**Proposal Title**

The original title of this proposal was:

“Developing Cell-Free Genetic Circuits and their Electronic Counterparts as Educational Tools for SynBio Students”

Since the project direction has changed, the new title is:

“Bacterial photography and edge detection: engineering light sensitive circuits in *E. coli*”

**Who We Are**

The CUSBS committee is composed of the following members:

* Andre Zylstra (az308) - Biological Project Manager
* Bill Jia (bzjz20) - Biological Project Manager
* Stefan Grossfurthner (sg791) – President
* Irina Danila (imd27) - Vice President
* Victoria Johnson (vpj21) – Secretary
* Edoardo Gianni (eg492) - Treasurer
* Michael Casey (mjc259) - Publicity and Media Officer
* Jaza Syed (js2612) – Hardware Project Manager
* David Chong (dtwc3) – Webmaster

In practice, the project is led by our biological project managers and conducted by interested members of the society and committee. Society membership is made up of a diverse group of students, ranging from Natural Sciences Biology and Physics students to Engineering and PhD students of various years.

**Sponsor for the research and cost centre**

Professor Jim Haseloff, Senior Treasurer to the Society

Department of Plant Sciences

University of Cambridge

Downing Street

Cambridge CB2 3EA

Email: jh295@cam.ac.uk

**The idea**

The focus of the biological project this year is to explore how synthetic biology can enable the combination of natural and engineered genetic parts, by creating an exotic functionality not typically found in nature. The project aims to reproduce the work published in two papers by Levskaya *et al.* (Nature, 2005) and Tabor *et al.* (Cell, 2009). These publications describe synthetic genetic circuits in *E. coli* capable of responding to light and detecting edges in images. Edge detection is of interest because nature is typically low-pass, and because it has a direct analogy in engineering applications including signal processing.  Generally, the project aims to develop along two parallel “biological” and “computational” branches designed to be mutually informative and complementary. Theoretical design of genetic networks will focus on computationally-aided mathematical understanding of the system and selection of biological parts that match the desired behaviour, hence bridging biology and engineering. Depending on the progress made, we hope that our theoretical exploration may guide novel experiments not shown in the work to be replicated and improve the edge detection system. We will make our work available to other groups in collaboration to support novel applications and enable open innovation. Alongside the practical project, invited speakers will develop some of these topics in more detail, present current research, or expand on wider areas of synthetic biology.

**Implementation**

Funding will primarily go towards biological and hardware materials. The wet-lab aspects of the project will be run in the newly established Biomakespace. Computational meetings will be run in the Department of Engineering.

A general outline of the steps and activities planned for this year’s biological project is provided below. It is worth stressing that participation in all or any of these steps is not enforced, and completely dependent on student availability, interests, and needs. Ideally, students will attend most sessions/activities.

Biological

* Prototyping in cell-free systems
* Construction of plasmids and sequences from iGEM BioBricks using Gibson Assembly
* Basic techniques for molecular biology including PCR, gel electrophoresis, and Sanger sequencing
* Basic microbiological culture techniques
* Hardware development (light input and masks for edge detection)
* Experimental design and data analysis

Computational

* Basic coding in Python with an emphasis on biological applications
* Numerical solutions to differential equations
* Modelling biological systems mathematically (e.g. enzyme kinetics, etc.)

The activities above are best viewed as “sub-modules” or “sub-workshops” to be completed towards the overall realisation of our project. Breaking down the work in this way will allow for easier organisation, hand-over of completed work (if people cannot make to the next session), and greater flexibility in project commitment. Each of these modules will be further expanded and accompanied by much more specific task breakdowns. These will be updated as the project progresses through the tasks, and will be detailed case-by-case via our online collaboration platform (Slack).

Participating in CUSBS projects is intended to be an extremely rewarding and enriching activity as we foster a culture of interdisciplinary cross-over and reciprocal learning. This year we are lucky to have members from all areas of science (biology, physics, engineering, medicine, mathematics), and all levels of expertise (from first year undergraduates to masters and PhD students). The amount of learning a student can expect is strictly dependent on them, their interests, their participation and their engagement with others. However, we decided to have a more clearly-defined set of goals based on our experience with last year’s project – a cumulative project with results to show at the end will give students a sense of purpose and accomplishment, much like in project-based societies run in the Department of Engineering, such as Eco-Racing and Cambridge University Spaceflight.

Scientific Skills:

* Experience with bacterial cultures as well as potentially bacterial transcription- translation cell-free systems.
* Experience with recombinant DNA technology: plasmid design, PCR, plasmid assembly and delivery
* Working with primary literature and reviews
* Theoretical understanding of gene regulatory networks and motifs, feedback loops, basic control theory
* Experience with computational methods to answer biological questions

Transferable skills

* Working in research teams
* Cooperation with students of different backgrounds
* Networking
* Creativity, original thought and independent research
* Possibility of joining project sub-committee

Those undergraduate members doing NST Part IB CDB, Part II Genetics, Engineering Tripos Part IIA Bioengineering, or Engineering Tripos Part IIA Information Engineering will find this project as a very useful opportunity to further develop or strengthen topics mentioned during lectures. We strongly encourage members to contact us and let us know what technique/topic/area they would like us to focus on in the future, and member feedback is an essential part of the project planning process.

**Benefits and Outcomes**

As part of the biological project, CUSBS is running coding sessions aimed at the investigation of simple and complex circuit dynamics using numerical solutions to differential equations. This series of workshops is developing quickly, with each session being accompanied by written teaching resources summarising and expanding on the topics covered. We have already written code that successfully reproduces the computational simulations shown in Tabor et al., and members use it to explore different hypothetical cases and come up with ideas to improve the system. We have additionally conducted a four-hour introduction to scientific computing, focused on basic programming literacy, Michaelis-Menten kinetics, and modelling the dynamics of the *lac* operon. The workshop was held in conjunction with the Cambridge University Biological Society to increase our reach and emphasize the increasing importance of interdisciplinarity in biological sciences. We welcome any other student society, school, or university initiative to make use of our resources and improve them/modify based on individual needs. We believe this holds an important potential for outreach by introducing anyone to basic principles of interdisciplinarity and complementarity between STEM fields.

On the biological side of the project, CUSBS is working towards the replication of Tabor et al. We have obtained access to consistently available laboratory space in Biomakespace and have conducted PCR and gel electrophoresis on donated BioBrick stocks containing the parts we desire to use to verify their integrity. We have additionally obtained a sponsorship from New England Biolabs, obtaining reagents necessary for Gibson Assembly and bacterial transformation at no cost. We had initially hoped to use cell-free systems to rapidly prototype portions of our genetic circuit, and hence ran a workshop introducing them to our members at the beginning of the academic year. Unfortunately, the systems available to us already contain the reporter protein in our circuit, producing false positives. We are currently looking into other alternatives to leverage the utility of cell-free systems in our project. We ultimately hope that we can create a general high-pass filter in a synthetic genetic circuit, which would be a culmination of our members’ abilities to learn in an interdisciplinary environment, read primary literature critically, and innovate.

**Budget**

|  |  |  |  |
| --- | --- | --- | --- |
| **Description** | **Price (GBP)** | **Quantity** | **Amount (GBP)** |
| Sterilin Petri Dish 90 mm, x20 | 3.36 | 3 | 10.08 |
| Invitrogen Lennox LB Agar Base, 500 g | 68.5 | 1 | 68.5 |
| Invitrogen Lennox LB Broth Base, 500 g | 40.08 | 1 | 40.08 |
| NEBuilder® HiFi DNA Assembly Master Mix E2621S | 121 | 1 | 121 |
| Expression vector plasmid | 49.45 | 1 | 49.45 |
| Oligonucleotide primer for PCR | 6 | 15 | 90 |
| Kanamycin sulfate, 1 g | 34.3 | 1 | 34.3 |
| S-Gal, 100 mg | 57.4 | 1 | 57.4 |
| Ferric ammonium citrate, 1 kg | 213.5 | 1 | 213.5 |
| iProof HF Master Mix, 100x | 126 | 1 | 126 |
| EMD Millipore Agarose, 25g | 44.75 | 1 | 44.75 |
| Tris Acetate-EDTA buffer, 1 L | 44 | 1 | 44 |
| Invitrogen 100 bp DNA Ladder, 50 ug | 69.5 | 1 | 69.5 |
| Invitrogen UltraPure Ethidium Bromide 10 mg/mL, 10 mL | 46.94 | 1 | 46.94 |
| Thermo Scientific DNA Gel Loading Dye 6x, 5x1.0 mL | 29.98 | 1 | 29.98 |
| Constructed plasmids | 47 | 3 | 141 |
| Inoculation Loops x250 | 47 | 1 | 47 |
| Ampicillin, 5g | 45 | 1 | 45 |
| **Total** |  |  | 1278.48 |