Australian
National
University

Research strengths and directions

Research School of Biology

Never has the study of biology, in all it dimensions, been more exciting or important. We can now build organisms from scratch and so gain unparalleled understanding of how they work. At the same time, accelerating environmental change and novel pathogens challenge agricultural and natural ecosystems, and our own species.

Research Mission

The Research School of Biology (RSB) undertakes fundamental research to understand the function, diversity and evolution of animal, plant, fungal and microbial life. Our research is driven a passion for discovery and application of new knowledge. Working at the cutting edge of modern biology, we combine experimental, field-based and comparative approaches with the latest advances in 'omics and computational biology. RSB has a large and diverse body of early-career researchers who enrich our intellectual environment and are trained in high-level experimental, analytical and communication skills.

Organisation

RSB is the largest School at ANU and is structured into 3 Divisions - Biomedical Science and Biochemistry (BSB), Ecology & Evolution (E&E) and Plant Sciences (PS). Following a large number (11) of retirements in 2021, many of whom remain active in research and teaching, RSB has 41 lab leaders in ongoing positions; 11 in BSB, 16 in EE and 14 in PS. These researchers are supported by 63 postdoctoral scientists and 141 PhD students. RSB also benefits from the expertise of 76 technical staff (35 RSB-funded and 41 on external funding). There

Research performance

RSB is a large and a high performing research school that provides a collegial and well-resourced environment for early-career researchers and lab leaders. We are largely responsible for ANU's high global and national rankings in Biological Science and we have 38 academic staff listed among the global top 2% of scientists by discipline, 3 recognized as highly-cited researchers, and 9 as Fellows of Australian and/or overseas academies. Our researchers frequently publish in top-rated journals, e.g. leading ANU in papers in Science, Nature, PNAS and PLoS Biology. RSB consistently performs very strongly in national competitive (ARC, NHMRC) funding with a high success rate and aggregate income, and, over the past 5 years, 4 ARC Laureates, 8 Future Fellows and 14 DECRA Fellows.

Research impact

Most fundamentally, the high quality of our researchers underpins our strong international reputation, which serves to recruit the best students and researchers. RSB has a focus on fundamental research spanning biological processes from the cell biology of plants and of pathogens, to the evolution of biodiversity at multiple scales.   Our translational research addresses National Research Priorities in:

- Food security - Future-proofing major crops by increasing photosynthetic efficiency and resilience to climatic stress and pathogens.
- Environmental change – Improving resilience of species and ecosystems by understanding ecological and evolutionary responses to rapid or prolonged environmental change.
- Health – Improving capacity to respond to known and novel pathogens and parasites, e.g. by identifying new targets for drugs to control malaria or toxoplasmosa, and developing new algorithms for interrogating genomic data from Covid-19 tracing.

Long-term superb fairy-wren case study

The superb fairy-wren is one of Australia's most recognised and well-loved birds. In 1988, Professor Andrew Cockburn established a long-term study of fairy-wrens in the Australian National Botanic Gardens in Canberra. Each year, researchers monitor the breeding and

survival of every fairy-wren in the Gardens, and a massive dataset documents the complete life-history of many generations. This information is used to study everything from the genetic basis of reproductive success and the male fairy-wrens' blue plumage, to the environmental factors that affect survival. The genetic data show that most chicks are not the genetic offspring of their mother's social partner, indicating some of the highest levels of 'extra-pair paternity' known in any animal. The work also provides important insights into effects of current climate change. For example, warmer spring temperatures mean earlier breeding, but the increased frequency of summer heatwaves has carry-over costs that reduce winter survival, which has led to a declining population size. The data allow researchers to determine whether the effects of climate change on wild animal populations reported in milder temperate zones in Europe and North America can be applied to Australia where the climate is naturally hotter and drier.

Research strengths – current and emerging

The current research strengths of RSB are most simply characterised as: (i) plant biology, spanning from crops to natural ecosystems, (ii) evolutionary biology and functional ecology, (iii) membrane biology, and (iv) parasitology. Underpinning these general strengths is high-level capacity in genomics, metabolomics and quantitative biology. While some core research strengths are largely centred within individual divisions, many span two divisions or the School as a whole (Figure 1). In many areas there is strong collaboration between researchers in RSB and other units at ANU and with CSIRO. **It is imperative that RSB maintains critical mass in these core research strengths.**

Research in the Division of **Ecology & Evolution** can be grouped into 2 broad themes - (i) phylogenetics and evolution of biodiversity, and (ii) behavioural and physiological ecology. In both, we develop and apply advanced computational and quantitative methods to understand how evolution works in the past and present, and to predict how species will respond to the challenges of accelerating environmental change in the Anthropocene.

Plant Sciences at the ANU seeks to understand, across a range of scales, the fundamental biological processes that control plant growth, survival and reproduction, and to translate that knowledge into applied outcomes. Core research strengths include photosynthetic biology, cell-signaling and development and plant-pathogen interactions. Research outcomes include: improving crop productivity and stress tolerance to ensure global food security in the future;

understanding how future climates will affect plant growth and survival in natural ecosystems; and, predicting the direction and magnitude of ecosystem-atmosphere feedbacks

Food security

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As one example:

Food Security; one focus topic might be increasing environmental stress tolerance of crop plants. This aligns with national priorities. There are worrying projections indicating that in the absence of significant adaptation to a changing climate, by 2060 grain farmers in some regions face a drop in productivity of 50 per cent below 2018 levels (Commonwealth Bank of Australia, 2019. 'CBA Annual Report 2019'. Accessed at: https://www.commbank.com.au/about-us/investors/annual-reports.html); meanwhile our goal is supposed to be to increase crop production by 2-3 per cent annually in line with increasing international demand, and in order to achieve the vision for Australia's annual farm gate output to exceed $100 billion by 2030 (Agrifutures, 2019. 'A 100bn industry by 2030?'. Accessed at: https://www.agrifutures.com.au/news/agriculture-a-100b-sector-by-2030/). A lot of change is needed to switch from a projected drop of 50% to a gain of 2-3% p.a., and RSB could help work towards leading a charge to figure out exactly what changes are needed.

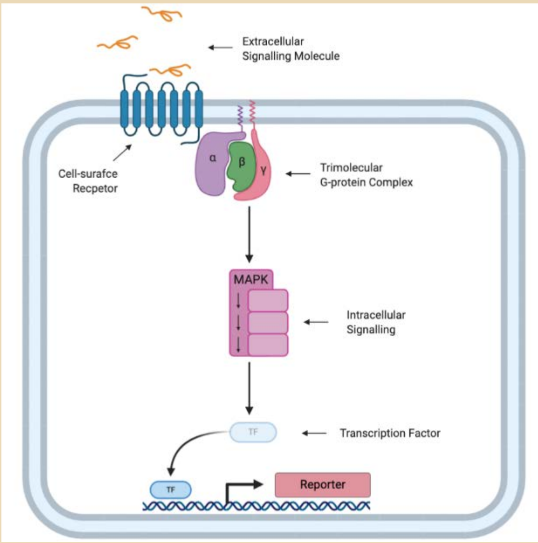
Research in the Division of **Biomedical Science and Biochemistry** has focussed on two core strengths - membrane biology and pathogen (parasite and microbe) biology, with recent additions in evolution & development. The emphasis is on understanding interactions of hosts and pathogens via the membrane interface, leading to better understanding of how drugs work and can be targeted for improved health outcomes.

Synthetic biology enabled biosensors

G protein coupled receptors (GPCRs) are the biological "inbox" of the cell. Residing in the cell membrane, they receive external chemical messages with exquisite sensitivity, and relay that message with chemical signals to the inside of the cell. This affects which genes are expressed and allow the cell to adapt and respond to its extra-cellular environment. Using the tools of synthetic biology, it has now become possible to engineer cells like the humble bakers yeast (Saccharomyces cerevisiae) with GPCRs from other organisms, so that the yeast becomes a specific and sensitive biosensor for a particular chemical. With cheap synthetic

DNA that can be quickly assembled into bigger pieces like Lego, and genetic engineering tools like CRISPR/Cas9, the chemical relay can be hijacked, and directed to the expression of a reporter gene instead. A common choice is Green Fluorescent Protein (GFP), but something that can be seen with the naked eye, such as a brightly coloured pigment from coral, can also be used. In this way, yeast can be used to detect minute concentrations of a specific chemical with exquisite sensitivity. Last year, my lab helped mentor a team of undergraduates as part of the Australian SynBio Challenge (https://www.aussynbiochallenge.org/) to design a diagnostic biosensor for Cryptococcus, an important human fungal pathogen that is the leading cause of death in AIDS patients. But this approach can also be used to detect and quantify almost any chemical that binds to a GPCR, from the pheromones of plant pathogens to illicit drugs.

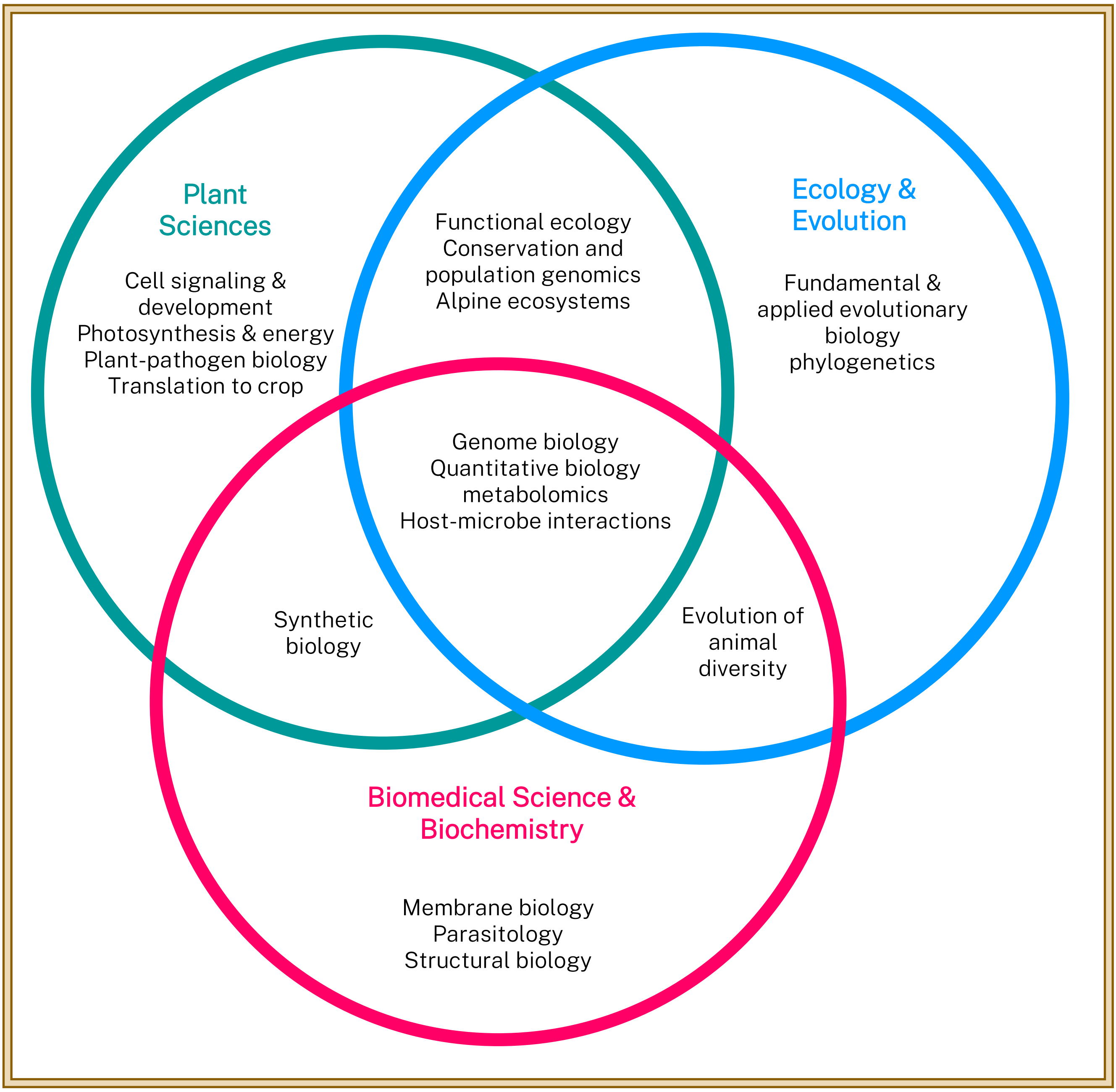
Since evolution has honed different GPCRs to be highly specific to a particular chemical, this research has the potential to create, affordable and fast biosensors that are exquisitely accurate. These biosensors can also be designed to detect many different compounds in parallel. We have recently started a multi-GPCR biosensor for the many different female sexual hormones that fluctuate across a menstrual cycle, with the aim to assess if this pattern is different in women suffering from Endometriosis and potentially creating a novel diagnostic test for this important, and under studied condition.



Despite the demonstrated ability of Synthetic Biology in engineering organisms, biology often has other ideas. A key challenge in the design of these biosensors is the integration of GPCRs from different organisms (for e.g. humane sexual hormone receptors) with the engineered G-protein signalling subunits from yeast required for downstream signalling in the cell. Structural biology however, the field in which I was trained, has illuminated the details of these interactions in exquisite detail in recent years, via the revolutionary advances in cryo-electron microscopy. This has allowed these molecular interactions to be understood, anticipated and reverse engineered when needed. Despite this, some educated guesswork combined with an effective screening assay is often still fundamental to creating a functional and accurate biosensor using this method.

From an RSB-wide perspective, there are many opportunities for synergy across Divisions and externally. Common to all 3 divisions is high level expertise in Genome Biology and Quantitative Biology. Both PS and EE have a shared focus on conservation biology and population genomics, PS and BSB intersect in research on host-pathogen biology, and EE and PS on evolution of animal diversity.

Three ***emerging*** areas where RSB can make particularly strong contributions are: (i) host-microbiome interactions, (ii) alpine ecosystems and (iii) synthetic biology. The first (with JCSMR) builds on the breadth of RSB research across host-microbe interactions in humans, plants, insects and their pathogens or associated microbes, from both mechanistic and eco-evolutionary perspectives. Eco-evolutionary studies of the function and dynamics of alpine species and ecosystems is a natural focus for RSB (with FSES) given our location and increasing climate-driven pressures on these systems. Synthetic biology is a global growth area with extraordinary potential; RSB is partnering with RSC and CSIRO to provide model biological systems to test novel constructs.



Research collaborations

As expected, RSB researchers collaborate actively with scholars from different parts of ANU and with colleagues elsewhere in Australian and overseas. RSB academics are participating in multiple ANU Grand Challenges and lead major ANU initiatives in data analytics, in developing partnerships with industry and CSIRO in Agricultural science, and with CSIRO and Univ. Canberra in Biodiversity Science. Strategically, our co-location with the Black Mountain campus of CSIRO is a major asset and advantage that is still not sufficiently exploited for national benefit. Here, an ANU-CSIRO *National Agricultural and Environmental Science Precinct* is a logical focus for further building interactions, beyond those already in place through individual researcher interactions and the activities of BDSI, CEAT and CBA. Each of these institutional collaborations is creating opportunities for EMRC researchers and broadening training options for PhD students and postdoctoral scholars in RSB.

Infrastructure

RSB is well-served by current infrastructure including recently built or renovated buildings. Infrastructure hubs include plant and animal facilities, the Ecogenomics & Bioinformatics Laboratory, RSB and central computing (incl. NCI), the RSB mass spectrometry facility is shared with RSC. Discussions are underway to consolidate more equipment into more infrastructure hubs to increase competitiveness for external or central ANU support, and to maximise efficiency of professional staff support. Key areas for renewal or expansion include (i) plant and animal facilities (BioXchange), (ii) a Biological Transformation Facility to underpin synthetic biology and host-microbe initiatives, and (iii) a mobile field laboratory and remote sensing capability for wild populations (e.g. Alpine ecosystems initiative).

More information

The RSB web site has more information on our research, including examples of exciting, recent work lead by our staff.

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