Australian Government
Chief Scientist

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MERSON LECTURE

Getting Ahead

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Queensland Brain Institute
BRISBANE

Let me begin tonight by flexing our brains.

We're going to travel back in time, by the power of thought: to Egypt, 2000 BC.

You're an investor in a pyramid scheme.

You've gone to inspect the progress on the construction site…

…when suddenly, a careless slave dislodges a chunk of sandstone… that hurtles from 100 metres above and clonks you square in the head.

You open your eyes… and you're lying in the sand, staring at the clouds, and bleeding profusely.

It's ugly.

But you're in luck! You're wealthy. So your slaves pick you up, dust you off, and carry you for treatment by the most expensive doctors.

The doctors immediately consult the medical literature – or in this case, the medical hieroglyphics.

It's a document we can still read today, called the Edwin Smith Papyrus.

What treatment does it recommend?

First, the diagnosis. The doctors will poke around with their hands and watch to see if you shudder or start leaking any interesting fluids.

Then, the treatment. They will fetch a nice cow, and slaughter it – cutting out a juicy steak to slap on your head to staunch the blood.

They'll get some honey and smear your head.

They'll wrap you in linen, pour milk in both your ears, and hand you the bill. And probably barbecue the rest of the cow.

Anyone who has reservations about the benefits of modern medicine is welcome to try the good old-fashioned way at home.

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But we shouldn't think too badly of the Ancient Egyptians. At least they had a grasp of basic anatomy, and a knack for cutting up corpses. For the next four thousand years, that was about as sophisticated as it got.

The secrets of the brain were locked so firmly in our skulls that we could learn next to nothing about its structures, its functions or its disorders.

You can only record what your technology actually allows you to see.

And whatever you see, you have to try to *interpret*.

The Ancient Romans thought of the brain in terms of their most advanced technology: aqueducts and waterways.

Enlightenment scholars, in the seventeenth century, thought of it as a clock.

The Victorians compared it to electricity.

The Edwardians compared it to the telephone network.

At university, I was taught to imagine it as a computer.

Today, we think of the brain as something akin to the internet – a web of complex pathways and interconnections.

I'm reminded of the saying about economic models. All are wrong, some are helpful.

The same is true of metaphors. They inch us closer to the truth.

For every useful metaphor, of course, we came up with a lot of bad ones – and bad theories to match.

Dualism: the pineal gland is the conveyor belt between the brain and the soul.

Phrenology: you can spot a criminal by the shape of the head.

Parapsychology: stare at a spoon, and you can bend it with the force of your mind rays.

Nonsense.

The father of modern physics, Isaac Newton, said that he stood on the shoulders of giants.

The father of modern neuroscience was Ramon y Cajal: he found himself standing in a quagmire of crackpots.

He was a nice man so he put it more kindly: he called it "my forgotten corner", so dark it didn't have a name.

But in that corner, in the late nineteenth century, he found a window. And he opened it – with drawings of the brain so meticulous, so accurate and so beautiful that we still publish them in textbooks today. Art books, and science books.

We looked through that window – we saw with his eyes – and we glimpsed for the first time the awesome scope of the final frontier in science.

Not the distant stars. Not the deep oceans. The brain. *The human brain*. Ourselves.

And from that point on, there would be no turning back.

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Now let's jump forward to Australia, 2017.

This time you're an ordinary person. In a good way!

But something's wrong. Your speech is slurred. Your vision is blurry. You feel dizzy.

So you get yourself to the hospital for an emergency CT or MRI.

They find a blood-clot in your brain: yes, it's a stroke.

They can give you clot-busting drugs that dissolve the obstruction.

Or if they can't, they'll insert a catheter through an artery in your groin and feed it to your brain to physically remove the clot.

All this, in less time than it would take a doctor in Ancient Egypt to fetch a cow.

You'll be transferred to a stroke unit for monitoring and follow-up care.

You might find all of these technologies astonishing.

But, to the doctors, they are simply routine: the standard care, for the average patient, on a typical day, in a nation like ours.

To be astonished, they say, look at what comes next: and not just in the treatment of stroke, but across the full breadth of that final frontier.

Imagine if we could help people suffering from chronic pain, not with addictive painkillers, but with an implant in the lower back that sends an electric current into the spinal cord nerves to mask the pain … and then records the signals from the nerves, in real time, so the current can be fine tuned to deliver maximum relief.

Imagine if we could install a pacemaker in the brain, for conditions like Parkinson's disease, blocking errant signals from faulty brain cells, and reducing tremors, enabling mobility, perhaps even restoring speech.

Imagine if we could learn from the way the brain collects and stores and processes enormous volumes of information, consuming a tiny amount of energy, in such a little space.

What if we could replicate something as intricate as a neural network in *silicon*, on a computer chip?

All of those technologies are not just plausible – they are in production.

It is an extraordinary moment to witness: the early pay-off on decades and decades of painstaking work to image the brain, to study its mechanisms, to learn from its secrets.

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About twenty years ago, I was sitting in the audience listening to the presenters at a neuroscience symposium. Hearing about the breakthroughs and the new research avenues that they opened, I said to myself that we probably knew about one percent of all there is to know about the brain.

Every year, I repeat the exercise.

Every year, there's an avalanche of discoveries.

And every year, I'm still saying exactly the same thing: *now* we know about one percent of all there is to know about the brain.

The more we learn, the more complex the puzzle appears.

And so we have extraordinary advances in science, on the one hand… and on the other hand, next to *no* traction in the metrics that dominate our lives.

What is the leading cause of death for Australian women? Dementia. It overtook heart disease this year. We're getting much better at treating heart disease. We're not getting much better at treating dementia.

What is the average life expectancy of a person diagnosed with motor neurone disease? Two and half years. There is no known cure, and no effective treatment.

What is the annual cost of depression to Australia? About $13 billion.

The human toll is infinitely worse: suicide is now the leading cause of death amongst young Australians.

I lost a dear friend, the great composer Allan Zavod, to glioblastoma late last year. The survival rates for brain cancer have not improved in the last three decades.

Is there a person in this room who hasn't longed desperately for answers – answers that with every step forward, just slipped further away?

But slowly, slowly, we are bringing the insights together, from molecular neuroscience, to cellular neuroscience, to systems neuroscience, to behavioural neuroscience.

We are seeing that first wave of truly breakthrough therapies. And so I am now prepared to say it: *we are entering the era of translation*.

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The story can be told in just one device: the Stentrode. And I have some tiny attachment to this story, at the start.

At an unspecified time in the past, I completed my PhD: patch-clamping snail brains to measure the electrical activity between neurons.

Back then, it was extremely hard going. The tools I needed were not commercially available – I had to engineer them myself.

It was the start of my company, Axon Instruments…. but that's another story.

And I was only one small part of what followed, a whole new generation of experimental tools, capturing progress in computing, and genetics, and machine learning, and bio-fabrication, and so much more.

With these tools, scientists were able to not just record electrical activity – but to translate it into computer code.

The next step was to translate the code back into a signal – a signal that would prompt a device to move. Think about it: we could pick up electrical frequencies, convert them to code, and then into an action. We could control a device by controlling our thoughts.

What might that device be? What device would we want to literally control with thought?

How about an exoskeleton, so a paralysed person could walk?

Enter the Stentrode: a device the size of a matchstick. It's an array of electrodes that can be inserted by a catheter into a blood vessel in the middle of the brain.

Once the Stentrode is expanded, the blood continues to flow, and the electrodes pick up the electrical signals from the adjacent motor cortex.

Feed those brain signals to an external computer. Interpret them to drive the motors of a bionic limb. Mobility in a matchstick.

And here I come into the story again, from the sidelines: the inventor Tom Oxley approached me in 2014, when I was Chancellor of Monash University. All I could offer him was enthusiastic encouragement. He didn't need much, and since that time I have followed his progress with admiration.

Did the world imagine the Stentrode when I was patch-clamping snails? No.

But everything that followed – the global investment in basic research, in building better research infrastructure, in training up a generation of researchers – all of it is contained in that matchstick.

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Let me pause there, because I'm conscious I've introduced two words: investment and infrastructure.

One of the first things I discovered as Chief Scientist is that those words are deeply interesting to a lot of people.

It's been put to me, for example, that the brain consumes about 20 per cent of the body's energy.

On that premise, brain research should get about 20 per cent of all the available funds.

It's certainly worth a try.

But on any measure, it is fair to say that the brain is already in the ascendant. The vital signs are strong.

We can measure it in blockbuster programs.

The Europeans have the 10 year Human Brain Project, one of the two largest scientific projects the EU has ever funded.

China has the 15 year China Brain Project, announced last year.

The United States has the BRAIN Initiative: that's B-R-A-I-N, in capital letters; kicked off with over $100 million from President Obama, and proposed investment in the order of $5 billion.

Along with the public funds, there's the corporate interest: with ventures like Neuralink, from the man who brought you Tesla and SpaceX; and the Allen Institute, from the co-founder of Microsoft.

But perhaps the best measure of the health of the field is the green shoots: the influx of young researchers, amongst them the best and brightest of their generation.

When I returned to Australia from the United States, I wanted to do something to foster that generation in Australia.

I established the Australian Course in Advanced Neuroscience, known as ACAN: an annual three week residential program that brings the cream of the early researchers together with experts working at the absolute edge of the field.

Strongly supported by the whole of the Australian and New Zealand neuroscience community, with intensive support from UQ and QBI, ACAN has been operating now for 13 years.

If the ACAN alumni are the future, then Ramon y Cajal would be proud.

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So what next? What next for Australia? What should our contribution be?

We could start with a quick head-scan.

If we think of the Australian brain research community *as* a brain – and we're all neuroanatomists here, or at least passable amateurs – we have a healthy cerebral cortex.

We have the capacity for genuinely world-leading research, with particular strengths in imaging.

The National Imaging Facility, for example, is gold-standard, and one of the few research infrastructures able to integrate the insights from the most advanced high-resolution scanners with the broader evidence from conventional imaging tools in widespread use.

At the local level, early on in my term as Chancellor at Monash University I was amazed to discover that we had just installed a '300 thousand electron-volt double-aberration corrected Titan transmission electron microscope’.

Eight years later, we had installed a more modestly named but more suitable for biology ‘cryo-electron microscope’, and our scientists were seeing the details of biological proteins that previously they could only imagine.

This year, Swiss, German and Scottish scientists received the Nobel Prize for the invention of cryo-electron microscopy.

So we have the tools, and we’ve also got the skills and reputation.

Sticking with the brain analogy, we could call that the limbic system. We have highly competitive research institutions, including the Queensland Brain Institute, and the biomedical cluster in my home town of Melbourne.

Just as important as the components are the connections. We’ve got them: we’re small enough to be a networked community, and large enough to be globally relevant.

We have a promising blood supply, in the Medical Research Future Fund, and the Biomedical Translation Fund.

And now we have the equivalent of cranial nerves, in the Australian Brain Alliance: relaying the messages from the brain research community to the rest of the body.

So yes, it’s a healthy brain. The synapses are firing. We want to put that organ to work.

It is not for me to define what the mission for the Brain Alliance should be. But I take a keen interest in its progress, and I seem to be in the habit of giving advice.

Let me offer three thoughts about the way forward.

FIRST*, set an ambitious goal.*

And by ambitious, I mean realistic for scientists and inspiring for everyday people. Both are important.

A goal that is ambitious to the point of absurdity is useless: we set out expecting to fail, and we forgive ourselves for falling short.

A goal that is hard but achievable is motivating: credible to our peers, credible to investors and credible to government.

But it can't just be credible, it should also be *exciting*. Excitement is the magic that makes the credible into the truly compelling.

Brain research to the Australian people is the hope of a life-changing miracle: a treatment for autism, an answer for dementia, eyes to see, legs to dance. Things we can be proud to call Australian.

At every conference I attend, someone is sure to mention the Big Three.

Stump Jump Plough.

Black Box Recorder.

Cochlear Implant.

Those who are more up to date will mention Gardasil.

Yes, I know, they're all great.

But my dream is to go to a conference and hear about the *next* Cochlear in neuroscience: the iconic achievement that makes Australians proud.

Let's set out to create it.

***SECOND**, put the focus on transformational research technology*.

Call me an engineer. I'll wear it.

But when it comes to neurotechnology, I'm not alone.

There is a very clear and very deliberate focus on technologies in both the American and European agendas.

The Americans front-end it in the full name for their capital-letters BRAIN Initiative: Brain Research through Advancing Innovative Neurotechnologies.

They back-end it in the program's goals: safe and effective medical devices for consumers.

Technology is the alpha and the omega – the driver, and the goal.

The ambition of that agenda is truly remarkable.

Last year I learned of a project in DARPA, the advanced projects wing of the US military.

They want to build a brain-machine interface with the capacity to bidirectionally communicate clearly and individually with up to a million neurons.

Communicating with a single neuron is insanely difficult. Communicating with a *million* single neurons, at the same time, is a million times insane… at least on the face of it. But what extraordinary breakthroughs could be made in the attempt!

And what extraordinary opportunities might arise for breakthrough thinkers, like the members of Robert Kapsa's team whom I met at St Vincent's Medical Research Institute in Melbourne.

They are well aware that the inability of axons to adhere to metal electrode surfaces is the limiting factor for connecting single neurons to electronic circuits.

It's like trying to stick gold onto aluminium: ask an engineer, it doesn't work. Unless… you coat the aluminium with an intermediate layer of nickel, then plate the gold to the nickel.

And you can do something similar with axons and electrodes. The prototype I saw at St Vincent's uses an intermediate layer of muscle cells. Muscle cells stick to metal where neurons won't. So let the muscles attract the axons to form neuromuscular junctions and presto – a stable connection to individual neurons might be possible!

A breakthrough idea, a transformational tool.

The physicist Dyson Freeman had a maxim: "New directions in science are launched by new tools more often than by new concepts".

Ask any neuroscientist: he was dead right.

I think, for example, of the MRI: magnetic resonance imaging.

This year, in July, we marked 40 years since the first human MRI scan.

It was supposed to happen seven weeks earlier, in May – but the first attempt failed. The subject was the lead inventor. And he had a little too much body fat for his own device to work.

Fetch a grad student!

And luckily for science, and the grad student, a crude image was obtained, a 2D view of the heart and lungs, reconstructed with colour pencils from a mere hundred data points.

That image was only possible because a physicist named Isidor Rabi wanted to study the nuclear spin of sodium, back in the 1930s, and was too lazy to put up for long with the cumbersome tools provided.

So he worked incredibly hard to make them better.

He observed the quantum phenomenon of nuclear magnetic resonance in 1937, with a tool that soon became standard in chemistry and physics.

It took another pioneer to think through its potential applications in the life sciences, and, in time, to the study of the brain.

Thirty years ago it was a challenge to take one low-resolution image in a session. Now we can take high resolution images every second.

At first we could just see grey matter – the cell bodies.

Now differential tractography MRI shows us the white matter – the connections across the brain – and it's revolutionised our understanding of cerebral networks.

To start, we just imaged structure.

Then, we imaged the functional areas of the brain.

Now, we're imaging thinking.

And we couldn't imagine neuroscience without it.

So it is technology that shifts the horizon of possibility for science.

But of course, that's not all: when the horizon shifts for science, it shifts for society as well.

Today the MRI is a standard part of medicine: a household name, with considerably more than a million scans performed across the world every week.

The technology has come so far that we can now do therapeutic ultrasound, guided by real-time MRI, to focus on a tumour, and destroy it. Extraordinary.

The lesson I take is that we can't expect to be competitive in science or innovation if we leave the toolmaking to other people.

I speak from experience, having deliberately given up an academic research career to make scientific instruments that helped the research careers of thousands of neuroscientists.

We need to be connected to the big global missions, in the thick of the action.

And we need to be adept in testing and refining and translating, here in Australia, because that's what pushes us forward.

***THIRD** and final, our research institutions should aim to be among the world's trusted information sources.*

Let me ask you a question.

How many of you would say your memory wasn't as good as it used to be?

How many of you would like to boost it?

Excellent – you will all be interested in the Brain Stimulator, one of the most popular examples of an outbreak of transcranial direct current stimulators.

The Brain Stimulator comes in the form of a kit. The device. The electrodes. A diagram of your head. And the positioning headband to stop the electrodes from falling off as they deliver zaps of memory-boosting electricity to your temples.

Nine volt battery not included.

If you are worried by the metallic taste in your mouth, the tingling or itchiness in your skull, or the occasional flashes of bright light, you can purchase the Saline Solution Applicator Bottle.

In other words, you can dab salty water on your head.

In the absence of a hypothesis for why it would work, or evidence that it actually does, the Brain Stimulator is a dreadful example of electronic snake-oil.

The good news is that the Brain Stimulator and similar devices seem to be popular only with a small fringe of the do-it-yourself brain-hacking community.

But that's not true of the miracle cures for children with autism.

The magic pills and potions that promise to cure brain cancer.

The myths and stigma attached to conditions like schizophrenia.

All of these things are actively harmful, to many people.

And they are not just harmful to people in desperate situations: they are harmful to science.

They come cloaked as science, they take the focus from science, and they tarnish the good name of science.

We could all lament the reality that the internet is awash with quackery, anecdotes, PR stunts… and media releases.

But if it's a problem, it's also an opportunity.

I would like to see our institutions build their reputations as the go-to, trusted information sources, not just for Australians but for anyone looking for accurate, up-to-date and accessible information.

Take the Queensland Brain Institute. They have done extraordinary work in developing accessible guides and information pages on topics like depression and Alzheimer's.

The QBI web site is not the usual register of researcher interests and media releases. Instead, it's a go-to resource. It's the place I'll go to for trusted information about brain diseases.

Politicians and members of the public will eventually find it and they will remember QBI whenever they think about brain diseases.

Other institutions are also actively investing in their public information platforms.

Let's make that a collective focus and a strength.

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So, three things: have a bold ambition; focus on transformational technologies; and be the trusted source.

Easy to remember, with or without that nine volt battery.

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I began this speech in Ancient Egypt, 2000 BC.

Let me conclude by pointing to the day when our descendants look back at 2017; and our best tools seem about as primitive as the honey, the cow and the milk in both ears.

It won't take 4000 years. But the brain is so complex that the research to get there will keep many thousands of brilliant researchers occupied for decades, probably for centuries.

Neuroscientists in the audience, your careers will not be limited by lack of questions to answer.

The possibilities stretch out beyond our imaginations…

… but the potential is right here, in our brains.

Let's tackle the future, *head on*.

THANK YOU