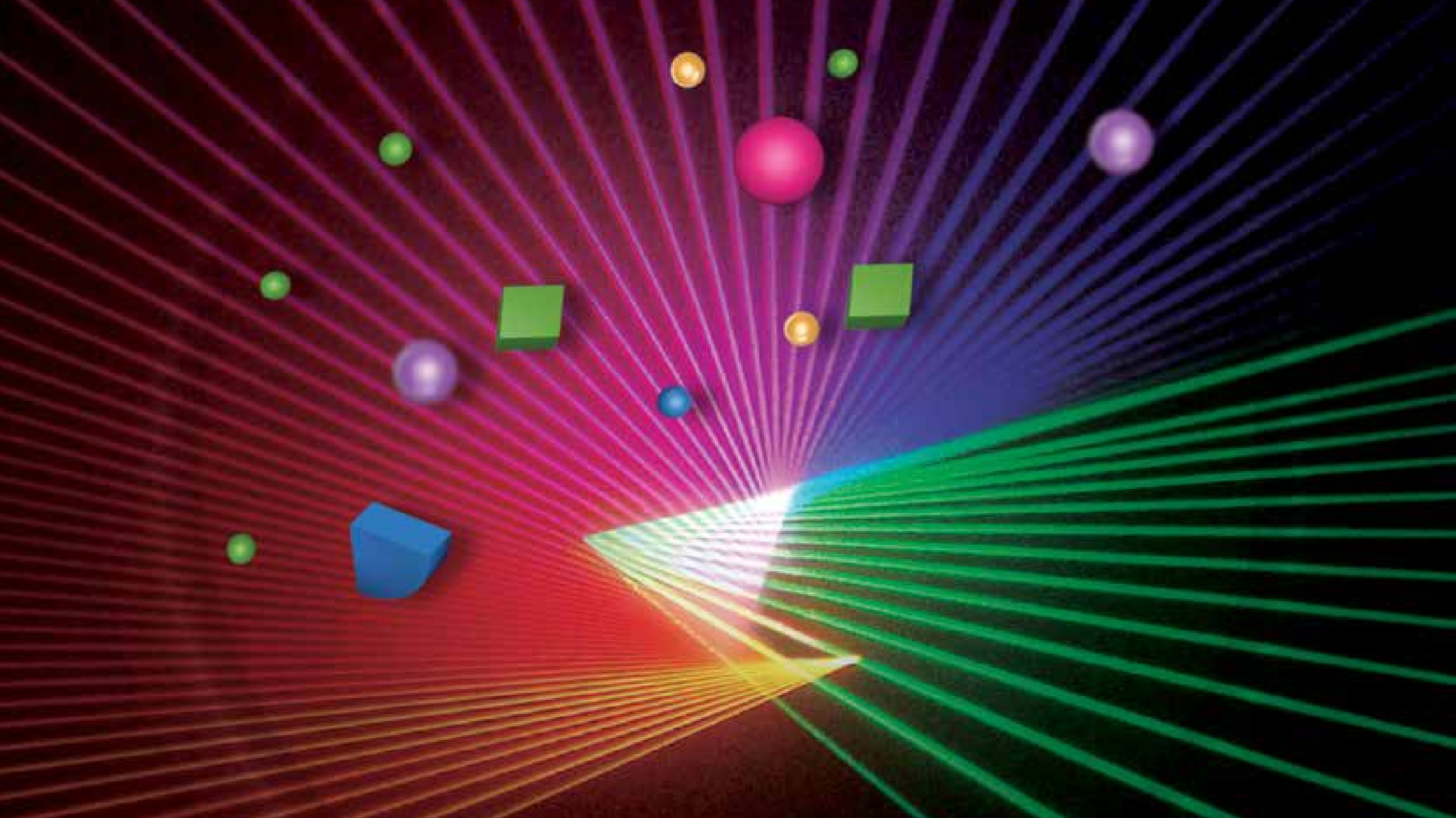
The Centre for Nanoscale BioPhotonics

The power of light to measure



Centre *for*
Nanoscale
BioPhotonics
ARC CENTRE OF EXCELLENCE

Welcome

Centre for Nanoscale BioPhotonics

We operate at the nanoscale at the CNBP, investigating the living body and dynamic systems more generally, by use of new and exciting light-based technologies.

In using the power of light to measure we seek to 'see' and understand molecular and chemical processes at play—how they influence the health and well-being of the individual, as well as how they impact the wider world around us.

Transdisciplinary in nature, we bring together a unique team of people and expertise, pursuing research at the intersection of nanoscience, biomolecular science and photonics.

With our investigative and industry partners from around the world, we are focused on pushing the very frontiers of nano-exploration and measurement. In doing so we are creating novel methodologies and approaches that are truly transformational and disruptive.

Ours is a fantastic voyage of discovery. It is one filled with high expectations and an awareness that we are increasing human knowledge and understanding.

It is also one in which our efforts will have enormous social and clinical translation potential.

Welcome to the CNBP!

Professor Mark Hutchinson
CNBP Director

Contents

A new high-tech medical device to make brain surgery safer.

What we do

At the CNBP we use the power of light to measure, seeking to understand the complexity of the living body, and of biological and dynamic systems more generally, all at a chemical and molecular level.

In doing so, we are developing revolutionary new tools and techniques, able to sense and quantify in real-time, those extraordinary nano-sized processes, operating at the very edge of our ability to observe.

> Excitingly, the molecular sensing tools we are devising today will underpin the diagnostic devices of the future.

SENSING IN THE LIVING BODY

Taking our technologies to the body, we hope to shed light on the 'machinery of life', to understand those real-time bio-molecular processes impacting health and disease, and the well-being of the individual.

Fertility, pain, stroke, heart disease and the brain, these are all areas that we target—where our molecular sensing activities look to provide new and illuminating answers, assessing influence and impact, of the 'very small' on the larger living body as a whole.

Excitingly, the molecular sensing tools we are devising today will underpin the diagnostic devices of the future.

Patient samples will be able to be quickly and effectively analysed for specific molecular biomarkers, supporting clinicians in their diagnoses and point-of-care activity for patients.

NEW COMMERCIAL OPPORTUNITIES

Sectors other than human healthcare, benefit too from the sensing tools that we create and develop.

We are seeing new and exciting commercial opportunities opening up in the veterinary, animal healthcare, agriculture, manufacturing and food production sectors.

The ability to undertake real time molecular analysis with tools that have been customised to measure specific molecular targets, offers tangible benefits to business, in both the taking and monitoring of quality and conditional assessments.

From sensors monitoring food quality, food-borne pathogens or contaminants, to novel tools to aid in the manufacturing and quality control process, our measuring technology has the potential to add significantly to many organisations and their bottom line.

At the CNBP our tools are literally measuring things that have never been measured before, achieving outcomes that previously were unimaginable.

CNBP Researcher
Dr. Michelle Zhang

How we do it

CNBP science is focused on creating scientific breakthroughs that will have long-term social and economic benefits.

Our approach is transdisciplinary, we bring together world-leading researchers and expertise—in physics, materials science, chemistry, biology, neuroscience, embryology, cardiology and more.

It is the ability of our teams to stretch the very limits of knowledge in each of these areas, and to then come together in collaboration to solve a shared goal, which allows us to undertake research that is truly unique and meaningful.

Advanced lasers, optical fibres, nanoprobes, chemical sensors, and leading imaging and microscopy techniques—these are just some of the methodologies employed by our team in support of our biophotonic science.

Consisting of over 120 researchers located at three outstanding Universities, with access to first-class facilities at the University of Adelaide, Macquarie University and RMIT University, we are positioned to succeed, and dedicated to the delivery of outstanding scientific research.

Four key pillars underpin everything we do—Academic Excellence, Commercial Impact, Quality Communication and a Nurturing Environment.

This means we conduct amazing science. But it also means that the way that we do this science is creating adventurous, innovative and open practices in our researchers.

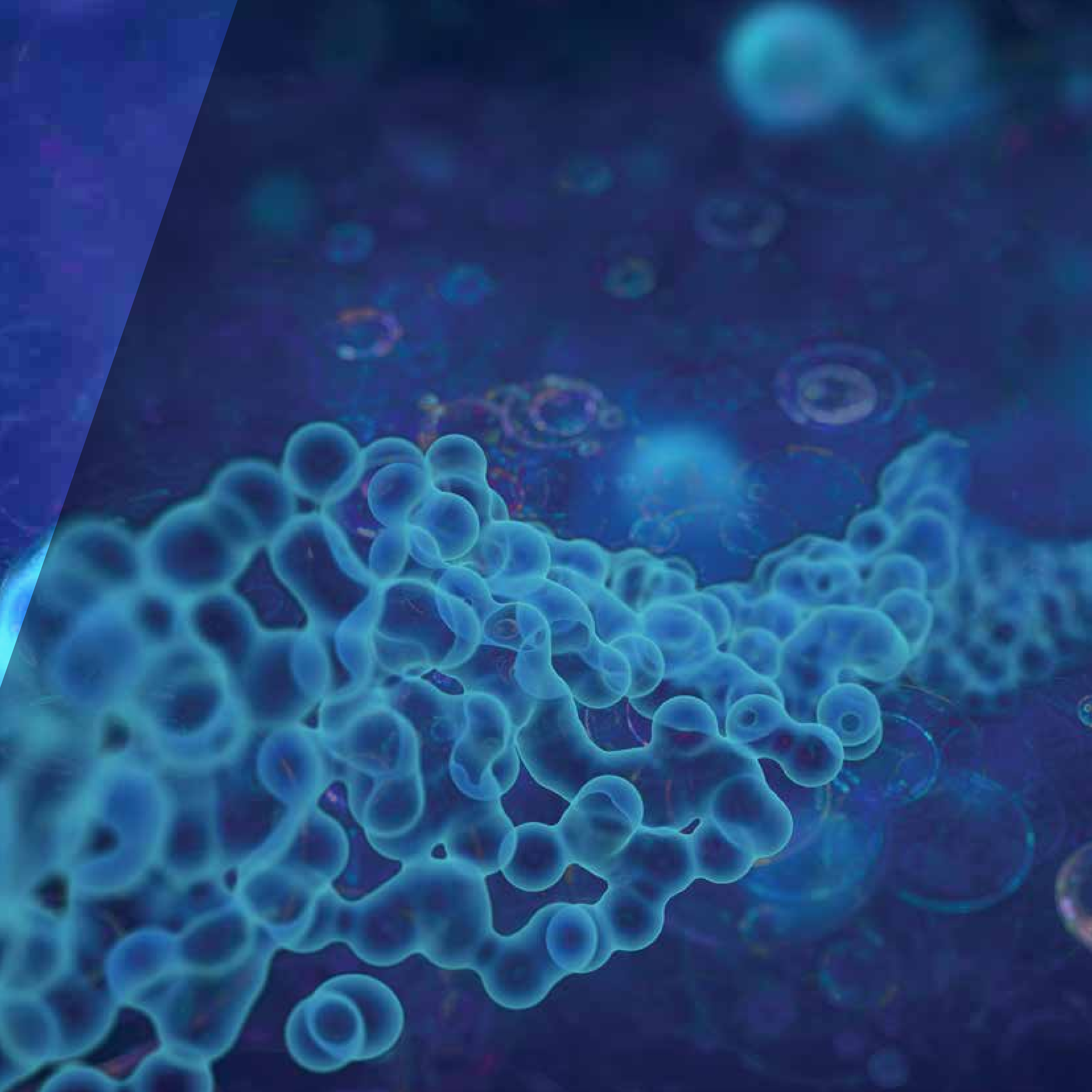
> We keenly encourage an outcome-focused culture and we actively work with our academic and commercial partners to create innovative and disruptive technologies.

Importantly, the scientific discoveries we make are only the beginning of our transdisciplinary journey.

We keenly encourage an outcome-focused culture and we actively work with our academic and commercial partners to create innovative and disruptive technologies.

These technologies and services will support multiple markets from veterinarians treating family pets, through to outback farms focused on animal production through to doctors treating their patients.

In delivering this vision and in looking to create economic and social value for all our communities, we are focused on a forward thinking strategy and meaningful project implementation in all of our day-to-day activities.



Work with us

At the CNBP we actively look to develop strong partnerships, building networks with major national and international research centres as well as with industry, to deliver exciting research, translational and commercial outcomes.

We firmly believe that our strength is significantly enhanced by engaging closely with our partners in an active and collaborative manner with the end-benefit that our research is pushed in new and exciting directions that could not be achieved alone.

Working with partners helps us to strengthen research outcomes, drive development activity, achieve global competitiveness, and also provides exciting new collaboration opportunities for our researchers.

Current CNBP research partners include the following leading facilities:

- CSIRO
- Leibniz Institute of Photonic Technology (IPHT), Jena
- University Health Network, Toronto
- City University, London (CUL)
- University of Southampton

We also have strategic discipline specific partners at:

- SA Health & Medical Research Institute (SAHMRI)
- The University of Colorado, Boulder
- Peking University, Beijing, China
- Huazhong University of Science & Technology (HUST), Wuhan, China

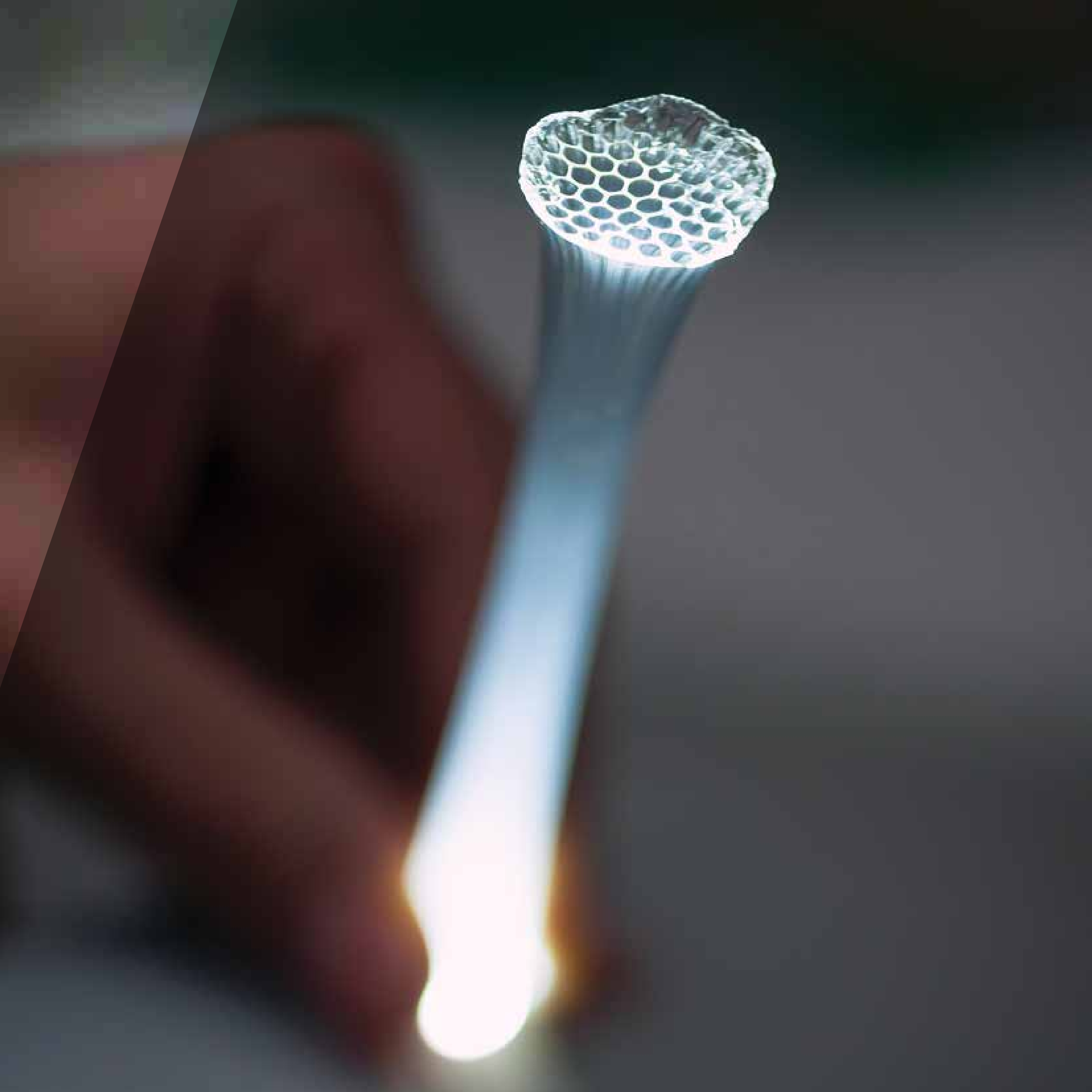
> Working with partners helps us to strengthen research outcomes, drive development activity, achieve global competitiveness, and also provides exciting new collaboration opportunities.

Corporate partners include:

- Imaging giant, Olympus Australia
- Heraeus, a global leader in fused silica
- BioPlatforms Australia, a leading biomolecular analysis provider

There are a wide range of benefits to partnering with us which includes:

- Access to pioneering new technologies
- Access to internationally renowned scientists and know-how
- Creation of measurement solutions that will have long-lived financial benefits
- Reputation and esteem benefits of collaboration with a world-class ARC Centre of Excellence
- New funding opportunities with the Australian Research Council linkage scheme and other grants
- Opportunity for commercial development
- Capability building through on-site co-creation of required solutions
- Opportunity for PhD student internships with your business



Developing market solutions

At the CNBP translational urgency and addressing commercial industry needs are central to our technology development.

We are committed to providing deployable solutions through successful translation of our 'light-based' sensing expertise.

We are here to facilitate the effective and efficient adoption of our research outcomes into products and services that can create a commercial return and positively impact society.

Our process is simple—to engage early with industry partners, to fully understand their market needs and to then provide solutions which will positively impact on the bottom line.

As such, we employ a range of technology transfer and IP investment approaches across differing market sectors to openly facilitate successful commercial outcomes with our partners.

Areas of application include next-generation molecular sensing tools, in the longer term to create clinical point-of-care diagnostics. Here we work closely with clinicians and end-users, focused on the needs of both the specialist and the patient.

We are also building on the disruptive science developed in our current research program—to modify existing tools, and to build brand new tools for animal healthcare, and to improve quality, quantity and sustainability across agricultural and food production supply chains.

To date we are the only major research centre in Australia building these high-tech light-based sensors able to monitor food quality and packaging, and able to provide reagent–free measurements in the manufacturing process.

> Our process is simple—to engage early with industry partners, to fully understand their market needs and to then provide solutions which will positively impact on the bottom line.

For us, the commercialisation process starts on the very first day of our projects.

We engage proactively with industry from the paddock to the plate, and from the factory floor to the boardroom to identify information gaps within systems.

We then deliver the measurement solutions that support decision making processes—that add to business efficiency, creating commercial return and impact.

At the CNBP we want to engage early with our commercial partners, to cultivate a collaborative approach, to develop solutions together, to increase knowledge and to have a real-world impact.

CNBP Chief Investigator
A/Prof. Jeremy Thompson

Revolutionary IVF Discoveries

THE SPARK OF LIFE

A/Prof. Jeremy Thompson

Every animal, including humans, start life as the fusion product between a sperm and egg, producing an embryo. And it is this process by which an early embryo forms and develops which continues to fascinate scientists around the world.

Some of this fascination is directed towards just how unique these two cell types are. Whereas a sperm is a mobile packet of condensed DNA, the other is the largest cell in the body (the egg, also known as the oocyte).

The uniqueness of the sperm and the oocyte, and the complexity of how they come together in the reproductive tract of any animal, is only part of the reproduction story.

Pregnancy requires an orchestrated series of hormonal events in females that entail communication between brain, gonads and in females, the reproductive tract.

Furthermore, it is not only the endocrine hormones, such as progesterone, that are important, but increasingly we recognise that reproduction involves the immune system as well. These signals culminate to provide the environment that sperm, oocytes and embryos operate within.

Studying these events present difficult challenges that are being tackled by the CNBP. Our major challenge is that we don’t understand just how dynamic life is, for a sperm or egg in the reproductive tract. All of our knowledge has been gained using *in vitro* assessments.

> Our team is already seeing research success in this challenging and intriguing area.

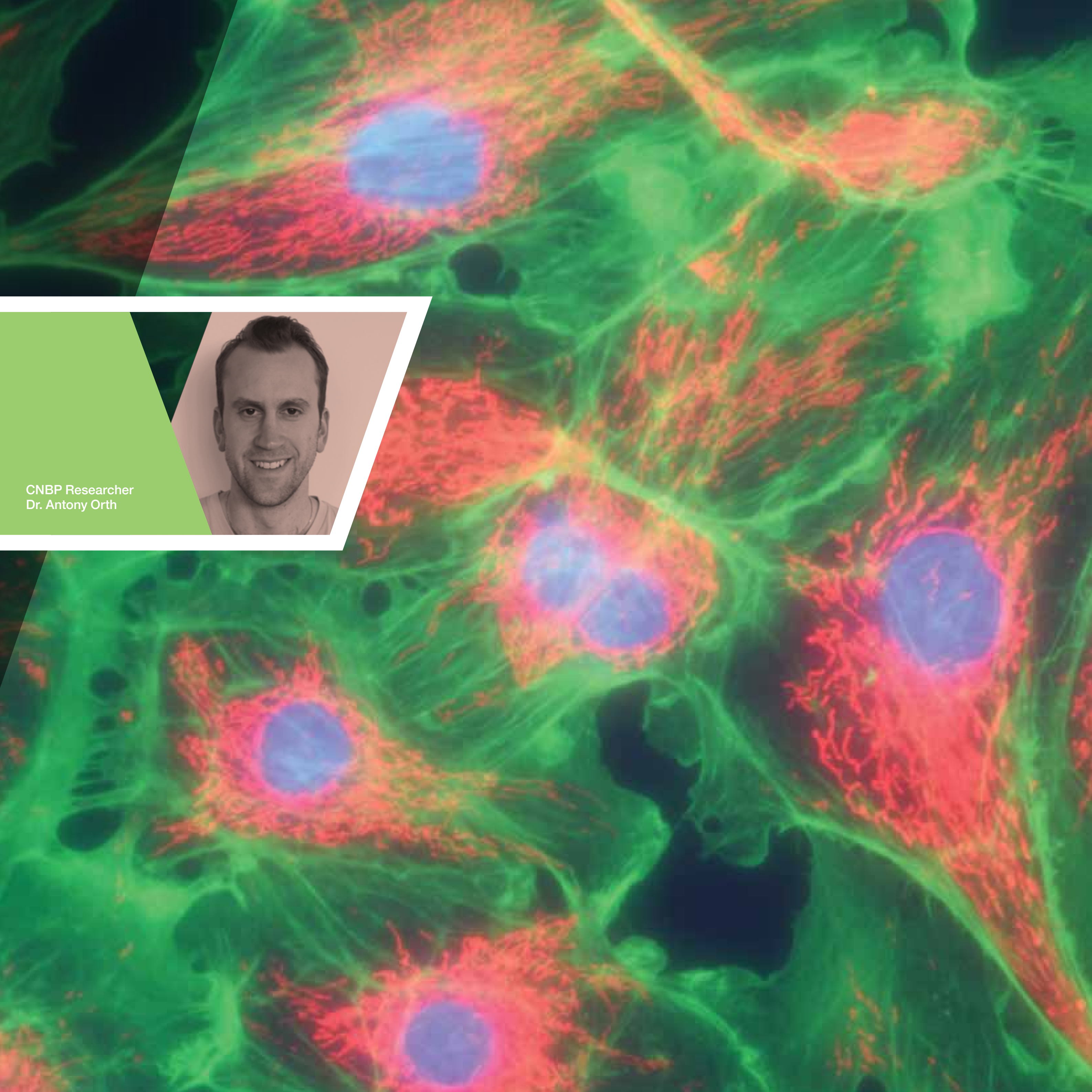
Our photonic probe approaches are enabling us to access the lumen of the reproductive tract in a way not achievable before. We are exploring the measurement of cations such as H^+ (pH), Zn^{2+}, and Ca^{2+}, plus H_2O_2.

Both Zn^{2+} and Ca^{2+} are involved in the fertilisation process—but never visualised in the reproductive tract.

Combinations of hyperspectral autofluorescence functionality or Raman spectroscopy and Optical Coherence Tomography (OCT) imaging are also accompanying our photonic probes approach.

Our team is already seeing research success in this challenging and intriguing area.

Recently reported was the development of our new fibre-optic sensor that can measure H_2O_2 and pH in solution, potentially aiding the tricky process of monitoring early-stage embryos during the IVF process.



CNBP Researcher
Dr. Antony Orth

Innovative Microscopy Techniques

IMPROVED MULTIPLEXING

Dr. Antony Orth

Fluorescence microscopy is one of the most widely used techniques in biology. Light emitting molecules called fluorophores tag specific targets in cells, each with a unique and identifiable colour.

Colour filters in the microscope can then select emission from any one of the types of fluorophores while blocking light originating from all others, resulting in information-rich images.

This approach is versatile, but there is a major limitation. The visible spectrum, where most fluorophores operate, can get crowded. The visible colour spectrum spans the range from 400nm to 700nm and only about 200nm of this range is available for fluorescence emission.

A typical fluorophore emits over a 50nm range of the colour spectrum. For colour filtering to work well, the fluorescent emission from different species should not overlap—in other words they should have distinct enough colours.

However, in dividing up 200nm of the visible spectrum into 50nm segments, the colours of fluorescent emitters blend together when you attempt to squeeze in more than four colours. In order to highlight more targets for more highly multiplexed experiments, there is a need to use another property to differentiate between fluorescent species.

At the CNBP, we have developed a technique called “bleaching-assisted multichannel microscopy” (BAMM) to increase multiplexing in fluorescence microscopy.

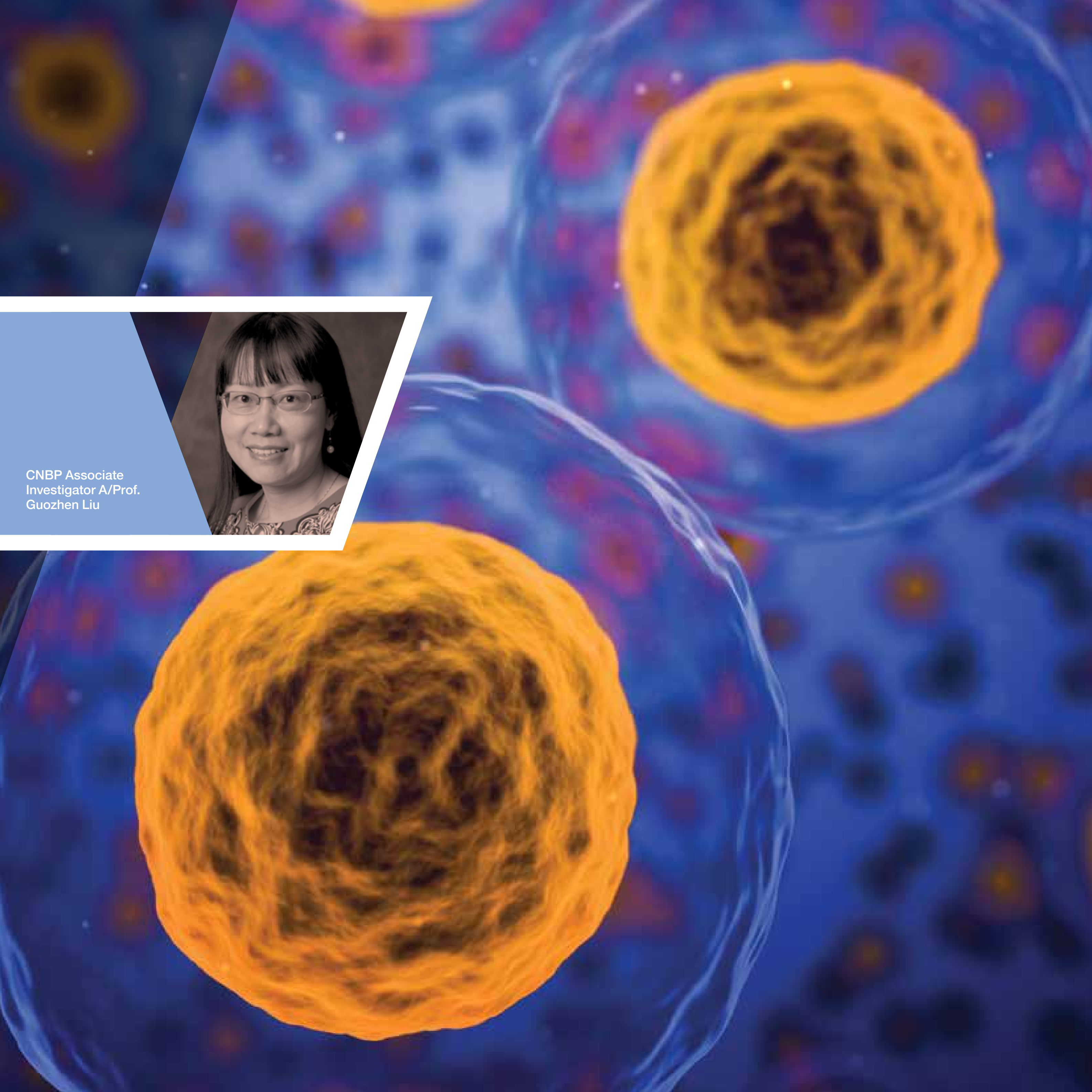
> In leveraging photo-bleaching for increased multiplexing, the CNBP has turned what has historically been considered a detrimental effect into an extremely useful phenomenon.

Instead of using colour to differentiate between fluorophores, we use the 4th dimension of time and exploit a phenomenon called photo-bleaching—the dimming of a collection of fluorophores or pigments under repeated exposure to light.

Because each type of fluorophore photo-bleaches at a different rate, we can differentiate between fluorophores without using any colour information. When paired with colour information, this added dimension of contrast enables scientists to use 2-3 times more types of fluorescent molecules, all in a single sample.

Current approaches to increased multiplexing involve significantly expensive hardware. In contrast, BAMM actually simplifies microscope design by obviating the need for colour filters in some cases.

In leveraging photo-bleaching for increased multiplexing, the CNBP has turned what has historically been considered a detrimental effect into an extremely useful phenomenon.



CNBP Associate Investigator A/Prof. Guozhen Liu

Next Generation Cell Therapies

UNDERSTANDING CYTOKINE SECRETIONS

A/Prof. Guozhen Liu

At the CNBP, we have developed advanced nanoscale sensing technologies that identify and select cells based on the secretion of cytokine molecules.

Utilising cutting-edge nanotechnology and bio-imaging research, our work is expected to have significant impact in areas including nanomedicine, drug discovery, immunology, oncology, regenerative medicine and vaccine related investigation.

Cytokines are proteins which are secreted by cells in the immune system. They are important in cell signalling and their release is frequently symptomatic of disease or health-related issues, such as arthritis, tissue trauma, inflammation, depression or even cancer. Consequently, monitoring cytokine secretions has enormous value in the understanding of basic physiology and how the body is actually working.

Until now, cytokines have been extremely hard to measure and quantify, due to low concentration, their small size, a complicated cytokine network, their dynamic and transient nature, and the fact that they exist in an environment of background 'noise' and interference.

We took an innovative approach, developing nanotools for monitoring cytokines *in vivo*. Surfaces of nanomaterials such as gold nanoparticles, graphene oxides and magnetic nanoparticles were engineered, 'tuned' to cytokine sensing and detection.

> Our technique offers benefits of superior performance, simplicity, stability, sensitivity and the capacity to sense in real-time.

This led to a major breakthrough in assay sensitivity (0.1 pg/mL), sufficient to probe cytokine secretion from a single live cell by altering an existing cell surface affinity assay.

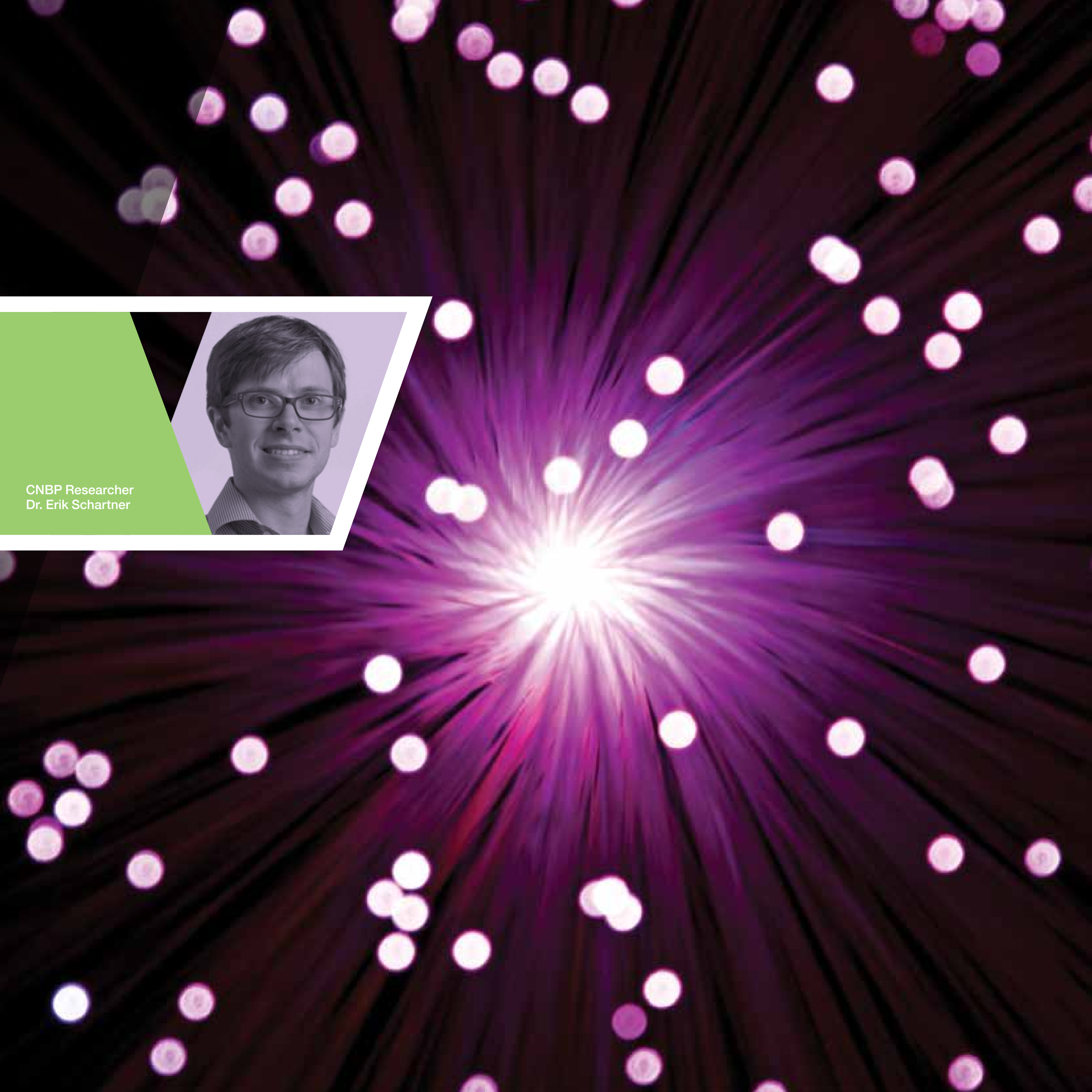
Compared to traditional enzyme-linked immunoassay methods, our technique offers benefits of superior performance, simplicity, stability, sensitivity and the capacity to sense in real-time.

This success saw the technology licensed to Regeneus, an Australian clinical-stage regenerative medicine company.

They aim to manufacture next generation cell therapies based on the identification and selection of high potency secreting stem cells.

More recently, our activity has seen the development of an optical fibre based cytokine test-strip to spatially monitor localized cytokine secretion *in vivo*.

This technology has initiated collaboration with the private sector and will impact current research on spinal cord injury diagnosis and monitoring.



CNBP Researcher
Dr. Erik Schartner

Cancer Margin Detection with Optical Fibres

HEALTHY OR CANCEROUS TISSUE?

Dr. Erik Schartner

CNBP researchers, in collaboration with clinicians at the Royal Adelaide Hospital have developed a sensor which can potentially aid surgeons in differentiating between healthy and cancerous tissue during surgery.

This is a key need in applications such as surgery for breast cancer, where current methods are limited in their effectiveness.

In 15-20% of cases the patient requires follow-up surgery to remove tumour tissue that was missed in the initial surgery.

This is naturally extremely traumatic to the patient, as well as adding a significant unnecessary burden to the healthcare system.

As such there's a strong need for a low-cost, rapid and sensitive method that can be used intraoperatively by the surgeon in the theatre.

The probe works by measuring the pH of the surface of the tissue, which results have shown correlates well with whether or not the tissue is healthy or tumorous.

The tip of an optical fibre is coated with a pH sensitive indicator, and the signal read out uses a low-cost light emitting diode and portable spectrometer.

A strong focus on this project was practical applications, with surgeons involved in the development of the project from the outset to ensure that the final outcomes involved a device that would be useful for real-world applications.

The probe works by measuring the pH of the surface of the tissue, which results have shown correlates well with whether or not the tissue is healthy or tumorous.

This work was the basis for successful University of Adelaide Commercial Accelerator Scheme funding and Medical Devices Partnering Program support that has allowed for further development of the probe towards clinical registration, deployment and eventual commercialisation.

Currently the focus of this activity is on collecting additional clinical relevant data, with an emphasis towards being able to engage with commercial partners in the near future.

Left: CNBP
Senior Investigator
Prof. Robert McLaughlin

Right: CNBP Researcher
Mr. Stefan Musolino

Sensors for the Brain

A SMART NEEDLE

Prof. Robert McLaughlin

A new high-tech medical device to make brain surgery safer is being developed by CNBP researchers at the University of Adelaide.

The tiny imaging probe, encased within a brain biopsy needle, lets surgeons 'see' at-risk blood vessels as they insert the needle, allowing them to avoid causing bleeds that can potentially be fatal. The 'smart needle' contains a tiny fibre-optic camera, the size of a human hair, shining infrared light to see the vessels before the needle can damage them.

Utilising optical coherence tomography (OCT) the imaging needle is able to be connected to a range of OCT scanners, with computer software then able to recognise blood vessels and alert the surgeon in real-time as the probe is being used.

The smart needle has already been used in a pilot trial with 12 patients undergoing neurosurgery at Sir Charles Gairdner Hospital in Western Australia. It will soon be ready for formal clinical trials.

The team are in discussions with a number of international medical device manufacturers and are seeking to manufacture the smart needles in Australia.

> The smart needle will soon be ready for formal clinical trials.

BRAIN TEMPERATURE

Mr. Stefan Musolino

The brain is the most temperature sensitive organ in the body—even small deviations in brain temperature, as a result of disease, brain injury or drug use are capable of producing behavioural change and neuronal cell death.

In order to measure and understand these temperature changes and how they are influenced by various biochemical pathways in the brain, a transdisciplinary team at the CNBP has developed an optical fibre-based temperature sensor, capable of pinpoint brain temperature measurement in freely-moving animals.

The sensor tip, minimised to only a few microns, provides for precisely localised temperature monitoring where conventional technology would struggle. Due to the small size of the fibre tip it has the possibility to be combined with existing sensors and implanted with identical methods without inducing additional stress or damage.

A fully developed probe could find potential application in human brain temperature monitoring after traumatic brain injury, stroke, or subarachnoid haemorrhage. It could also be utilised for tracking hypothermia in infants with neonatal encephalopathy to aid in neuroprotective therapy efforts during the first 72 hours after delivery.

> CNBP has developed an optical fibre-based temperature sensor.

Left:
CNBP Researcher
Dr. Philipp Reineck

Right: CNBP
Associate Investigator
Dr. Yiqing Lu

Brighter Signals from Nanoparticles

PHOTOSTABLE NANO-PROBES

Dr. Philipp Reineck

Fluorescent nano-probes allow us to label specific parts of a biological cell. In principle, this allows us to observe biological processes on the scale of single cells in real time such as the active transport of cell components along a microtubule, which is one type of intracellular 'highway'.

A great challenge is that most fluorescent probes used today stop to fluoresce rapidly when imaged—an effect known as photo-bleaching.

We develop fluorescent diamond nano-probes that are perfectly photostable. Our probes are not only photostable, but can also sense temperature and magnetic fields.

We have recently discovered a new fundamental phenomenon: an increase of diamond fluorescence caused by a magnetic field. In our interdisciplinary team within the CNBP we also develop diamond probes that are sensitive to important cellular signalling molecules. This way we will be able to track movement and detect cellular signals simultaneously.

We continue to push the boundaries of fundamental science to develop brighter and smaller diamond probes, which has uncovered a new class of very bright fluorescent nanodiamond.

> Our probes are not only photostable, but can also sense temperature and magnetic fields.

NANO LASER CRYSTALS

Dr. Yiqing Lu

The use of nanoparticles in microscopy imaging holds tremendous potential for researchers, aiming to examine dynamic biomolecular processes in ultra-fine detail in the body.

Issues however, include the need for high illumination power requirements that can damage biological samples as well as unwanted background noise in the biological sample that limits the contrast of what can be seen.

Our research breakthrough has been to develop a new generation of bright luminescent nanocrystal—one in which the chemical element thulium, extensively used in lasers, has been added at high concentrations.

This new particle exhibits a unique "photon avalanche" effect, whereby emission photons are generated at higher efficiency, substantially amplifying brightness using low-power infrared illumination light. It has allowed us to achieve images with a super resolution of 28nm, together with multiple other benefits—the suppression of unwanted interference as well as reduced complexity and cost, across the total imaging system.

Our work illustrates that tiny laser nanocrystals offer substantial potential as a new generation of luminescent probes for optical microscopy at the nanoscale level.

> Our breakthrough has been to develop a new generation of bright luminescent nanocrystal.

CNBP Chief Investigator
& Co-Deputy Director
Prof. Ewa Goldys

Big Data to Help See Small Cells

NEW CELL COLOUR TECHNOLOGY

Prof. Ewa Goldys

Our newly developed technology enables colour to be used as a uniquely powerful diagnostic and detection tool for medicine, with additional applications across the life sciences, manufacturing and the food industry.

Our pioneering hyperspectral imaging technique allows us to extract specific biomolecular information, hidden in the fluorescent colour signatures of living cells and tissues.

Using this information, we can non-invasively determine cell biochemistry. We are able to test hypotheses about the similarity (or otherwise) of cells and cell populations and about the effects of chemical interventions in those cells, such as drug treatment.

In our approach, we obtain fluorescence images of live cells and tissues at a number of selected excitation wavelengths, capturing their fluorescence emission at multiple specified, wavelength ranges. This accurately quantifies their fluorescence (colour).

We then analyse micrographs of cell populations using custom-developed software to gather information about hundreds of quantitative features including cell size, shape, brightness and texture.

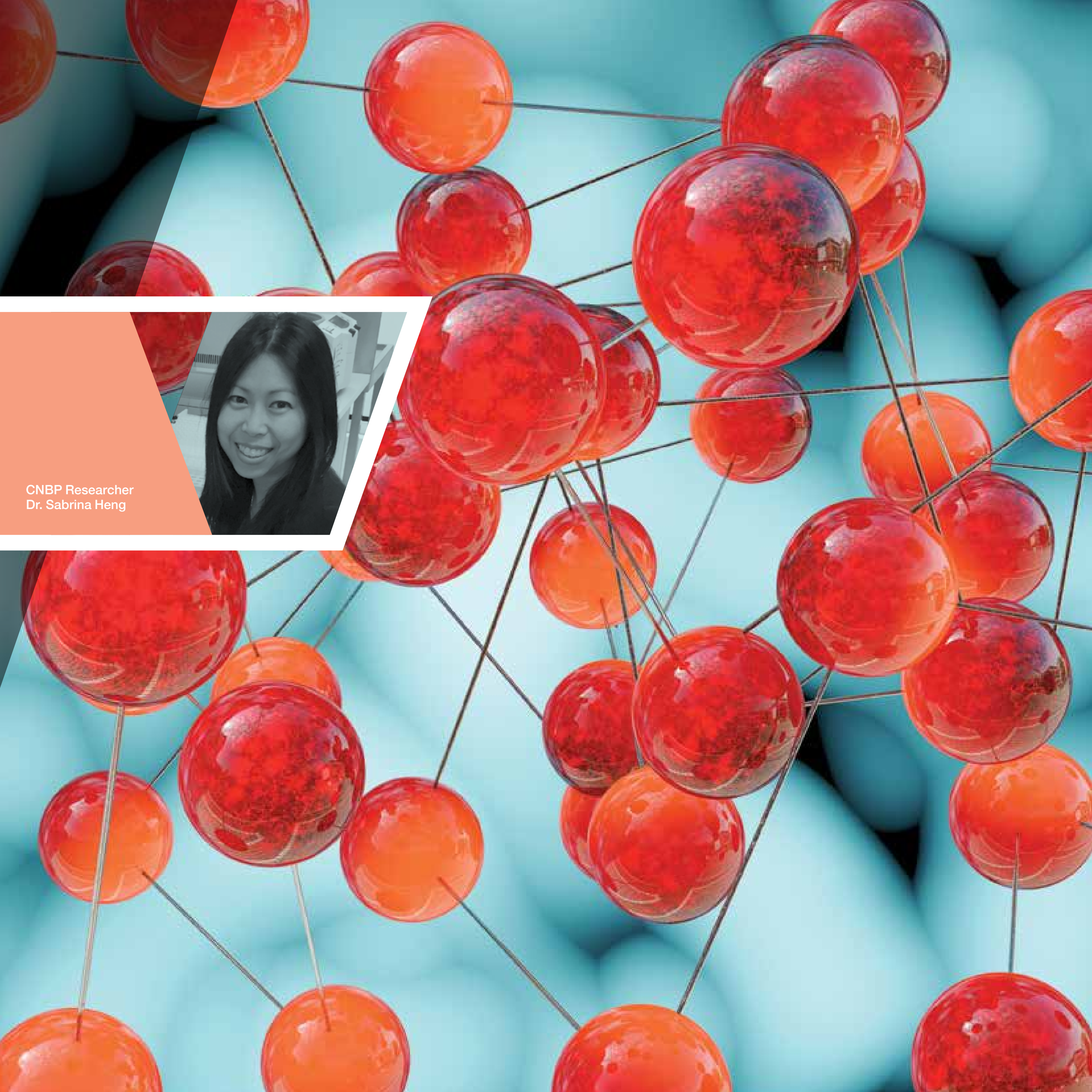
This dataset provides richly detailed information about living cells, letting us unveil the presence of biomolecules such as NADH, flavins, retinoids, cytochrome C, and many others, and their cellular content.

> This next-generation methodology allows our team to non-invasively and rapidly detect major health conditions including neurodegeneration, cancer and diabetes.

This next-generation methodology allows our team to non-invasively and rapidly detect major health conditions including neurodegeneration, cancer and diabetes. Notably, these cellular and molecular measurements can be done non-invasively, in living organisms. The method offers the potential for healthcare decisions to be based on the health needs of the individual, and their unique biological characteristics.

Using our technique, we will ultimately be able to look at the colour of a patient’s cells and tell if the patient is sick or healthy, and how they respond to treatment.

We also see commercial applications for our ‘cell colour technology’ beyond healthcare, in industrial and environmental monitoring—such as in determining the quality of fresh and processed foods; and in industrial processes to identify microbial contamination.



CNBP Researcher
Dr. Sabrina Heng

Probing Metal Ions in the Body

DEVELOPING METAL IONS SENSORS

Dr. Sabrina Heng

Metal ions are vital in most of life's processes. Their crucial role in cellular function means that a change in the level of metal ions in the body is often associated with diseases.

Fluorescent metal ions sensors offer the potential to answer biological questions e.g. how do metal ion concentrations change in response to cellular events, environmental changes, or onset of disease or how do cells regulate metal dynamics, and how do metal dynamics impact cellular function?

To gain a deeper understanding into the dynamic roles that metal ions play in regulating our health and disease, it is important to develop new sensor technologies that can be used to probe metal ions within the body.

For a sensor to be used within the body, it needs to be non-toxic and small, while requiring only a minute sample, to produce a rapid and accurate response.

In addition, at a real advantage are reversible sensors, where the sensor can be made to turn 'on' and 'off' using a switch of some kind.

Reversibility means that multiple measurements can be made without the need to change the sensor. This permits continual and non-invasive study, while also increasing the sensor's useful lifetime.

In our efforts to investigate these metal ions, we have recently developed new metal ion sensing molecules that have two parts, each with specific functions.

For a sensor to be used within the body, it needs to be non-toxic and small, while requiring only a minute sample, to produce a rapid and accurate response.

One part changes its structure, opening to become fluorescent and closing back to its colourless form when exposed to visible light. The other part can be tailored to bind different metal ions. When metal ions are bound, they lock the chemical in the open form, which then fluoresces.

Treating the complex with white light drives off the metal ion and reverts the sensor chemical to its starting state, ready to be used again. This switching can be done many times without losing reliability or sensitivity.

We have also developed ways of combining these molecules with liposomes for biocompatibility. Adding such molecules to our sensing devices is important as it gives us the ability to control our sensing devices with the flip of a light-switch.

Incorporating the custom designed light-driven molecules into sensing platforms such as micro-structured optical fibers and nanoparticles, represent advances in developing fast, sensitive ion sensing methods that will eventually allow us to create exciting new 'windows into the body'

CNBP Researcher
Dr. Nima Sayyadi

Detection of Prostate Cancer Cells

SENSITIVE IMMUNODETECTION OF PROSTATE CANCER CELLS

Dr. Nima Sayyadi

Rapid, sensitive, and non-invasive diagnostic tests for prostate cancer have the potential to lead to better treatment outcomes and lower healthcare costs. However, less than ten cancer cells need to be detected in large volumes of urine for useful diagnosis. Current urine cytology approaches lack required sensitivity at this level.

Detection of prostrate cancer cells (PCCs) in urine would be far more preferable than the current approach of invasive needle biopsy. More than 50% of the biopsies are negative for prostate cancer partially because the prostate specific antigen (PSA) biomarker in serum can be elevated for reasons other than prostate cancer. The low sensitivity (33%) widely used PSA have been increasingly recognized.

A highly specific IgG antibody (MIL38) was developed to specifically recognise PCCs by our collaborator Minomic International Ltd. However, at present, immunofluorescence urine cytology detection of PCCs is not sensitive enough as a diagnostic approach.

The fundamental problem in the detection of these low abundance PCCs in urine is the weak signal-to-noise ratio (SNR) obtained when using common fluorescence probes, such as fluorescein isothiocyanate (FITC), because of the overlapping of the fluorescent signal with the commonly encountered auto-fluorescent molecules within the cells and urine matrices; these factors combine to greatly reduce detection efficacy.

> The capacity to quantify single prostate cancer cells has the potential to revolutionise the diagnostics industry.

We have developed time-gated immuno-luminescence detection of PCCs with up to two orders of magnitude greater sensitivity than the commercially available fluorescence probes.

Using long-lifetime lanthanide probes in conjunction with time-gated imaging, the cellular autofluorescence background is totally suppressed, allowing the capture of vivid, high contrast images of immunestained PCCs.

We are developing the application of orthogonal scanning automated microscopy (OSAM) techniques for fast scanning of the luminuscently stained PCCs on a microscope slide (in ~3 min) with high precision and high signal-to-noise ratios.

We are also currently working on a systematic analysis of the urine sample of pre-biopsy patients for the detection of PCCs using our technology in collaboration with Minomic International and Prof. Gillatt from Macquarie University Hospital.

The final goal is performing analysis of the urine of pre-biopsy patients in parallel with existing diagnosis methods, including PSA and MiCheck tests. The capacity to quantify single prostate cancer cells has the potential to revolutionise the diagnostics industry.

Ours is a fantastic voyage of discovery. It is one filled with high expectations and an awareness that we are increasing human knowledge and understanding.

We would love to hear from you. To discuss how we can work together, please feel free to contact us.

Professor Mark Hutchinson
Director, CNBP
T: +61 (0)8 8313 0322
E: mark.hutchinson@adelaide.edu.au

Professor Ewa Goldys
Co-Deputy Director, CNBP
T: +61 (0)2 9850 8902
E: ewa.goldys@mq.edu.au

A/Professor Brant Gibson
Co-Deputy Director, CNBP
T: +61 (0)3 9925 3649
E: brant.gibson@rmit.edu.au

Melodee Trebilcock
Business Manager, CNBP
T: +61 (0)8 8313 2981
E: mel.trebilcock@adelaide.edu.au

The latest information on our research can be found at CNBP.org.au/sciencepapers.

Centre *for* Nanoscale BioPhotonics
ARC CENTRE OF EXCELLENCE

cnbp.org.au @CNBPscience