The Physics Foundation presents

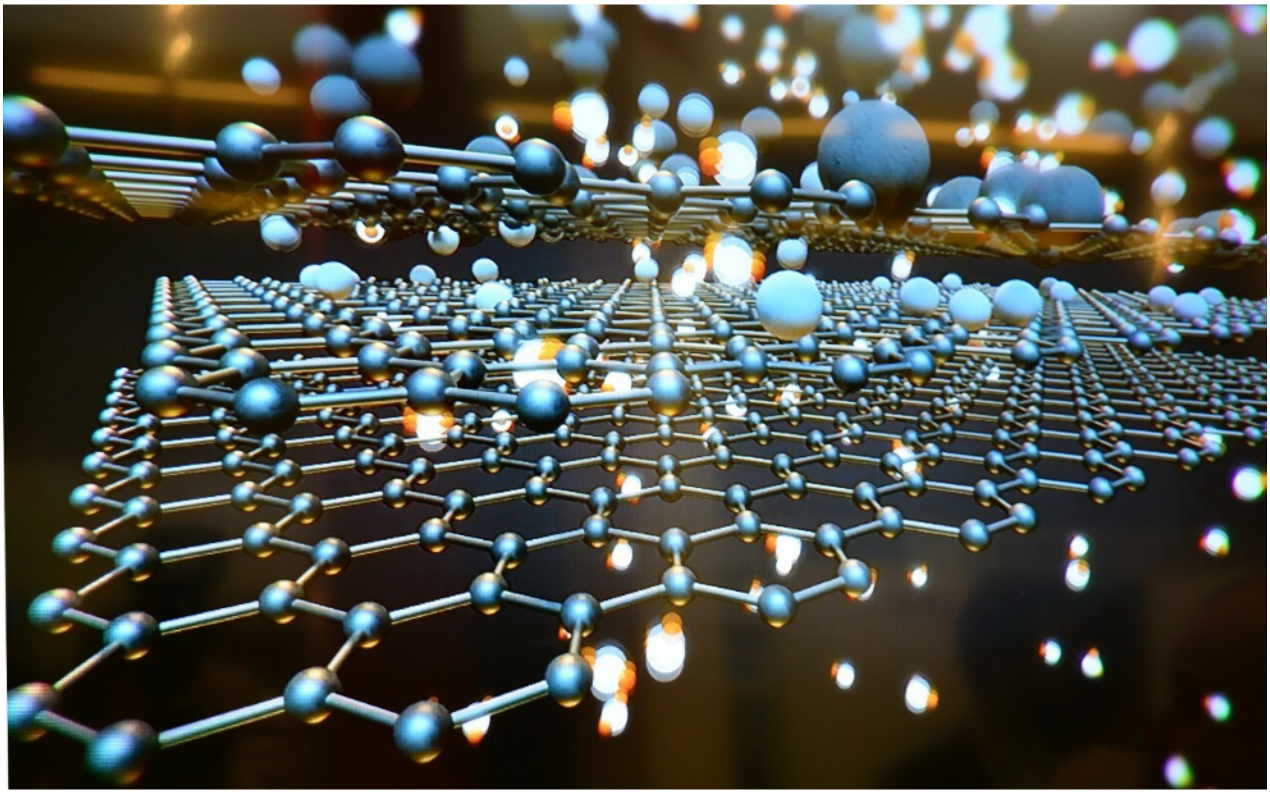
The Nucleus

Issue No. 2 December 2022

THE UNIVERSITY OF SYDNEY

Issue No. 2 – November 2022

We acknowledge the tradition of custodianship and law of the Country on which the University of Sydney campuses stand, The Gadigal People of the Eora Nation. We pay our respects to those who have cared and continue to care for Country.



President's Welcome
Michael Winternitz

Welcome

The Nucleus continues a tradition of reporting key matters from within the School of Physics.

We invite you to explore the inner sanctum of the School of Physics - to witness the cutting edge, world class research & teaching being undertaken.

The School has a proud tradition of excellence. A leading research institution in this country, and indeed on the world stage - playing host to several Australian Research Council Centres of Excellence (ARC), in addition to a range of other acclaimed research centres.

In our feature article, we hear from a Grand Challenge winning team, Dr Ben Fulcher & Dr Shelley Wickam, as they explore targeted drug delivery to the brain, via nanorobots.

We hope you enjoy exploring the journey of laser powered space sails, also a Grand Challenge winning team, led by Professor Martin De Sterke, where he is part of a global team that aims to send small probes to the Alpha-Centauri system, the star system closest to Earth.

It is a pleasure to announce that three inspiring teams were awarded Grand Challenge Prizes in November 2022, entitled:

- Universal Neurophotonic Interface: Bionics with Feeling (Assoc Prof Stefano Palomba)

- X-ray Imaging Based on Metal Halide Perovskites (Prof Rongkun Zheng)

-Quantum many-body techniques for machine learning (Dr Sahand Mahmoodian)

This edition explores the successful delivery of the 2022 online Professor Messel International Science School (ISS).

The Physics Foundation is very pleased to announce that ISS 2023 will return to being held in person at the University of Sydney - providing scholars a truly remarkable campus experience.

Head of School Professor Celine Boehm will step down from her role in December. I would like to thank Celine for her hard work leading the School, during what have been very difficult times.

Professor Boehm leaves a strong legacy of strengthened research and education initiatives within the School, as well as founding the Grand Challenges initiative which have been immensely successful.

On that note, I am pleased to offer on behalf of the Physics Foundation, a warm congratulations to Professor Tara Murphy, who has been awarded the Head of School role, and will commence from December 2022.

Tara is a world class Scientist in her own right, and is current Deputy Head of the School - and therefore brings an in depth understanding of the challenges and opportunities ahead.

The role of the Physics Foundation has never been as important, having a proud history of ensuring that the School of Physics is supported through the many initiatives.

We hope you enjoy this newsletter and look forward to sharing many more exciting pieces of research, from within the School of Physics.

Thank you for your ongoing support & interest.

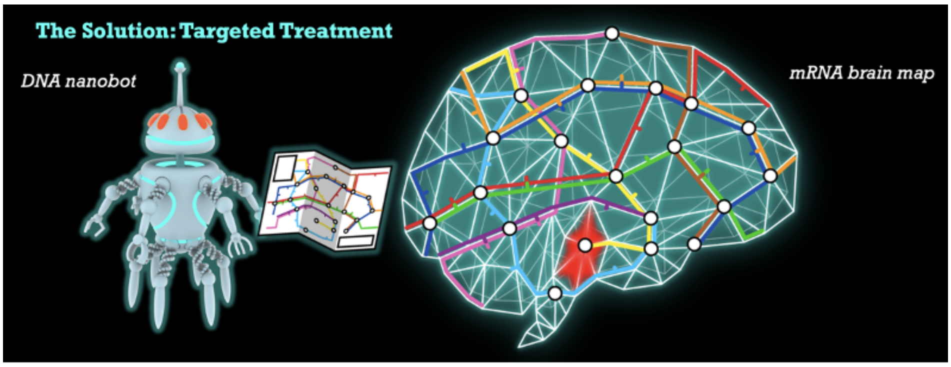
Yours Sincerely,

Michael Winternitz

President of the Physics Foundation

Nanorobots: Cutting Edge Drug Delivery

Ninety-two percent of Central Nervous System drugs fail due to off-target toxicity. Grand Challenge funding from the Physics Foundation has enabled Dr Ben Fulcher and Dr Shelly Wickham's team to design nanorobots to tackle this problem.



Ben and Shelley's interdisciplinary team brings expertise in whole-brain molecular maps, molecular devices and cognition and brain disorders to create nanorobots capable of targeting areas on the brain.

One of the greatest challenges we face is how to deliver drugs to specific parts of the body. This is especially hard in the brain.

Brain disorders like severe mental illness, dementia, and brain tumours cost Australia over $74 billion a year. In 2018, over 4.3 million Australians received a mental health related prescription. That's one in six of us.

Frighteningly, 92% of new Central Nervous System drugs fail at clinical trials, mostly due to off-target toxicity.

Even when they are effective, they can have debilitating side-effects caused by flooding the entire brain. For example, in Parkinson's Disease, clinicians replace the dopamine that is missing from the dorsal striatum, curing tremors. But this overloads other parts of the brain that control decision making, leading to addictive behaviours like gambling that can be life destroying.

If we could precisely target neurochemicals in the brain, we could transform a wide range of treatments to maximise patient well-being.

"Our goal is to design and validate a nanoscale machine (or 'nanorobot') with molecular logic circuits to deliver drugs to specific brain cells."

We came up with this idea as three friends chatting over coffee: a theoretician (Dr Ben Fulcher, who analyses whole-brain molecular maps), an experimentalist (Dr Shelley Wickham, who makes molecular devices), and a clinician (Mac Shine, who studies cognition and brain disorders).

And since this conversation, we have made important steps towards our vision, with the Physics Foundation having supported two groups of physics undergraduates, a PhD student, and a postdoc currently working in this area.

You can get a sense for the problem by imagining the brain as a network to be navigated, like a subway system. By reading the station sign you know when you're at the right stop. We can define station names in the brain using incredible whole-brain maps of over 20,000 genes.

But there are major statistical challenges involved in finding a unique molecular signature of an individual cell in an individual part of the brain that you might want to target. We are currently using methods from neuroinformatics, big data, and artificial intelligence to develop new algorithms to tackle this problem.

Our current aim is to identify which diseases have the best molecular data to build the most detailed brain maps for navigation, focusing on neurodegenerative disorders such as Alzheimer's disease.

Once we've worked out some good molecular rules that could target the right brain cells, we need to build nanoscale devices that can implement these rules. DNA is the molecule that contains all our genetic information, but it can also be used to construct programmable molecular logic gates.

Just like electronic circuits, DNA circuits can perform sophisticated information processing, but using molecules in solution.

We are currently building barrels out of DNA that act as nanoscale circuit-boards for molecular DNA circuits.

These nanostructure circuits will be able to sense their local environment and compare the information with the molecular signatures calculated from the brain-map data.

What's exciting here is that we're not merely characterising brain maps, but using them to guide drug delivery for the first time.

Furthermore, we're going beyond simple on–off sensors, but using nanoscience to build sophisticated targeting systems that take into account many cell markers concurrently, like a barcode.

It is only in The School of Physics that we have the unique combination of world-leading expertise across neurophysics, nanoscience, and computing to achieve these goals.

Collaborating with other experts across campus also makes this a really fun interdisciplinary project with huge potential for real-world impact.

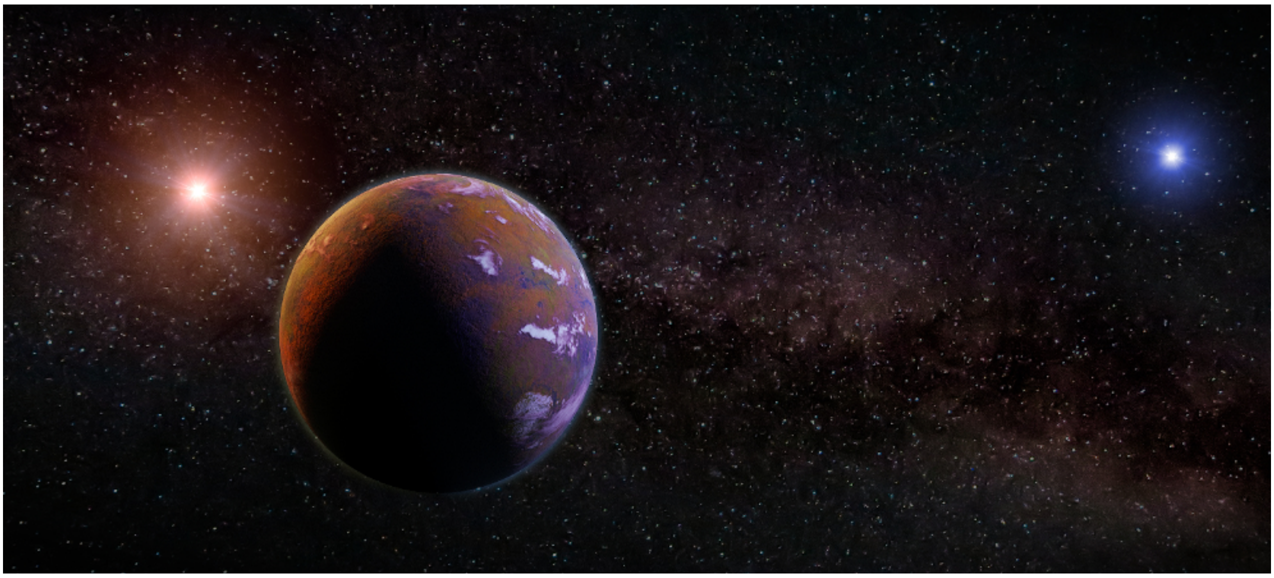
- Dr Ben Fulcher &
Dr Shelley Wickham

Dr Ben Fulcher leads the Dynamics and Neural Systems Group in the School of Physics at Sydney University. He has a diverse and interdisciplinary training in physics, dynamical systems, brain modelling and statistical learning.

Dr Shelley Wickham is an ARC DECRA Fellow, Westpac Research Fellow and Senior Lecturer in the Schools of Chemistry and Physics at the University of Sydney.

(Team photo)
From left: Mac Shine, Annie Bryant, Ben Fulcher, Shelley Wickham, Minh Luu.

Voyage to Alpha Centauri in our lifetime



Conventional spacecraft would take 80,000 years to reach our nearest star system, Alpha Centauri. The StarShot program aims to build laser-powered sails that could complete the journey in just 20 years.

How can you reduce an 80,000 year trip to just 20?

Read how Professor Martijn De Sterke's team are tackling one of the biggest challenges in accelerating a laser-propelled light sail to 50,000 g.

The Breakthrough Starshot project, coming out of the United States, aims to send small probes to the Alpha-Centauri system, the star system closest to Earth.

The idea is that the probes will be propelled by an Earth-based laser which accelerates them to 20% of the speed of light in approximately 15 minutes.

It would then take approximately 20 years to reach Alpha-Centauri, covering an enormous distance of 4 light years.

The probes will have the shape of a sail with a diameter of a few metres, but with a mass of only a gram.

This is a very ambitious project that requires major advancements in several areas in science and in engineering including material science, space communications, lasers, heat management, etc.

The Physics Foundation Grand Challenge project Mission to Alpha-Centauri aims to contribute to one aspect of this large project by analysis of the launch phase.

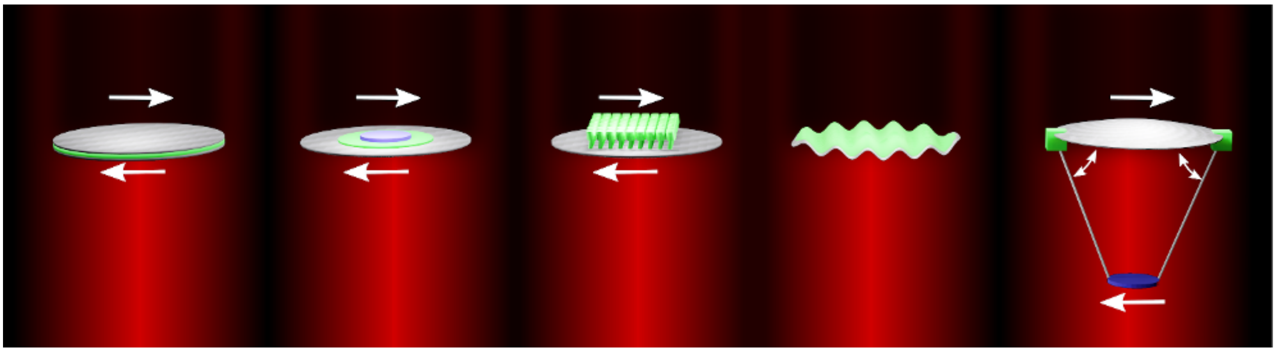
The launch phase is very delicate as the motion of the light sail tends to be unstable. That is, any unavoidable imperfections in the light beam cause the sail to shake and to veer off course, leading to a failed mission.

We have been working on the stabilisation of the light sail while it is being propelled by the laser.

Our approach is schematically summarised in the image below: the sail consists of different parts that can move with respect to each other (indicated in blue and in grey).

When they do so, there is friction (green), which not only reduces the relative movement but also damps the shaking of the sail as whole.

Using advanced techniques in theoretical mechanics, our analysis of the movement of the sail demonstrates that it can be stabilised in this way.



Components in the sail move independently of each other which causes friction reducing the relative movement and dampening the shaking of the craft as a whole.

We also show that the heat that is generated by the friction is likely to be small compared to the unavoidable absorption of energy from the laser beam.

So far, existing research has been based on unrealistic assumptions including infinite 'stiffness' of the sail and so does not bend and only modelled in 2D. We have extended modelling into 3D and demonstrated viability without ‘infinite stiffness’.

Our work has been published in Physical Review Applied. However, we also found that achieving stability is not guaranteed and appears to depend on the details of the sail properties in a way that we do not understand yet.

Acquiring this understanding is on the agenda for 2022-23. We are fully embedded in the Starshot program and have acquired further funding to tackle these challenges.

- Prof Martijn de Sterke

Above: Professor Martijn de Sterke PhD, FAIP, FOSA.

Prof Martijn de Sterke PhD, FAIP, FOSA is a physics theorist here at the University of Sydney, with research interests in optics, photonics and electromagnetism.

Using Physics to solve Cystic Fibrosis

Miro Alexander Astore is one of our bright recent post-docs. Miro set out to understand the root cause of Cystic Fibrosis by applying computational physics to biology. In this interview he tells us how he leveraged expertise from both the Schools of Physics and Biology for work on his PhD.

Hi Miro, thanks for chatting with me. Do you mind if I start by asking you how long you have been in the School of Physics?

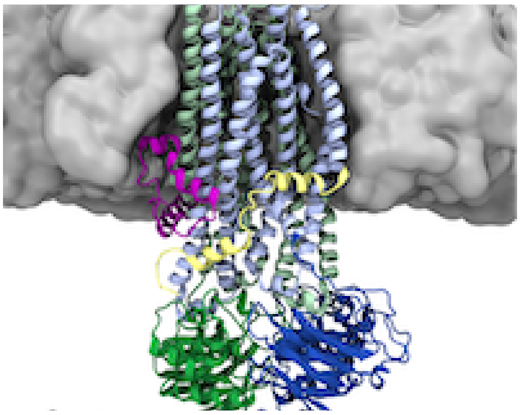
Nearly 8 years! I started here in 2015 and it's flown past.

Wow, a long time for a young person. What have you been doing that whole time?

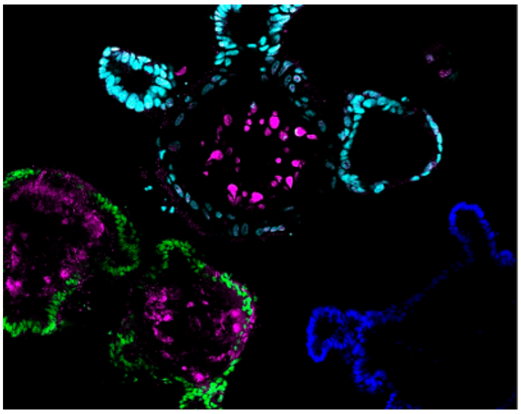
For my first three years I was studying pure mathematics and physics. The combination of the two was definitely tough and I wasn't as suited to it as some of my friends-but coming to campus everyday and getting their perspective on abstract problems was invaluable. It's been surprisingly helpful for my PhD which was very different from all of that.

So what did you do for your PhD?

I changed gears a little bit, I did a PhD in biophysics. I used computational models to study the molecular motions of a protein called CFTR with atomic precision. This protein forms



The CFTR ion channel embedded in a model cellular membrane. By using supercomputers, Miro simulated the motion of nearly 200,000 atoms in and around this protein to learn how it works inside healthy cells, and how it malfunctions to cause Cystic Fibrosis.



Lab-grown gut organoids generated from the stem cells of a cystic fibrosis (CF) patient. Drugs which treat CF can be tested on these organoids, giving a pathway for those with rare forms of CF to access life-saving medications.

an ion channel, and when it malfunctions due to genetic mutations it causes Cystic Fibrosis (CF).

Cystic Fibrosis? You mean the lung disease?

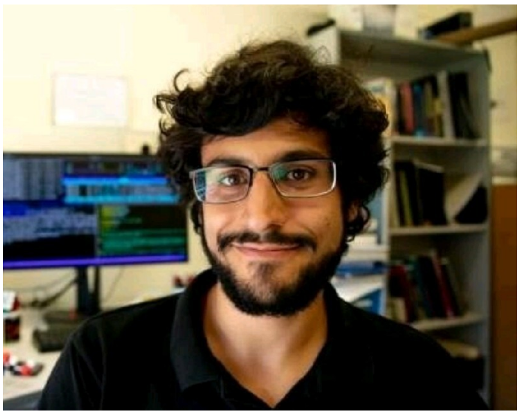
Yeah it was really interesting. I took all the abstract knowledge I built up in my undergraduate studies and used it to learn how to compare the molecular motions in both healthy and mutant CFTR proteins, to understand how disease was being caused.

I achieved this by combining a technique called molecular dynamics and a LOT of time on supercomputers. I complemented the functional research carried out by Dr. Shafagh Waters and her team of cell biologists in the molecular and integrative CF research laboratory at UNSW. They're trying to figure out which kind of CFTR mutations they can treat with existing medications.

Developing targeted therapies and selecting the most effective medication is a huge problem for patients with CF at the moment. People with rarer forms of the disease struggle to access life saving medication. To help them, Dr. Waters and her team take biopsies directly from patients with Cystic Fibrosis and grow them into mini-organs called "organoids".

These tissues are grown in such a way that they mimic the behaviour of a full organ. In this case, they're grown to mimic the lungs or the intestines. They can then be used as models to test different drugs-to choose which ones will be most effective in each patient.

Wait so where does physics come into all of that?



Miro Astore has been using supercomputer modeling at a molecular level to understand the malformations of the CFTR protein that cause cystic fibrosis.

Well working in parallel with Dr. Waters' team I used supercomputers to model the motions of both the healthy and the diseased CFTR protein, to figure out why it was malfunctioning with a given mutation. My models have given me a computational microscope to see, down to the atom, what's going wrong inside the mutant CFTR proteins. This let me build up a molecular understanding of how different genetic mutations might cause similar types of dysfunction in the protein.

Then, the cell biologists and I can get an idea of what kinds of genetic mutations we can treat with different drugs. Eventually, this means that each patient will be able to choose the medications which will work best for them.

There's a lot more to do, but I think our findings have demonstrated that we can do this kind of personalised medicine. I'm also excited to see what the next generation of physicists will do with biological problems. They'll have bigger computers and more data.

That's a very interesting project. Did you find it difficult to work with doctors and biologists with a background in physics?

At first a little bit, there was so much to learn and figuring out how to speak different languages to different experts took some time. But networking, reading and asking questions really paid off, even though I'm still learning.

Doing this work in a School of Physics has been great too. Physicists are really good at breaking down problems and finding abstract solutions. For example, my supervisor Serdar Kuyucak has an incredibly deep insight into the physical nature of biological and chemical systems. His training really helped me conceptualise the physics that's happening inside all our cells.

Throughout my degree I would also knock on the door of the particle physics office for help with the maths in my simulations, or over lunch I would ask an astrophysicist for technical help with the supercomputers. Putting all this physics together helped me get so much more out of my PhD I think.

And you've finished up now? Congratulations! What's next for you?

I'm starting a postdoctoral fellowship in New York City at a place called the Flatiron institute. It's part of a huge charity, the Simons Foundation. I'm really excited. I'll be studying how cells sense temperature. I was surprised to learn that we're not sure how this works yet. The problem involves a lot of really difficult statistical mechanics so it's a perfect project for a physicist like me. It's also really important, since the sensation of heat and pain are closely linked. So my research might help us find new, non-addictive, ways of treating pain.

I'll definitely be keeping in touch with Dr. Waters and her team though. There is so much more work to do with CFTR and more specifically, I think there is so much more that a physical perspective can do to help treat CF.

Sounds exciting, good luck Miro!

How the Foundation inspires young minds

The Professor Harry Messel International Science School (ISS 2022)

Alumni from the International Science School 2019. Due to Covid-19, the ISS2021 and ISS2022 were run online. ISS2023 will return in-person where we will bring scholars together from around the world.

We are passionate about inspiring & honouring Excellence in our young scientists across the world, through the Professor Harry Messel International Science School. Check out what happened at ISS 2022!

After a hugely successful trial of the International Science School's online program in 2021, we looked forward to returning to the traditional in-person ISS this year.

The ongoing covid-19 pandemic had other ideas, and in late 2021 we decided to once again run the ISS in virtual mode in July 2022 under the theme of Looking Forward.

We were determined to make ISS2022 as big, as inspiring and as engaging as ever. With the experience gained from 2021, we produced a 9-day program of talks, experiments, tours and activities.

The Scholars and Staff

In total 139 scholars took part in the program, all highly talented and enthusiastic students in their final two years of secondary education. While 2021's program was limited to Australian students, this year we brought the 'International' back to the Science School with ten students taking part from Japan, ten from New Zealand, three from the USA, and two from Vanuatu, alongside their peers from every state and territory of Australia.

Leading them was a fantastic team of volunteer 'Staffies', all alumni of the ISS program from recent years — including two staffies from New Zealand and, for the first time, one from Japan. The global nature of the ISS is such an important aspect of the program, and we are delighted to see that reflected in the staffie team.

The Program

After the success of the five-day event in 2021, we expanded the program across eight days of talks, hands-on experiments, live-streamed lab tours, discussion panels, and a huge variety of social events.

The Grand Challenges opened at the University of Sydney's Messel Lecture Theatre, with a crowd of alumni, university staff and students, and invited guests and VIPs in attendance, the ISS scholars and staff joining online.

Under the warm guidance of our MC, A/Prof. Alice Motion, the event began with words of welcome from the University's Vice Chancellor, Prof. Mark Scott, and Mr Michael Winternitz, President of the Physics Foundation. ISS2022 was then formally opened by our patron, Her Excellency The Honourable Margaret Beazley AC QC, Governor of NSW.

The Hon Alister Henskens SC MP, NSW Minister for Science, Innovation and Technology, and Minister for Skills and Training, then addressed the scholars before introducing Australia's Chief Scientist, Dr Cathy Foley, who spoke about the scientific and technological nature of the global challenges ahead, and the need for talented, science-literate young people to take up those challenges.

Following the formal opening event, the live audience in Sydney and the online scholars around the world recieved a fascinating and inspiring opening lecture on The Revolution in Radio Astronomy, delivered by the University of Sydney's Professor Elaine Sadler.

The lecture series continued with one talk each day:

- The (Second) Golden Decade of AI, with Google Fellow and VP Blaise Aguera y Arcas
- Green Engineering and Micro-Factories, with Prof. Veena Sahajwalla (UNSW)
- Biomedical Engineering, with Jacinta Cleary (PhD student at USyd)
- Next-Generation Solar Cells, with Prof. Anita Ho-Baillie (Sydney)
- The Hydrogen Revolution, with Prof. Francois Aguey-Zinsou (USyd)
- and the ever-popular Dr Karl Kruszelnicki (USyd) with his rollercoaster ride through science, Dr Karl's House Party.

The lecture series was recorded and by the end of 2022 will be uploaded to the official ISS YouTube channel.

After the lecture, each day featured online workshops designed by the University of Sydney's Science Communication team to actively engage the students in their own homes. The scholars sifted sand samples for microplastics, produced 'fake meat' burgers from scratch (and taste-tested them, of course), created home-made electrolysis labs, and explored the seemingly ubiquitous mathematics of the Golden Ratio in nature.

The scholars also participated in several seminar sessions: they quizzed science communicator and School of Physics alumnus Derek Muller, a.k.a. YouTube's Veritasium; they debated issues of ethics and leadership in science; and they absorbed advice and wisdom from a panel of ISS alumni across four decades of the program.

One of the highlights of a traditional ISS is visiting research spaces and labs around the university. To capture a flavour of this for the online program we organised a series of virtual lab tours streamed directly from research labs across campus. Scholars were treated to a guided tour of Prof. Ho-Baillie's solar cell lab, met Dr. Ann Kwan and her team at the Kwan Lab, a cross-disciplinary research group based in the School of Life and Environmental Sciences, and explored Prof. John Bartholemew's amazing Quantum Integration Lab.

To recreate some of the rich social life of the ISS program, the staffies hosted daily events for the scholars outside of the formal program, including quizzes, games tournaments, and a streamed movie night. With scholars participating from their homes, and sometimes their schools, across Australia and around the world, the social program was instrumental in bringing the students together and helping them to bond. Thanks to the ingenuity, enthusiasm and dedication of the staffie team, we managed to give the scholars a truly personal and enjoyable week.

Live and In-Person in 2023?

With the world gradually opening back up again in 2022, we will be returning to an in person ISS in 2023, and look forward to welcoming the world's youngest movers

As ISS2022 was online we sent out packs with various materials to all of our scholars. Within each were the components to conduct experiments and participate in 'Virtual-lab' activities from the comfort of their own homes. The image to the left is from a task to create a meat-alternative burger from scratch.

The Grand Challenges – 2022 Winners

The Physics Grand Challenges was established in 2019 and aims to support unconventional, innovative, interdisciplinary research projects with a total of $250,000 each to be awarded, up to two projects. Five project leads presented brilliant submissions to the Selection Panel with a 10-minute Pitch followed by a 5-minute Q&A each on 14th November, at a live event at the Messel Lecture Theatre.

The 2022 Selection Panel included several Foundation Council members

- Michael Winternitz, President of the Physics Foundation.
- Professor Gemma Figtree, a world leading cardiovascular researcher and practitioner, (Council Member).
- Mr Trevor Danos AM FTSE, company director and strategic adviser for a range of government and private organisations (Physics Foundation Life Governor).
- Dr David Mills AM, a prominent expert on non-imaging optics (Physics Foundation Life Governor.
- Mr Adam Lister, a senior business executive.

The projects were of such high calibre this year that the Foundation decided to award two projects the full amount of $250,000 each and seed funding of $50,000 to a third project.

Assoc Prof Stefano Palomba – Universal Neurophotonic Interface: Bionics with "Feeling" – Awarded $250,000 s

More than 1 billion people worldwide are affected by a Peripheral Neuropathy-related disability (PNS). PNS is a serious condition resulting from damage to your peripheral nerves – outside your brain and spinal cord. 80% could be helped by a bionic device connected to the PNS with a universal bi-directional nerve interface in a bionic prosthetic. The team are working on a long-term vision allowing the brain to control the prosthetic and receive sensory feedback, i.e. to "feel".

Prof Rongkun Zheng – X-ray Imaging Based on Metal Halide Perovskites – Awarded $250,000

This project aims to demonstrate single-pixel X-ray detectors and multipixel X-ray imagers based on their patented direct epitaxy of high-quality single-crystalline Metal Halide Perovskites. The expected outcome is X-ray imaging technology with much higher sensitivity and greater confidence in the accuracy of imagery than current MRI and X-Ray imaging. Additionally, this new approach will exhibit much lower radiation dosage than current X-Ray technology, and is expected to be of significantly lower cost than current MRI technology.

Dr Sahand Mahmoodian – Quantum many-body techniques for machine learning – Awarded $50,000

This project combines two incredibly important and exciting topics in modern science: quantum physics and machine learning, for the analysis of time-dependent signals. Time dependent signals are ubiquitous and are central to solving problems in industries as diverse as biomedicine, mining, social media, and finance. The project brings together world-leading expertise in quantum many-body physics, time-series machine learning, and neural networks to develop cutting-edge time-series classification methods that leverage powerful techniques from quantum mechanics for the first time.

The winners and the panelists for the 2022 Grand Challenges.
FROM LEFT TO RIGHT: Mr Michael Winternitz, Dr Feng Li,Mr James Kirby, Assoc Prof Stephano Palomba,Dr Alessandro Tuniz,Mr Adam Lister, Dr David Mills

2022 Physics Foundation
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- Professor Celine Boehm, Head of School of Physics
- Mr Justin Noble , Liaison Officer
- Ms Sian Edwards, Administrative Officer

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- Her Excellency the Hon. Margaret Beazley AC QC

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(initial year of directorship shown)

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- Emeritus Professor Richard Collins FTSE (1997)
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Sponsors
& Donations to the Foundation

The Messel Endowment

The Physics Foundation established the Messel Endowment in 1999 to ensure the Professor Harry Messel International Science School (ISS) continues in perpetuity.

Currently there are over 200 supporters to the Messel Endowment. These generous supporters are acknowledged in the Messel Endowment Honour Board that is published on the Physics Foundation website.

The two largest donors to date have each donated over $1 million. These donors are classed as Extra Galactic Donors and are:

- Australian Government through the then Department of Industry.
- Mr Lee Ming Tee, through Mulpha Australia

The Physics Foundation is appreciative of all our donors to the Messel Endowment.

Without this valued support the ISS could not continue its important work of honouring excellence in outstanding Year 11 and 12 science students from Australia, China, India, Japan, New Zealand, Thailand, the UK and the USA and encouraging them to pursue careers in science.

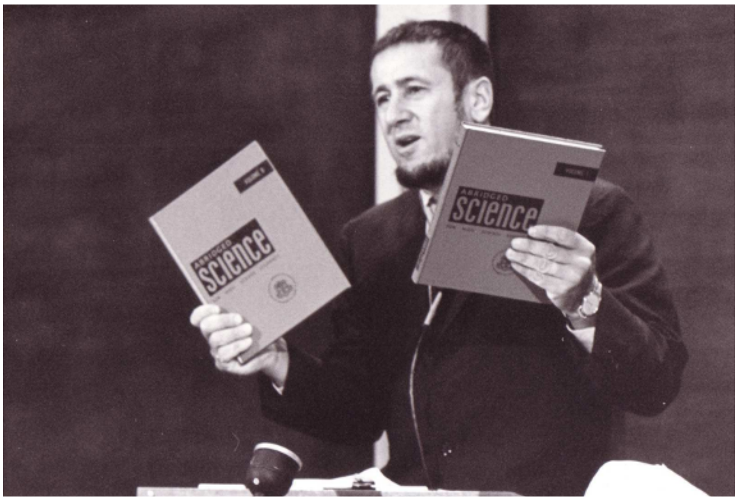
The Professor John Graham Bequest

In 2018 the Foundation Council and the School of Physics were saddened to hear of the passing of Emeritus Professor John Graham, a distinguished astronomer and long-time supporter and enthusiastic friend of the Physics Foundation.

In 2020 the Physics Foundation received a very generous donation, from John Graham's Estate (via the USA Foundation) for programs of science education at the University of Sydney.

Careers and achievements

The ISS now has over 5,000 alumni with many going on to outstanding career achievements in their chosen fields including science, medicine, engineering and technology.



The Nucleus
Supported by The Physics Foundation

The pursuit of excellence is at the heart of our mission.

For over 50 years, the Physics Foundation's philanthropic work in supporting scientific research, education and outreach has continued, thanks to support from business, industry and government.

The Foundation's financial support contributes significantly to the School of Physics, providing scholarships and prizes for students and academic staff, teaching infrastructure and equipment and programs in science education and communication.

The Foundation's Council is made up of representatives of business and industry, community leaders and senior office holders and academic staff of the University of Sydney. Council members are elected at the Foundation's annual general meeting.

Our objectives

- Inspire senior secondary students to pursue studies in science and science careers through the Professor Harry Messel International Science School and other School education programs.
- Provide funding to the School of Physics to support the Julius Sumner Miller Fellow as well as strategic and education initiatives run by the School such at the Physics Grand Challenges.
- Reward academic excellence via funding for undergraduate, and postgraduate academic prizes & scholarships
- Increase the resources of the University to assist the Senate and the Vice-Chancellor in the promotion of science, in particular physics.
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