Decoding and Designing: Out and about at Midlothian Science Festival

Submitted by synbio on Wed, 10/31/2018 - 14:19

Alazne Dominguez (right, postdoc in Jamie Davies lab) and Cigdem Selli (left, postdoc at The Queen's Medical Research Institute) came up with a clever, hands-on approach for building a dialogue around these technologies. Here they explain what happened.

During the Midlothian Science Festival we had the chance to engage 94 kids (aged 5 to 11) with the concepts of synthetic biology and bioinformatics through an activity titled: Decoding and Designing. Why? Because we felt that not enough effort had been devoted to explaining these relatively new fields, which remain largely unknown to the public. We wanted to show the simplicity of these apparently complicated concepts in a fun and educative way through interactive activities.

We attended two events within the festival: First, the 'Science Alive Gala Day' at Lasswade High School, Bonnyrigg and then the 'Computer Festival' at IKEA, Straiton.

First, we provided tips to the children to recreate a short DNA sequence using soft mega blocks of four different colours (representing the four nucleotides, ATCG). Then we asked them to guess what the sequence might encode. Clearly, this was impossible without bioinformatics tools to facilitate the reading of that text.

Once they could decode the DNA, we suggested that they start to design and build novel biological systems using synthetic biology. We described some real examples of useful synthetically produced products such as insulin. However we also raised awareness of the potential ethical issues such as intentional misuse (e.g. bioweapons) and perhaps unintended consequences (e.g. prohibitively expensive spider silk fabrics).

Finally, we encouraged kids to choose a synthetic biology application and build it, from a set of instructions, using the soft blocks. If the construction was correct, they were rewarded with a Polaroid picture. It was fascinating to realize that for most of the kids this was their first experience with those 'magic pictures' and the nostalgia in parents' faces.

To make a long story short, the experience was really fun and rewarding. Next time, please do come and join us!

Alazne Dominguez & Cigdem Selli

iGEM Success - Gold for Edinburgh Teams

Submitted by synbio on Mon, 10/29/2018 - 10:56

Congratulations to both Edinburgh teams who won gold medals at the 2018 Giant iGEM Jamboree – the annual showcase of student-driven synthetic biology projects. Interdisciplinary teams of undergraduate and overgraduate (or postgraduate) students spent their Summer designing and building and their hard work has paid off at this year's competition.

The Undergraduate team was also nominated for best foundational advance project. A fantastic achievement that highlights the aim to introduce something that benefits synthetic biology as a discipline, underpinning a wide variety of other projects. Their project 'MaxED OOT' looked at providing improved characterization to facilitate the use of Maxicells - achromosomal E. coli cells - as a safe and minimalistic chassis for future use in Synthetic Biology. Read more at http://2018.igem.org/Team:Edinburgh_UG

The Overgraduate team looked at producing bio-based and biodegradable thermoplastics from industrial co-products. Read more about their project 'Valeris.ed' at http://2018.igem.org/Team:Edinburgh_OG

Thanks to all team instructors and advisors who volunteered their time, lab space and resources.

Learn more about iGEM: http://igem.org/About

New light-based systems turns off protein production

Submitted by synbio on Mon, 10/29/2018 - 09:54

A novel light-controlled 'off' switch for proteins will open up new ways to explore how many important cellular processes work.

A collaboration between the UK Centre for Mammalian Synthetic Biology (Jamie Davies and Elise Cachat) and groups based in Germany, have harnessed optogenetics – light controlled switches of gene expression – to switch off protein production.

Most researchers study what a protein does in a cell by artificially manipulating its production. Many use chemicals to control the process but these can be toxic and have unexpected side effects.

Optogenetics offers a solution. Researchers build light-sensitive detectors into the molecular controllers of protein production and then trigger these with a beam of light. The technique can target cells with higher accuracy then chemicals and works in both cell cultures and in living animals. However, it has proven very difficult to create optogenetic systems that turn off protein production.

To address this, the team built a two-component, blue light-responsive optogenetic OFF switch ('Blue-OFF'), which quickly reduces how much protein is made when illuminated. They combined a light responsive unit (KRAB-EL222), which halts protein production on illumination, with a module (B-LID) that marks proteins for degradation. So blue light targeted both gene expression and protein stability creating a fast and powerful response.

The researchers then showed that they could use the system to control cell death in a culture of human cells. This exciting new approach opens up novel perspectives in fundamental research and applications such as tissue engineering.

Dual-controlled optogenetic system for the rapid down-regulation of protein levels in mammalian cells Baaske, J et al. *Scientific Reports* Volume 8, Article number: 15024 (2018)

Edinburgh's first Cafe Synthetique

Submitted by synbio on Fri, 10/12/2018 - 11:53

On 9th of October, researchers from Biology, Informatics and Engineering hosted Edinburgh's first Café Synthetique event. This monthly event aims to address the lack of public and informal events for those curious about Synthetic Biology. The first meeting, titled "The What, How and Why of Synthetic Biology", featured talks from Dr Stephen Wallace and Dr Leonardo Rios Solis. The sold-out event attracted attendees from the public, academia, and industry which shows an appetite for informal conversations about synthetic biology across communities. Future events will take place on the second Tuesday of each month, with the next event (6.30pm 13th November at Harry's Southside) exploring ideas in mammalian synthetic biology.

To keep up to date with the Café Synthetique, follow @Cafesynthedin on twitter

Professor Andrew Millar appointed Scotland’s CSA for Environment, Natural Resources and Agriculture

Submitted by synbio on Mon, 10/08/2018 - 15:38

Professor Andrew Millar, previously Director of Edinburgh’s Centre for System Biology (2007-2012) and SynthSys, has been appointed as the Scottish Government's Chief Scientific Adviser for Environment, Natural Resources and Agriculture (ENRA).

Professor Andrew Millar, Director of Research for Biological Sciences at the University of Edinburgh, will provide scientific advice on issues such as the environment, agriculture and the wider rural economy.

One of the challenges facing Professor Millar will be to develop and secure Scotland's science base in these areas, through the Brexit process.

Cabinet Secretary for Environment, Climate Change and Land Reform, Roseanna Cunningham, said: "If the Scottish Government is to effectively address current and future challenges facing our environment then sound scientific advice is integral. I'm looking forward to working with Professor Millar to tackle some of Scotland's most crucial environmental, agricultural and rural issues, and the positive impact scientific developments could have on these."

Professor Millar said: "Scottish science has an enviable track record and our natural resources are among the country's most critical assets. I am happy to contribute to Scottish policy at a time when change and opportunity in this area are coming from social and political development, as well as from new scientific understanding, technologies and the changing environment."

The main functions of the CSA ENRA role are to provide independent science advice to inform our work across policy areas, and champion the use of evidence to inform policy development and delivery.

Professor Millar succeeds Professor Louise Heathwaite, who held the Scottish Government position until 2017.

Doors Open day attracts more visitors

Submitted by synbio on Mon, 10/08/2018 - 15:19

The University's Doors Open event attracted even greater numbers with thousands braving the lively Scottish autumn weather to explore the science going on at the King's Buildings Campus.

This year, the Centre welcomed 367 visitors to the Roger Land Building on Saturday 29th September where they explored science as varied as synthetic biology through to infectious diseases.

The Centre provided hands on arts and crafts activity, designed by Dr Gaynor Campbell, to explain how we can engineer in novel features to cells to make them useful tools to fight major global challenges. Kids also got involved with designing and building plasmids to encode their features of choice – from oil munching bacteria to new enamel for teeth.

This year, other groups from across the School of Biology got involved with topics such as immunology, animal parasites and malaria.

The University constructed the Roger Land Building in the 1960s to house the Animal Research Organisation. The architect, Sir Basil Spence, is renowned for his modernist design of Coventry Cathedral, destroyed during WWII.

The Roger Land Building then housed the Institute for Stem Cell Research before being renovated for the School of Biological Sciences and the hub for the UK Centre for Mammalian Synthetic Biology.

Young Frankenstein – cautionary tale or valuable lesson

Submitted by synbio on Fri, 07/27/2018 - 17:54

A Sci-Screen event provided a light-hearted backdrop for Centre members to engage the audience of Edinburgh Skeptics in a more serious dialogue about science, its representation and its communication. And what could have been more appropriate than the hilarious 'Young Frankenstein' (starring Gene Wilder) in what is the 200th anniversary of the publication of Mary Shelley's classic novel Frankenstein.

Before the screening, Marie-Anne Robertson, Science Communications Manager for the School of Biological Sciences and Dr Jane Calvert of SynthSys and Science, Technology and Innovation Studies, provided an introduction to media monsters and the necessity for human connectivity respectively.

Throughout the media, literature and film, scientists fall into wearingly familiar stereotypes. Whether it is the hapless scientist losing control of their discovery or the mad scientist hell-bent on global domination – they all tell a familiar tale, and reveal a very important lesson.

In Young Frankenstein an angry mob of villagers circle Dr Frankenstein's castle; they are not only furious about the creation of the monster but also deeply suspicious of the doctor's motives.

But look closely and you see this is not a fear of science itself. What really troubles the villagers is power. When ordinary people feel they have little control over new breakthroughs, or the people who may exploit them, alarm bells start ringing. If history has taught us anything, then it is that shrinking away from the debate does us no good.

The fallout from major media scandals and contentious issues, such as GM foods and the MMR vaccine, had profound and far-reaching consequences on policy and public attitudes. It was a wakeup call that shook all those responsible for communicating science. Many lessons have been learnt on the importance of two-way communication.

New approaches like synthetic biology require not only skill in explaining the science but willingness to openly tackle concerns about power. Who gets to decide how to use the technology, who regulates it, who gets to exploit it? This is not only the job of journalists, press officers and scientists but also everyone who is involved in funding, regulating, buying and using the products of science. Discussion about the regulation and use of new technologies, including the practical, ethical and moral issues, is as important as communicating the basic science itself.

As Dr Frankenstein learnt, his creation wasn't the problem, it was his neglect and failure to take responsibility for his creation and the unintended damage that it caused.

Marie-Anne Robertson, Science Communications Manager, School of Biological Sciences

Image: Creatice commons CC0

Building superbugs in the Meadows

Submitted by synbio on Mon, 06/04/2018 - 09:36

Centre members braved the erratic Edinburgh summer weather to build bugs with kids of all ages at the annual Meadows Festival.

Over 100 children came along during the event to design and build bugs with super powers that could help to save the planet.

The activity, designed by Dr Gaynor Campbell, explains very simply how we can engineer in novel properties to cells to make them useful tools in the fight to address many global challenges.

Participating kids totally got with the programme and built some fantastic creations – and all in a friendly GM-free environment. It also provided an opportunity to explain the Centre's research to parents and carers.

Centre hosts future trends workshop

Submitted by synbio on Fri, 06/01/2018 - 11:54

A group of 50 leading synthetic biologists gathered at the Edinburgh Centre for Carbon Innovation (see image) in Edinburgh on May 16 and 17 to discuss 'Future Trends in Synthetic Biology.'

Hosted by the UK Centre for Mammalian Synthetic Biology the purpose of the 2-day workshop was to discuss and report on current research progress in the field of synthetic biology, and discern focal points for future, related disruptive technologies and applications. The workshop was an invitation-only, closed-door event to provide an opportunity for participants to discuss their perspective without bias.

During the event there was animated discussion around a range of topics, from the application of synthetic biology to accelerate the production of high value chemicals, materials and medicines, through to heated debate on issues such as proportionate governance, biosecurity and ethics. At the end, delegates discussed what measures might be needed to help move synthetic biology to the next levels. Issues such as universal standards, identify 'grand challenges' focusing the community on a shared goal, and coordinating all relevant stakeholders were discussed.

A white paper discussing the discussion of the meeting and its recommendation will be shared with the community when completed.

The Centre would like to thanks the US Office of Naval Research Global and the Department of Homeland Security for sponsoring this event and in particular to Dr Patrick Rose (ONR Global) for all his support with its organisation and delivery.

Science as Muse

Submitted by synbio on Tue, 05/08/2018 - 16:34

What happens when a leading scientist visits a group of first year illustration students at the Edinburgh College of Art (ECA)? The birth of a new field where the scientist becomes the muse.

The idea was the brainchild of Astrid Jaekel, a teaching Fellow and course coordinator of first year illustration at the ECA. Astrid was keen to bring science into her classroom; the resulting - 'Long Story Short' - is based on the idea of the Illustrator becoming part of the storytelling chain. First, they absorb and process information and then they turn the resulting story into artwork that will serve as a storytelling device.

As part of a 5-week long storytelling project, first year Illustration students met with three practitioners from different fields: Master storyteller David Campbell, Sculptor Duncan Robertson and Scientist Prof Bill Earnshaw. Each gave insight into their professions and the relevance of storytelling within their practice.

The final task of the project took inspiration from scientific methods of research as well as collaborations between artists and scientists. On the first day, students were introduced to the ASCUS lab at Summerhall, who provided them with basic microscope training, followed by an exercise of how to extract their cheek cells and stain them to reveal the cell membrane and nucleus. In the afternoon, the group then met Bill Earnshaw, Professor of Chromosome Dynamics at the University of Edinburgh and a member of the UK Centre for Mammalian Synthetic Biology, who spoke about his research, his ideas on art and science and shared his personal journey of becoming a scientist. Most interestingly, Bill pointed out similarities between Art and Science processes and how he himself was torn between becoming Artist or a Scientist.

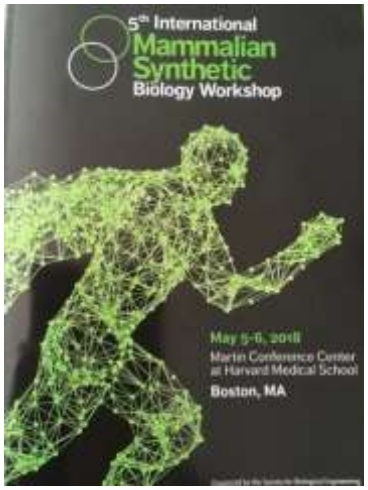
In response to the events of this day, students had to create an illustrated, sequential, narrative piece containing a minimum of four panels. Any discoveries arising from the day could serve as a starting point, and a playful approach was welcomed, which saw fact and science being turned into imagination and fiction.

The young artists particularly enjoyed the creative freedom they were given and the fact that they could revisit and apply a lot of their learning from throughout their first year at ECA. There was a variety of outcomes including the educational, humorous, self-reflective and personal and they were very excited to share their work with the scientific community.

Astrid and her team are grateful to Prof Earnshaw, the UK Centre for Mammalian Synthetic Biology, and the ASCUS lab for making this exciting collaboration happen.

Mammalian synthetic biology comes of age

Submitted by synbio on Tue, 05/08/2018 - 16:30



Mammalian synthetic biology will make a huge impact on medicine and healthcare if just a fraction of the many exciting projects discussed at the 5th Annual Mammalian Synthetic Biology Workshop in Boston (May 5 and 6) come to fruition.

The opening keynote speaker, Prof Crystal Mackall of Stanford University, set the scene with a review of the success of CAR Technology, the 'poster child' for mammalian synthetic biology. Last August, the US FDA approved Novartis' Kymriah for treating certain paediatric and young people with a form of acute lymphoblastic leukaemia (ALL). Kymriah is a personalised T-cell therapy and offers a route, in some patients, for prolonged control of ALL, arguably a full 'cure'. However, CART is not without its challenges including 'exhaustion' of the T-cells over time and/or excessive toxicity: Mackall provided an overview of her elegant studies to explore ways of using synthetic biology to address these problems. Clever use of drug-controlled CART systems, which can turn the therapy on and off as necessary, could be one way to prevent T-cell exhaustion. Generating bi-specific CARs may be a viable route for avoiding off-target toxicity. Other speakers in the 'synthetic immunology' session explored alternative strategies for fine tuning routes to address these challenges including Crispr engineering of defective T-cells and creating synthetic T-cell receptors using *notch* receptors. The next challenge will be to use a synthetic immune system to attack and eliminate solid tumours.

Another highlight of the meeting was the 'viral vectors and gene therapy' session. Adenoviral vector (AAV) is the most widely adopted viral vector for human gene therapy. AAV offers a handy way of shuttling large pieces of synthetic DNA into cells and comes in at least 68 different 'flavours' (serotypes), making it suitable for personalised therapy. However, Nature did not design AAV to be an illicit gene 'trafficker' and so it is not particularly effective at infecting many cells types with sufficient capacity to be of any use in gene therapy. Here synthetic biology can really make a difference. O'Shea's lab have found ways create to make a cut and paste modular system of the different serotypes, producing a useful viral toolbox. Dr David Schaffer of the University of California, Berkeley is using directed evolution to modify the viral capsid, the component that directs viral infection. He has now developed AAV that can target retinal cells and will be suited to treating blindness caused by retinal degeneration.

The microbiome continues to attract the attention of the big names of the synthetic biology world, Profs Jim Collins (MIT) and Pam Silver (Harvard Medical School). They are engineering bacteria to explore the mode of action of antibiotics or even to work as antibiotics themselves. Silver is harnessing E. coli to prevent Salmonella infection – engineering detection and killer functions into common gut bacteria. Ingenious.

Others sessions included topics such as genes and circuits, the funding and investment landscape (apparently microbiome companies are the ‘Marmite’ of VC investments - they either love ‘em or hate ‘em) multicellular systems. There were excellent presentations on modelling of complex systems, which will continue to be vital if we are to be able to engineer cells with any reproducibility.

George Church (Harvard University) closed the meeting with a review on his very many projects and a brief update on progress with the Human Genome Project Write, which had been the topic of a meeting earlier in the week in Boston.

While still relatively small in number, the mammalian synthetic biology research community is big on ambition and creativity. The challenges ahead are still substantial but with the success of CART in the clinic, the prize does not seem quite so unachievable any more.

To date, the Mammalian Synthetic Biology Workshop has only been held in Boston, but the organisers have seen the need to broaden its horizons. Next year, the event will be in Chicago, and we hope to welcome it to Edinburgh in 2020.

SAW Trust inspires again

Submitted by synbio on Tue, 05/08/2018 - 16:08

The SAW Trust were back in Edinburgh on May 3 to deliver what was their third successful training day in science communication.

A group of 32 teachers, scientists, writers and artists attended to learn more about the SAW Trust's fun and innovative approach to teaching science through pictures and words.

Jenni Rant (SAW training lead and scientist) and colleagues Mike O'Driscoll (writer) and Chris Hann (poet) inspired the room with ways to explore DNA and cells using everything from pipe cleaners and paints to balloons and polystyrene balls. The 'class of 2018' excelled themselves in their creative interpretations of the cell structure (see photo).

All too often, the 'arts' and 'sciences' are referred to as separate disciplines but, as discussed in class, they are more similarities than differences. The arts can also help open up science to children who feel disengaged with science or have preconceptions that it is simply 'too difficult' for them.

At the end of the day, the trainers selected seven teams to develop and take workshops into schools in the Edinburgh and the Lothians. We are particular grateful to the SAW Team, all our enthusiastic volunteers, and Lorna MacDonald from Edinburgh City Council who has helped to connect us to schools.

You can read more about the SAW Trust and their activities here www.sawtrust.org

Professor Susan Rosser awarded Royal Academy of Engineering's Chair in Emerging Technologies

Submitted by synbio on Wed, 04/25/2018 - 08:54

Susan Rosser, Professor of Synthetic Biology, is the recipient of a prestigious Royal Academy of Engineering's Chair in Emerging Technologies scheme. The Chair provides research visionaries with support in developing technologies with high potential to deliver economic and social benefit to the UK.

Susan is Director of the Edinburgh Mammalian Synthetic Biology Research Centre and Co-director of the Edinburgh Genome Foundry. She previously held a prestigious EPSRC Leadership Fellowship in Synthetic Biology.

Her ambitious project aims to genetically engineer cells that can simultaneously combine diagnosis of a disease with a targeted treatment that prevents disease progression or provides a cure - so called theranostics. Developing implantable or circulating 'surveillance' cells that recognize and process the information associated with disease-related changes would allow earlier detection. The disease could be treated before it develops or progresses by programming the cells to produce a therapeutic molecule, such as an antibody or drug. The advantage of this approach is that the treatment would be administered at the correct location, at the right dosage, providing a more personalised, customised treatment.

Most diseases are treated with "one size fits all" therapies, such as drugs, which have a broad action and sometimes cause unintended side effects through their effects on other parts of the body. Current treatments often don't reflect differences between individual patients or constantly changing disease states mean that the timing, location and dosage is often far from ideal.

The Royal Academy of Engineering will provide funding of £1.3M for Professor Rosser to focus full-time for 10 years on research, development and exploitation. The University of Edinburgh was the only institution to be awarded multiple Chairs, being successful in two of the ten available.

International workshop to discuss unmet needs in ‘design-build-test’ for synbio

Submitted by synbio on Tue, 03/27/2018 - 15:24

In little over a decade, synthetic biology has evolved from demonstrating proof-of-concept gene circuits in bacteria to developing a new class of therapeutic devices (theranostics). However, despite a thriving community, and some noteworthy successes, the task of assembling a predictable gene network from biomolecular parts remains a challenge. It can take many months of trial and error to produce a gene circuit with the desired behavior or phenotype. In engineering terms, we are still far from the efficient, rational ‘Design-Build-Test’ cycle deployed in industrial manufacturing contexts.

To gain consensus about the challenges, and to discuss potential solutions, the UK Centre for Mammalian Synthetic Biology hosted a workshop on February 22nd and 23rd 2018 in Edinburgh. A principal aim of the workshop, besides knowledge exchange across the different communities, was to start to develop a roadmap document and a focused community to address these challenges through targeted funding applications.

Over 50 people from US, UK and Europe attended the workshop and enjoyed two days of talks and lively discussion. They discussed four key areas:

- How to automatically design synthetic gene circuits - *Bio-design automation*;
- How to design the most informative experiments to characterize such circuits - *Optimal Experimental Design;*
- How to use such experiments to obtain reliable mathematical models - *Making sense of data;*
- What kind of technologies those experiments should be based on - *Technology*.

Outputs of the meeting will be used to develop a community position paper.

You can find out more and join the conversation via the online forum here.

The organisers are very grateful for financial support from Scottish Universities Life Sciences Association.

Tapping bacterial survival strategies for ocean navigation

Submitted by synbio on Tue, 03/27/2018 - 14:30

Funding to understand how bacteria swim to stay alive could lead to the development of bacterial 'biosensors' to help the U.S. Navy navigate at sea.

The new study aims to explore whether tailoring the sensory machinery that allows bacteria to detect and respond to changes in their environment, could unleash their potential as bio-sensors. Using bacteria to sense changes in ocean currents, depth and the salinity of seawater could lead to a self-sustaining source of sensitive and real time data that aids navy vessels, such as submarines.

Bacteria, such as *Escherichia coli*, have sophisticated cellular machinery, called the chemotactic network, that can quickly sense tiny changes in their environment. By sensing minute changes in chemicals and nutrients, they can swim away from harm and maximise their chances of survival. Bacteria may also respond to changes in water pressure and flow, which could be used to detect changes in speed or ocean currents.

Dr Teuta Pilizota, Chancellor's Fellow in the Centre, will measure how bacteria respond to changes in salinity, which varies at sea depending on location, depth and time of year.

Environmental changes are picked up by specialised bacterial receptors that trigger the rotation of tiny hair-like strands, called flagella, on the surface of bacteria allowing them to swim. Bacteria control the way they swim by altering the speed and direction of rotation of the 'molecular motors' that power the flagella.

Bacteria are already used as biosensors, for example, to detect toxins in water. But, the process is slow as it relies on the production of fluorescent proteins, which can take several minutes. However, the Dr Pilizta sensitivity and speed of bacteria's chemotactic network, which reacts in seconds, could make it ideal for real-time navigation if it is able to work across a range of ocean conditions.

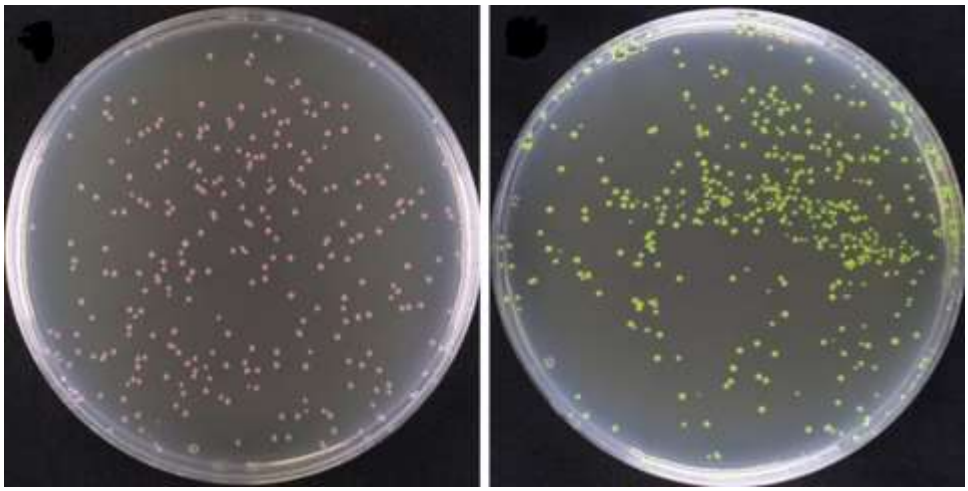
Dr Pilizota and her team will also investigate if bacteria can sense multiple signals at the same time and if there is potential to couple the chemotactic network to electrical outputs.

The study is funded by the Office for Naval Research and Defence Advanced Research Projects Agency. The funding will not only aid understanding of bacteria's potential as biosensors, but also lead to insights on why they swim and if it helps them to evade the body's defences and cause infection.

iStock image of bacteria

New user-friendly DNA assembly toolkit

Submitted by synbio on Tue, 03/27/2018 - 12:56



The development of a more versatile, simple and efficient DNA assembly kit will offer researchers unlimited ways of building complex molecular constructs by combining different DNA parts.

The ability to assemble different DNA parts is essential to synthetic biology, which enables researchers to construct new biological pathways or redesign existing biological systems. Existing DNA assembly toolkits typically compromise on either simplicity, the complexity of the assembly process, or capacity, the number of DNA parts that can be combined. Dr Naomi Nakayama and her team in SynthSys have tackled those issues by creating Mobius Assembly, which combines unlimited assembly capacity in a simple, streamlined process.

Synthetic biology uses engineering principles on a nanoscale, to assemble different DNA parts into longer stretches of DNA that result in new cell functions, and sometimes to create entire biological pathways. Mobius Assembly uses a two-stage design that allows a complex DNA construct to be made by combining a series of smaller DNA parts – similar to building a computer. In one step researchers pick from a library of standardized DNA parts, to build a functional unit, similar to combining the right parts together to make a USB port or the circuit board. In the second stage, these larger functional units are joined together to make a system – rather like bringing all the bigger parts together to make a working laptop. Mobius Assembly allows researchers to switch back and forth between these stages, called levels, so that new parts can be continually added to the system, allowing a complex DNA sequence to be assembled.

Mobius Assembly users can also visually distinguish between the different assembly levels and identify successful DNA additions by the use of coloured chromogenic proteins. The chromoproteins are produced by bacteria, eliminating the need for researchers to add toxic and expensive chemicals to screen for successful DNA assembly. By breaking genomes down to their individual parts researchers gain a better understanding of how living systems work. Synthetic biology also allows the design of new biological processes, such as developing drug-producing bacteria in which a whole new biosynthetic pathway has been introduced. Living cells, such as yeast or bacteria, act as a ‘blank canvas’ which house the new, synthetic DNA constructs – effectively turning them into biofactories. Assembling even simple DNA

constructs is more complex than building a computer. The way the DNA parts interact is complex and sometimes unknown - making it similar to working in black box. The most common method for DNA assembly uses enzymes, called endonucleases, to cut out the DNA parts at specific sites leaving sticky ends, or overhangs. These overhangs pair to other complementary ones on other DNA parts, allowing different DNA parts to combine in a specific order. To improve its versatility, the researchers built the Mobius Assembly toolkit using sticky overhangs most commonly used by researchers allowing its parts to be shared widely. The researchers also introduced a rare-cutter endonuclease, which is more specific and ensures the DNA parts can be extracted intact with less modifications needed - speeding up the assembly process.

"We made Mobius Assembly as user-friendly as possible. We currently use it with Escherichia Coli and plant cells, but we hope it will be used widely and adapted to many different types of organisms."

Andreas Andreou, School of Biological Sciences

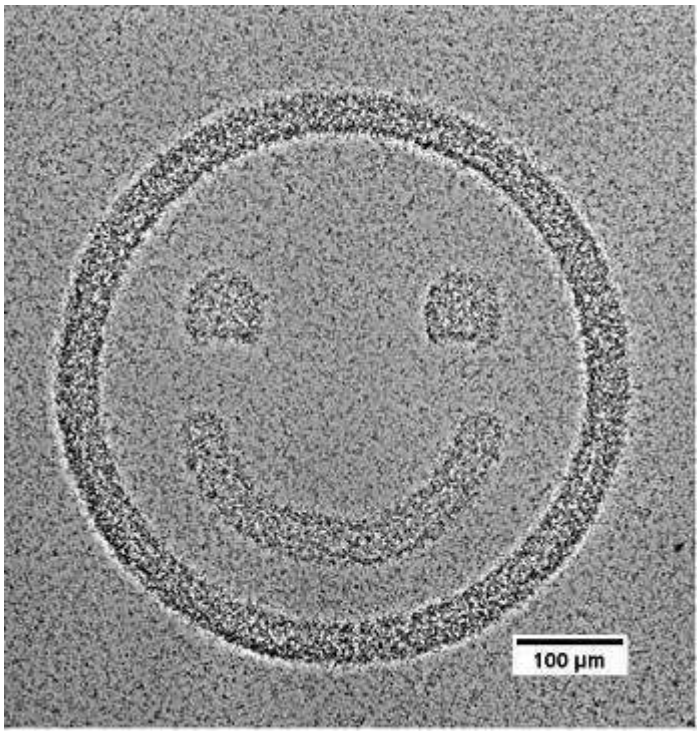
Publication:

Mobius Assembly: A versatile Golden-Gate framework towards universal DNA assembly, PLOS One

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0189892

Painting with light-powered bacteria

Submitted by synbio on Fri, 03/09/2018 - 14:40



Dr Teuta Pilizota, a PI in the UK Centre for Mammalian Synthetic Biology, is part of a research team who have used genetically modified bacteria to produce light-induced patterns as a potential route for engineering smart materials.

Micro- and nano-fabrication can revolutionise many areas of technology, including personalised medicine. There are two conceptually distinct ways to construct such structures: 'top-down' techniques such as lithography use 'scalpels', while in 'bottom-up' techniques, microscopic 'Lego components' move themselves into position and self-assemble. The University of Edinburgh team demonstrated a novel method whereby arbitrary patterns can be assembled in a fluid environment and reconfigured in real time using light-controlled motile bacteria as the 'Lego' blocks.
The researchers demonstrated this method by constructing a bespoke mutant of Escherichia coli bacteria and used it to assemble the initials of the University of Edinburgh as well as a smiley face.

The method is shown to be programmable, that is the self-assembled patterns can be switched in real time. The physics and biology controlling the rapidity of switching and the sharpness of the patterns is investigated in detail, allowing the team to 'tune' the pattern formation.

This protocol provides a new paradigm for self-assembly of structures on a scale (10-100µm) which presents difficulties for many if not all current fabrication methods. At the same time, this methodology has significant implications for the burgeoning field of 'active matter' science.

Paper in Nature Communications (link is external)

Crossing Kingdoms and Disciplines: Living Art at SynthSys

Submitted by synbio on Wed, 02/28/2018 - 11:25

For two weeks in January 2018, SynthSys and Science Technology and Innovation Studies (STIS) jointly hosted pioneering biological artists Ionat Zurr, Oron Catts and Tarsh Bates from SymbioticA: the Centre of Excellence in Biological Arts at the University of Western Australia.

There is a tendency for living things to join up, establish linkages, live inside each other, return to earlier arrangements, get along, whenever possible. This is the way of the world. The new phenomenon of cell fusion, a laboratory trick on which much of today's science of molecular genetics relies for its data, is the simplest and most spectacular symbol of the tendency. In a way, it is the most unbiologic of all phenomena, violating the most fundamental myths of the last century, for it denies the importance of specificity, integrity, and separateness in living things. …Cytoplasm will flow easily from one to the other, the nuclei will combine, and it will become, for a time anyway, a single cell with two complete, alien genomes, ready to dance, ready to multiply. It is a Chimera, a Griffon, a Sphinx, a Ganesha, a Peruvian God, a Ch'i-lin, an omen of good fortune, a wish for the world.

(Oxford University Professor Henry Harris, Roots: Cell fusion 1985)

As new life forms are being created but are yet to be named, there is a need for people from different disciplines – artistic, cultural and scientific – to discuss and articulate a new language for shaping our evolving relationships with the living world. Novel life forms created in the laboratory (either constructed or created unintentionally) evoke many questions: scientific, ontological, ethical and poetic.

While at SynthSys, Zurr, Catts and Bates initiated a research on a project on cross-kingdom cell fusion in synthetic biology between mammalian and yeast cells, to explore how the novel entities produced by these cell fusions challenge existing scientific and cultural classification systems. When borders are crossed – be they biological, geographical or conceptual – the sense of excitement and exhilaration is blended with unease.

Cell fusion is used routinely in science. However, in this on-going project the team is attempting to fuse cells from different kingdoms in an *in vitro* setting. To identify the conditions that will enable cells from both kingdoms to thrive together requires the expertise of different groups, so the project involves the Cachat lab, the Menolascina lab and the Rosser lab (all at SynthSys). Jane Calvert and Erika Szymanski, social scientists from the Engineering Life project at STIS, are also part of the highly interdisciplinary team.

In short, the plan is to open up the membranes of the mammalian and yeast cells, momentarily, in a micro-fluidic system, and to enable the cells to fuse and hopefully

replicate. Metaphorically this could be described as artificial endosymbiogenesis. It raises fundamental questions about the use of an engineering approach to cross the boundaries between biological kingdoms.

During their visit Zurr gave a talk at the SynthSys Open Centre, Bates gave a STIS seminar, Zurr and Catts give a public lecture at Summerhall.

Their work-in-progress will be exhibited at the Edinburgh International Science Festival (31st March - 15th April 2018) and the Western Australia Art Gallery in September 2018. The SynthSys/SymbioticA collaboration will also be the topic of a panel at the Quite Frankly Conference, which will take place at the University of Western Australia in October 2018, and opportunities will be explored for further developing this collaborative work.

Quite appropriately, this project on the creation of novel life forms, conducted in Scotland, happens in the same year (2018) that marks 200 years since the publication of Mary Shelley's *Frankenstein: or, The Modern Prometheus.* Scotland (Orkney) is the place where Frankenstein attempted to make a bride for the "Creature", but decided to abandon this endeavour, on moral grounds.

The work is supported by a Research Collaboration Award from the University of Western Australia, the UK Centre for Mammalian Synthetic Biology, and the ERC Engineering Life project.

Image: Pig Wings. Credit: The Tissue Culture & Art Project (Oron Catts & Ionat Zurr)

Medium: Pig mesenchymal cells (bone marrow stem cells) and biodegradable/bioabsorbable polymers (PGA, P4HB)

Dimension of original: 4cm x 2cm x0.5cm each

Date: 2000-2001

Should vegans eat yeast?

Submitted by synbio on Tue, 02/06/2018 - 09:21

SynthSys social scientist, Dr Erika Szymanski, wowed the audience at the Big Bang Weekend in Wigtown with a sparkling presentation on yeast.

Armed with a rather unusual prop, her pet sourdough yeast starter (see photo below), Erika started with a tricky question: Should vegans eat yeast? Those diminutive microbes may not have tooth and claw but they are certainly very much alive. Indeed, it is perhaps because of their very small scale that we may not be taking them seriously enough. Erika took the audience on a whirlwind tour of the world of yeast and asks whether we should take another took at life on a small scale.

She asks: how is synthetic biology changing our relationship with these highly valuable microbes? We have relied for centuries on yeast for bread and brewing. Today we are rapidly extending their natural remit. We are genetically reprogramming them to make flavours and fragrances, medicines and materials. We are re-constructing them *de novo* (aka Synthetic Yeast 2.0 project). We are even planning to send them in a rocket to Mars to make the planet inhabitable. Time, perhaps, to take a little more note of our microbial collaborators.

Erika is a Research Fellow in the Engineering Life project led by Dr Jane Calvert in Science, Technology and Social Sciences. This project, funded by the European Research Council, is exploring social dimensions of what happens when engineering principles are applied to biological systems. Erika is also working on the history of yeast genome sequencing in another European Research Council-funded project, TRANSGENE, led by Dr Miguel Garcia-Sancho.

The Big Bang Weekend is an annual event that explores different aspects of science for the public. This year the topic was ‘Is it alive?’ which explored what we mean by life at both large and small scales. There were great presentations on robots and artificial intelligence, whether or not there is life out there in space, and a comedian’s exploration of human consciousness (or lack thereof).

http://www.stis.ed.ac.uk/engineeringlife

Single-cell variability in multicellular organisms

Submitted by synbio on Wed, 01/31/2018 - 12:50

A newly published paper has extended studies of noisy gene expression to multicellular organisms.

While gene expression noise in single-celled organisms is well-understood, it is less so in the context of tissues. Dr Ramon Grima of SynthSys and his PhD student, Stephen Smith, use modelling to show that coupling between cells in tissues can increase or decrease cell-to-cell variability depending on the type of gene regulatory networks in each cell. The modelling predictions are verified using experimental data from mammalian and plant tissues.

The results suggest that cell-cell coupling may be one of several noise-control strategies employed by multicellular organisms, and highlight the need for a deeper understanding of multicellular behaviour.

Smith S., and Grima R., 2018. Single-cell variability in multicellular organisms. Nature Communications 9, 345 (2018) PDF
DOI: 10.1038/s41467-017-02710-x

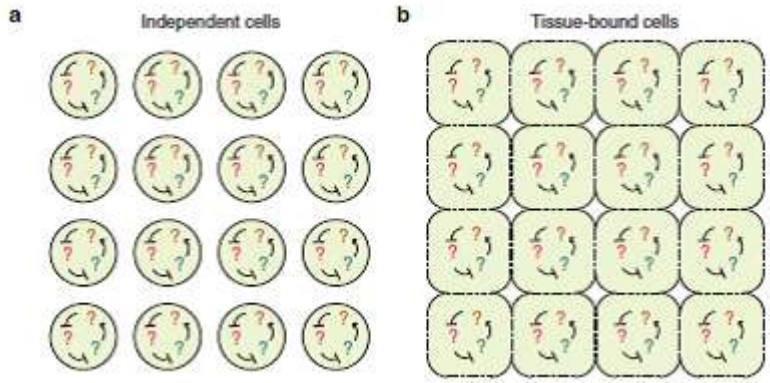


IMAGE Differences between a population of isolated cells and a tissue of cells.
a A population of isolated cells: each cell contains an identical genetic network.
b A tissue of cells: each cell contains an identical genetic network and some molecules can be transported between neighbouring cells (dotted lines)

Welcome to the new SynthSys Director

Submitted by synbio on Wed, 01/17/2018 - 14:16

Dr Meriem el Karoui of the University of Edinburgh's School of Biology has become the new Director of SynthSys.

Meriem received her PhD in Microbiology in 1998 from the University René Descartes (Paris, France), where she focused on understanding DNA repair in bacteria. For her post-doctoral training she moved to the University of Oxford, where she worked with Prof. Jeffrey Errington on cell division in Bacillus subtilis. She then started her group at INRA (France) to study chromosome organization in bacteria. In 2009, as a visiting professor at Harvard Medical School, she developed an in vivo single molecule imaging technique, and stochastic models of DNA repair.

In 2013, she was awarded a prestigious Chancellor's Fellowship at the University of Edinburgh where she has established a group with merged expertise in mathematics, microbiology and biophysics. Meriem is a Wellcome Trust Investigator and her research focuses on the integration of bacterial physiology in the understanding of the molecular processes underlying DNA maintenance and antibiotic tolerance.

Meriem will interact across several schools and colleges and help build bridges between the different disciplines. The rotating directorship reflects the multidisciplinary research of the Centre. Meriem takes over from Professor Alistair Elfick from the School of Engineering.

Find out more about Meriem's research interests:

Lab website: www.elkarouilab.fr

Twitter: @MEKlab

Wellcome Trust
video: https://www.youtube.com/watch?v=72d4U5TuebI&feature=youtu.be

A fine balance between stress and success in synthetic circuit design

Submitted by synbio on Wed, 01/10/2018 - 12:33

A new study has provided insights into how varying the number of synthetic circuits introduced into host cells influences their behaviour may provide a guide to improved synthetic circuit design.

Dr Baojun Wang of SynthSys and collaborators from the National University of Defense Technology, Changsha (China) and Imperial College London (UK) have interrogated these host-synthetic circuit interactions using RNA transcriptome analysis using an exemplar 'AND gate' circuit in *Escherichia coli.*

Synthetic biology approaches rely on introducing foreign (heterologous) gene networks into a host to program cells, with the assumption that expectation of the introduced synthetic network is orthogonal (i.e. not self) to the host background. However, synthetic circuits do still interfere with the host cell's physiology by either posing a strain on host metabolism or inducing unintended interactions with host native gene pathways.

The team showed that the number of copies of synthetic circuits added had a more influential effect on host-cell interference than circuit composition per se: medium numbers of plasmids showed more prominent interference than low numbers. In contrast, the circuits have a stronger influence on host growth with an increasing metabolic load as the number of copies of the exemplar circuits increased. They noted that as they varied circuit copy number, from low to medium, the components behaved differently and, counterintuitively, attenuated output.

The study demonstrates the number of copies of the plasmid is a key factor that can dramatically affect the orthogonality, burden and functionality of the heterologous circuits in the host chassis. The results provide important guidance for future efforts to design orthogonal and robust gene circuits with minimal unwanted interaction and burden to their host.

Publication

Liu Q, Schumacher J, **Wan X**, Lou C and **Wang B**, "Orthogonality and burdens of heterologous AND gate gene circuits in *E. coli*", ***ACS Synthetic Biology***, (2017) doi.10.1021/acssynbio.7b00328 (pdf)

Published: December 14, 2017