# Guide to Human Practices

PixCell, iGEM 2018

Imperial College London



## 1 Introduction

*"A society that permits biology to become an engineering discipline, that allows that science to slip into the role of changing the living world without trying to understand it, is a danger to itself "* (Woese, 2004)

As part of the international Genetically Engineered Machine (iGEM) competition in synthetic biology, we developed PixCell, a foundational technology that enables electronic control of gene expression. The system consists of genetically engineered bacteria encoding genetic networks, that are activated or deactivated at specific voltages. We developed the hardware (an electrode array), software (*in silico* models and computational controller) and genetic networks (DNA circuits which produce fluorescence in response to electrical signals) to build a predictable and programmable system for spatial patterning of cells.

Here we review our considerations on the impacts that our technology could have on the world. However, investigating the outcomes of a foundational technology, such as PixCell, is not easy. For example, no one was able to predict the far-reaching consequences of connecting devices together in a network: the internet was born, heralding major societal transformations. Analogously, predicting all possible effects of our technology is equally challenging, with discourse surrounding electrical-biological interfaces emanating from art, music and literature rather than the natural and social sciences. With the world approaching the stage of the "internet of things", will our technology one day approach a similar stage of the "internet of beings"?

When developing this technology we envisioned that its ability to precisely control gene expression had immediate applications in tissue engineering, synthetic meat production, biological system modelling, biomaterial engineering, bio-containment and directed evolution, alongside all other fields where spatio-temporal control is required. We framed our human practices aims to effectively communicate and explore the potential of our technology and synthetic biology in general, and analysing how these beneficial applications could come to fruition, alongside mitigating the harms of undesirable applications. We hope that this guide will be useful for other synthetic biologists, when thinking about the human meaning of our work.

# 2 Communication

Our project revolves around an interface between microbes and machines. Simply speaking, we are creating a means for which machines can exchange information (e.i. communicate) with microbes. Like the internet, an interface between different computers, the applications of such a technology are far-reaching and possess emergent properties. Hence, finding potential applications and more importantly societal impact will require extensive communication, which serves as our recurring theme for Human Practices.

Communication is also the key that links both integrated human practices as well as education and outreach. To enhance communication between scientists such as ourselves and the public, we have devised a science communication framework and custom guide, along with an audio-visual guide complemented with survey data. The framework encompasses communications between both academia and non-academic members and thus is flexible for both outreach purposes as well as for finding feedback for integrated human practices. To enhance communication between scientists in a team, we have handed out surveys and created a team cohesion app. Lastly, we thought of our project in a philosophical way, by exploring the divisions between life and machine and what it means when the lines between the two blur.

## 2.1 Communications Strategies Guide (CSG)

Communicating science has always been a struggle for scientists, who are only used to communicating with people in their niche field of science. As a nascent field, it is very important for synthetic biologists to be able to communicate with members of the public, as it fuels public interest and funding for future projects.

With the engineering design framework in mind, we designed a science communication framework to create, design, implement and improve on science communication protocols. Based off of this framework, we came up with a list of questions which will generate a custom guide for science communication based on the user input. The steps for the framework are briefly described below:

1. Identifying audience
2. Evaluating familiarity
3. Designing communication
4. Improving Design

We have used the Communications Strategy Guide extensively for Integrated Human Practices and Outreach. More information on the guide can be found on the wiki.

## 2.2 Surveys and Upstream Engagement

Our survey tested whether people that are more knowledgeable about the science behind biotechnology are generally more positive towards GMOs. We included 66 participants in our survey. We conducted our surveys at multiple different locations in central London including the Science Museum, the Victoria and Albert Museum, the Natural History Museum and exhibition road in South Kensington. Our survey was divided into two parts: in the first we asked scientific questions on the area of biotechnology, in the second part we asked whether the participants are in favour or against certain future applications of our technology. During data analysis the participants were divided into knowledgeable/unknowledgeable and Favourable/Unfavorable towards GMOs. A chi-square test was performed and showed no correlation between background knowledge on GMOs and acceptance of biotechnology with a p-value of 0.99. This result showed that our upstream engagement should focus directly on the ethical concerns around our project rather than purely educating around the science behind GMOs. This defined our entire human practise and outreach strategy. Our findings led us to host a public debate discussing ethical issues associated with synthetic biology. The insight gained during the survey also fed into the creation of our science communication guide - focusing on the ethical concerns of the audience rather than focusing solely on explaining the science behind the technology. Our art exhibition is also aimed at changing the perception around our technology rather than focusing on the science alone.

Next, we analysed how the general public perceived the use of electrical control in our project. This was important to us as electronic control is often negatively connotated as for example the Frankenstein monster in Shelleys' goth novel Frankenstein. Data analysis showed that the use of electricity in potential applications does not influence the acceptance of our technology.

The next step was to analyse whether acceptance varied between potential applications of our technology. Data analysis showed that the type of application does have a statistically significant influence on acceptance.

### 2.3 Team Communication: Let's Talk About This (LTAT)!

When we started our project, we soon realised that communication between members in the group is the limiting step for the dynamics of the team. Two weeks after the beginning of the iGEM Project (2nd week of July) we experienced a problem within our team. A member almost left the team. In order not to repeat the same mistakes, we designed an interactive questionnaire to foster the communication of problems within the team. Problems can be different and so are classified as personal, technical and team-related. Depending on the answers, a different branch of a pre-compiled question tree appears as output on the interface. At the end of the questionnaire, the user has the choice to submit the form with his/her/its name or anonymously. All the answers and data are collected and sent automatically to the Imperial iGEM mail (or whatever mail specified in the code). By answering the questionnaire, the user does not only have the chance to communicate a specific problem to the team, but is also a chance to analyse the type of problem, a first fundamental step in being able to solve it. This web tools is not only useful for us, to improve the dynamics of the team, but we hope it will be a useful tool for other teams as well.

## 3 The Societal Impact

*"Our task now is to resynthesise biology"* (Woese, 2004)

Synthetic biology is a multidisciplinary field of research that applies engineering principles to biological systems. This is generally achieved by reducing the functional units of biology into discrete elements, such as promoters, RBSs (Ribosome Binding Sites), CDSs (CoDing Sequences) and terminators. By assembling these genetic components in a rational way, synthetic biologists aims to engineer functioning modules, alike those created in computer science, which when combined can perform desired functions, such as drug synthesis, bioremediation or energy generation. This modular approach provides a powerful heuristic method to biology: building genetic programs de novo allows us to understand how genetic networks operate from first principles. Synthetic biology enables unprecedented control over living things. However, as the evolutionary biologist Carl Woese wrote in his seminal paper "A New Biology for a New Century", the field's reductionist approach poses threats to a society which does not try to understand biological systems and the consequences of their use prior to their wider application. Unlike the nuclear technology developed in the early 20th century, it is key that synthetic biology is developed with humanity and the world as a whole firmly in mind.

### 3.1 The Organism-Machine Interface

Our project merges the advancing technologies of electronics and synthetic biology to control patterning, a key requirement to be able to create complex biological systems. Ever since Descartes (Descartes, 1637), the idea that living beings are a type of complex machine has fascinated philosophers and scientists alike. The discovery of DNA, as the software that controls the "hardware" of these living machines, provides molecular evidence to the hypothesis that biological system can be described mechanistically. The name of the competition itself (international Genetically Engineered Machines - iGEM), suggests that we are treating living cells as machines. Indeed, we are engineering our biological system using standardised components and protocols and with control theory notions in mind. Organisms hack algorithms and algorithms can hack organisms However, is this assumption correct ? Can we rationalise all the processes in living systems and treat cells as machines? Or is there an intrinsic stochasticity in living system that is out of human control? As some of our mentors wrote, "how do we distinguish between life and non-life, between the animate and the inanimate, and thus between the organism and the machine? Does a clear boundary exist between the animate and the inanimate, and if so, are we challenging this boundary? (Freemont et al., 2012). We addressed these questions in a bioethics discussion, organised with the support of the student-led synthetic biology society (SynBIC) at Imperial. The results of this discussion, are publicly available in the "Outreach" section of our wiki.

## 4 Integrated Human Practices

In order to identify potential issues and applications of our system, we engaged in direct dialogue with stakeholders, as per the Communication Strategies Guide (CSG) -we previously elaborated. This approach allowed us to devise potential applications for our system, as well as correct design flaws such as the use of toxic pyocyanin as a redox-cycling molecule. This led us to repurpose our system with a safer molecule (phenazine methosulfate -PMS-), which also resulted in being a cheaper inducer molecule even when compared with broadly used inducers. We also identified that internal friction in teams is a common issue as proven to us by our experience as well as a survey that we conducted amongst 67 iGEM members from 14 other teams. To address this issue we developed our team communication app (LTAT) to help improve team communication both internally and in other teams.

| **Project Area** | **Integrated Human Practice** |
|---|---|
| Biosafety | Characterisation of alternatives to pyocyanin |
| Wet Lab | Biocontainment application |
| Dry Lab | Change in electrode set-up |
| Human Practices | Development of a science communication framework |
| Team | Development of the team communication app |

## 5 Education and Public Engagement

During the summer, while working in the laboratory, we dedicated some time to organise and engage in outreach activities, with the aim to communicate our project with the rest of society. Below is a table that summarises the major events that we organised

### 5.1 London iGEM Troubleshooting

Together with other iGEM teams in London (UCL, King's College, Westminster...) we organised a sessions for iGEM teams aimed at helping to solve issues related to the competition.

| Event | Date | Location |
|---|---|---|
| UK iGEM Meetup | July 12-13 | Oxford University |
| London iGEM troubleshooting meet-up | September 16 | King's College London |
| New Scientist Live | September 20-23 | ExCel, London |
| Fresher's Fair | October 2 | Imperial College London |
| SynBIC + iGEM socio-ethics discussion | October 9 | Imperial College London |

### 5.2 New Scientist Live

We collaborated with the Oxford iGEM team to present our work at the New Scientist Live exhibition, in London between the 20th and 24th of September 2018.

### 5.3 Art Exhibition at the Centre for Synthetic Biology

Art involves conceptual frameworks, fields of association, and avenues of inquiry not investigated by scientists and engineers (Yetisen et al., 2015). In order to understand broader applications of our project, we have commissioned a few artists from Royal College of Arts and University of the Arts London (UAL) to produce art pieces with our PixCell and patterning in mind. The theme of the commission is in line with our human practice strategy: communication. Specifically, we asked to the artists to think about:

- Communication between individual cells to form complex patterns
- Communication between cells and computers

The works will be exposed at the opening of the new Centre of Synthetic Biology at Imperial College. We also plan to create a portfolio with the works, a brief description and the author, to be uploaded on the wiki.

### 5.4 PixCell Board Game

We developed a board game to provide a way of educating people on key concepts in synthetic biology such as modularity, metabolic burden and depicting the effect of a gene on cell physiology in a fun and interesting way. This board game is available for download on our wiki.

## 6 Useful Reading

Freemont P., Kitney R, Baldwin G., Ellis T., Polizzi K., Synthetic Biology: a Primer...
Woese, C.R. (2004) A New Biology For a New Century. *American Society for Microbiology.* p. 173–186