Synthetic Biology Research Centre Newsletter

University of Nottingham

Issue 2 February 2015

Synthetic Biology Research Centre – Nottingham Launch Event

The BBSRC/EPSRC Synthetic Biology Research Centre - Nottingham held its formal Launch event on 14th January 2015. Over 180 guests including international academics, industrial partners, research funders and leaders in the field of C1 gas fermentation gathered to celebrate the launch of the SBRC-Nottingham in the University's flagship research facility: the Centre for Biomolecular Sciences Building. An impressive line-up of distinguished speakers marked the launch. In opening the proceedings, the University's Vice-Chancellor, Professor Sir David Greenaway highlighted why the partnerships that the SBRC has already created with industry, the Research Councils and with academics in many disciplines are essential in making the new centre successful. He particularly paid thanks to the Research Councils for their support and their vote of confidence in Nottingham by awarding £14.3m of funding for Synthetic Biology to the University.

Left to right: Sir David Greenaway Vice–Chancellor, University of Nottingham; Prof Ian Shott CBE Shott Trinova LLP; Dr Celia Caulcott, BBSRC; Prof Nigel Minton, SBRC–Nottingham Director and Mr Steve Bagshaw, CEO FUJIFILM Diosynth Biotechnologies

Senior Candidate roles in Industrial Biotechnology, Synthetic Biology & Biology required.

We invite applications from suitably qualified candidates for Chairs in the following areas:

- Chair in Enzyme Evolution/Design
- Chair in Process Engineering
- Chair in Fungal Genetics
- Chair in Biocatalysis & Enzyme Engineering

For more information and how to apply please visit: http://www.nottingham.ac.uk/jobs/currentvacancies/ref/ACADIB

Closing date 10 April 2015

Research Fellows in Biology & Mathematical/Computational Modelling required.

For more information and how to apply please visit: http://www.nottingham.ac.uk/jobs/currentvacancies/cat/210

Closing date 13 & 18 March 2015

Dr Celia Caulcott, (Executive Director, Innovation & Skills, BBSRC), spoke of the importance that synthetic biology will play in our lives.

This was echoed by Mr Steve Bagshaw (CEO FUJIFILM Diosynth Biotechnologies) who spoke about why industrial biotechnology and synthetic biology were essential to industry and Professor Ian Shott (Chair of the SBRC-

Nottingham Strategic Advisory Board) who noted that synthetic biology and industrial biotechnology were developing from positions of strength at Nottingham. He stated that the University had excellent international credentials in synthetic biology which, although the technology was currently EU-and USA-centric, was spreading increasingly globally.

Professor Nigel Minton, (SBRC-Nottingham Director) spoke of the vision of the Centre and its ambition to demonstrate that society's current dependency on oil, coal and natural gas for chemicals can be broken and that our chemical industries can become greener and more sustainable. He said that the SBRC-Nottingham would carry out the underpinning research work to modify the metabolisms of existing bacterial species using synthetic biology approaches and make them act as mini-factories in biorefining. These adapted bacteria will use waste greenhouse gases such as carbon dioxide, carbon monoxide and hydrogen to create useful chemical feedstocks.

The packed programme continued with guided tours of the specialist gas-fermentation research laboratory facilities, networking, poster sessions and a thought-provoking Social Sciences seminar on Responsible Research and Innovation by Professor Paul Martin of the University of Sheffield. The University has invested significantly in bespoke facilities for the SBRC-Nottingham and, with the landmark

investment from BBSRC and EPSRC in the new centre, it is well-set for advancing our knowledge and application of microbial fermentation using cutting-edge science.

Research News

Improved pMTL80000 Modular Vectors for the SBRC

By Dr Jonathan Baker

Plasmids have become an integral part of modern molecular biology and are employed in a wide range of techniques including; gene modification, transposon library construction and protein expression. By 2008, several plasmids had already been employed in Clostridium but they did not share a common structure as they had been created by different groups. This caused some problems as directly comparable plasmids were required to identify which combination of vector elements were the most suitable for a chosen application in the particular bacterial species being studied. Also, once the desired elements had been identified the shuttle plasmids could not be constructed quickly, reliably or in a consistent way.

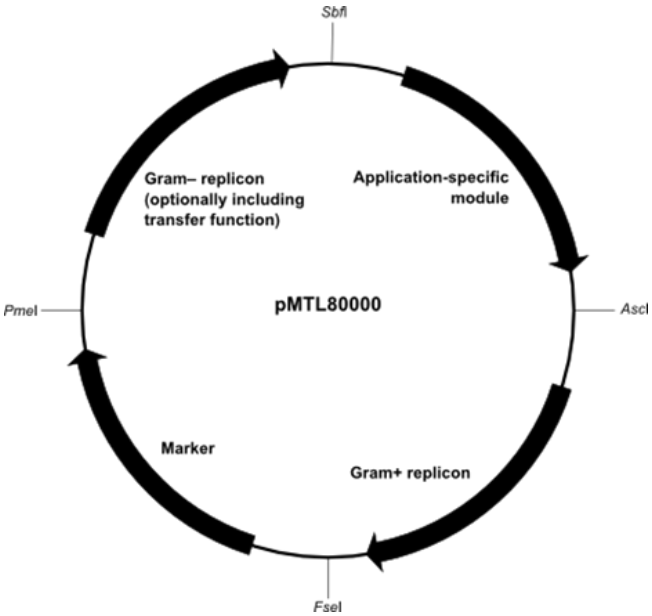
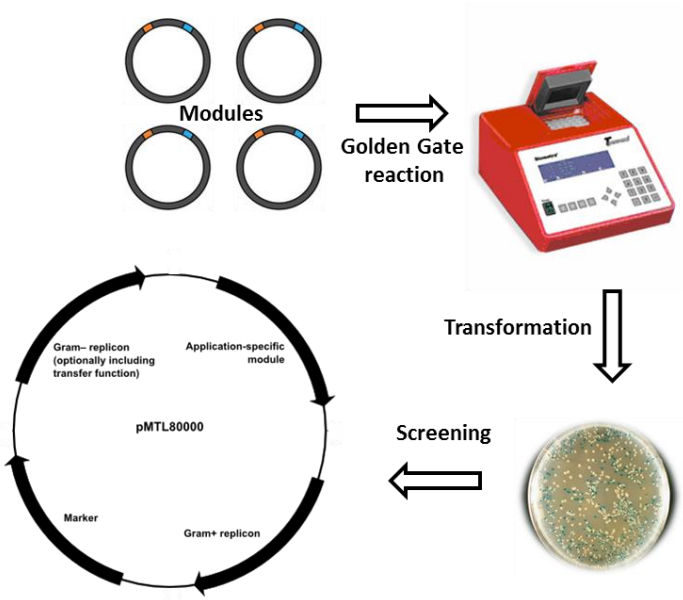


Figure 1. The pMTL80000 modular vector

The pMTL80000 modular vectors were developed by the University of Nottingham Clostridium Research Group to overcome these issues and create a systematic approach to shuttle plasmid construction (Heap et al., 2009). A standard plasmid arrangement consisting of four modules provided a straightforward means of in vivo vector element comparison. In addition, Individual modules could be easily replaced through using pairs of the four rare restriction enzymes included in the pMTL80000 design (Figure 1). This system has since been exploited by many research groups and is referenced in numerous publications.

Figure 2. Automated Golden Gate cloning builds entire pMTL8000 vectors from single modules in one quick reaction.



Modern synthetic biology is constantly changing to utilise the most cutting-edge methods and equipment available. Automation of classic molecular biology techniques is allowing researchers to greatly increase both the breadth and speed of their molecular research. However, the four restriction enzyme design of the original system is not suitable for automation and still necessitates manual DNA digests, agarose gel extractions and ligations to create the desired vector. Therefore our pMTL80000 plasmid system is currently being modernised at SBRC-Nottingham to overcome

these limitations. The powerful "Golden Gate" DNA cloning technique allows for large DNA constructs to be assembled using only one Type 2 restriction enzyme in a single digestion/ligation reaction (Engler et al., 2009). We are currently redesigning the pMTL80000 system to use Golden Gate cloning whilst retaining the module nature of the vectors. This preserves the useful features of the original pMTL80000 plasmids whilst allowing construction to become automated in a single reaction using premade single modules encoded on carrier vectors (Figure 2). This new methodology has been tested successfully in the lab, where a functional pMTL80000 plasmid was created in one 30 minute Golden Gate reaction.

Our new system of rapid automated Golden Gate vector construction will provide the necessary tools for the SBRC-Nottingham to create bespoke modules and devices in the application of synthetic biology.

Engler, C., Kandzia, R., Marillonnet, S. (2008). A one pot, one step, precision cloning method with high throughput capability. PLoS One. 3(11):e3647.

Heap, J.T., Pennington, O.J., Cartman, S.T., Minton, N.P. (2009). A modular system for Clostridium shuttle plasmids. J. Microbiol. Methods. Jul;78(1):79-85.

Dr Jonathan Baker
SBRC-Nottingham
email:
jonathan.baker@nottingham.ac.uk

My Research Area - Dr Jamie Twycross, Computer Science, SBRC-Nottingham

I am an Assistant Professor in the School of Computer Science at the University of Nottingham, and a Co-Investigator in the SBRC. I have a background in computer science, biology and mathematical physics, and research experience in both academic and corporate institutions. I currently hold a University of Nottingham Advanced Research Fellowship. In general, my research focusses on understanding how complex behaviour in biological, physical and artificial systems arises. Aside from the pleasure of simply finding out how something works, I use this understanding to predict and guide the behaviour of these systems, and to engineer similar behaviours into other distinct systems. A key feature of my research is its interdisciplinary nature: working with scientists from different disciplines to understand the complex systems that exist in their fields.

One of my main areas of expertise is in the development of multiscale computational and mathematical models of complex systems in fields such as systems biology, synthetic biology, and systems medicine. Building a model of a complex system helps to capture, rationalise, consolidate and extend our intuition and understanding of how a system works. Once we have developed a sufficiently accurate model, we can use the model system as a proxy for the actual system and, for example, rapidly explore different scenarios which would be much more costly in terms of time, money and effort to perform on the actual system. Working with researchers from a diverse range of disciplines, I have developed models of a wide variety of biological systems, including human immune system pathogen recognition, hormone signalling in plant roots, and bacterial quorum sensing signalling.

As a Co-Investigator in the SBRC, I lead the team of computer scientists, mathematicians and bioinformaticians working within the Centre. Our goal is to develop an integrated software suite which facilitates the rapid development of microbial chassis able to produce a range of platform chemicals, and which encapsulates cutting-edge research in novel modelling and analysis approaches. The software suite will provide a virtual lab for rapid prototyping and analysis of novel platform microbes, allowing wet and dry lab researchers to explore in silico a range of what-if scenarios before undertaking expensive and time-consuming wet lab experiments.

A key novel aspect of the software suite will be the integration of metabolic engineering and synthetic biology approaches. We also aim to develop synthetic biology devices which can be integrated into metabolic pathways and permit the monitoring and regulation of these pathways.

Dr Jamie Twycross
SBRC-Nottingham
email:
jamie.twycross@nottingham.ac.uk

Intellectual Property and Commercialisation

The SBRC–Nottingham has been established to accelerate the development of our understanding of how microbial metabolism can be tailored to economically generate chemical feedstocks sustainably from waste gases. From this fundamental science approach, the SBRC–Nottingham will develop new synthetic biology tools and resources to be utilised by industry as well as academia, globally. The SBRC-Nottingham will work closely with the University of Nottingham's Technology Transfer Office to identify, assess and protect IP as it arises. The objective is to ensure that, as far as possible, all IP that has exploitable value is identified and used appropriately to maximise research, environmental, societal and economic impact from the Research Council funding that underpins the Centre. The ambition of the SBRC-Nottingham is that the tools and resources it generates will be actively promoted to global audiences of academics and industrialists. The SBRC intends that, wherever practicable, any research tools it develops will be made widely available to industry through non-exclusive research and / or commercialisation licences. Patented technologies associated with the SBRC that are currently available through the University are listed below. They are available to companies either as commercial or research licences. To discuss your licensing needs please contact Dr Alan Burbidge, SBRC-Nottingham Centre Manager. Alan.burbidge@nottingham.ac.uk

SBRC-Nottingham Patents

Patent title	**Synthetic Operon Construction in Clostridia Allele Coupled Exchange (ACE)**
Publication number	WO 2009/101400
Description	An homologous recombination system that avoids the need for a heterologous reporter system and which enables large tracts of DNA to be inserted into a host bacterium such as *Clostridium acetylbutylicum*.
Academic publication	**Integration of DNA into bacterial chromosomes from plasmids without a counter-selection marker.** John T. Heap, Muhammad Ehsaan, Clare M. Cooksley, Yen-Kuan Ng, Stephen T. Cartman, Klaus Winzer, and Nigel P. Minton* Nucleic Acids Res. (2012); 40(8): e59. **Expanding the repertoire of gene tools for precise manipulation of the Clostridium difficile genome: allelic exchange using pyrE alleles.** Ng YK, Ehsaan M, Philip S, Collery MM, Janoir C, Collignon A, Cartman ST and Minton NP, (2013). PloS one. 8(2), e56051

Patent title	**A negative / counter selection marker for use in clostridia: Cod A selectable marker**
Publication number	WO 2010/084349
Description	The cytosine deaminase gene (*codA*) of *Escherichia coli* as a heterologous counter-selection marker for genetic manipulation of wild-type *C. difficile* strains. CodA not only converts cytosine to uracil but also converts the innocuous pyrimidine analog 5-fluorocytosine (FC) into the highly toxic 5-fluorouracil (FU) leading to incorporation of fluorinated nucleotides into DNA and RNA. It is this latter activity which allows CodA to be an effective counter-selection marker.
Academic publication	Cartman ST, Kelly ML, Heeg D, Heap JT, Minton NP (2012) Precise manipulation of the *Clostridium difficile* chromosome reveals a lack of association between *tcdC* genotype and toxin production. Applied Environmental Microbiology 78: 4683–90

Patent title	**ClosTron**
Publication number	**US 20110124109** (US-only patent)
Website	http://clostron.com/
Description	A type II intron system based on TargeTron which enables gene knock-outs through intron insertion in Clostridia
Academic publication	**The ClosTron: A universal gene knock-out system for the genus Clostridium.** Heap, J.T., Pennington, O.J., Cartman, S.T., Carter, G.P. and Minton, N.P., 2007. Journal of Microbiological Methods. 70(3), 452-464 **The ClosTron: Mutagenesis in Clostridium refined and streamlined.** Heap JT, Kuehne SA, Ehsaan M, Cartman ST, Cooksley CM, Scott JC, Minton NP. J Microbiol Methods. 2010 Jan;80(1):49-55.

Conferences

CALENDER

Of Key Synthetic Biology Activities and Events

19 March 2015
Public Lecture – PhD Student Florence Annan 'How to make jet fuel and other useful things from greenhouse gases'
18.00-19.00 B1, Physics Building, University Park, Nottingham, UK

21 March 2015
British Science Association
11.00-16.00 Science in the Park, Wollaton Hall, Nottingham, UK

25-26 March 2015
ACI Gasification Conference
Prague, Czech Rep
http://www.wplgroup.com/aci/conferences/eu-ecg4.asp

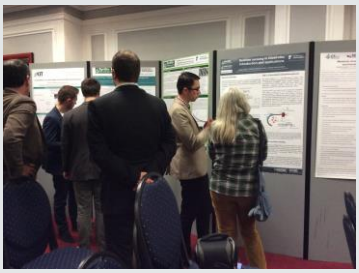
9 May 2015
Mayfest 2015
SBRC and C1net will be running hands on activities at the University of Nottingham's Community Open Day
Nottingham, UK

10-13 June 2015
Synthetic Biology: Engineering, Evolution & Deisgn
Boston Park, USA
http://synbioconference.org/2015

5-9 July 2015
Synthetic and Systems Biology Summer School ,
Sicily, Italy
http://www.taosciences.it/ssbss2015/

Chemicals from C1 Gas Conference 14-16 January 2015, Hilton Hotel, Nottingham

Hosted by C1net a BBSRC-NIBB this was a FREE two-day conference, which brought together academic and industrial partners, to identify and address key challenges in the study of those organisms able to grow on C1 compounds and commercially exploit them as platforms for chemical manufacture. The programme included talks from selected submitted abstracts, as well as from key academics and industry representatives. Some of the expert speakers included: Sean Simpson (LanzaTech), Peter Duerre (University of Ulm) and Auxiliadora Prieto (National Spanish Research Council). There was also a poster session and plenty of opportunities for networking.



Poster Session at the C1net Conference

Craig Woods, PhD student, University of Nottingham

Synthetic Biology Leadership Council Meeting 27 November 2014, Royal Academy of Engineering, London

The seventh meeting of the Synthetic Biology Leadership Council was the second open meeting to which members of the synthetic biology community and wider public were invited. Alan Burbidge (SBRC Centre Manager) gave a presentation outlining the scope and ambition of the SBRC-Nottingham, its focus on C1 gas utilisation for chemical feed-stocks and highlighting the importance of Responsible Research and Innovation to the mission of the centre. For more information: https://connect.innovateuk.org/web/synthetic-biology-special-interest-group/synbio-leadership-council

Industrial Biotechnology Showcase 11-12 February 2015, QEII Conference Centre, London

The Industrial Biotechnology Showcase organised by Innovate_UK's IB Special Interest Group brought together leaders in the field of IB and Synthetic Biology from both industry and academia. Nigel Minton, the SBRC-Nottingham Director gave a well-received overview of progress and activities being undertaken by the 'C1net', a BBSRC Network in Industrial Biotechnology and Bioenergy (NIBB) which he is leading and whose interests align closely with the SBRC-Nottingham. Over the two days of the Showcase, there were presentations on exciting high-throughput discovery programmes, synthetic biology approaches and the industrial application of IB and Syn-Bio making the showcase a valuable place to be for anyone interested in how the UK is harnessing the power of biology. For more information: http://ibts.meeting-mojo.com/

New to the Team

Hanna Doughty

I have recently joined the School of Life Sciences as a Laboratory Technician, working in the Synthetic Biology Research Centre. Before this, I was working as a Microbiology Technician in 2 Sisters Food Group, where I was screening food for a number of pathogens on behalf of companies such as Marks and Spencer, Aldi and Tesco. I graduated from Nottingham Trent University in the summer of 2014 with a BSc in Forensic Biology, with an emphasis on Molecular Biology. Whilst I was there, I developed my interest in microbiology through my dissertation which centred around evaluating molecular techniques for defence against Category A bioweapons. I am very much looking forward to expanding on my experience and working with the research teams within the School.

James Winter

I have recently joined the School of Life Science as a member of the newly formed Synthetic Biology Research Centre. After graduating from Nottingham-Trent University with a BSc honours degree in Forensic Science, I spent four years working for Abbott Laboratories as a Fermentation Technician where I manufactured targeted proteins for use in diagnostic blood testing kits. Later I moved into Technical Product Development where I investigated process issues and tested planned process improvements. Subsequently I worked for Coca Cola Enterprises as Senior Microbiology Technical Operator where I monitored and dealt with issues concerning contamination throughout the factory, after which I worked for BioProduct Laboratories as a Plasma Processing Technician. I have long aimed to leave the commercial working environment for an academic and research based career, so I am very excited to be working at this renowned University. I look forward to making many new friends during the next five years and exploring everything the University has to offer.

Andrew Mutch

I have recently joined the School of Life Sciences as a Research Technician in the Synthetic Biology Research Centre, having just completed a MSc in Molecular Cell Biology. Prior to studying for my masters I worked both in the NHS and in the formulation development wing of the pharmaceutical company Aeisca as a pharmaceutical analyst. I am very much looking forward to working in a research lab environment and expanding both my knowledge and skills.

Tom Bailey

Following my undergraduate studies in Sheffield, I joined the Clostridia Research Group in 2008 as a PhD student. At that time there were less than 10 researchers! The group saw rapid expansion during my four years of study, and has continued to grow since then. I graduated in 2012, and continued to work for the University in a number of roles over the subsequent two years. These included work for the Student Lifecycle, Market Intelligence, Research and Graduate Services and the International Office. I have recently returned to Nigel Minton's lab, primarily to manage the upcoming Marie Skłodowska-Curie ITN, titled 'CLOSPORE'. In addition, I will be supporting the GASCHEM researchers and managing the group's finances.

Other News

Vice-Chancellor's Achievement Awards 2015
University of Nottingham

Professor Nigel Minton
(SBRC Director)
Nominated by Klaus Winzer, Associate Professor.

Professor Minton is being awarded for his outstanding achievements in the area of industrial biotechnology, which have not only enhanced the reputation of the University but also resulted in considerable positive impacts for both staff and students.

Prof Nigel Minton, SBRC Director and Prof Sir David Greenaway, Vice-Chancellor, University of Nottingham

SBRC Website & Twitter

The SBRC Website has now been officially launched!!

www.sbrc-nottingham.ac.uk The website will be a dynamic portal with several important and key global audiences. This will be updated on a regular basis with news, features, events and outreach activities.

SBRC Twitter is also now available and we have reached over 70 followers**!** Keep up to date daily with all SBRC news as well as synthetic biology news and activities.

@SbrcNottingham

Outreach Activities

SBRC Outreach Primary School Visit

Huntingdon Academy, Nottingham

19 November 2014

As part of the BBSRC's Great British Bioscience Festival, Louise Dynes and PhD student Sarah Mastrangelo made a visit to Huntingdon Academy in Nottingham to introduce pupils from Year 5 into a world of microbiology and how bacteria can help us produce biofuels. Pupils explored what different bacteria looked like, all the weird and wonderful things they can do and who are the bacteria heroes and who are the bacteria baddies. The pupils used what they learnt to design their own bacteria to take home!

Nottingham University Academy of Science and Technology Opening Evenings

The SBRC and C1net have now attended 4 open evenings at NUAST since November 2014. NUAST is a new type of academy offering a specialist curriculum at KS4 and KS5 for students with an interest in science, engineering or computing. The academy has various links with industry and both Nottingham Universities.

Prospective Year 10 and Year 11 students and their parents got to hear straight from the young scientist's themselves about how and why they got into science. It provided a great opportunity to engage and educate both pupils and parents on research going on in the SBRC.

More details about the academy and what they offer can be found here: http://www.nuast.org.uk/index.php

Louise Dynes
Synthetic Biology
Outreach and Communications Officer
Centre for Biomolecular Sciences Building
The University of Nottingham
University Park
Nottingham, NG7 2RD

SynBio
SBRC Nottingham
a BBSRC/EPSRC Synthetic Biology Research Centre