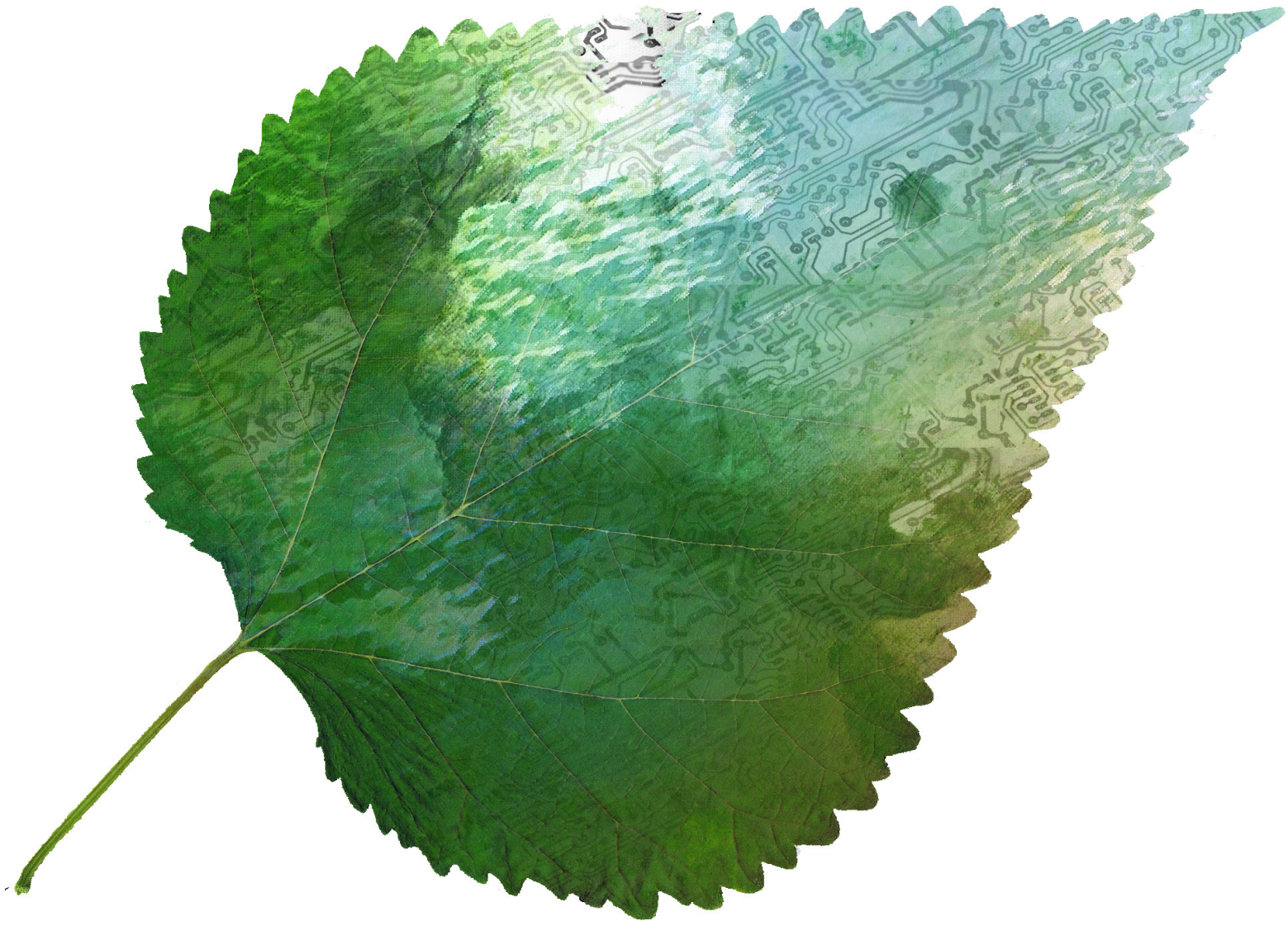
# Developing Plant Synthetic Biology in the UK



## Opportunities and Recommendations

# Developing Plant Synthetic Biology in the UK

Report from the 2013 GARNet meeting

*An Introduction to Opportunities in Plant Synthetic Biology*

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## Table of Contents

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## Abbreviations

BBSRC: Biotechnology and Biological Sciences Research Council

EPSRC: Engineering and Physical Sciences Research Council

RCUK: Research Councils UK

SBLC: Synthetic Biology Leadership Council

SynBio SIG: Synthetic Biology Special Interest Group

TSB: Technology Strategy Board

# 1 Executive Summary

Synthetic biology is the design or re-design of biological processes. In living systems, synthetic biologists use innovative DNA assembly and editing tools to build synthetic systems from the bottom up with orthogonal DNA 'parts,' or intervene in other ways to alter a biological component or process in a predictive way.

To date, most *in vivo* synthetic biology has been done in microorganisms, but as the technology matures it is becoming necessary to trial synthetic biology in multi-cellular systems. Plants are the logical choice as they are sessile, self-sufficient, have self-maintaining and repairing organs, and are free of many of the ethical issues that surround synthetic biology in animals.

UK plant scientists are in an excellent position to join the global community in pushing the boundaries of plant synthetic biology. UK plant science has a track record of embracing new research areas; for example two out of six systems biology centres funded in 2005–6 had a plant science focus, and today a number of plant scientists are key players in the systems biology arena. Since synthetic biology depends upon predictable systems, this expertise provides a good foundation for the future.

Additionally, UK plant researchers are supported by two formal networks: GARNet works alongside basic plant science research groups to provide training and information about new technologies, and acts as a link to their major funder, BBSRC; and the UK Plant Sciences Federation, which represents all plant science stakeholders at policy level, and connects research institutions to agriculturalists, educators and industry.

UK plant synthetic biology has an excellent research base and community structure to build on. To establish the community among the world leaders in synthetic biology, GARNet proposes the following actions. We expect that OpenPlant, one of three multi-disciplinary research centres funded jointly by BBSRC, EPSRC and TSB in 2014, will carry out a number of these recommendations.

**Enabling community sharing of biological parts** and **establishing an open source software repository** will provide plant scientists with the resources they need to explore synthetic biology approaches with low financial risk.

**Inspiring a generation of plant synthetic biologists** by ensuring opportunities for students to explore synthetic biology, and **enabling training, partnerships and collaborations** in order to equip researchers at all career stages with the appropriate skills to explore this new area.

**Stakeholder mapping and public engagement**, working with groups such as the SynBio SIG and Sense About Science, to improve the regulatory environment and **explore licensing options** surrounding synthetic and genetically engineered plants.

**Incentivising development of new tools and approaches** will ensure continued expansion of the scope of plant synthetic biology.

## 2 Introduction

Synthetic biology is an emerging field that unites scientists from all disciplines with the aim of designing or re-designing biological components, processes and systems. It is a broad church even within biology, spanning molecular biology, bioinformatics, genomics, developmental and cell biology. In recent years, exciting synthetic biology breakthroughs have come from the physical sciences, including chemistry, physics, computer science, materials science, mathematics and a range of engineering disciplines.

In some expert views, synthetic biology must produce something useful for commercial or altruistic purposes (Arkin *et al.*, 2009). However, fundamental research is inherent even in product-driven synthetic biology research: designing something means understanding it. For biologists, designing biological parts, processes and systems for any purpose means reprogramming them, often from the DNA level up.

To biologists, the idea of approaching science like an engineer by designing, building and testing biological processes is novel and exciting, but it is not the whole story. It can be helpful to approach synthetic biology more as an architect would: to consider the whole package from a creative perspective rather than a purely mechanical one. This can give rise to novel ideas, which may be quite different from simply applying synthetic biology to standard biological research (Ginsberg, 2012). Additionally, commercially viable synthetic biology needs to be marketable and desirable, so considering its aesthetic and realistic application is as important as the mechanics of what is feasible.

The UK Government is investing in synthetic biology as an attempt to drive innovation in science and, in the longer term, to be of benefit to industry and the economy. In early 2012 the Minister for Universities and Science David Willetts announced the launch of a Synthetic Biology Roadmap to plan the development of a world-leading synthetic biology industry in the UK. In November 2012 the Chancellor George Osborne announced a £20 million investment, and in 2013 that investment materialised as funding for several interdisciplinary synthetic

biology centres. One of three centres announced in 2014 is OpenPlant, a research centre aiming to promote open innovation and new developments in plant synthetic biology.

There are already a few standout synthetic biology projects at UK institutions. A team at the University of Bristol has developed an elegant tool kit of coiled-coil peptides (Moutevelis and Woolfson, 2009; Fletcher *et al*., 2012) to standardise *de novo* protein construction. The kit has now been applied to a growing number of *de novo* protein structures including self-assembling cages (Fletcher *et al*., 2013). Inorganic chemical cells with porous membranes, which have the capacity for redox activity and self-repair (Cooper *et al*., 2011), have come out of research at the University of Glasgow. A UK consortium led by the University of Nottingham has shown that synthetic molecules can even interact with biological systems; a custom designed polymer can both sequester cells from suspension and inhibit quorum sensing in *Vibrio harveyi*, sister species of cholera-causing *V. cholera* (Xue *et al*., 2011). Imperial College London is a key collaborator in the Yeast 2.0 initiative, which aims to build and test a chassis with a minimal synthetic genome; an important goal for synthetic biology (Dymond *et al*., 2011).

GARNet, the UK Arabidopsis Research Network, ran a workshop in April 2013 to address questions surrounding plant synthetic biology: what are the advantages of doing synthetic biology in plants? Which synthetic biology tools are available to plant scientists? What is needed to build a strong plant synthetic biology research base in the UK?

This report is a summary of issues raised and conclusions drawn in discussion sessions at the GARNet workshop (see Appendices 2 and 3), intended to assess the status and potential of plant synthetic biology in the UK.

# 3 Why Plant Synthetic Biology?

## *3.1 Intrinsic advantages to plants as synthetic biology systems*

To date most synthetic biology has been at the single cell or molecular level. The next step is to build or re-engineer multi-cell pathways and test synthetic signalling and processes in multicellular organisms. Plants are the obvious candidates for a multicellular model for synthetic biology because they are legally, ethically and economically easy to work with compared to animals or animal tissue. In the laboratory, if not in the field or commercial market, plant science is not affected by ethical considerations. They are sessile and their cells are organised into fixed tissues and organs.

Plant cells are themselves compartmentalised, with predictable pathways governing where metabolites are sent, presenting the opportunity for whole systems to be siloed into organelles rather than affect the overall genomic or metabolomic profile. Plants can fuel themselves with minimal outside input and are self-generating and self-repairing, so most changes to a plant's molecular biology or phenotype can be removed or reset easily.

Additionally, plant science presents a partially characterised but wholly untapped reservoir of genetic diversity that has not been considered from a synthetic biology viewpoint before. Finally, it would be possible to reproduce and disseminate any plant synthetic biology product simply by collecting seeds.

### *3.2 The UK plant science community as an excellent synthetic biology research base*

Although not unique to plant science, the established plant science research base is an important benefit to UK plant synthetic biology. The plant science community is fast to adopt new technologies and research approaches. For example, several plant scientists have become national and international experts in systems biology in the short time since systems biology centres were funded by RCUK. Some research groups have already embraced synthetic biology (see Section 4); the Sainsbury Laboratory appointed a Head of Synthetic Biology in 2013; and the BBSRC/EPSRC/TSB-funded multi-disciplinary OpenPlant Centre, based in Norwich and Cambridge, aims to deliver a number of synthetic biology tools, resources and training opportunities for plant science.

### *3.3 High impact applications of plant synthetic biology*

Beyond the short-term practicalities of plants as synthetic biology systems, plant synthetic biology can be applied to several major world challenges.

Food security is an RCUK cross-council priority and a priority for G20, the international consortium behind the Global Food Security and Agriculture Programme. Population growth and the expectations of an expanding global middle class are putting ever-larger demands on fertile land. Global climate change is gradually changing the agricultural landscape, and extreme weather events regularly devastate harvests. Although agri-technology is only part of a solution, synthetic biology has many applications in this area. Regulations in some parts of the world, including the European Union, make it unlikely that fields of synthetic plants will become commonplace. On the other hand, simply applying synthetic biology approaches and ideas to crop science can impact crop improvement. A tool developed by synthetic biology approaches has already

been used to develop non-transgenic rice plants resistant to *Xanthomonas oryzae*-induced blight (Ti *et al*., 2012).

Soil quality and nutrient use efficiency are significant factors in agricultural sustainability. Nitrate and phosphate fertilisers are extensively applied to farmland, but this activity is not sustainable. Nitrate run-off and release of nitrogen in the form of $N_2O$ and $NO_x$ gases have environmental consequences (Good and Beatty, 2011), while the finite supplies of phosphorus are dwindling (Elser, 2012). A phosphorus-fixing pathway would need to be built from scratch, but it is a conceivable application for synthetic biology. Nitrogen-fixing staple crops are already a realistic goal, as described in Section 4.1.

Plants have been known to synthesise compounds with medical properties for many decades. High-profile examples are the cancer drugs vincristine from *Catharanthus roseus* and paclitaxel from *Taxus brevifolia*, and anti-malarial artemisinin, found naturally in *Artemisia annua*. Traditional molecular biology approaches failed to provide efficient plant factories for vincristine and paclitaxel, which are currently produced in yeast and by chemical means respectively. In 2013, synthetic biology approaches enabled efficient production of artemisinin in yeast; in future they may be applied to the *in planta* commercial production of as yet undiscovered plant metabolites.

Plant synthetic biology could also be applied to the production of high value goods; indeed 'luxury' goods may be the first marketable synthetic biology products in some countries. It is conceivable that part-synthetic houseplants could provide home fragrance, decoration, or gas or carbon monoxide detectors. Equally, new luxury foods fusing two flavours or colours together may be produced for novelty value.

Generally speaking, plants are well received in every human environment. Synthetic microbes have a plethora of exciting applications, but in homes and public spaces people may be likely to favour synthetic or re-designed potted plants than microfilms of man-made bacteria.

# 4 Plant Synthetic Biology in Progress

## *4.1 Impact-driven plant synthetic biology*

There are several on-going plant synthetic biology projects aiming to deliver high-impact end products at various stages of development.

Previous work from Giles Oldroyd (John Innes Centre) characterised the components of the pathways underlying rhyzobium symbiosis (Xie *et al*., 2012; Capoen *et al*., 2011; Oldroyd *et al*., 2011). Over the last two years, two grants have been awarded to the group enabling them to focus on re-creating the pathways in wheat. Their goal is to build wheat plants with a completely synthetic pathway allowing the plants to have a symbiotic relationship with nitrogen-fixing rhizobium species. If achieved, this will effectively make wheat crops self-fertilising and will eliminate the need for nitrate fertiliser.

June Medford and her group at Colorado State University have been working on a synthetic plant for over ten years, and have built a functional synthetic pathway in *Arabidopsis.* The group's goal is to develop plants containing biosensing pathways that detect dangerous levels of volatile compounds in public spaces.

Medford's biosensor pathway is based on a prokayotic signal transduction pathway. Importantly, this means the synthetic system is isolated from endogenous activity, minimising cross-talk within the plant cellular environment and maximising signal detection. The plant biosensors, or 'sentinels', can be adapted to detect any molecule. The proof-of-concept studies used TNT:

- TNT was detected in the apoplast by a computationally re-designed bacterial periplasmic binding protein (PBP), a trans-membrane chemotactic protein (Looger *et al*., 2003).
- A Trg domain on the PBP detected TNT and the histidine kinase domain activated a synthetic PhoB molecule (Antunes *et al*., 2011).
- The DNA-binding PhoB molecule targeted a specifically designed PhoB-responsive promoter (Antunes *et al*., 2009), triggering rapid chlorophyll loss and de-greening the leaves.
- The de-greening circuit was re-set once TNT levels become undetectable (Antunes *et al*., 2006).

### *4.2 Experimental plant synthetic biology*

The two projects described above fit what might be considered goal-oriented, impact-driven synthetic biology. Other plant scientists are using synthetic biology approaches to push the boundaries of their fields, and many are exploring and quantifying certain aspects of plants to serve the wider plant science community, in addition to progressing their own research.

An orthogonal 'toolkit' for plant synthetic biology may be derived from recently identified operon-like clusters (Field *et al*., 2011; Mugford *et al*., 2013). In bacteria, novel antibiotics have been biosynthesised by identification, characterisation, and re-arrangement of gene clusters (Gottelt *et al*., 2010;

Gomez-Escribano *et al*., 2012). The discovery that some plant secondary metabolite genes, such as antimicrobial triterpenoids in oat, are encoded by gene clusters (Mugford *et al*., 2013) presents the possibility of shuffling genes within a cluster to generate novel compounds in plants. This works in much the same way as in bacteria, thus expanding the possible biomedical applications for plant synthetic biology beyond simply working with existing plant metabolites.

It is not appropriate to put off synthetic biology until the data-gathering groundwork is done as it is impossible to know every biological process in a living organism. However, understanding the system you wish to re-design or put a synthetic process into is important. Jim Haseloff's lab at the University of Cambridge is working toward building self-organising switches with the ultimate possible goal of re-programming plant morphogenesis, or other aspects such as plant–microbe interactions. The starting point was new imaging tools to visualise cellular dynamics (Federici *et al.*, 2012) and models to predict and test self-organising circuits (Rudge *et al*., 2012).

Despite the advantages of plants as a model for synthetic biology, it remains a fact that plants are far more complex than any existing synthetic biology models. They have complicated signalling pathways, many organs, and often have very large genomes. A group of international collaborators propose the lower plant liverwort *Marchantia polymorpha* as a new model for synthetic biology due to its streamlined genome architecture (Ohyama *et al*., 2009) with less redundancy than *A. thaliana*, developmental simplicity, and easy cultivation in culture on agar or on soil. If 'explorative' plant synthetic biology is to become an established field in the UK, adoption of new model systems like Marchantia may be necessary.

# 5 Horizon Scanning

## *5.1 Laying the road to the future*

The plant synthetic biology endeavours above, inspirational as they are, are only the start of what can be achieved. There is a Kickstarter project to source crowdfunding to make luminous *Arabidopsis thaliana* plants – will motorways one day be lit by glow-in-the-dark grass? Will the gardeners of the 23rd century be intercropping phosphorus-fixing runner beans with personalised medicinal tomatoes? Will parts for pre-fab houses be grown in orchards? If some of these ideas are improbable, others are not only possible, but are arguably predictable profit-makers for their inventors and investors.

The UK is well placed to deliver these or similar plant products. Firstly, the UK plant science community has an excellent research base. It is second only to the

USA in terms of publication impact (SCImago, 2007). It also has a good history of adapting to new challenges, for example in 2005/2006 seven new systems biology centres were established, two of which had a plant science focus. GARNet, the grassroots network for plant researchers, played an important role in promoting systems biology to plant scientists and liaising with BBSRC about what was needed in order for the community to lead the field. GARNet can play a similar role in encouraging the uptake of plant synthetic biology approaches and enabling community initiatives, for example to define standardised 'parts,' if required.

Furthermore, UK funding of pure and applied research, and crop and model species, has traditionally been balanced but separated. The UK Plant Sciences Federation, founded in 2011, encourages and facilitates networking between these groups, so opportunities for collaborations between very varied plant science stakeholders are available.

Finally, members of the Research Councils UK (RCUK) consortium have a requirement that outputs generated from their funding be made open access. To date, synthetic biology initiatives all over the world have taken an open approach to their work, making software open source and donating gene constructs to community-based repositories. The RCUK policy ensures any resource or tool from a publically funded project will be accessible for others to use, thus saving time and money for UK plant scientists and guaranteeing visibility for the UK on the world stage when researchers based elsewhere use the resources.

If we are to make inroads towards establishing a successful and economically important plant synthetic biology research base in the UK, there are a number of barriers to be overcome.

## *5.2 Community resources*

### *5.2.1 Challenge 1: Accessing synthetic biology tools*

Synthetic biologists aim to design, or redesign, DNA to build biological systems in much the same way that engineers design machines. Being a core component of synthetic biology approaches, much of synthetic biology will initially focus on designing new biological 'parts'. A list of biological parts repositories and molecular tools is found in Appendix 1. Thus far, the synthetic biology community has been open and willing to share biological parts on a share and share alike basis.

A common approach, and the way in which the majority of DNA parts described in Appendix 1 can be synthesised, is to use open source data. In fact, Gibson Assembly and *de novo* assembly are the two most common assembly standards

or methods used by synthetic biologists (Kahl and Endy, 2013). Some synthetic biology tools can also be purchased as a commercial kit. However, for many researchers working with a limited budget and exploring synthetic biology for the first time, *de novo* synthesis or purchasing commercial kits are not viable options. For example, services provided by Gen9, DNA 2.0 and Genescript start at between $0.29 and $0.35 per base pair for the synthesis of sequence-perfect clones. As most research projects require multiple constructs, and a number of replicates are necessary, the costs may mount into thousands of pounds.

In addition to the financial cost of synthesising parts, it is important to consider the redundancy in man-hours and funding incurred when groups synthesise the same constructs. Individual research groups may be synthesising the same modules and primers independently, for example a widely used promoter or antibiotic resistance gene, which is an inefficient use of time.

There are community-based repositories that enable sharing of parts, although currently none specifically serve plant scientists. According to a survey of synthetic biologists (Kahl and Endy 2013), the most extensively used parts database in 2013 was iGEM's (international Genetically Engineered Machine) Registry of Standard Biological Parts. This repository was founded to record and distribute biological parts developed in the annual iGEM synthetic biology competition for undergraduate students, so that each year teams could use and build on parts from previous years. Today anyone from industrial researchers to postgraduate students can register as a user, but the Registry still relies on community contribution and policing. Users deposit and request DNA parts including promoters, primers, ribosome binding sites and protein domains, all at no cost. Quality of parts is tested but not assured centrally; the results of the tests are online for users to assess before ordering the part. Users are also encouraged to review the part once they have used it.

Addgene is a commercial US-based not-for-profit organisation, which, like the iGEM model, depends on the willingness of the community to share products from their lab. According to the survey by Kahl and Endy, it is the third most commonly used parts registry (the second being ATCC, a resource for microbiologists). Plasmids are around $65 for non-commercial labs, which allows central quality assurance and a straightforward website and distribution structure. More advanced 'kits' are also available from Addgene, for example the Golden Gate TALEN kit, which is available for $425. However these costs can become prohibitive when many components are required, and there are potential issues of control, longevity, access and delivery from a US base.

### *5.2.2 Challenge 2: Tools to manage, curate, and mine information*

In plant science the extensive 'omics databases delivered by systems biology research projects are a valuable resource and an important advantage to plants as synthetic biology models. Having as much information as possible about the cell, tissue or organism in which they are working is crucial for synthetic biologists; re-engineering or co-opting a natural process is easier than building a system from scratch.

Additionally, synthetic biologists must work around complex and often unpredictable processes that keep cells alive and functioning. Reliably predicting how synthetic parts will interact with essential processes is important, and is only possible if systems data is available and re-usable. It is therefore vital that scientists have the means to mine and re-analyse large datasets.

### *5.2.3 Action 1: Setting community standards and a mechanism for parts sharing*

The lack of global standards for synthetic biology means that the parts repositories mentioned above do not provide a reliable alternative to *de novo* synthesis, even for commonly used parts. This presents a financial barrier to synthetic biology that some research groups are unable to overcome. Numerous but niche software tools may act as a barrier or disincentive for plant scientists to engage with synthetic biology.

The first step towards community sharing of biological parts for plant synthetic biology is to establish a set of community agreed standards. A very successful model to do this is Minimum Information about a Microarray Experiment (MIAME). This was agreed over a two-year period at several meetings (Brazma *et al*., 2001), and abiding by MIAME guidelines is now a requirement of authors when publishing results from microarray experiments. Once agreed, researchers could be encouraged to use a standard assembly tool, set of promoters and antibiotics, and agreed software for specific applications. This need not be obligatory: every group could assess the needs of each project individually, and the agreed standards would be used when two or more options are suitable. In a short amount of time, there would be a critical mass of standardised 'parts,' making community sharing easier. GARNet has successfully facilitated a similar process in the past for genomics tools, and will make it a priority over the next five years.

OpenPlant, a synthetic biology community and research programme co-led by Anne Osbourn (John Innes Centre) and Jim Haseloff (University of Cambridge), plans to work with the UK and European communities to set standards and explore options for a pilot scheme for open distribution of biological and software parts. GARNet will work with OpenPlant to engage with the community about such a system. It may be necessary to incentivise the contribution of parts to a physical central repository, for example by giving each biological part an ID

number that can be quoted in publications, thereby allowing users to track the use of their parts.

#### *5.2.4 Action 2: Open source software repository*

At present there are many open source tools to facilitate synthetic biology: Infobiotics Workbench, GenoCad and J5 from JBEI are just three. However, there is no central software repository offering an overview of the tools available in order for a user to make an informed decision about which modelling or experimental design tool to use for their application. As more plant scientists explore synthetic biology, a central database of up-to-date online and open source synthetic biology resources, including brief descriptions, dates of updates and manuals where applicable, would be very valuable. Although the website itself need not be new, such a database would need a team of experts to regularly assess the suitability of the resources to which users are directed.

OpenPlant will develop a database for software-defined parts, synthetic biology programmes or online apps, for example to perform automated quantification and assembly. New tools, with tutorials, will be developed via a special seed fund and all OpenPlant-initiated resources are expected to be shared centrally on www.openlabtools.eng.cam.ac.uk.

Ideally, a central plant synthetic biology repository would allow users to build custom constructions *in silico*, using community standard methods. The only similar resource available is J5 from JBEI, which was exclusively licensed to spin-out company TeselaGen in 2012, making its long term future as an open resource uncertain; and the soon to be public SynBIS from Imperial College London. Neither resource was designed for or by plant scientists. It is hoped that the OpenPlant platform will build into a valuable resource for the global synthetic biology community, in addition to the UK plant synthetic biologists for whom it will be designed. It will also be an excellent education and outreach tool for plant science education and for promoting synthetic biology to new researchers.

### *5.3 Skills and training*

#### *5.3.1 Challenge 3: Multidisciplinary skills and collaborations*

Synthetic biology is inherently interdisciplinary, which presents a challenge to traditional science education and training. In the early stages of synthetic biology, where the UK plant science community currently stands, common collaborators are mathematicians, computer scientists, chemists and social scientists. As a project develops towards application, plant scientists may find

themselves working alongside designers, agriculturalists and engineers. It is therefore important that biologists have sufficient understanding of these disciplines in order to collaborate efficiently in multi-disciplinary projects.

The interdisciplinary research centres and initiatives funded by RCUK, the iGEM competition and multidisciplinary doctoral training centres are essential hubs for encouraging the interdisciplinary collaborations that synthetic biology requires. However, they do not have a sufficiently broad scope to give all scientists wishing to use synthetic biology the necessary skills.

### *5.3.2 Challenge 4: Reluctance to explore new technologies*

Among some scientists, there is wariness of new tools and technologies – and for some good reasons. Many of the tools listed in Appendix 1 are very new, for example the CRISPR/CAS9 genome editing method, which was first described in plants in August 2013. As discussed in Section 5.2.1, there is also a financial barrier to synthetic biology approaches. Some research groups will decide they cannot afford to invest in novel synthetic biology approaches using funds from an existing grant, and many groups operate on very limited funds while preparing grant proposals. The actions suggested in Section 5.2.3 are intended to lower the financial barrier, but the risk that a protocol will be problematic when there is no expert to guide and advise, nor a critical mass of publications with descriptions of the method in different species, would still apply even if the biological parts were easily available.

### *5.3.3 Action 3: Inspiring a generation of plant synthetic biologists*

Biotechnology YES is an entrepreneurial competition in which teams of UK PhD students write business plans for a hypothetical business, based on real science. A plant-focused Biotechnology YES or spin-off competition would both encourage plant scientists into a synthetic biology mindset and promote plant synthetic biology to other disciplines.

Establishing a plant-focused synthetic biology competition similar to the iGEM model would again encourage plant scientists to use synthetic biology and promote plant science to other synthetic biologists. Some plant science projects have been entered into iGEM in the past, and OpenPlant plans to expand opportunities in plant synthetic biology for the Norwich and Cambridge iGEM teams, but the long timescales involved in working with plants – as compared to bacteria – limit opportunities in plant systems. GARNet will work with the Synthetic Biology Special Interest Group (SynBio SIG) to explore the possibility of establishing a spin-off competition for plant synthetic biology with a plant-appropriate timescale and rules.

Recent advances have made plants a more viable option for synthetic biology competitions, and for Masters and undergraduate projects:

- Wisconsin Fast Plants® is a rapid cycling variety of *Brassica rapa,* which grows into a seedling in three days and flowers in 13–17 days. They were developed for experimental science lessons, but their accelerated life cycle makes them a good system for the iGEM competition timescale of a few months.
- Marchantia has a short life cycle and is easily maintained and transferred between agar, soil and tissue culture. Both *Brassica rapa* and Marchantia can be transformed with high efficiency.
- The CPMV-HT transient expression system allows rapid, extremely high-level, transient expression of foreign proteins (Sainsbury and Lomonossoff, 2008; Vardakou *et al.*, 2012) in *Nicotiana benthamiana,* and is another excellent tool for a short-term plant synthetic biology project.

### *5.3.4 Action 4: Enabling training, partnerships and collaborations*

Researchers considering synthetic biology approaches would benefit from a reliable, curated, central online guide to synthetic biology methods. Excellent online resources already exist for some synthetic biology tools (see Table 1). A central website would link to good protocols, either pre-existing or commissioned, and have a 'frequently asked questions' page for each method, containing expert explanations of its applications as well as technical advice. GARNet has provided the community with similar resources for genomics and systems biology in the past, and is well placed to deliver an informative online guide to synthetic biology.

Summer schools to deliver intensive training to graduate students and early career researchers have been successfully run by the Gatsby Foundation and the Centre for Plant Integrative Biology (CPIB) at the University of Nottingham. The summer school model could be used to train early career scientists in skills relevant to plant synthetic biology: Golden Gate cloning, software engineering, computational modelling, or use of a synthetic biology CAD tool, for example. However, it is important that in the long term, basic computing and modelling training is integrated into undergraduate programmes to make young scientists aware of possibilities in synthetic, integrative and systems biology, and to equip them to embark on related career paths.

For more senior researchers vying for funding, the EPSRC IDEAS Sandpit model has been well received and is suited to innovation and networking for synthetic biology. The 'Sandpit' is an intensive residential workshop model in which participants from a wide range of backgrounds, industries and disciplines are challenged to come up with a novel research project and plan its delivery. After

the event, teams write proposals and funding may be awarded to projects from the Sandpit. A Synthetic Biology Sandpit, run jointly with the US funding body NSF, distributed £6 million between five projects, including Syntegron (http://www.syntegron.org/), Cyberplasm (http://cyberplasm.net/) and Synthetic Aesthetics (http://www.syntheticaesthetics.org/). A plant synthetic biology community would attempt to secure funding for a repeat event, and would strongly encourage plant scientists to attend.

A more informal alternative to a Sandpit, more suitable for early career researchers and without the hefty funding incentive, are hackathon-style 'Research Hotels.' Groups of scientists would use existing sequence, pathway and metabolite data and open source tools to design a potential synthetic plant pathway or product. A similar model has been successful in the 'Mathematics in the Plant Sciences' workshops run by CPIB. During these workshops, teams of mathematicians and computational biologists work on problems pitched to them by plant scientists. With funding, this workshop could continue as a synthetic biology event.

OpenPlant will establish laboratories in Cambridge and Norwich. These will provide access to specialised equipment, and will form the physical bases for training workshops, and incubators for collaborations and new projects.

## *5.4 Biotechnology regulations and licensing*

### *5.4.1 Challenge 5: EU regulations and public support*

A major challenge to commercial applications of synthetic biology is the public perception of genetically modified organisms (GMOs) in Europe. Current EU regulations on genetically modified crops make this a particular challenge for crops with a synthetic part, but it is likely to present problems for synthetic microbes too. Although the UK Government actively funds GMO research and is vocal in support of field trials, EU regulations are too restrictive for industry to profit from investing in bringing GMOs to market. Politically, public opinion in Europe makes changing agricultural technology regulation difficult.

Public engagement linked to GMOs has been accused of being condescending, of simplifying and polarising the debate, focusing on technical rather than political issues, and of being one-sided and defensive. Professional science communicators are not common, and scientists need guidance when they engage with the public over a political issue. Equally scientists and learned societies must take a strong stand on GM, and work with social scientists to communicate the real risks and benefits of synthetic biology effectively.

### *5.4.2 Challenge 6: Intellectual property*

As described in Section 5.2.1, the academic synthetic biology community has an ethos of 'share and share alike' via community repositories, and the right to use commercial materials is usually granted for free or at a very low cost, either informally or formally. Biotech companies, however, do not share the same benefits and have to negotiate a minefield of potential patent infringements (Ledford, 2013). For them, doing synthetic biology is like building a bridge while negotiating and paying for the right to use every single part and technique.

In some cases, legally using technology in a commercial laboratory is impossible. For example, use of some materials of academic origin by commercial companies may be restricted by their originators in research institutions and universities from use in commercial research or processes, and greater flexibility is needed to negotiate or discuss options with the owner of the material. Consequently, companies must spend time – sometimes months – finding or developing an alternative method.

Some sections of the synthetic biology community are beginning to tackle this issue. Biotech company DNA2.0 has released the gene sequences of three fluorescent proteins, which were designed from scratch after finding that pre-existing proteins could not be used without buying expensive licences. Anyone, from PhD students to multi-national companies, can use DNA2.0's products for academic research or commercial product development. Parts repository Addgene allows companies to both contribute and buy parts, although the parts available to industry are limited as donors must explicitly give permission for their parts to be shared with non-academic users.

### *5.4.3 Action 5: Stakeholder mapping and public engagement*

Overcoming the regulations barrier will require a concerted effort from every current or potential synthetic biology stakeholder. Stakeholder mapping is needed to ascertain a suitable area for early investment in commercially driven synthetic biology.

It is possible that luxury goods, such as cut flowers for example, may be a suitable halfway house between restrictive GM regulations and a freer market for synthetic biology: smaller quantities are needed compared to food products, so they can be grown in closed environments, and there is unlikely to be any ethical objections to the involvement of large industry. If this is the case, luxury plant products may be a worthwhile investment for plant synthetic biologists. It would be necessary for designers, economists and marketing professionals to be involved from the outset of the project, since their expertise would be as important to the outcome as would those of the plant scientists.

OpenPlant plans to run annual forums to discuss responsible innovation. The forums will consist of working groups, general meetings and academic exchange. They are intended to consider and report on important factors in synthetic biology research and commercialisation. Planned topics include new business models, third world exchange and evaluating environmental impact. GARNet, representing the basic plant science community, can work with Sense About Science to begin engagement with the public on these issues.

### *5.4.4 Action 6: Exploring licensing options*

As discussed in Section 5.2, a good investment for UK plant synthetic biology would be a community repository for biological parts. If such a resource was developed, it would be important that sharing with start-ups and small and medium enterprises (SMEs) is considered in the planning. There are several possibilities for a community resource used by academic and commercial users alike. There could be a number of options for donors, for example an opt-out of sharing with commercial or academic users. Alternatively, the commercial users could pay a fair fee, determined by the size of the company, and agree a percentage of any profit from the research product for the right to use the part.

It is important to note that the UK Government invests in research for the economic and societal good of the country. While not all research results in a useful application, the impact of a small number of commercial products or processes outweighs the initial cost of investing in a large number of research projects. New materials, production processes, medical and agricultural products and much more can all originate from government-funded research, and all crucially generate businesses that pay tax and provide jobs.

It is therefore appropriate that, when relevant, researchers and/or their institutions apply for patents and exercise their rights to licence or restrict access to their product. However, we suggest that research institutions have a moral duty to make reasonable efforts to work out agreements with start-up companies and SMEs, including where material has not been patented. For example, the company could pay an up-front fee, appropriate to its size, and agree to pay royalties from any profits made from products using the invention.

As a trusted point of contact for UK plant researchers, GARNet will represent plant science-specific issues and interests to the TSB Synthetic Biology Special Interest Group and the Synthetic Biology Leadership Council, for whom intellectual property problems across the academic–industry interface is a matter of concern. Additionally, intellectual property is expected to be a topic of consideration in the OpenPlant Forum, where these possibilities and others are likely to be explored.

## *5.5 Technical tools to build a world-leading plant synthetic biology community*

### *5.5.1 Challenge 7: Efficient transformation*

**Crop transformation**: Building a synthetic pathway into a plant may require transformation with many genes and genetic parts, so it is important to be able to transform large constructs. As DNA synthesis services and tools such as Golden Gate cloning and Gibson Assembly enable cloning of large multi-gene constructs, the real technical barrier is the transformation event itself. Wheat transformation is technically challenging and although up to 30% transformation efficiency is possible with the limited availability PureWheat® technology, it is a bottleneck that will have to be overcome if synthetic biology in wheat is to be carried out outside of a handful of expert groups. Barley transformation has a high efficiency of around 25% (Harwood, 2012), however, like many other crop species including wheat and rice, transformation efficiencies and techniques in barley vary between varieties.

**Algal transformation**: The ability to express foreign genes in algal cells is also a major challenge. A high recombinant protein level is 2% total soluble protein (TSP) in algae (Specht 2010), but 30% TSP can be achieved in lettuce chloroplasts (Kanamoto *et al*., 2006).

**Chloroplast transformation**: As mentioned in Section 3.1, a potential advantage of synthetic plant 'producers' over microbe factories is the opportunity for compartmentalised gene over-expression presented by plastids and chloroplasts. Chloroplast micro-factories are integral to many synthetic biology ideas, as the chloroplast can tolerate far higher levels of proteins and metabolites that may be toxic or that would otherwise interfere with cellular processes if produced in the cell lumen. It should therefore be a priority to optimise chloroplast transformation in major crop species.

In the model plants tobacco and Arabidopsis, as well as in solanaceous crop plants, chloroplast transformation methods are efficient and reliable. In tomato and potato, transgene expression can be as great as 45%. However, in monocot species, which include the major global staple food crops wheat, rice, barley and maize, chloroplast transformation is more difficult because of the regeneration method used after the transformation event. In dicot plants, leaflets in tissue culture are transformed and the plant regenerated by organogenesis. In monocots, regeneration is from transformed somatic embryos, and although there have been reports of high transgene expression in maize somatic embryo

chloroplasts, this was not translated into high expression in the explant and seedling (chloroplast engineering reviewed by Bansal and Saha, 2012).

### *5.5.2 Challenge 8: Predictive biology*

The engineering approach fundamental to synthetic biology demands a predictable toolbox: engineers cannot design bridges if the parts used to build them do not act the same way in each construction. Biology is not yet predictable, but systems and predictive biologists aim to be able to predict gene, protein or metabolite functions in certain environments.

Ideally, product-driven industrial plant synthetic biology should be entirely predictable, while cutting-edge research – by its nature – will never be wholly predictable. In practice, basic explorative plant synthetic biology requires predictability in two key processes: site-specific recombination and promoter activity.

TALE technology, zinc finger nucleases and RNAi mutagenesis allow site-directed mutagenesis and have revolutionised molecular biology. However, site-specific gene insertion remains an important goal. This would enable researchers to be sure that an insertion will not interfere with natural plant processes, or to simply replace natural genes with synthetic ones if required. A possible means of site-specific insertion is the synthesis or characterisation of 'landing pads'; predictable, conserved regions where a foreign segment of DNA can be inserted by homologous recombination.

Transcription factors and promoters determine transcription of a gene. In synthetic biology, controlling gene expression begins with understanding and manipulating promoters. Natural gene regulatory systems involve many signals, transcription factors and pathways, and are hard to predict. It is important for synthetic biologists to be able to work with predictable promoters that are likely to be isolated from endogenous pathways. Such a system has not been developed, but would contribute to the development of toggle switches and synthetic pathways, as well as simply facilitating predictable gene expression.

### *5.5.3 Action 7: Incentivising development of new tools*

The OpenPlant initiative has received funding dedicated to new tool development, including tools for new models such as cyanobacteria and Marchantia as a plant synthetic biology chassis. The focus will be on genome assembly methods, gene regulation, genome engineering including a synthetic chloroplast genome, and digital tools. Satellite research projects, such as the nitrogen-fixing wheat research programme and a novel plant products programme led by Cathie Martin (John Innes Centre), will be key in the development of transformation technologies for specific crop species.

Beyond this dedicated development fund, solutions to the issues highlighted above, and new challenges that arise as the field matures, could be outlined at a hackathon or Biotechnology YES competition as suggested in Section 5.3. Developing the methods themselves will require funding.

Individual labs could make headway for the good of the community while working on their funded project if researchers had a financial incentive to optimise and publish a general protocol for other plant researchers to use, rather than using a highly customised project-specific protocol. A possible funding mechanism is to invite researchers to apply for supplementary funding to develop training materials for a new method derived from an existing project. There will be a tools and technologies seed fund from OpenPlant, which will award £5000 for the development of new digital tools.

In practice, a predictable synthetic biology system might be a set of TAL driver lines targeting well-characterised synthetic promoters and specific cell types. With such a resource, researchers would be able to test gene functions and other hypotheses quickly and reliably. Looking further ahead, a predictable plant super-host with a minimal genome may be the model organism for future synthetic biologists.

A potential solution to the challenges of transforming plants and algae with large constructs is an entire artificial chromosome that can be inserted into a callus, seed, or platelet whole. It would contain genes encoding everything needed to express a synthetic molecule or pathway, independent of the natural genome (Gaeta *et al*., 2012). Another target for research is the CPMV-HT protein expression system, which enables extremely high-level transient expression of a foreign protein in tobacco. It has not yet been trialled in algae or crop species, but would be an excellent expression system for some applications.

# 6 A UK Plant Synthetic Biology Community: Conclusions

Excellence in fundamental research and a history of embracing innovative research methods mean plant science in the UK is in a good position to develop a plant synthetic biology research base with scientific and economic impact. The recently funded OpenPlant initiative demonstrates confidence in the UK plant research community's ability to make an impact with synthetic biology within the scientific community and funding bodies.

The UK plant science community has a good community structure and excellent research strengths to build on, and several plant synthetic biology projects and

tools are already established within UK research groups. However, there are obvious gaps in the synthetic biology pipeline:

**Challenge 1: Access to synthetic biology tools** can be difficult for some groups. *De novo* synthesis of custom primers or parts – for example, for genome assembly – is too expensive for small research groups or for researchers trying new approaches for the first time. There are two large community parts repositories, but as neither were specifically developed with plant scientists in mind, even commonly used plant science parts may be absent.

**Challenge 2: Tools to manage, curate and mine information** are essential. The extensive 'omics databases delivered by plant systems biology are an important benefit to plant synthetic biology, but these very large datasets must be accessible and re-usable.

**Challenge 3: Multidisciplinary skills and collaborations** increasingly form part of undergraduate courses and early career training but will not prepare the majority of early career researchers for the very close interdisciplinary partnerships required in synthetic biology.

**Challenge 4: Reluctance to explore new technologies** is natural, since there is a risk that embarking on a new protocol will waste time and resources. Most plant scientists will be unable to access expert advice when trying a synthetic biology method for the first time.

**Challenge 5: EU regulations and public support** present particular problems for plant synthetic biology. Regulatory systems surrounding GM crops in Europe reflect negative public views and make it difficult to deliver impact in those areas where plant synthetic biology has the most potential: food security and sustainable resource management.

**Challenge 6: Intellectual property** is a traditional sticking point between academia and industry. The fledgling UK synthetic biology industry is made up of SMEs, many of which cannot access resources developed at universities or research institutions because they are unable to pay or negotiate on the fee requested. This is a direct impediment to impact and economic growth from synthetic biology in the UK.

**Challenge 7: Efficient transformation** of crop and algal species is not yet a reality. Transformation has been optimised to a reasonable standard in some varieties of a number of crop species, but wheat can only be transformed by a limited number of service providers. Algal transformation is very unreliable in the majority of species.

**Challenge 8: Predictive biology** is an important goal for synthetic biologists. Being able to reliably model the biological and environmental response to synthetic parts or systems will improve the process of product delivery from synthetic biology.

Meeting these challenges requires a formal UK plant synthetic biology community. As a grass-roots elected forum for plant researchers, GARNet is ideally placed to develop a UK Forum for Plant Synthetic Biology with underpinning resource funding from BBSRC. The plant synthetic biology community must serve two overarching purposes: first to work with plant scientists to progress the development of a UK resource centre and repository, to promote synthetic biology approaches and facilitate networking and training events; and second to work within the synthetic biology community to promote plant science and make connections with relevant contacts from other disciplines.

To serve its internal needs the plant synthetic biology community must be outward facing; as well as plant scientists doing or considering synthetic biology, it should involve all potential stakeholders. Synthetic biology is inherently interdisciplinary, and both plant scientists and other research groups will benefit from shared expertise and collaborations. Traditional and systems plant biologists are central to plant synthetic biology, as are synthetic biologists from chemical, computational and microbiological backgrounds.

Looking to the future, plant biologists will need to interact with a wide range of professionals in order to deliver commercial impact. Agricultural and structural engineers, architects, food scientists, marketing experts, designers, economists and social scientists may all cross paths with plant synthetic biology outputs at some stage. This is true of many other branches of synthetic biology, so it is not necessary for these groups to be part of a plant-specific synthetic biology community. It is therefore critical that the UK plant synthetic biology community acts as a specialised niche within the wider UK synthetic biology community.

With leadership from GARNet and the support of OpenPlant, which will act on many of the recommendations in this report, the UK plant synthetic biology community has the potential to produce significant scientific knowledge and innovation by working with the above groups. We recommend the following actions to establish a world-leading plant synthetic biology community in the UK:

**Action 1: Enabling community sharing of biological parts**. The community should work together to build a comprehensive biological parts registry to avoid duplication of effort, and to lower the financial and technical barriers to entry.

**Action 2: Establishing an open source software repository**. This should provide a directory of widely available online resources, with an associated user guide and relevant information.

**Action 3: Inspiring a generation of plant synthetic biologists**. This should build upon current UK capacity to provide relevant training to undergraduate students and early career researchers to ensure they have the knowledge and means to explore synthetic biology.

**Action 4: Enabling training, partnerships and collaborations**. Using new techniques is inherently risky, and synthetic biology tools often have to be custom-designed and synthesised at cost to the user. Training in specific techniques, and an associated network of expert users and collaborators, will enable researchers at all levels to use synthetic biology approaches confidently.

**Action 5: Stakeholder mapping and public engagement**. Commercial impact from plant synthetic biology will be limited if current EU regulations on GMOs do not change.

**Action 6: Exploring licensing options**. Intellectual property regulations are another limiting factor for commercial impact from synthetic biology. Start-up companies and small and medium enterprises struggle to access basic materials, such as transformation vectors, which are freely available to non-profit research institutions.

**Action 7: Incentivising development of new tools and approaches**. This will facilitate the uptake of synthetic biology by a wide range of users, helping to overcome barriers to the adoption and growth of plant synthetic biology and the manufacture of synthetic products in plants.

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## Appendix 1: Synthetic biology toolkits suitable for plant science

| Name | Options for use | Reference | Useful link |
|---|---|---|---|
| Tools for DNA or Genome Assembly | | | |
| Gibson Assembly | Self-assembly or Gibson Assembly® Master Mix from NE Biolabs | Gibson *et al.*, 2009 | www.synbio.org.uk/dna-assembly/guidetogibsonassembly.html |
| Golden Gate Cloning | Self-assembly | Engler *et al.*, 2008 | www.j5.jbei.org/j5manual/pages/23.html |
| MoClo | Self-assembly | Weber *et al.*, 2011 | |
| Golden Braid | Self-assembly | Sarrion-Perdigones *et al.*, 2011, 2013 | |
| Gateway® cloning | Invitrogen kit | Karimi *et al.*, 2007 | |
| Tools for DNA Editing | | | |
| Transcription activator-like effector / nuclease | Self assembly, AddGene, or GeneArt® Precision TALs from Life Technologies | Schornack *et al.*, 2008; Romer *et al.*, 2009. | www.taleffectors.com |
| Zinc finger nucleases (ZFN) | OPEN Reagents via Addgene, self assembly, or CompoZr® ZFN from Sigma Aldrich | Bibikova *et al.*, 2003; Maeder *et al.*, 2008 | www.addgene.org/zfc/open |
| CRISPR-Cas | Self assembly | Jinek *et al.*, 2012; Shan *et al.*, 2013; Nekrasov *et al.*, 2013 | www.genome-engineering.org/crispr |
| Expression Systems | | | |
| HT-CPMV | Contact inventors | Sainsbury and Lomonossoff, 2008 | |

## Appendix 2: Workshop programme

Day 1

| | |
|---|---|
| 09:30 | Registration |
| 10:00 | Welcome and introduction |

**Session 1: What is synthetic biology, and what can it be used for?**

| | |
|---|---|
| 10:15 | Jim Haseloff (University of Cambridge)<br>Engineering plant form |
| 10:40 | June Medford (Colorado State University)<br>Rewiring a plant and Digital-like Controls |
| 11:05 | Andy Boyce (BBSRC)<br>BBSRC perspective |
| 11:30 | Belinda Clarke (Technology Strategy Board)<br>Funding new frontiers in synthetic biology |

**Session 2: From molecules to cells and circuits**

| | |
|---|---|
| 11:55 | Dek Woolfson (University of Bristol)<br>Generating and applying toolkits of de novo peptide components for synthetic biology |
| *12:20* | *Lunch* |
| 13:20 | Cameron Alexander (University of Nottingham)<br>Synthetic polymers – new containers and communication materials for synthetic biology |
| 13:45 | Lee Cronin (University of Glasgow)<br>Bottom up meets top down: From inorganic biology to synthetic biology manipulations in 3D printed wet-ware |
| 14:05 | Martin Howard (John Innes Centre)<br>Implementation of analogue arithmetic circuitry in plants |
| 14:30 | Anne Osbourn (John Innes Centre)<br>Making new molecules |
| 14:55 | Rob Edwards (University of York; FERA)<br>Plant Synthetic Biology: a New Platform for Industrial Biotechnology? |

**Session 3: Plant synthetic biology**

| | |
|---|---|
| 15:20 | Nick Smirnoff (University of Exeter)<br>Synthetic metabolons |
| *15:45* | *Afternoon tea* |
| 16:05 | Giles Oldroyd (John Innes Centre)<br>Redesigning the symbiotic signalling pathway for rhizobial recognition |
| 16:30 | Sebastian Schornack (The Sainsbury Laboratory Cambridge)<br>Targeted variation of genomes using TAL effectors |
| 16:55 | Breakout groups: What can plants do for synthetic biology? |
| 19:30 | Dinner at the NCSL |

Day 2

| | |
|---|---|
| 08:45 | Tea and coffee |

**Session 4: Synthetic biology tools**

| | |
|---|---|
| 09:00 | Susan Rosser (University of Glasgow)<br>Recombinases as tools for synthetic biology |
| 09:25 | George Lomonossoff (John Innes Centre)<br>eVLPs for plant synthetic biology |
| 09:50 | Tom Ellis (Imperial College London)<br>Assembling designer genomes |
| 10:15 | Sylvestre Marillonnet (Icon Genetics)<br>Developing tools for synthetic biology: Golden Gate Cloning and the MoClo System |
| 10:40 | Jim Ajioka (University of Cambridge)<br>A guide to Gibson assembly |
| *11:05* | *Coffee break* |
| 11:30 | Breakout sessions to discuss future community needs |
| *13:00* | *Lunch* |
| 13:45 | Feedback from breakout groups |
| 14:10 | Claire Marris (Kings College London)<br>Responsible Research and Innovation for Synthetic Biology |
| 14:30 | Alistair Elfick (University of Edinburgh)<br>iGEM |
| 14:50 | Natalio Krasnogor (University of Nottingham)<br>Computational tools for rapid model prototyping in synthetic biology |
| 15:10 | Jim Haseloff (University of Cambridge)<br>PlantFab registry of DNA parts for plants |
| 15:30 | Richard Kitney (Imperial College London)<br>Foundational Resources from cSynBi |
| 15:50 | Guy-Bart Stan (Imperial College London)<br>Taking a forward-engineering approach to the design of synthetic biology systems? |

## Appendix 3: Breakout Group instructions

Your breakout groups are the same for the two discussion sessions. The dots on your badges represent the group you will be in. The groups are also labeled in the delegate list. Your group chair, rapporteur, and meeting location is given in the table below.

| | **Chair** | **Rapporteur** | **Location** |
|---|---|---|---|
| Group 1 | Andrew Spicer | Jim Beynon | B35a |
| Group 2 | Rob Edwards/Jonathan Jones | Tom Ellis | B35c |
| Group 3 | Anne Osbourn | Dek Woolfson | B1 |
| Group 4 | Susan Rosser | Jim Murray | LT1 |
| Group 5 | Giles Oldroyd | Ruth Bastow | CS Atrium |

**Breakout Session 1: What can synthetic biology do for plants?**
Tuesday
16:55 Discussion in breakout groups
18:00 Feedback
18:30 Finish

1) What are the benefits of undertaking synthetic biology in plants?
2) What can plants contribute to synthetic biology?
3) If you were not limited by technology or resources, what new plants or plants products would you construct using synthetic biology approaches?
4) Which plant system(s) would provide a useful starting point for synthetic biology research?
5) What barriers would need to be overcome in order to carry out the projects outlined above?

**Breakout Session 2: A plant synthetic biology community**
Wednesday
11:30 Discussion
12:30 Lunch
13:30 Feedback

1) What current tools and resources exist to support plant synthetic biology?
2) What new tools and community resources are needed to allow plant researchers to make progress in this new sphere?
3) To what extent is the UK plant science community well placed to take advantage of the current opportunities in synthetic biology? What are the current barriers?
4) If there was an initiative to bring together a plant synthetic biology community, who should it include and what purpose would it serve?
5) Should such a community be limited to plant science, or should it be linked to communities that are already beginning to emerge in microbial or other areas?