2nd RoSBNet Workshop

12th – 14th July 2010, St Anne's College, University of Oxford

Summary of Breakout Sessions

Food and Crop

Discussion took place on how engineering could contribute to plant synthetic biology projects, but it became clear that there were many challenges to plant synthetic biology and that perhaps a novel approach was needed, for example designing a "chassis" plant with the minimal features of a plant on which synthetic biology could be based. The main problems of plant synthetic biology applications is the fact that plants are multi-cellular organisms and systems level models of multi-cellular organisms are lacking. In particular, modelling genotype to phenotype is extremely challenging but needs to be overcome for most applications of synthetic biology to plants. In the meantime, focusing on cell-based traits, such as immunity could be more feasible.

Points made during discussion:

Problems:

- Plant genomes have been sequenced but very few crops. There are huge varieties within species. Genomes are huge via domestication/ploidy.
- Possibility for breaking down genome for sequencing?
- Mathematical modelling – do not know very many parameters. We know lots of phenotypes but very few links to genes
- How transferable are components from one plant/system to another
- Whole plant projects are challenging – cell level more do-able

What would we want to do:

- Grow rice with reduced water – should we pose the question more simply.
- Grow in bioreactors
- Gain understanding – artificial links in networks so understand underlying systems
- Find minimum genomes – know what to add and manipulate
- Developmental aspects
- Find models with reduced lifecycles
- Sensor for pathogen infections
- Maintain yield under environmental stress conditions.
- Immunity in plants is cell-based therefore "do-able", can more easily manipulate.
- Solutions to plant problems could be ex-plant – solution trade off.
- Growth rate – model fast systems.

What do we need for a minimal synthetic biology in plants?

- Good reporters (difficulties of cell walls)
- Position dependent expression
- Can do transient expression

- Can we develop a “chassis” for synthetic biology in plants. Make it plant like but it would enable necessary experiments.
- Models must range in scale from big to small – models of phenotypic traits (eg. water use) must be connected to genes.
- Targeted insertion of DNA
- Knowledge of how to drive tissue specific expression.

Ethics:
- Affecting livelihoods – farmers
- How to manage public opinion

Environment and Energy

The need to use synthetic biology for environmental and energy use was questioned as investment could be made in other technologies, but a move towards complementary technologies was recommended. Although initial investments tend to be high, long term manufacture brings efficiency. A more open dialogue with the public would help address difficult issues rather than create hidden concerns, positive campaigning could help.

Areas that could benefit include:
- Biosensors/antibodies
- Bio-fuels with improved infrastructure
- Recycle waste to produce energy, through a synthetic ecosystem that would fill a niche and then evolve.
- Water ultra filtration with specialised equipment
- Creating life in hostile environments e.g. arid/freezing/hot climates

Problems:
- How do biosensors respond to a changing environment?
- How would mutations/change of phenotype be counteracted? Population stability?
- Will evolution intervene and selective pressures reverse input?
- Synthetic Organisms could be a new type of pollutant introduced to the environment?
- Quality of control of communities tools; not working as advertised, lack of repeatability?

Action:
- Molecules must be designed for a specific purpose.
- Biological organisms must be able to assess the environment, and have an ability to correct and reproduce effectively. Prevent with selectable marker feedback control.
- Security at a local level would be desirable. Planning for potential future problems necessary.
- Photosynthesise genes into animals so they don’t have to eat so much.
- Continue to develop mathematical modelling to determine risk factors. Pick the right organisms, experience through screening, Stable isotope labelling, Need broader diversity.
- Control population growth, less pressure on resources.
- Clearly define research agenda for the future.

Signalling and Metabolic Networks / Biomedical Applications

The participants were enthusiastic about the long term impact of Synthetic Biology on biomedical applications but there were concerns as to how easy it will be to initiate clinical trials and to deliver a product; there was uncertainty about the length of the path towards that achievement. There were questions on alternative ways to construct sensor-control-actuator types of devices and how to ensure they perform reliably and safely.

There was widespread concern regarding therapeutics and the long term effects of biomedical applications of Synthetic Biology. The main issues need to be identified and the system understood well before design is undertaken.

With regards to metabolic engineering, a question arose whether we know what/why/how to engineer a pathway, given the complexity of its environment. It is challenging enough to do design on mono-cellular organisms let alone multi-cellular ones. The challenges lie also on how to interface the designed system, as well as whether it is possible to employ a sensor-control-actuator paradigm in this case too (what is the sensory platform etc).

On the ELSI side, it was obvious that eventually a new technology, based on Synthetic Biology, would be replacing an existing one. Hence the effects that this would have on a population should be analyzed. The Ethics of research were discussed and how one could regulate for personalized medicine. It was agreed that there are several issues to be considered; small studies should be undertaken first before longer term, larger tests are undertaken. We should prioritize the questions that need to be addressed in this context and answer them, engaging the public before these constructs are implemented.