the basis of human behaviour and actions. While each brain is unique, all healthy human brains share the same basic structures and functions. It's the specific ways in which our brain cells communicate that makes each of us different, and this is influenced by both our genetics and interactions with our environment. With experience, whether physical or emotional, our brain remodels itself, strengthening and weakening existing connections and making new ones. Understanding how these unique connections are forged and modified will help us truly comprehend the link between the physical brain, our behaviour, and what makes us individuals.

2 To understand and enhance healthy brains

By exploring and mapping the inner workings of how a normal brain functions and how it can instantaneously create new thoughts, learn new things and recall memories, we can harness that knowledge to enhance brain function. This will require identifying and categorising the thousands of types of brain cells and their connections with one another, monitoring and recording their activity patterns in real time to reveal how the brain processes information, and understanding how each connection fits into larger networks across the brain.

3 To understand and treat brain diseases and disorders

Dealing with the tide of neurological diseases and disorders is one of the biggest challenges of our time. Neuroscience advances in the 21st century will revolutionise health care just as the development of vaccines and antibiotics did in the past 200 years. To effectively treat brain diseases and disorders, including dementia, schizophrenia, depression, motor neurone disease and many others, we need to understand how the healthy brain functions and what makes these processes go awry.

The most exciting part is that by studying how the brain works, we open up numerous possibilities for treating the vast range of mental and neurological disorders prevalent in our community.

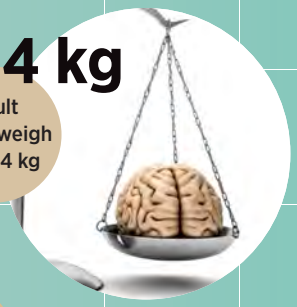
Brain basics

100 billion

There are around 100 billion neurons (brain cells) in the average adult brain

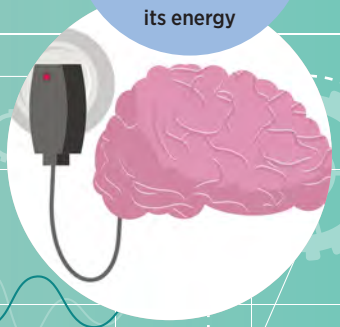
1.3-1.4 kg

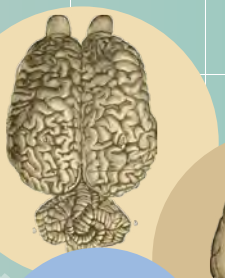
Adult brains weigh ~1.3-1.4 kg

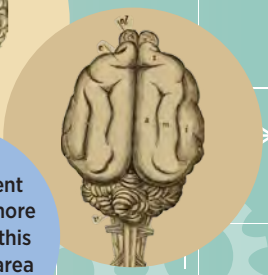


20%

The brain accounts for about 2% of the body's weight but uses 20% of its energy







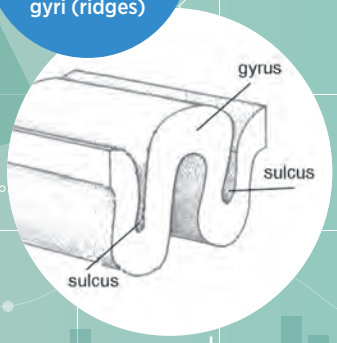
More intelligent species have more brain folds as this increases the area for connections

The brain has trillions of connections between neurons

100,000

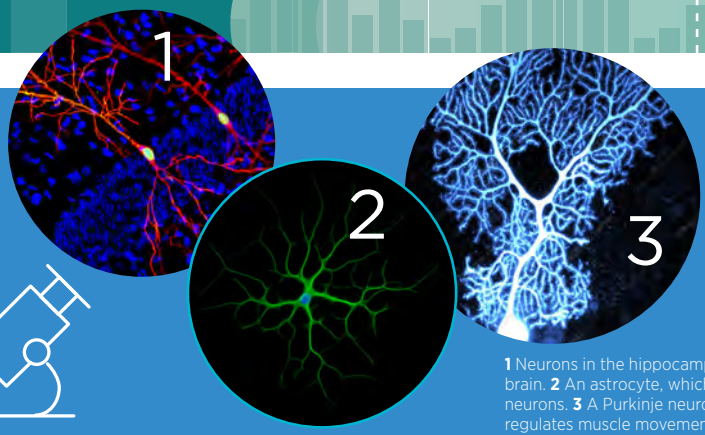
Brain tissue the size of a grain of sand has about 100,000 neurons

Folds in the human brain are called sulci (grooves) and gyri (ridges)



70%

The brain uses about 70% of a human's 22,000 genes, mostly to control connections between neurons as we learn and remember



1 Neurons in the hippocampus of the brain. **2** An astrocyte, which supports neurons. **3** A Purkinje neuron, which regulates muscle movement.

Types of brain cells

Neurons are the basic building blocks of the brain and the nervous system. They send and receive signals, which allow us to think, form memories, move our muscles and much more.

Neurons have different shapes, sizes and functions, and while there are three primary types of neurons in the spinal cord, the brain is another story.

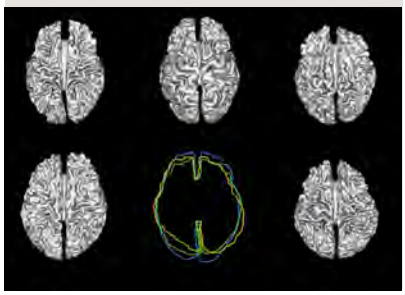
There may be hundreds or thousands of specialised types of neurons in the mammalian brain. With so much diversity, it is important to have ways of identifying and distinguishing between the different types and their roles. Unfortunately, this is not straightforward, but some possibilities include considering a neuron's shape, location, where its branches project out to, what genes it expresses, and where its inputs begin.

Researchers are still trying to determine how to classify neurons. This is a fundamental step to delving even deeper into how the brain operates.

A-Z

What's a brain disorder?

When the brain is operating normally, all of its parts – including cells, electrical activity and chemical messengers – work together to make our bodies and minds function as they should. A brain disorder is anything that disrupts any of these aspects of normal brain function and affects quality of life.



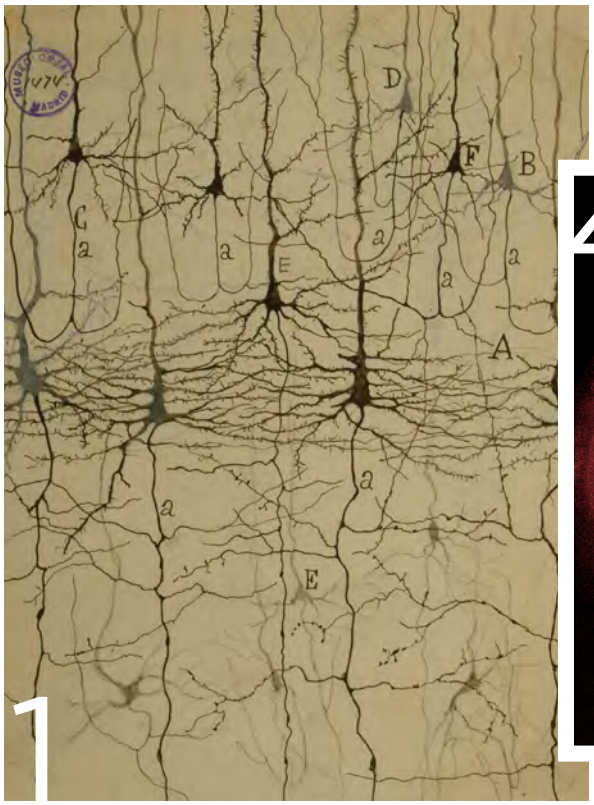
ISTOCK; 1.RODRIGO SUAREZ, 2. STEPHEN WILLIAMS

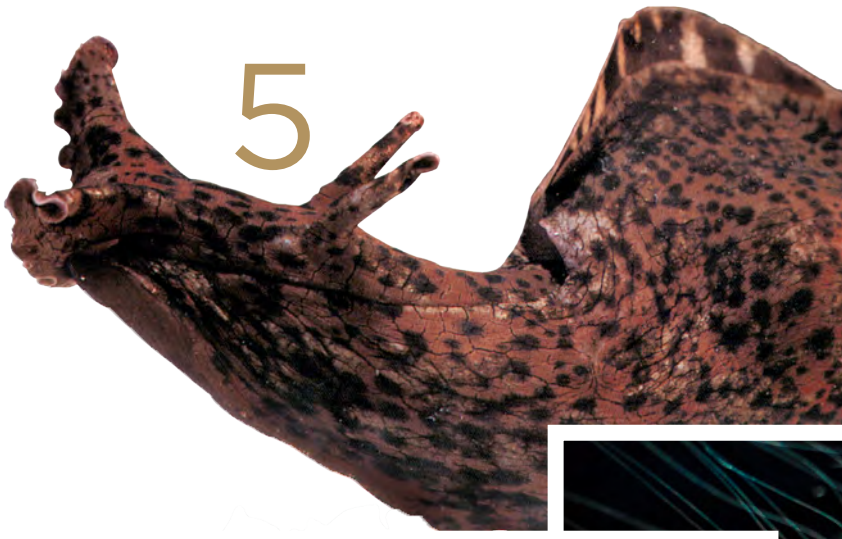
Key leaps inspired *by nature*

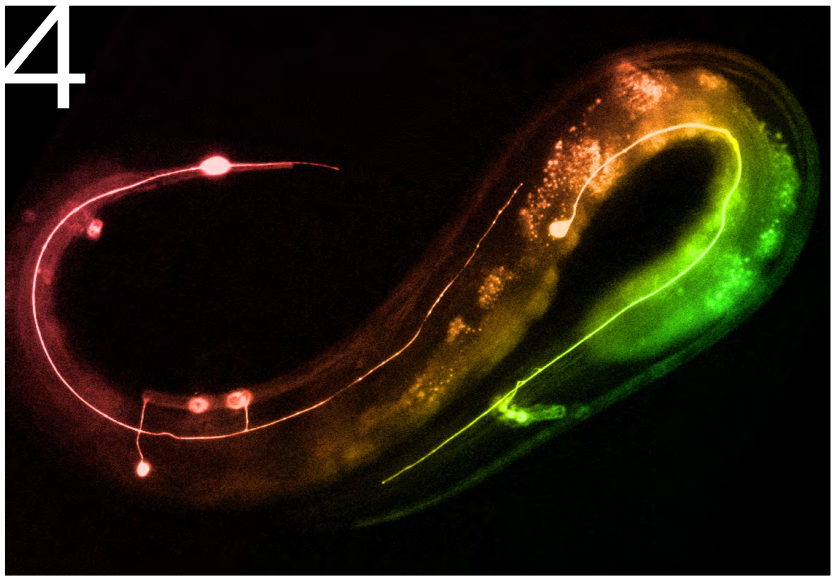
Our current work in neuroscience wouldn't be possible without these developments in tools, techniques and knowledge.

1 The nervous system has units

Santiago Ramón y Cajal had a passion for art but followed his family into medicine. At the time, the prevailing theory was that the nervous system comprised one connected network of tissues. Using Camillo Golgi's staining technique on microscopic slides of brain cells, Cajal saw through artistic eyes what others could not: that brain tissue was made of individual cells, called neurons. This was a major shift in knowledge of the brain at the time, and Golgi and Cajal were awarded a Nobel Prize for this discovery in 1906.







2 How neurons communicate

Sir Alan Hodgkin and Sir Andrew Huxley studied the neurons of squid, to show for the first time that signals travel along these nerve cells via electrical impulses from the movement of charged particles called ions. Sir John Eccles extended this work to explore what happens at the junction between two neurons, called a synapse. He showed that chemical signals can produce electrical currents that allow neurons to communicate. The trio was awarded the Nobel Prize in 1963 for these discoveries.

3 Shedding light on the visual brain

David Hubel and Torsten Wiesel advanced our understanding of vision. They showed different images to cats and noted which parts of their brains were activated. They devised a way to record the activity of a single neuron and then mapped out the visual cortex of the brain. They made discoveries about how the brain processes visual information. Importantly, they showed there's a critical period in the early stages of life when connections of the brain can be changed, and after that, visual pathways are set. They were awarded a Nobel Prize in 1981.

4 Roundworms: a simple model for the nervous system

Sydney Brenner was a geneticist whose contemporaries included the scientific luminaries James Watson and Francis Crick, who first described DNA's structure as a double-stranded helix. Brenner, together with John Sulston and Bob Horvitz, turned their attention to mapping out the cells of a simple organism, the roundworm *Caenorhabditis elegans*. Their Nobel Prize–winning work opened up a new way for scientists to study neurons, of which roundworms have just 302. They showed that some neurons are programmed to die, and discovered the genes that regulate this process—which also happens in humans. This tiny worm (see p16) can regenerate damaged neurons, providing a model to understand their growth and repair.

CREDITS (CLOCKWISE): WIKIMEDIA COMMONS, GETTY, GETTY, GETTY, NICK VALMAS/QBI

5 Where memory is stored in the brain

Only recently have scientists started to understand how we remember things and where memories are stored in the brain, at the level of neurons. Neuroscientist Eric Kandel was awarded the Nobel Prize for Physiology in 2000 for his work in showing that neurons change their connections when learning occurs. Kandel used a species of sea slug, *Aplysia californica*, as a simple model for studying what happens to neurons as an organism learns.

6 Lighting up the brain

Taking inspiration from nature, Professor Martin Chalfie wondered if the green glow of a jellyfish could be used to visualise cells in the body. Following the biochemical isolation of green fluorescent protein (GFP) by Osamu Shimomura, and mapping of its DNA sequence by Doug Prasher, Chalfie used GFP to visualise neurons in worms. Roger Tsien then developed many fluorescent proteins, which have been used in myriad ways, including to show how neurons grow and connect. Chalfie, Shimomura, and Tsien were recognised with the 2008 Nobel Prize in Chemistry for their transformational work.

7 Harnessing the gene editing power of bacteria

One of the most significant recent scientific developments has been the ability for scientists to easily target and modify DNA at specific places in the genome—known as gene editing. This game-changing technique, called CRISPR, came about when Professor Jennifer Doudna and Professor Emmanuelle Charpentier harnessed a natural defence that bacteria use to slice up and destroy viruses that invade them. Neuroscientists are using CRISPR to alter gene expression by editing DNA in mammalian brains under a variety of conditions. This may one day help us treat heritable brain disorders such as Huntington's and Alzheimer's diseases, or to treat brain diseases caused by acquired DNA mutations, such as some brain cancers.

8 Human genome sequenced

In 2003, a 13-year project to map the whole human genome (3.2 billion base pairs of DNA) was completed. This key milestone in science couldn't have happened without the development of Taq polymerase, an enzyme derived from heat-loving bacteria that were first found in Yellowstone National Park's famous geysers. The mapping of 23,000 genes has enabled scientists to link particular genes with normal brain function, and find others that play a role in brain diseases and disorders.

9 Optogenetics - controlling the brain

Optogenetics is the process of using genetic techniques to enable light to turn cells like neurons on and off. This leap in neuroscience came initially from observing proteins in green algae that control movement in response to light. Scientists genetically engineer groups of neurons they want to study by inserting light-sensitive proteins called opsins. When light is shone on those neurons, they activate. This kind of stimulation is much more specific than using electrical stimulation, and can reveal how neurons connect and how they contribute to different behaviours.

The state of neuroscience today

In 1980, Nobel Prize–winner Sydney Brenner said: "Progress in science depends on new techniques, new discoveries and new ideas, probably in that order."

Despite decades of study, the limited ability to peer inside a living, working brain has meant that neuroscientists must continually develop new technologies to progress what we know.

Key milestones in understanding the brain include early observations made by the 4th century Greek philosopher Hippocrates, who believed the brain to be responsible for intelligence; the amazing drawings of individual brains cells in the early 1900s by Cajal, who was able to identify them thanks to Golgi's staining technique; and the discovery of how brain cells talk to each other through chemical signalling in nerve cells of animals, by Nobel Prize-winning Australian neuroscientist Sir John Eccles and colleagues.

Explosion of neuroscience

An explosion in our understanding of the brain has come in the last 40 or so years, and has been accelerating at an unprecedented pace as technology rapidly improves. Importantly, these amazing advances (see p4) have been propelled by scientists who are inspired by nature and connect seemingly unrelated discoveries to open new fields of brain research. Nobel laureates Sydney Brenner and Eric Kandel, for instance, recognised the importance of studying simple animals to provide a deeper understanding of the human brain. Kandel used the California sea hare, *A. californica*, to study memory, and Brenner used the roundworm *C. elegans* to study genetics.

The study of the nervous systems of simple organisms like roundworms, and the behaviour of fruit flies, bees, sea slugs, and other animals, has taught us much about how they sleep, see, fly and navigate. Harnessing animals' evolutionary specialisations has expanded our toolbox for neuroscience research—for instance, using the glow of a jellyfish to light up brain cells.

The next leaps

Although we've made real progress, there is still much to learn. The brain is among the most complex systems known, and there are many important functions that remain a mystery, such as how memory is stored, how the brain processes information, how many types of neurons exist, and why people develop brain diseases like dementia.

Today, with cutting-edge, nature-inspired technologies, we are entering an accelerated era of discovery about the brain. Scientists can now look at the cells inside a living brain, control the actions of specific cells with light, and correct errors in the cells responsible for brain function. Many big questions will be answered by scientists who turn to nature for inspiration.

Some big questions include:

- How does the brain encode and process information?
- How is memory stored?
- How do our brains adapt in real time to experiences?
- How does the brain use energy?
- How are our brains so efficient?
- What is consciousness?
- Can we regrow or repair our brains?
- Can we treat or cure brain diseases?

Our brains are the most complex systems on Earth and there are many important functions that remain a mystery...

CHAPTER 2

ANIMAL INSPIRATION

Though humans are most genetically similar to primates, with 98 per cent of the same genes, we nevertheless share many of our genes with the simplest of organisms—about 61 per cent with fruit flies, for example. Despite differences in size and complexity between the human brain and smaller animal brains, the similarities mean that much can be learned from studying these simpler models. We can better understand sensory processing, such as how animals see colour and make sense of visual information; we can learn how animals navigate their environment, including through flight; and by looking at how animals sleep, we can learn more about our own sleep behaviours. All of these animal models and behaviours give us important insights into understanding the human brain.

As with all discoveries, animal research can also be a source of inspiration for developments in new technology. Take, for instance, the ability of the mantis shrimp to see polarised light, which humans cannot detect without special glasses. Scientists are now working on an underwater navigation technique using this process. Likewise, understanding how birds fly in flocks without colliding can help us fly groups of drones or develop better crash-avoidance systems for aircraft.

CREDITS: ISTOCK

Flight: learning from nature's best

A honeybee can return home quickly and precisely after flying several kilometres from its hive to find food. A budgie can fly rapidly through a dense thicket, avoiding all the branches. How do these tiny-brained creatures navigate so well? How do they avoid collisions? These are just some of questions that Emeritus Professor Srini Srinivasan from UQ's Queensland Brain Institute has been trying to answer.

His team has uncovered how bees are able to fly safely through narrow passages, regulate their flight speed, gauge how far they have flown, and orchestrate smooth, safe landings. More recently, their research has shown how bees flying in swarms can make coordinated turns to move safely in busy air spaces and avoid collisions with each other.

"Bees are very smart," says Emeritus Professor Srinivasan. "They can learn colours, shapes and smells, detect camouflaged objects, and even fly through complex mazes."

His team also studies how flying creatures avoid obstacles. Their research has revealed that budgies are very body aware: while flying through a narrow space, they close their wings in advance, but only when the space is narrower than their wingspan. They also found that budgies flying head-on toward each other avoid collisions by using a simple rule: each bird veers to its right. This strategy, which birds evolved millions of years ago, has also been adopted by aircraft pilots to avoid collisions.

Combining biology, neuroscience and engineering, Emeritus Professor Srinivasan's team has designed new vision systems to guide the flight of autonomous aircraft like drones, so they can avoid collisions with other aircraft or obstacles in their environment.

"We are gaining new knowledge about how small animals with relatively simple nervous systems have evolved elegant strategies for guidance and navigation, and are incorporating the findings into new technology," he says.

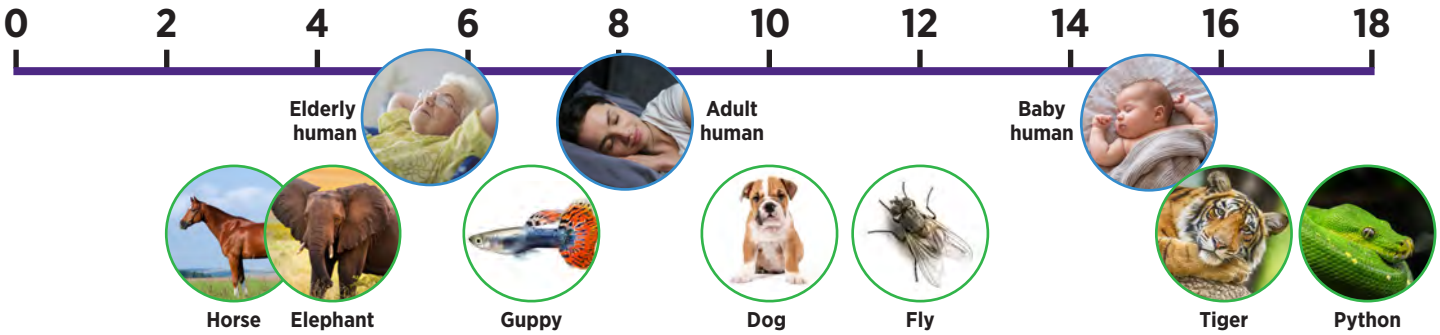
CREDITS: GETTY

Flies sleep like babies

Any animal with a brain sleeps. Some sleep more than others, but surprisingly, the amount of sleep they need is not related to their body size or brain size. Fruit flies, for instance, have sleep patterns that are remarkably similar to humans—they sleep mostly at night for about 8 to 10 hours, have a midday siesta, sleep more when they are young, and sleep in stages of varying intensity, such as deeper and lighter sleep, just as humans do. Furthermore, fruit fly sleep is affected by the same stimulants and sedatives that work on humans, and if the flies are sleep deprived, they sleep longer and more deeply to catch up.

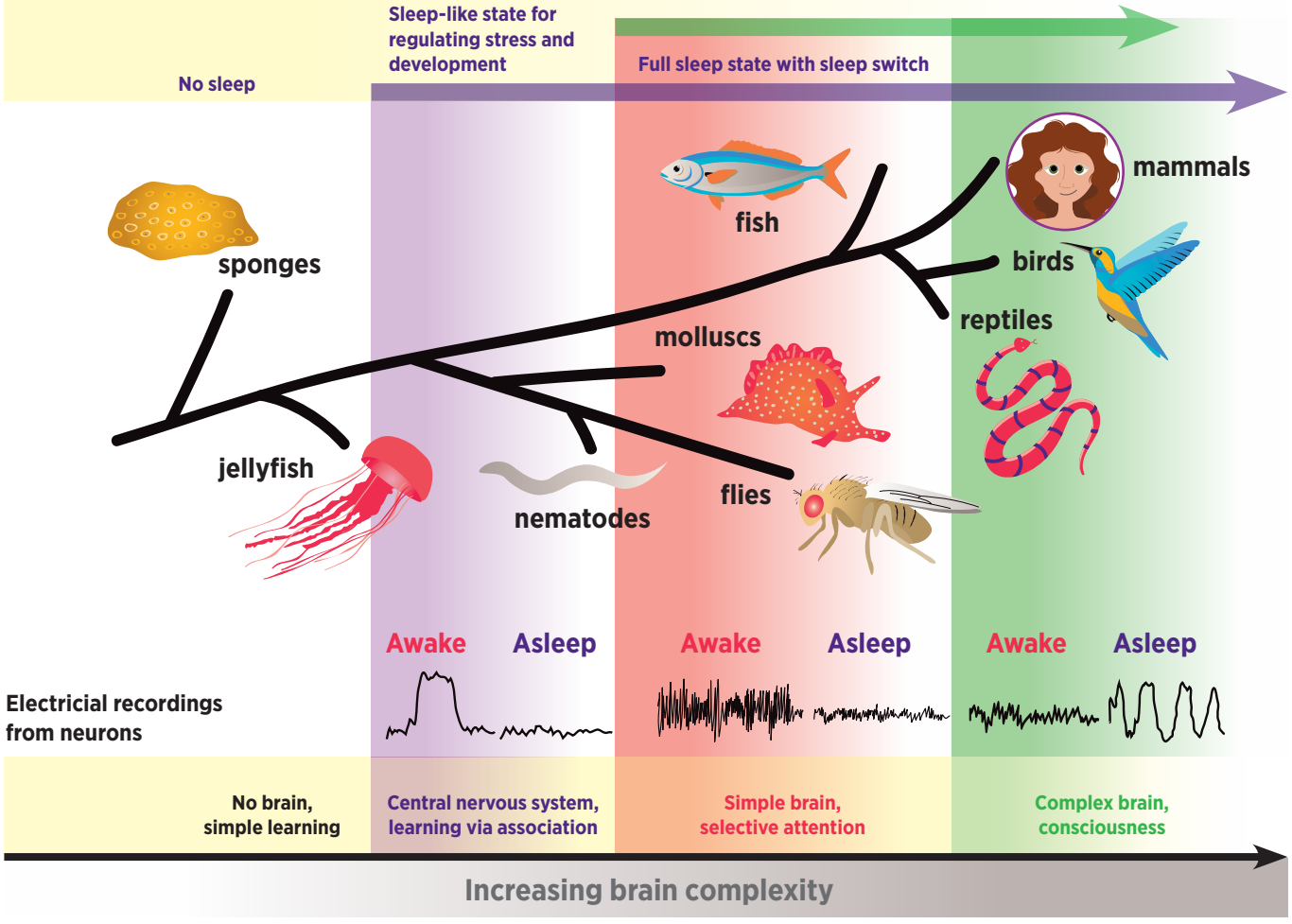
Associate Professor Bruno van Swinderen's team at UQ's Queensland Brain Institute are studying fruit flies to further understand which genes are important for regulating sleep, why we sleep, what triggers sleep, and what causes sleep disorders. They are also investigating the roles that different stages of sleep have in how the brain functions. These insights may also help us understand the mechanisms that support consciousness.

Sleep hours in a day

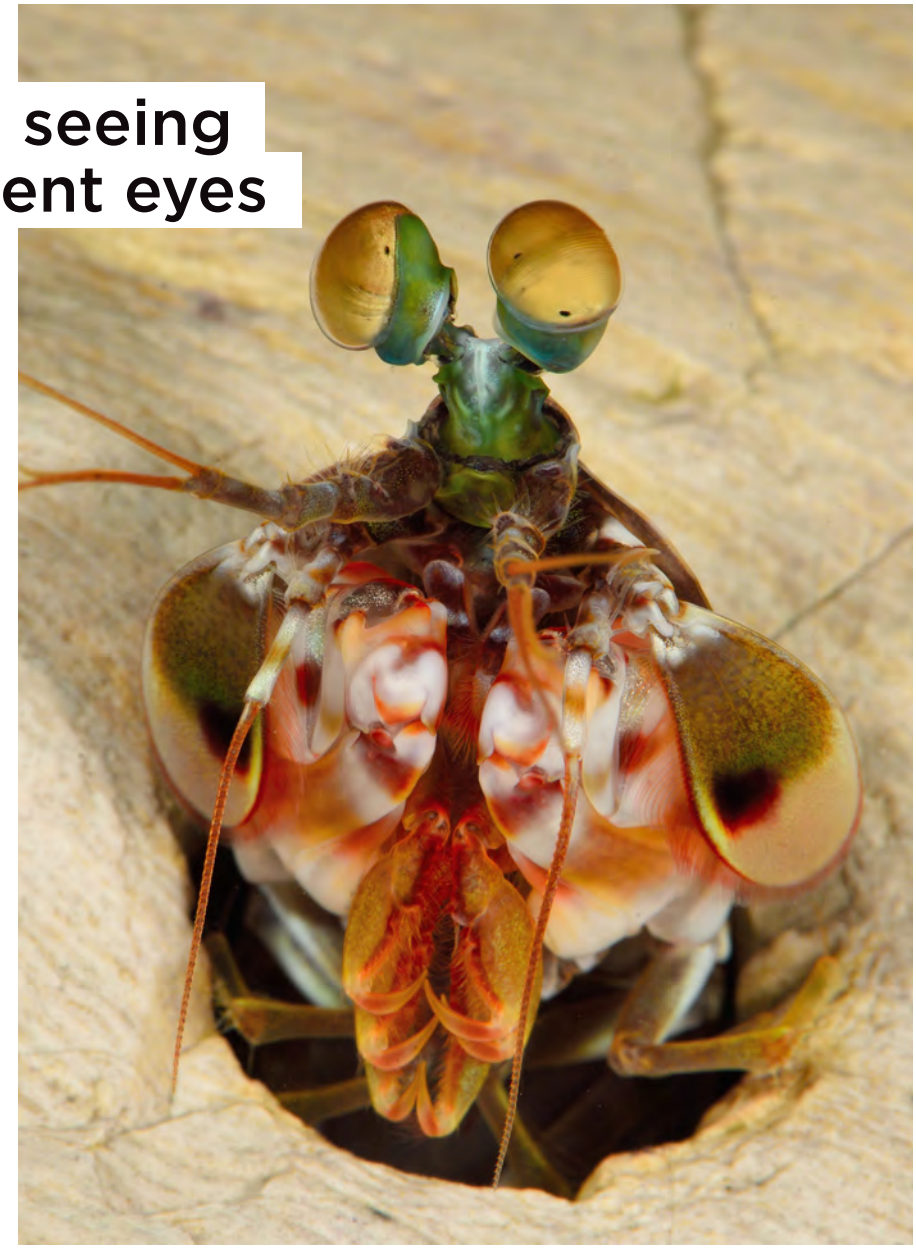


The evolution of sleep

Ancient cellular sleep functions have been preserved through evolution and in more complex organisms, occur during specific sleep stages. Different sleep functions have developed for organisms with more complex brains, including having different stages of sleep.



Animal vision: seeing through different eyes



Making sense of all the visual information we receive every second we're awake uses about a quarter of the brain's processing power at any one time. The human eye, our primary sensory organ and source of information, is often seen as highly advanced, so it might be surprising to learn that we may have only a quarter of the colour vision capability of a mantis shrimp and are at least six times slower in visual reaction time than a fly.

Mantis shrimp have the most complex retinal visual system known to science, says Professor Justin Marshall, from UQ's Queensland Brain Institute, an expert in animal vision. The crustaceans use polarised light for attracting a mate, with only males reflecting this light. Mantis shrimp also see colour and have 12 input channels, or sensitivities, in their eyes for this. Humans only have red, green and blue, and yet we can distinguish millions of different colours. "How mantis shrimps use colour remains shrouded in mystery," says Professor Marshall, whose research has uncovered these amazing findings. "At the moment, we understand more about how their vision system works than how they use it. There is a lot of exciting research to come."

Many animals out-perform humans in some form of vision and some, including the octopus, can see forms of light that humans cannot. Octopuses also see polarised light, a form of light that humans only see with the aid of sunglasses and other optical devices. Surprisingly, they are also completely colour-blind and seem to have swapped colour for polarised information from the world around them. How do they manage their feats of amazing camouflage, blending perfectly with the ocean

...many animals out-perform humans in some form of vision...

Navigating underwater, thanks to mantis shrimp

Global positioning systems (GPS) are so commonly used now that most fitness trackers and smart watches have them embedded. But while GPS can be accurate on land, under the ocean it's a different story. "Most modern navigation techniques don't work underwater," says Dr Samuel Powell from the Marshall lab at UQ's Queensland Brain Institute. "Satellite-based GPS, for example, only works to a depth of about 20 cm."

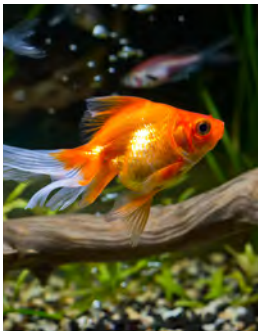
Dr Powell and colleagues are devising a new technology to extend navigation capabilities underwater, taking inspiration from marine animals including mantis shrimp and cephalopods like squid, cuttlefish and octopuses, which communicate using polarised light. The scientists have built polarisation sensors that can determine the sun's position in the sky, based on patterns of light underwater.

This new method will enable more accurate and cost-effective long-distance navigation, and could enable navigation at depths up to 200 metres below the ocean's surface, ideal for submarines or submersibles used in exploration and recovery. "Our method would allow for real-time navigation underwater with more accurate long-distance results, without the need to resurface periodically," says Dr Powell.

CREDITS: GETTY, MARSHALL LAB/QBI, ODONTODACTYLUS HAVANENSIS / ROY CALDWELL, JUSTIN MARSHALL/QBI

floor? And why do some, such as the blue-ringed octopus, use colours they don't see themselves? These cephalopods are very sensitive to contrast patterns and even the texture of their surrounds; they can mimic their environment almost perfectly and have evolved to 'know' the colour of the ocean bed. The iridescent blue of the tiny blue-ringed octopus is likely there to warn animals that can see colour that its bite is laden with potentially lethal toxins.

"Instead of colour, cephalopods have developed polarisation vision for tasks that mostly remain obscure to us," says Professor Marshall. "Some certainly communicate with polarised light but the meanings of those messages are yet to be decoded."



Among the vertebrates, even the goldfish with its tiny brain can detect more colours than a human, and it can see ultraviolet (UV) wavelengths, a range of light that humans cannot normally see. Many reef fish, birds, lizards and mantis shrimp use UV light, some for covert communication among themselves, most likely for attracting and choosing mates.

Studying how these small-brained animals can see and process such complex visual information helps us understand more about how our brains process our visual world. Scientists, inspired by this vision in nature, are also working on developing better underwater navigation and camera technologies. (See box, opposite).

Colour vision

These are the colour channels present in the visual systems of these animals—in other words, the colours on the spectrum that their eyes see.

Stomatopod

Bird

Bee

Reef fish

Human

Dog

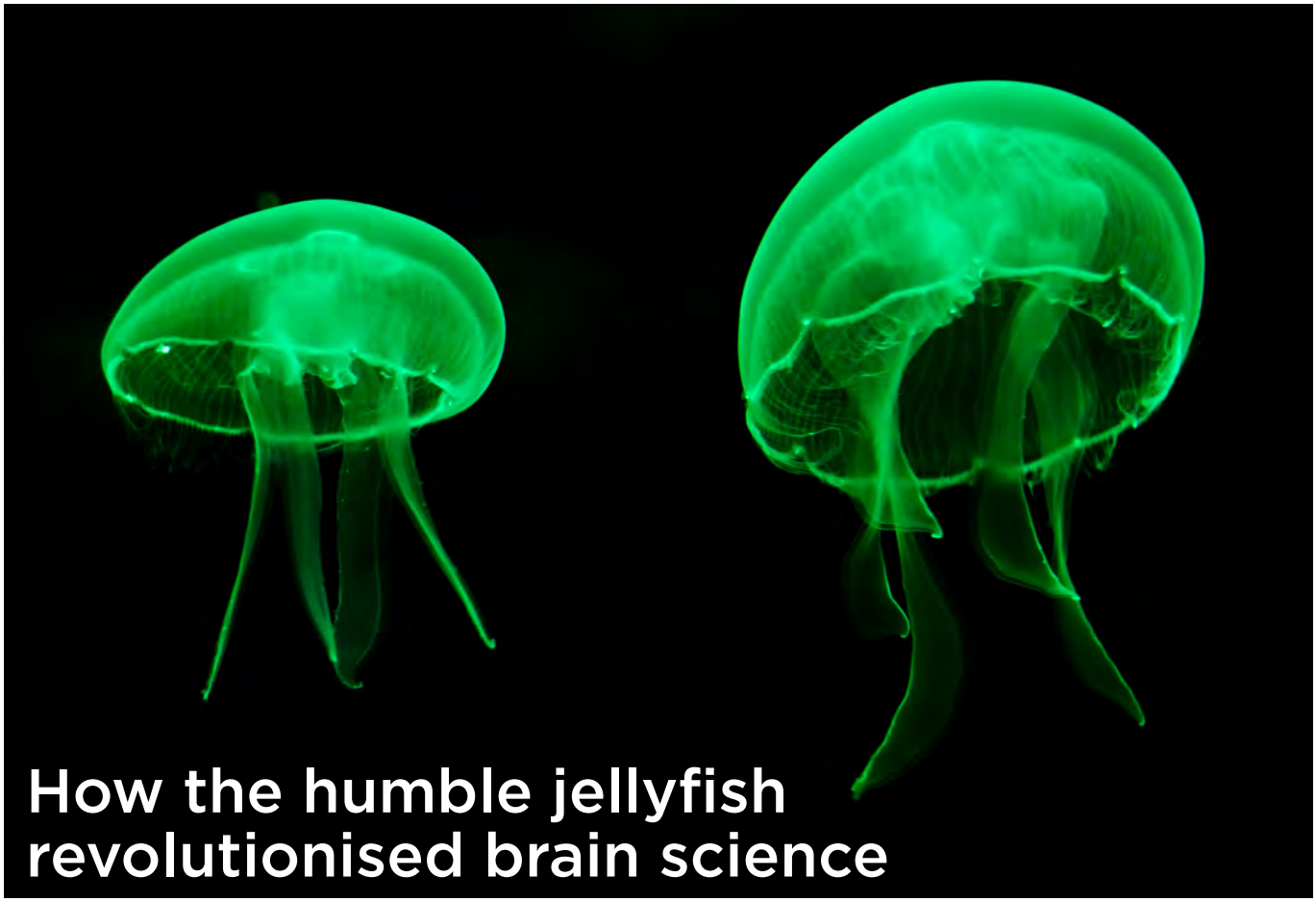
Octopus

CHAPTER 3

LIGHTING UP THE BRAIN

Because the brain is protected in our skulls, it is not easy to study its inner workings. Neuroscientists have relied on recording electrical signals, as well as looking through microscopes at stained cells. As advancements in technology have progressed, particularly with imaging techniques like MRI, PET and CT scans, scientists have been able to visualise more of the brain. But while those scans show the brain's anatomy, blood flow and coarse-grained activity, they don't provide any insights into how individual neurons or small networks of neurons communicate.

A truly remarkable development, from a seemingly obscure source, was harnessing the fluorescent glow of animals like jellyfish to light up everything, from whole animals to individual brain cells. Fluorescence can help us see some of the smallest molecules inside cells as they move around to make brain cells work. Scientists can also see how neurons talk to each other and how they repair themselves after injury. This allows us to understand more about how the brain works, how we learn and remember, and why disorders and diseases occur.

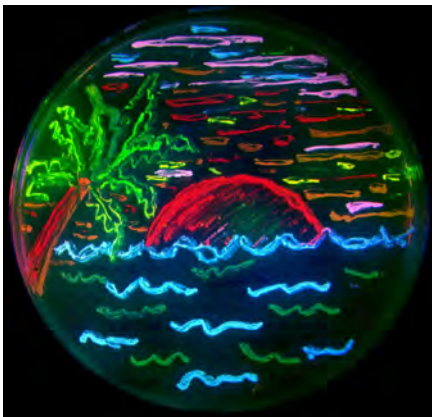


How the humble jellyfish revolutionised brain science

Often in science, being curious and asking simple questions can lead to amazing discoveries. One such story began in the 1960s with a scientist, Osamu Shimomura, asking the question: what makes a jellyfish glow? Shimomura was able to identify the particular protein—which he called green fluorescent protein (GFP)—from the jellyfish *Aequorea victoria* that produced its bioluminescent light.

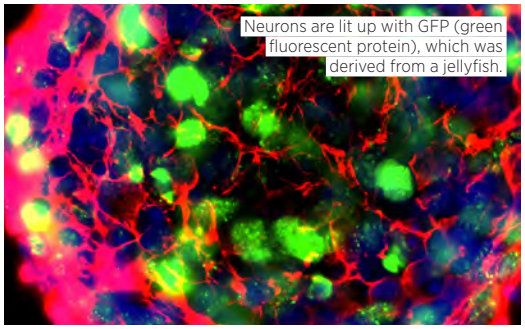
Years later, Professor Martin Chalfie heard about GFP and wondered if this protein could be used to highlight individual cells in other organisms. At the time, Professor Chalfie was using the tiny roundworm *C. elegans* (see p16) to study how nerve cells worked. In a groundbreaking study, he successfully labelled groups of connected neurons in roundworms, and a new era in visualising nervous system cells began.

Scientists then used GFP to make all kinds of cells glow, from neurons to plant cells. But the glow didn't last that long, and green wasn't always the most ideal colour to work with. Enter biochemist Roger Tsien, who

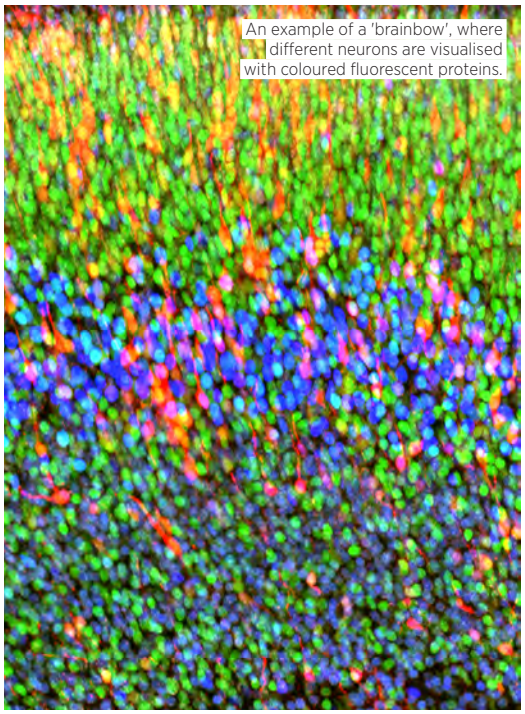


The beach scene that Roger Tsien's lab created with different variations of bioengineered jellyfish genes grown in bacteria.

CREDITS: GETTY, WIKIMEDIA COMMONS, QBI



Neurons are lit up with GFP (green fluorescent protein), which was derived from a jellyfish.



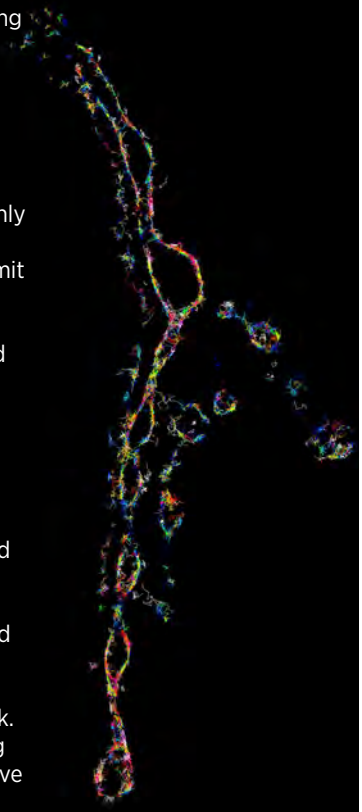
An example of a 'brainbow', where different neurons are visualised with coloured fluorescent proteins.

Lighting up the tiniest part of cells

One of the more exciting developments in neuroscience is using a fluorescent protein from the lobed cactus coral *Lobophyllia hemprichii* to highlight the workings inside a brain cell in real time. Using a highly sensitive super-resolution microscope to highlight important molecules that transmit signals at the junction (called a synapse) between neurons, Professor Frederic Meunier and his team at UQ's Queensland Brain Institute have been able to reveal what happens inside living nerve cells.

"We can now see molecules organise themselves in real time, viewing the nitty gritty mechanisms that allow neurons to communicate," says Professor Meunier. "You see molecules moving randomly and then, for a few milliseconds, interacting with each other."

"This is an exciting time, as we've opened the door for many more groundbreaking studies that will change our view of how molecules function to make the brain work. This work could further our understanding of memory, learning and neurodegenerative diseases," he says.



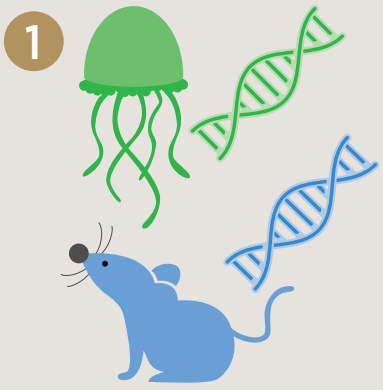
A visual representation of the movements of molecules inside neurons at the point where they connect with other neurons.

set about improving the brightness of GFP, as well as genetically engineering it to express more colours. He also isolated fluorescent proteins from other animals, to develop a broader range of colours. To showcase the array of colours, members of his team created a multicoloured beach scene with bacteria in a petri dish.

The use of GFP and other glowing proteins to light up the inner workings of organisms has revolutionised neuroscience. Before this, scientists weren't able to see such detail.

In brain research, GFP and other proteins have been used to visualise different neurons, to show how networks form in the brain, to identify individual neurons in slices of the brain, to study how neurons grow and connect, and to mark neurons affected by plaques that are hallmarks of Alzheimer's disease. For their transformational work that began with a question about glowing jellyfish, all three scientists were recognised with the Nobel Prize in Chemistry in 2008.

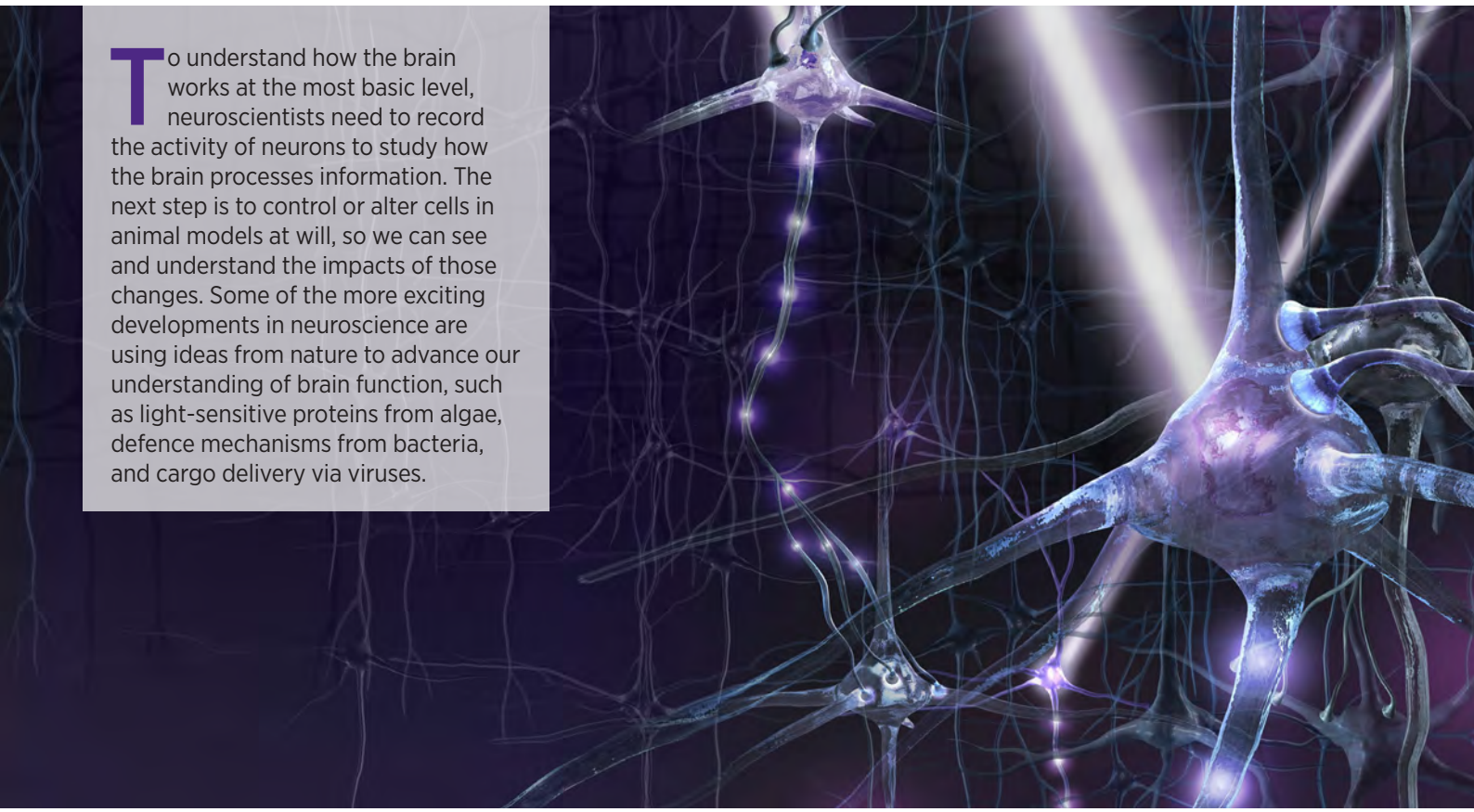
Using a jellyfish to light up the brain



CHAPTER 4

CONTROLLING THE BRAIN

To understand how the brain works at the most basic level, neuroscientists need to record the activity of neurons to study how the brain processes information. The next step is to control or alter cells in animal models at will, so we can see and understand the impacts of those changes. Some of the more exciting developments in neuroscience are using ideas from nature to advance our understanding of brain function, such as light-sensitive proteins from algae, defence mechanisms from bacteria, and cargo delivery via viruses.



Our brains are constantly receiving information from all around us via our senses, and generating movements that help us execute our goals. But our brains also have a rich repertoire of internally generated activity—our emotions, imaginings and memories—that isn't triggered by what we just heard or saw, or the next movement we want to make. How does the brain achieve this? By what logic do those millions and millions of neurons work together to create a thought, or to convert these black squiggles into meaningful words and sentences, or to hit a cross-court forehand? This is a big question in neuroscience, and to answer it, scientists must track brain activity at the level of individual cells.

A new approach is to measure calcium, a key ion involved in a range of critical processes in the body, from contracting our muscles, to cell growth, memory formation, and sending signals along neurons. A change in the concentration of calcium ions is a way of tracking the activity of neurons. By tracking calcium, it is now possible to measure thousands of individual cells in animals as they execute specific actions.

Neuroscientists are using a cutting-edge technology called two-photon imaging microscopy to measure these changes. At UQ's Queensland Brain Institute, Professor Stephen Williams and his team use this technique to explore the way that dendrites, the fine branch-like extensions of neurons, process information in the brain. They have pinpointed that active dendritic information processing is important in brain circuits that are activated at the moment an animal is engaged in a task. The mammalian brain is so complex that to narrow down neurons from the approximately 70 million in a mouse brain, to just a single group—and link it to a behaviour—is an incredible advance.

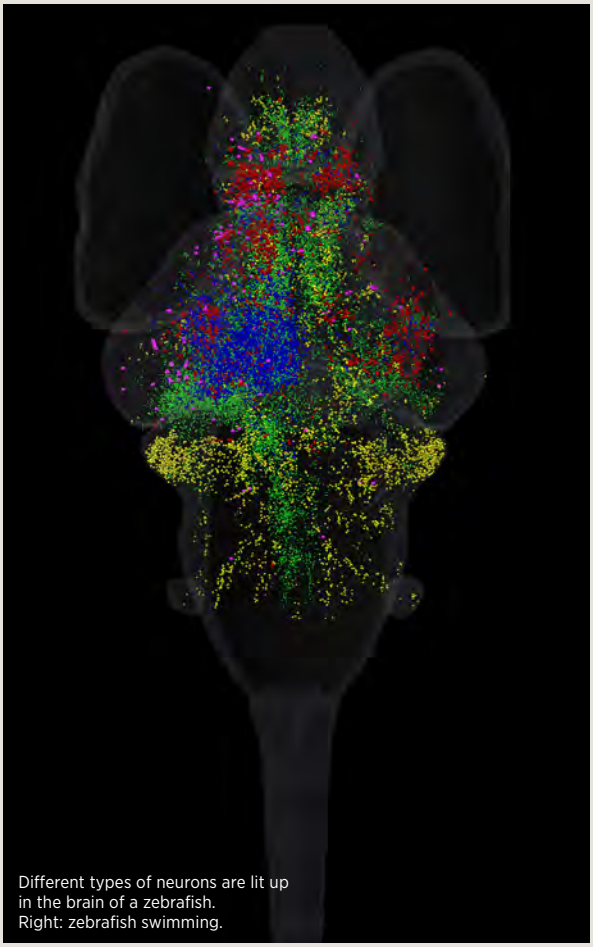
... it is now possible to measure thousands of individual brain cells in animals as they execute specific actions...

Switching on brain cells at will

To go one step further than recording brain cell activity, Professor Williams and his team have used a revolutionary light-based technique called optogenetics to study how these circuits process information.

For this technique, scientists genetically engineer channels in a neuron to respond to light, by inserting a light-sensitive protein derived from algae (see opposite). When a channel is exposed to light of a particular wavelength, say blue, it opens to let ions pass into the neuron to generate an electrical signal. Flashing a light can trigger or inhibit neurons expressing light-activated channels with amazing accuracy.

Using this technique, Professor Williams' team has been able to identify a system of neurons that were active when animals were engaging in a task. This 'cholinergic system' is disrupted in diseases of the brain that impact cognitive abilities, such as dementia, so future research may reveal ways to stop this disruption and slow the progression of brain diseases.



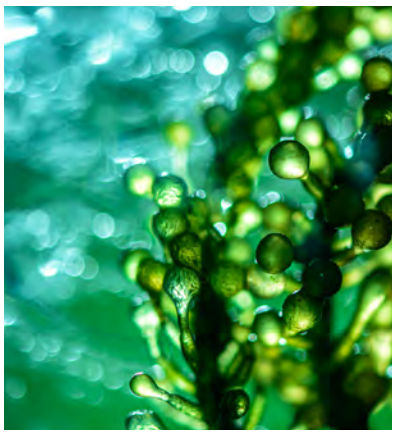
Different types of neurons are lit up in the brain of a zebrafish.
Right: zebrafish swimming.

The whole brain

To understand how neurons work together to process information, scientists can monitor how connected groups of neurons across the brain activate in response to a stimulus. Advances in technology have only recently enabled researchers to see the activity of networks of neurons in live animals, in real time. "It has always been hard to study these networks, because you have to observe the activity of thousands of neurons at the same time," says Associate Professor Ethan Scott, from UQ's Queensland Brain Institute. His work focuses on the circuits and networks of neurons responsible for animals' ability to sense the world and respond with appropriate behaviours. His team studies the tiny transparent zebrafish, peering into its simple brain using a cutting-edge technology called light-sheet microscopy to show nearly all of the neurons in their brains at once.

To understand how zebrafish make sense of their world, the team records brain-wide activity while presenting images, sound, and motion stimuli to the fish. Each stimulus activates different neurons, so the scientists can see how different networks are engaged to process those stimuli.

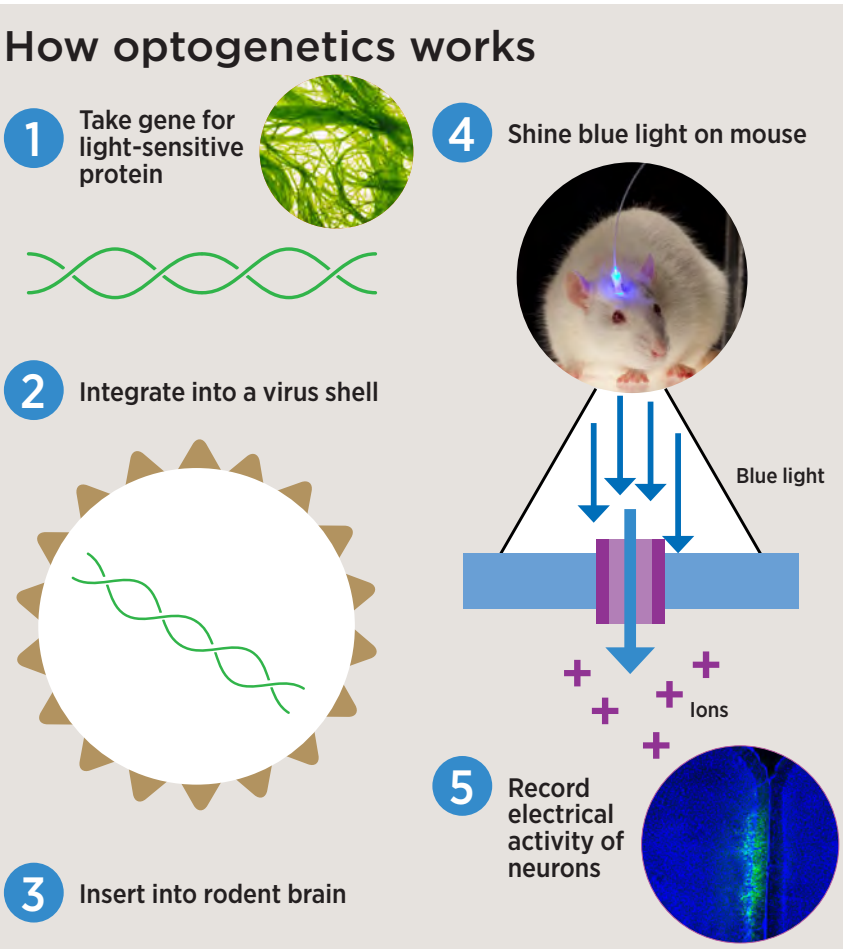
The scientists can then use optogenetics (see below) to stimulate neurons with light in very precise ways. They can customise the light patterns projected into the animals' brains, like a hologram, activating the exact neurons they think are responsible for visual, auditory, and vestibular processing (balance) and studying the fishes' responses.



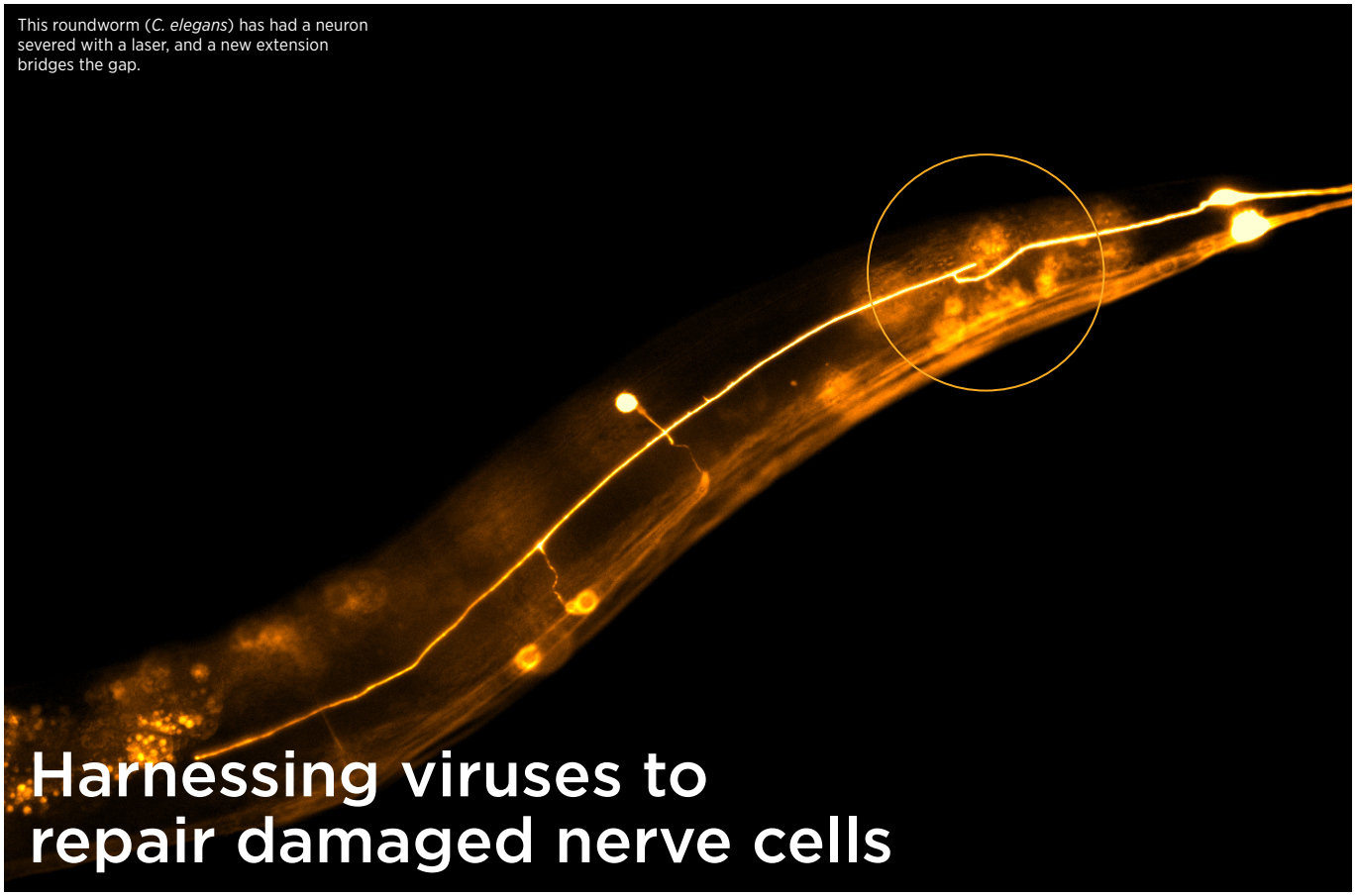
Algae controls the brain

Who'd have thought that a humble slimy algae could progress the next revolution in neuroscience? In the 1990s, scientists observed that electrical signalling in cells of green algae changed in response to light. That kernel of knowledge was used to isolate the light-sensitive gene that has opened up a new field in neuroscience research, called optogenetics: using light to control the activity of brain cells in living tissue.

How optogenetics works



CREDITS: GETTY, ETHAN SCOTT/QBI, GETTY, ROGER MAREK/QBI



This roundworm (*C. elegans*) has had a neuron severed with a laser, and a new extension bridges the gap.

Harnessing viruses to repair damaged nerve cells

In the late 1990s, biologists Professor Andrew Fire and Professor Craig Mello were studying how genes are expressed, or turned on, when they made a remarkable discovery about DNA's single-strand cousin, ribonucleic acid (RNA).

At the time, it was already well known that genes contain the instructions for making specific proteins—the building blocks of the body's cells and their functions—and that messenger RNA relays those instructions to the protein-making regions of the cell. Professors Fire and Mello and their colleagues found that by exposing cells to an artificial double-stranded RNA of a specific gene, it can interfere with, and destroy, the normal messenger RNA of that gene. This process is called RNA interference (RNAi) and allows scientists to silence specific genes as needed. Importantly, Professor Gary Ruvkun and Professor Victor Ambros discovered that cells in *C. elegans* also use a similar mechanism, via tiny pieces of RNA (microRNA), to turn off specific genes. At UQ's Queensland Brain Institute, Professor Massimo Hilliard and his team are using RNAi in *C. elegans* to help understand how to repair the long, cable-like axons of nerve cells, which can be damaged by trauma or degraded in many brain diseases.

A main challenge has been the delivery method: how do you get these small interfering RNAs into the right cells at the right time? For this, researchers have had help from some unexpected allies in nature: viruses.

Decades of research into infectious viruses, such as HIV and the herpes simplex virus, has revealed these viruses can be co-opted to deliver genetic material into human cells. By removing all the harmful genetic information and leaving the virus shell, scientists have effectively turned these viruses into tiny cargo containers that can deliver synthetic DNA or RNA.

Viruses can be made to target specific cell types at certain times, allowing, for example, the delivery of RNA to brain cells undergoing repair in a particular part of the brain. These technologies have now become indispensable research tools.

Associate Professor Tim Bredy is using virally delivered RNA to try to enhance memory, and Professor Jürgen Götz is using the technique to find new treatments for dementia.

The humble roundworm: a key player in brain science

The tiny *C. elegans*, measuring about 1 mm long, has done more for neuroscience than just about any other organism. With just 302 neurons and 7000 connections, it has a much simpler nervous system than our complex 100 billion neurons. Professor Hilliard's team has been able to slice the axon of a single neuron to see how *C. elegans* repairs it. They found it is able to spontaneously repair a broken nerve by stitching the two halves back together! (See image above). If we can figure out at the most basic level the signals and proteins used in that process, we may be able to apply that to humans to help repair nerve damage.

CREDITS: XUE YAN HO/QBI, ISTOCK, SCIENCEPHOTO

Tiny worm could hold the key to repairing injured nerve cells

The ability to reconnect nerve cells following an injury is a huge goal in science. Humans cannot do this spontaneously and it's why damage to the spinal cord is usually permanent.

But this ability does exist in nature: a number of invertebrate species, like the microscopic roundworm *Caenorhabditis elegans*, are able to re-fuse and restore the function of neurons that have been severed.

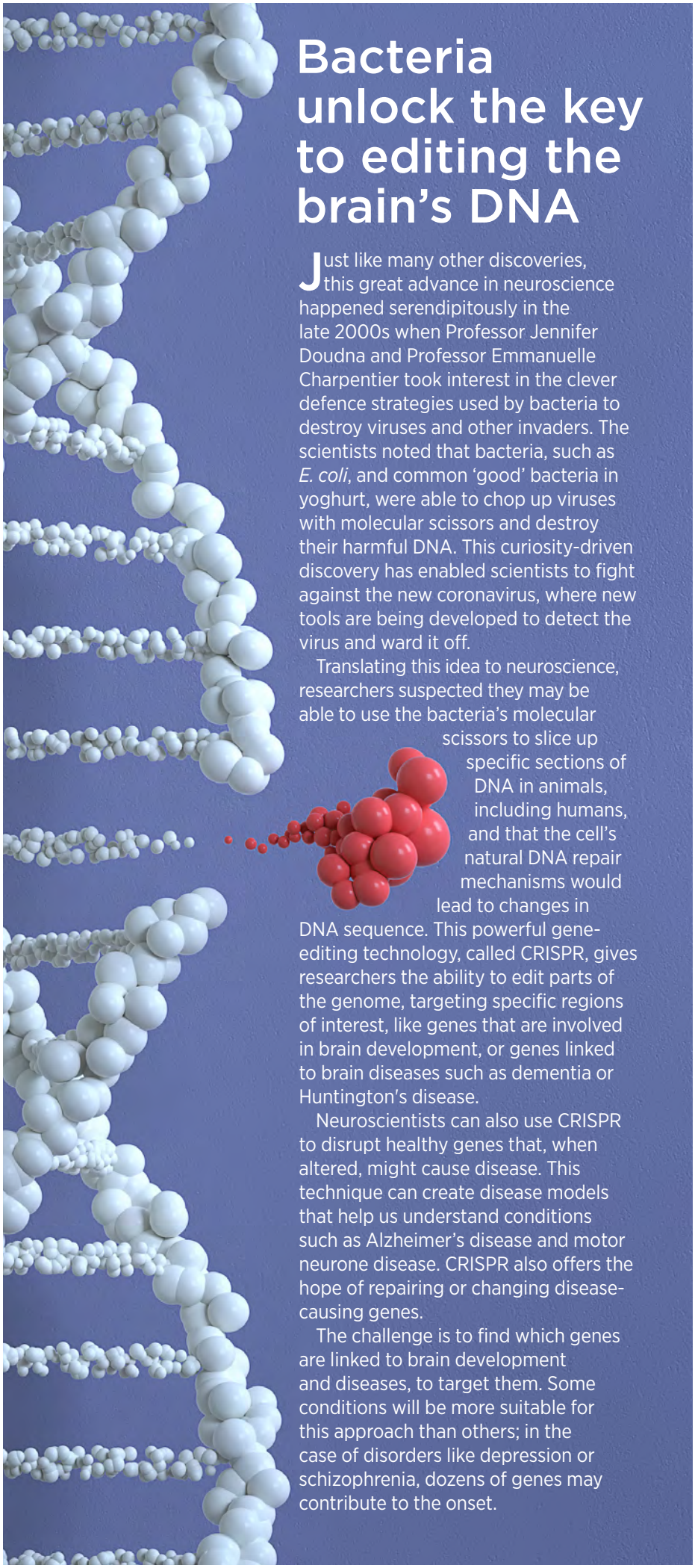
Professor Massimo Hilliard and his team at UQ's Queensland Brain Institute are studying this amazing capability in *C. elegans* in the hope of one day being able to treat nerve injuries, such as paralysis, in people.

They uncovered key information on how this process is regulated. Neurons communicate using lengthy, cable-like structures called axons. In 2015, Professor Hilliard's team discovered the ability of *C. elegans* to carry out a process called axonal fusion, where two halves of a cut axon reconnect.

"It's a very efficient process," Professor Hilliard says. "Instead of injured nerves having to regrow the full length to their targets, they are basically just bridging a gap to rejoin the nerve and allow it to function again." (see image, opposite top).

To undergo fusion, the axon still attached to the cell must first regrow, then position itself in close proximity to its separated axonal fragment. Once the two parts of the axon have reconnected, they fuse their membranes to form a cohesive whole with an outer membrane and the inner material of the cell.

It's a process that offers promise as a potential treatment for people with nerve injuries, which can cause life-long disabilities.



Bacteria unlock the key to editing the brain's DNA

Just like many other discoveries, this great advance in neuroscience happened serendipitously in the late 2000s when Professor Jennifer Doudna and Professor Emmanuelle Charpentier took interest in the clever defence strategies used by bacteria to destroy viruses and other invaders. The scientists noted that bacteria, such as *E. coli*, and common 'good' bacteria in yoghurt, were able to chop up viruses with molecular scissors and destroy their harmful DNA. This curiosity-driven discovery has enabled scientists to fight against the new coronavirus, where new tools are being developed to detect the virus and ward it off.

Translating this idea to neuroscience, researchers suspected they may be able to use the bacteria's molecular scissors to slice up specific sections of DNA in animals, including humans, and that the cell's natural DNA repair mechanisms would lead to changes in DNA sequence. This powerful gene-editing technology, called CRISPR, gives researchers the ability to edit parts of the genome, targeting specific regions of interest, like genes that are involved in brain development, or genes linked to brain diseases such as dementia or Huntington's disease.

Neuroscientists can also use CRISPR to disrupt healthy genes that, when altered, might cause disease. This technique can create disease models that help us understand conditions such as Alzheimer's disease and motor neurone disease. CRISPR also offers the hope of repairing or changing disease-causing genes.

The challenge is to find which genes are linked to brain development and diseases, to target them. Some conditions will be more suitable for this approach than others; in the case of disorders like depression or schizophrenia, dozens of genes may contribute to the onset.

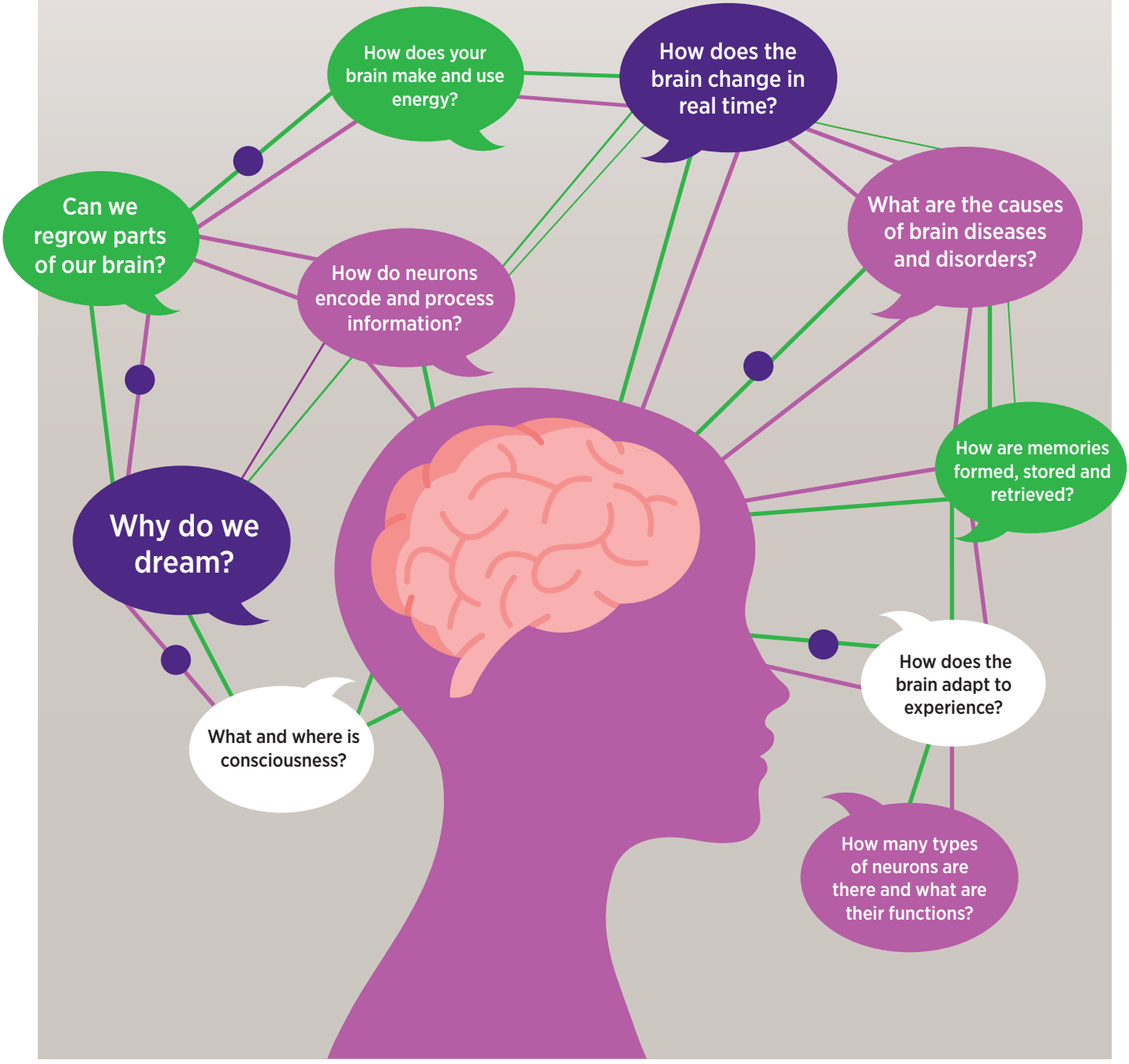
CHAPTER 5

FUTURE LEAPS IN BRAIN SCIENCE

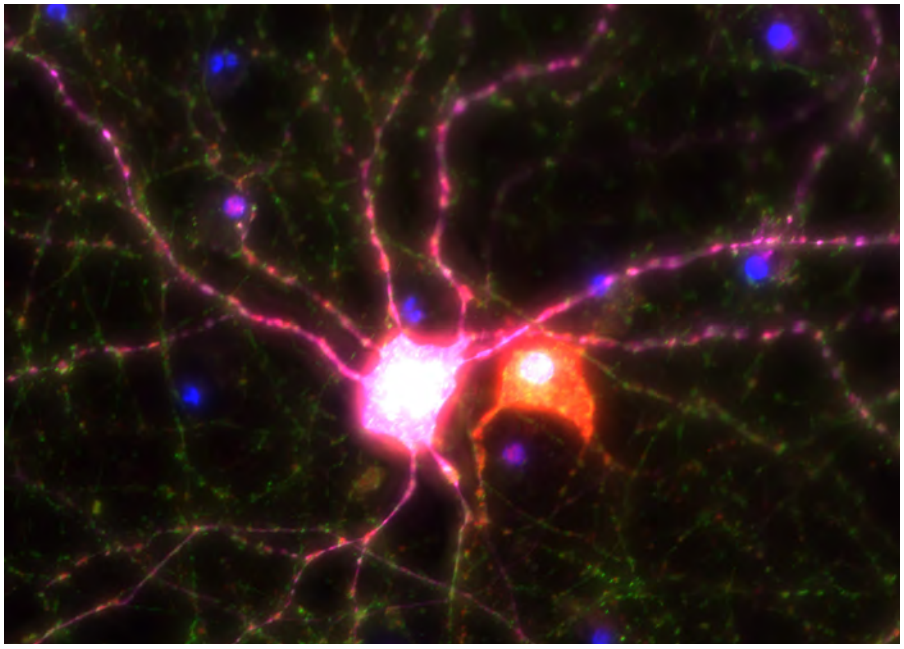
We have discovered more about the brain in the last 50 years than in the previous 500 years. We have learnt, for example, that certain regions in the brain are associated with particular parts of the body or with particular skills, such as language. We have learnt that individual cells called neurons are the fundamental units of the brain. We have learnt that our brains can change, and can adapt to experiences to store memories and learn, as well as adapt to damage. We have learnt that electricity and chemical signals are how neurons communicate with each other.

In this chapter, we look at some of the big questions in neuroscience yet to be answered, as well as some interesting potential applications.

Big questions in brain science



CREDITS: GETTY, QBI, SCIENCE PHOTO



Adapting on the go: the mysterious ways of epigenetics

The DNA code in genes inherited from our parents gives instructions for much of the way our physical bodies are made, our risk factors for diseases, our personalities, and individual directions for cells to develop into particular types—neurons, for example. But our environment and experiences also have an impact on how our bodies and brains look and work. The concept that a gene's function can be altered by experience—by turning it up or down without changing the underlying DNA code—is called epigenetics.

Studies on water fleas have demonstrated this epigenetic effect. These insects grew horns on their heads in response to predatory signals in the water and would pass these features on to their offspring as long as the signal was in their environment. As soon as the signals were gone, the next generation of offspring were born with normal heads. This is a classic example of an epigenetic change in response to an environment, which doesn't involve a change in the underlying DNA code.

Professor Oded Rechavi's lab at Tel Aviv University studies these mechanisms in the roundworm *C. elegans* (see p16). Their earlier work showed that epigenetic changes in worms can produce adaptations across generations. More recently, they discovered that epigenetic changes in neurons affect the ability of the worm's offspring and descendants to forage for food.

From simple organisms to the complex human brain

Researchers are now moving from studying epigenetics in simple organisms to looking at the complex human brain. Epigenetics in the brain, in principle, changes gene activity in response to a variety of experiences, including exposure to drugs of abuse or environmental toxins, changes in nutritional factors, and simple daily events such as social contact.

This was a very important moment in neuroscience because it revealed that our DNA is not our destiny and implies that our environment can profoundly affect the way our brains function

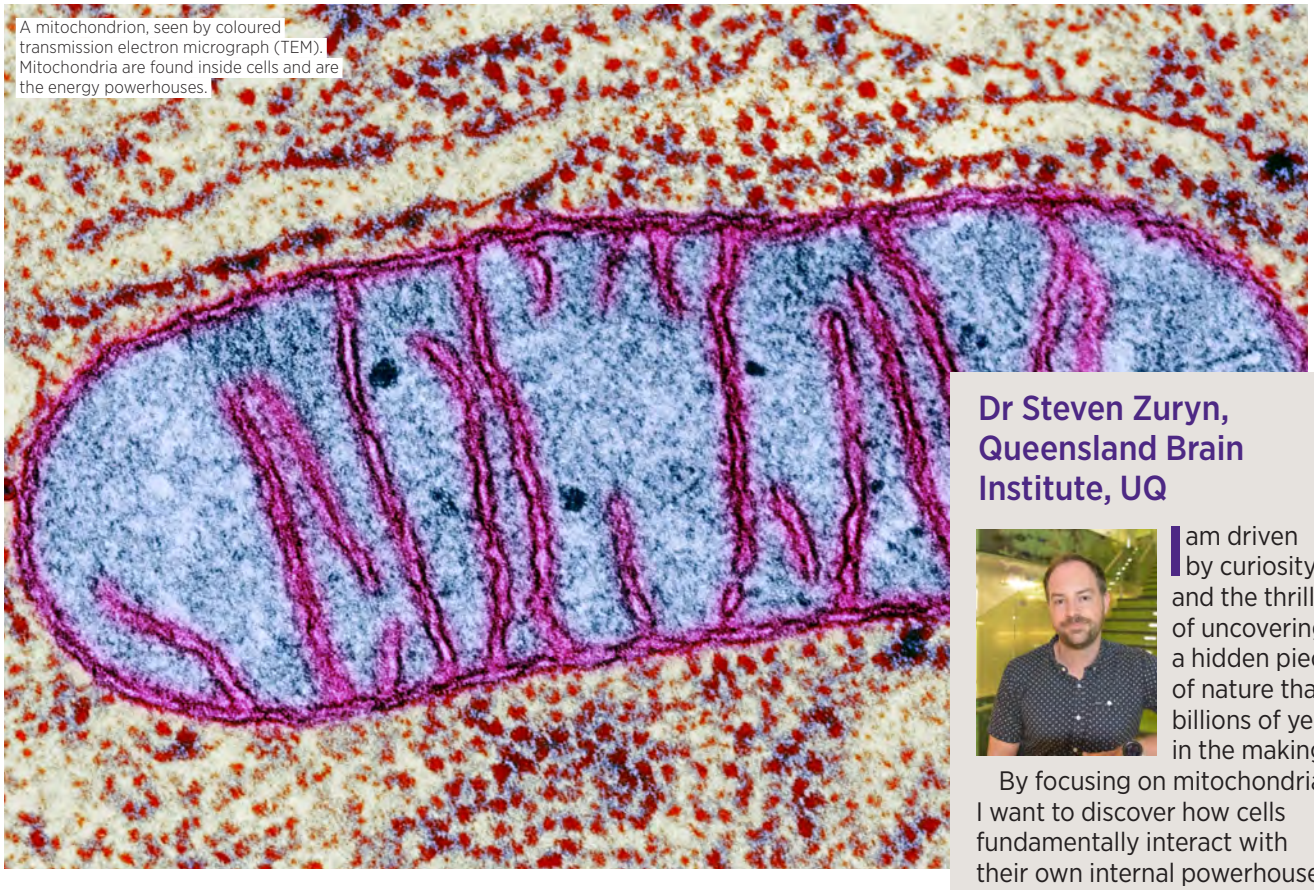
A water flea's normal body (right) and a water flea after being explosed to a predator (left) and inheriting a protective horn.

But how is a gene turned up or down after an experience? The answer is by reversibly modifying our DNA. Back in the early 1970s, Russian scientist Professor Boris Vanyushin was studying how learning affects DNA. He found that an increase in chemical tags, called methyl groups, that bind directly to DNA was related to the strength of memory. This major discovery changed the way we think about the relationship between our DNA and experience.

We now know that, like a dimmer switch, these tags on DNA can turn genes up or down depending on the circumstance. This was a turning point in neuroscience because it revealed that our DNA is not our destiny and implies that our environment can profoundly affect the way our brains function, all the way down to our genes—and these adaptations can be passed on to the next generation.

For the past two decades, Associate Professor Timothy Bredy and his team from UQ'S Queensland Brain Institute have been investigating how epigenetics affects memory. They have shown that all four DNA bases of the genetic code—A, T, G and C—are subject to these chemical tags and can work together to influence the strength of different kinds of memory.

The team has also found underlying ways in which these tags emerge, showing that a large part of our genome doesn't actively code for proteins that make our neurons function correctly, but is instead a sophisticated surveillance system that allows the environment to influence our genes. Their work has important implications for understanding how memory works and developing new treatments for fear-related anxiety disorders like PTSD.



A mitochondrion, seen by coloured transmission electron micrograph (TEM). Mitochondria are found inside cells and are the energy powerhouses.

Food for thought: how your brain makes and uses energy

Your brain is arguably the hungriest organ in the body, consuming roughly 20 per cent of your energy each day.

Most of that energy is produced by tiny structures inside cells called mitochondria, which break down complex carbohydrates from our food into simple sugars.

"Considering the brain is made up of around 100 billion neurons, that gives you an idea of how much energy the brain uses and needs to survive, and the mitochondria are responsible for that," says Dr Steven Zuryn from UQ's Queensland Brain Institute.

Intriguingly, much of what we know about mitochondria originated with the study of bacterial evolution.

Until around two billion years ago, mitochondria were separate organisms, much like bacteria. At some stage, an ancestor of our cells fused with one of them. After all this time, mitochondria still have their own genome. It's much smaller than our main genome, and encodes just 37 genes. But each mitochondrion has as many as 10 copies of its genome, and each cell contains hundreds to thousands of mitochondria. Consequently, changes in mitochondrial DNA can have a big effect on the body.

"We now know that there are more than 30 diseases caused by mitochondrial DNA mutations"

"We now know that there are more than 30 diseases caused by mitochondrial DNA mutations," says Dr Zuryn. He wants to understand how mutations in mitochondrial DNA change in individual cells and throughout the entire body during a lifetime. His research is focused on understanding how these mutations are passed on, or prevented from being passed on, from one generation to the next.

Such explorations could provide insight into degenerative brain diseases, which have been linked with mitochondrial DNA mutations.

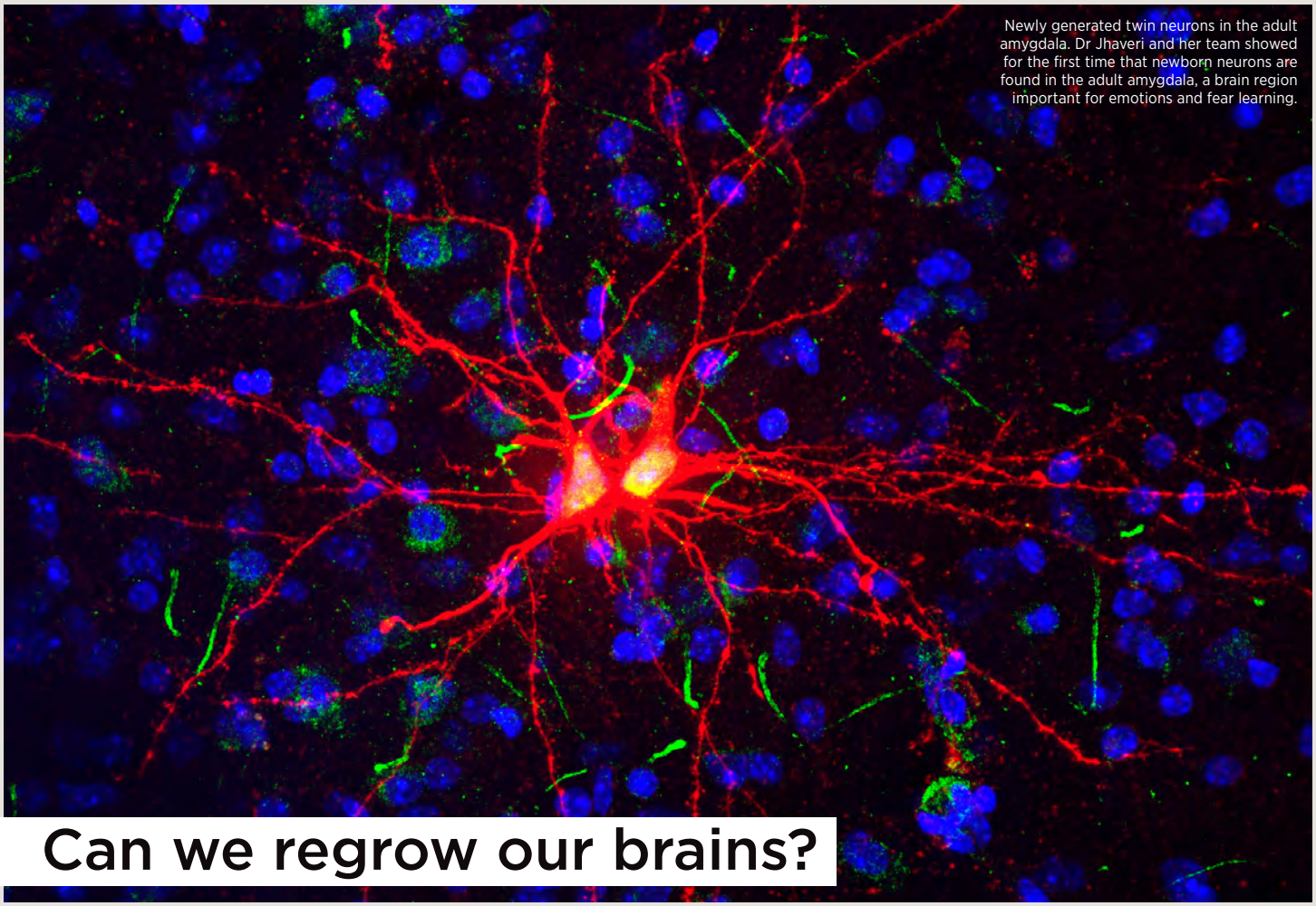
Dr Steven Zuryn, Queensland Brain Institute, UQ

I am driven by curiosity and the thrill of uncovering a hidden piece of nature that's billions of years in the making.

By focusing on mitochondria, I want to discover how cells fundamentally interact with their own internal powerhouses. From a biological point of view, it is mitochondria that have literally powered the explosion of evolution and complex life which is energetically demanding, resulting in the diverse array of species we see around us, both plant and animal. They need our cells and our cells need them. However, mitochondria can deteriorate as we age. This is why mitochondrial dysfunction lies at the core of many human diseases, including inherited mitochondrial diseases and possibly more common age-related diseases such as dementias and cancer. Understanding how cells can adapt and repair mitochondria is important for improving outcomes for people with mitochondria-related disorders.

The next frontier is to understand the nanoscopic mechanics of how this occurs and identify possible interventions to prevent mitochondrial damage, or improve damage repair, so that we can treat disease and, ultimately, prolong cell and neuron function in the face of ageing and disease.

CREDITS: SCIENCE PHOTO, JAVERI LAB, QBI



Newly generated twin neurons in the adult amygdala. Dr Jhaveri and her team showed for the first time that newborn neurons are found in the adult amygdala, a brain region important for emotions and fear learning.

Can we regrow our brains?

For years, the dominant theory on the brain's adaptiveness held that because the connections were so complex, they would be impossible to replace once formed. In the 1960s, however, the first clues about the brain's plasticity began to emerge. "Joseph Altman showed that new cells are made in the brains of adult rats," says Dr Dhanisha Jhaveri, a senior scientist at UQ's Queensland Brain Institute. Though these early results were controversial, they were followed by an explosion of research in subsequent decades, including pioneering work by the Institute's founding director, Emeritus Professor Perry Bartlett.

"The studies showed that stem cells reside in the adult mouse brain, and under the right environmental stimuli, these cells will divide and form neurons," says Dr Jhaveri.

More recently, studies of the hippocampus, a part of the brain critical for memory, suggest that as many as 700 new neurons are added to this region each day.

Dr Jhaveri's research, in collaboration with Emeritus Professor Bartlett and Professor Pankaj Sah, shows that new neurons also form in the amygdala, a brain structure central to emotional processing, and can integrate into existing brain circuits. Intriguingly, they discovered that chronic stress disrupts this process and leads to anxiety behaviour in mice. The finding suggests that the formation of new neurons and their correct connectivity is important to healthy brain function.

From such curiosity-driven research also comes the promise of new treatment avenues.

"Understanding how new neurons form connections could lead to new anti-depressants or new anti-anxiety medications," says Dr Jhaveri. It could also reveal ways to encourage brain repair after injury or to reduce the effects of neurodegenerative conditions like dementia or Parkinson's disease.

Could we ever regrow a whole new brain? Perhaps, says Dr Jhaveri, but it won't be as useful as you might think. "Instead of regrowing the whole brain, it will be more important to regenerate the right kind of neurons in the right place that make the right connections."

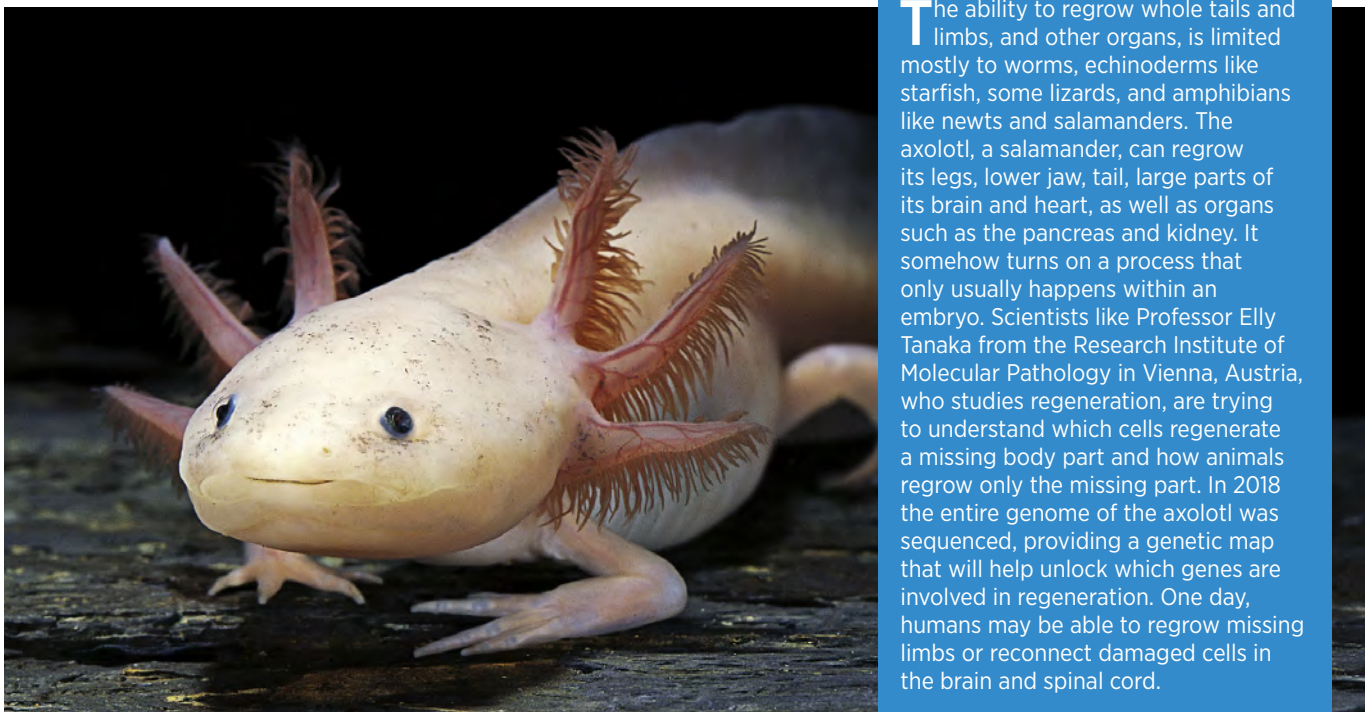
Dr Dhanisha Jhaveri, Queensland Brain Institute, UQ

What really motivates me is the fact that we have gone into an uncharted territory, opened up some new doors and there is a whole new world out there yet to be discovered. I'm really driven by understanding the fundamental brain mechanisms that contribute to our cognition and emotion: production of new nerve cells, how they are connected, how their activity is regulated and how they impact behaviour.

We require this understanding before we can rationalise and devise a design or a strategy that will help to fix the cells or the circuits in neurodegenerative diseases or in cases like anxiety or depression.

One day we could harness these amazing animal abilities

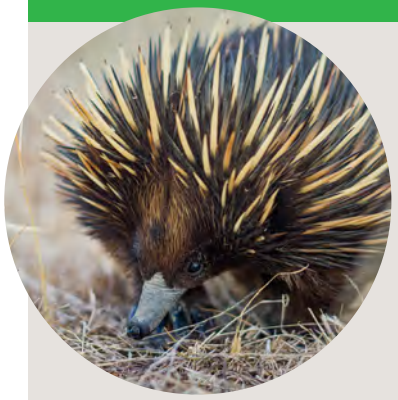
Some animal brains achieve amazing feats like regrowing tails and limbs and sensing electricity. Neuroscientists are working to figure out how they do it to inspire future technologies that can apply to humans.



How do animals regrow tails, limbs and parts of brains?

The ability to regrow whole tails and limbs, and other organs, is limited mostly to worms, echinoderms like starfish, some lizards, and amphibians like newts and salamanders. The axolotl, a salamander, can regrow its legs, lower jaw, tail, large parts of its brain and heart, as well as organs such as the pancreas and kidney. It somehow turns on a process that only usually happens within an embryo. Scientists like Professor Elly Tanaka from the Research Institute of Molecular Pathology in Vienna, Austria, who studies regeneration, are trying to understand which cells regenerate a missing body part and how animals regrow only the missing part. In 2018 the entire genome of the axolotl was sequenced, providing a genetic map that will help unlock which genes are involved in regeneration. One day, humans may be able to regrow missing limbs or reconnect damaged cells in the brain and spinal cord.

How do animals sense electricity?



Sharks, rays and eels are well known for being able to detect electricity, but platypuses, echidnas and bees can do the same. These animals have receptors called ampullae of Lorenzini, which detect electrical currents via pores on their snouts. Animals use electroreception for locating objects around them, often prey, and typically live in environments that are low light – murky rivers, deep in the ocean, or in caves. Some fish even communicate using weak electrical signals, for attracting mates. If this could be harnessed in humans, it could enable the development of electrical interface devices to connect our brains to computers for cognitive enhancement or for augmented reality.

Octopus intelligence

Although closely related to snails and slugs, octopuses show a level of unusual intelligence, setting them apart among the invertebrates. In some respects they are smarter than many mammals, able to perform tasks that would baffle a dog and display more cognitive capability than a cat. Octopuses have been known to grab coconut shells to protect themselves from a shark attack, solve mazes, plan notorious escapes from aquariums and devise creative solutions to getting food or being hunted. Many of the neurons an octopus uses to process information are in its tentacles, in addition to having a centralised brain. Neuroscientists can learn a lot from octopuses, including understanding neural networks, as well as investigating how camouflage could be applied for military use.

CREDITS: GETTY, ISTOCK

A question of ethics

Exciting developments in brain science, inspired by nature, are rapidly advancing our understanding of the brain. This science is important, but, as with all advancements, there are significant ethical implications, and we need to consider the ways in which neuroscience technologies and discoveries are managed and used.

Unknown consequences

One of the most significant leaps in neuroscience—using gene-editing technology to alter DNA in neurons (see p17)—has the exciting potential to cure genetic brain diseases like Huntington's. But there are potential unknown effects of making changes to a person's genome that may manifest decades later. Other considerations include whether to make pre-emptive changes in an individual's genome if they might be at high risk of developing a brain disorder. Using bacteria and virus shells to deliver genetic material (see p15) also has potential negative effects: the body's immune defence system may have an adverse reaction if it determines this foreign material should be eliminated.

Enhancing the brain

Developing treatments for brain diseases and disorders is an important goal in neuroscience. By definition, this involves enhancing a diseased or disordered brain. The next step is how we might enhance normal brains. There are upsides to cognitive enhancement: boosting memory or intelligence or creativity. But there are clear downsides too: who will have access to this technology and how should it be regulated? At what point should cognitive enhancement stop? What unintended consequences might there be? What kind of enhancement crosses a line into unfair advantage or brain doping?

Alternate use—or misuse—of neuroscience technology

While scientific advances may have the noblest of intentions, there will always be the potential for misuse, or uses that were not originally considered.

Brain augmentation technology designed to treat brain dysfunction —memory enhancement, for instance—may be applied in military settings to boost soldiers' capabilities. Gene editing technology has already gone a step too far in the eyes of many. For example, in 2018, a Chinese researcher announced, to the great concern of scientists around the world, that he used CRISPR to create the first gene-edited babies. The babies, purportedly had resistance to HIV, but they may also have genetic mutations that are life-shortening.

Manipulating the brain

Scientists can use light to control and alter neurons, and can use techniques and devices—for example, transcranial magnetic stimulation, or TMS—to change the brain, at least temporarily. These have the potential to affect someone's personality or identity. How much is a person responsible for their actions if their brain is artificially altered? In this context, what is the threshold of manipulation below which a person's brain would still be considered normal?

The big picture

Research is inherently interconnected with many scientific fields and is not performed in isolation from our values and policies in society. While researchers pursue their ideas to advance science, they do it knowing there are potential downsides along with the benefits.

Important ethical concerns in neuroscience

- Treatments that may change personality or identity
- Unintended or unknown effects of altering DNA in the brain
- How much should we be able to enhance function?
- Fair access to technology that enhances brain function
- Consent from people who have a brain disease or disorder
- How prediction of brain disorders and diseases may impact health insurance coverage
- Anticipating possible alternative use, and misuse, of neuroscience technology

Investing in the future

The ultimate aim of most research is to improve the human condition, from working on treatments for diseases like Alzheimer's, to improving crop yields and reaching for the stars. As we have explored in this magazine, discovery and fundamental science research has the potential for significant impact on our quality of life. It is with these foundations that UQ's Queensland Brain Institute was established in 2003, with the premise of focusing on fundamental discovery science and the aim of leading the world in neuroscience research.

The Institute now has a collection of internationally respected researchers who routinely have their work published in the top scientific journals. Our neuroscientists have made important discoveries, including that new neurons can be made in the adult brain, vitamin D plays a critical role in early brain development, and certain signalling molecules are important for neuron communication and repair.

... discovery and fundamental science research has the potential for significant impacts on our quality of life.

Almost two decades later, our body of fundamental research is contributing to more than our knowledge of how the brain works—it is also being translated into potential treatments for currently incurable nervous system disorders. QBI is progressing several clinical human trials, including two clinical safety trials which are being planned: a trial of a drug to slow MND progression, based on 23 years of research by the Institute's inaugural director, Emeritus Professor Perry Bartlett, and a non-invasive ultrasound treatment to improve memory functions in people living with dementia.

Importantly, this clinical research would not have been possible without first understanding how these diseases affect the brain at a molecular level, and indeed, how the neurons and molecules involved operate normally. Many of our laboratories are attempting to unravel what seem to be relatively simple processes but are, in fact, incredibly complex. For example, how do neurons communicate with each other? We have gathered extensive knowledge about how information is passed from one neuron to another and how neurons form networks, but there is still much to be learnt about the molecular and cellular machinery underlying these processes—with potential impacts on improving learning and memory, combating neurodegenerative diseases, and stimulating recovery from brain injury.

The Queensland Brain Institute's Discovery Research Endowment Fund has been established to embrace the critical role that philanthropic donations play in progressing new, out-of-the-box ideas that lead to scientific breakthroughs. Our long-term hope for the fund, through philanthropic support, is to address unmet needs—supporting young researchers; backing early stage, high-risk, high-reward projects; and providing seed funding to secure government support for larger initiatives. These niche areas are often not catered for by government, yet can have an enormous impact on solving major health issues facing society today, including dementia, depression, anxiety, and stroke.

Society's investment in fundamental research is an investment in future science that may solve some of our biggest health and ageing issues.

CREDITS: QBI

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

CREATE CHANGE

Owning the unknown at the Queensland Brain Institute

Our scientists are unlocking the mysteries of the brain to understand and treat disease, improve learning and memory, and inspire technology. Help them discover more.
qbi.uq.edu.au/discovery

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

CREATE CHANGE

w: qbi.uq.edu.au / e: qbi@uq.edu.au / p: +61 7 3346 6300