Visualization: A Guide for Synthetic Biologists

Imperial College
London
Introduction

When you do iGEM, you tend to have conversations that go like this:

“What exactly are you doing? And why?”

Most iGEM teams are able to easily answer this question, because their projects are focussed on solving real world problems that immediately affect almost all of us.

Foundational projects focus on the development of enabling technologies. Foundational projects have the unique challenge of explaining why they are relevant without immediate, real world applications. Most foundational projects choose a “hook” application, which limits people’s imaginations to that space. This narrows the scope and the impact of their project, but need not be the case. Each foundational iGEM project helps to enable a diverse group of future technologies such as composite biomaterials and distributed biocomputing, which will be relevant to everyone on our planet. In order to unlock

How can we enable understanding and inspire non-synthetic biologists? We can do this through visual media. After much consideration, the 2016 Imperial iGEM team formulated this experiential guidebook. The guide is a collection of researched techniques, software tools, and feedback we have received when trying to communicate our project to inspire future developments. It has four parts: principals of good visualisations; how to present your visualisations; how to quantify the success of your visualisations; and a culminating example of how we used these techniques to present our project at the New Scientist Live event in London. We hope you find it useful.
Principles of Visualisation

“I am very little inclined on any occasion to say anything unless I hope to produce some good by it.”
– Abraham Lincoln
Principles of Visualisation

First of all, we consider visualisations to be a collection of different graphics. That means a visualisation can be composed of drawings, videos, graphs, and other visual media. While visual media can act as a powerful language between different groups of people, expressing what words sometimes cannot, visualisations sometimes suffer from lack of structure and focus. This can cause their message to become lost. It is very important to consider what information you want to convey when creating visualisations.

Four key components should be considered when creating effective visualisations. Without these components, visualisations can become uninteresting and opaque. Different graphical components can appear disjointed, and the overall visualisation confusing. According to David McCandless, a renowned artist who curates and contributes to his blog, “Data Is Beautiful”, they are:

- Information
- Story
- Goal
- Visual Form

A good visualisation contains raw data which is linked together with a story. The story has to conclude with a strong message. All of this information has to be packaged in a form which is aesthetically pleasing and interesting so people are enticed to engage with it.

You must also consider the audience. Are you trying to present information to people in their specific field, to people in a general field, or to people with no scientific background at all? It is important to remember that an audience’s expertise with certain subject matter will determine the level of detail and content in the visualisation.
How will you say it?

“Think twice before you speak, because your words and influence will plant the seed of either success or failure in the mind of another.”

– Napoleon Hill
How will you say it?

Choosing what form your visualisation will take can be overwhelming. Will it be a diagram of a cell? Will it be a video of a biochemical process? Will it be a comparison of two species of cells? Needless to say, a categorization of the different kinds of visualisations available can help guide one’s decision. We found Felice Frankel’s book, Visual Strategies, particularly helpful. Here we have summarized some of her work where she outlines the broadest categories of visualisations, and then narrows them into specific subcategories which are applicable to both. This helped us determine what kind of graphics we wanted to create to support our overall message and visualisation. Moreover, after deciding the general form of the visualisation, we provided some editorial rules for the composition of the graphics in the visualisation. Furthermore, we included some graphs we found interesting and thought could be useful to synthetic biologists to display raw data in their visualisations. Finally, we included some tools we found helpful when developing visualisations for our project.

Categorization

Visualisations can be classified into two broad categories: explanatory or exploratory.
Explanatory Visualisations
Explanatory visualisations illustrate a specific concept, or draw attention to important information a scientist wants to emphasize. (Frankel & DePace 2012) For example, a diagram created with the SBOL Visual language which shows the components of a particular designed plasmid.

This would be an example of an explanatory visualisation because it illustrates the genes which will carry out a desired function in a cell.

Exploratory Visualisations
Exploratory visualisations allow the viewer to manipulate, or interpret the information they are presented with in their own way. (Frankel & DePace 2012) An example of this would be a collection of growth curves for cells under different conditions.

<table>
<thead>
<tr>
<th>MONOCULTURES OF B. SUBTILIS:</th>
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<tbody>
<tr>
<td>SPECIES</td>
</tr>
<tr>
<td>--------</td>
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<tr>
<td>B. subtilis</td>
</tr>
</tbody>
</table>

Optical Density over Time (hours)
The growth curves allow the viewer to make conclusions about the best conditions to grow cells. They might also allow the viewer to understand how they might restrict the growth of a certain type of cell. The viewer is left to make their own conclusions about the information they have been presented.

Within those two broad categories, there are the following subcategories. They are:

**Structure and Form**
Visualisations which explain or highlight specific components of a system. An example is James Chappell’s diagram from his paper, “Creating small transcriptional activating RNAs.” Chappell clearly labels the important, structural components a STAR in the diagram.

![Diagram of STAR system](image1)

**Process and Time**
Visualisations which show the transitional steps of a process in time. An example is an image of the steps required to activate the growth regulation module of our circuit this year.

![Diagram of growth regulation](image2)
Compare and Contrast
Visualisations which highlight the similarities or differences between two things. An example is an image of different populations of cells expressing different chromoproteins, with the center being a co-culture of the two.

Golden Rules for Composition
1. Elements should be organized logically in relation to one another. There should be some sort of visual hierarchy in the data presented. The viewer should be able to look at the visualisation and be guided through it naturally. For example, posters should be laid out in a fashion where they are read from top to bottom. Video games should have level icons are a progression of in colours, indicating level difficulties. Arrows should be used to indicate flow where it might otherwise be unclear.

2. Use shape and colour to emphasize, label, and show continuity in a diagram or graph. In order to show relationships between items in a visualisation, certain colours they have chosen to indicate that relationship should remain consistent. For example, if one is showing a “zoomed in” view of a cell in a video to show its inner workings, the cell should remain the same colour. Moreover, accent colours should be chosen to highlight key elements in a visualisation. For example, if one is trying to show the genetic circuitry within a cell, the constructs and their genetic components should be
in bright colours and the surrounding area should be dark. Make it obvious for the viewer what they should be looking at and where it originated.

3. Diagrams can be overlaid or associated with other data to better inform the viewer about their relationship. Show raw, graphical data with the diagrams in a visualisation that it represents. For example, this could be cross-talk experimental data next to the genetic circuitry which provides the cell with its quorum-sensing capabilities. Use graphs as “proof” that verify information you present in your visualisations.
Interesting Graphs

To help with supporting statistical data, the “Data Visualization Catalogue” online is an excellent resource for discovering inspiring and often unused graphs. We have chosen a few which we thought could be useful for synthetic biologists when composing visualisations.

**Bullet Graph**
Displays performance data. Could be used to compare growth data between different cell types.

**Nightingale**
Displays quantities, like a bar chart, but on a polar axis. Disproportionately highlights larger values, which could be useful during presentations.

**Stream**
Displays changes over time. Could be used for relative concentrations of key metabolites during the cell cycle.

**Circle Packing**
Organizes data in an hierarchical fashion. Could be used to quantify contributions from different cell populations to an overall output.

**Radar**
Displays data in a way that is easy to compare different values. Could be used to represent contributions of parameters in a sensitivity analysis.

**Bubble Chart**
Displays multiple variables on the same graph. Good for recognizing patterns and correlations in the data.
### Tools for Visualisation

These are the software tools we used to make our visualisations. Most of them are open source or should be available at your university. We used countless other programs, but these were the best at helping us with our project.

<table>
<thead>
<tr>
<th>Tool</th>
<th>What is it?</th>
<th>Why did you use it?</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBOL Visual</td>
<td>Standardized library of glyphs which represent genetic components.</td>
<td>We used it to enable efficient communication about our circuit designs with our PI's.</td>
</tr>
<tr>
<td>Pigeon CAD</td>
<td>Online web application which allows for the construction of expression constructs using the SBOL Visual language.</td>
<td>Because Pigeon CAD is simple to use and allows for the quick creation of labelled plasmids.</td>
</tr>
<tr>
<td>Simbiology</td>
<td>A MATLAB toolbox which allows for the quick development of reaction-based cellular models.</td>
<td>MATLAB is excellent software for modelling ODE’s. However, the block diagram editor of Simbiology made it easy to visualize the many reactions taking place within our model.</td>
</tr>
<tr>
<td>Gro</td>
<td>An open source software tool to develop population-based models.</td>
<td>We used Gro because it allows for the production of gifs which helped to visualize the co-culture experiments we modelled.</td>
</tr>
<tr>
<td>AfterEffects</td>
<td>A post-production software tool used to edit and create video animations.</td>
<td>Some aspects of our project were better understood when we depicted them with animations, like quorum molecules to communicate between different cells.</td>
</tr>
<tr>
<td>Inkscape</td>
<td>An open-source vector graphics software.</td>
<td>We needed software to allow us to make images for our infographics, posters and website, and slides for our presentation.</td>
</tr>
<tr>
<td>Unity</td>
<td>A multiplatform game development tool with a customizable and easy to use editor.</td>
<td>We wanted to make a mobile game for iOS and Android. Unity has “prefabrications” or pieces of software that make it easy to quickly build games.</td>
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Assessing Success

“Success is simple. Do what's right, the right way, at the right time.”

– Arnold H. Glasgow
At its core, our visualisation strategy is about better educating people concerning synthetic biology, through visualisations. In order to assess our success, it might be useful to use one of Bloom’s taxonomies to set educational goals. These can be measured through simple questions which can be classified into the different categories. Bloom’s taxonomies set a hierarchical framework for learning objectives. Learners must be able to complete goals at the bottom of the hierarchy before they advance to higher levels of learning. This knowledge-based taxonomy requires that students learn facts about a concept, analyze, and finally synthesize new information at the highest level of learning. The framework for the knowledge-based taxonomy from lowest level to highest is:

<table>
<thead>
<tr>
<th>Description</th>
<th>Level of Expertise</th>
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<tbody>
<tr>
<td>Knowledge</td>
<td>Recall terms, procedures, and theories.</td>
</tr>
<tr>
<td>Understanding</td>
<td>Interpret terms, procedures, and theories.</td>
</tr>
<tr>
<td>Application</td>
<td>Apply terms, procedures, and theories to concrete situations.</td>
</tr>
<tr>
<td>Analysis</td>
<td>Able to organize terms, procedures, and theories into minute parts.</td>
</tr>
<tr>
<td>Synthesis</td>
<td>Create new ideas from terms, procedures, and theories.</td>
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</tbody>
</table>
Culminating Example

“I try to lead by example”
– Usain Bolt
Visualisation has permeated our iGEM project this year. However, one piece that relied heavily on our research and critiques from students and faculty at the Royal College of Art was our infographic and game we presented at the New Scientist Live.

We had a goal of presenting two novel visualisations at the New Scientist live in order to get the general public inspired and thinking of new applications for co-culture. We reviewed McCandless’ considerations for an effective visualisation. We had raw data about co-cultured bacteria which occur in nature, and some data about how they could be used to improve some manufacturing processes, as well as some other research which had some inspired future applications. We had a story. We had a foundational project that we wanted people who were not synthetic biologists to learn about and help contribute novel applications for the future of our foundational project. We had a goal. We wanted our visualisations to be easy to understand so people could propose new ideas after learning about co-cultures.

After reviewing Felice Frankel’s text, we knew we wanted to present two different kinds of visualisations. One of the visualisations would be an explanatory infographic and the other an exploratory game. The graphic would highlight some of the technical background behind our project. The poster would explain the orthogonal quorum sensing systems, RNA logic, and growth regulation. The game be less technical, and would allow people to explore a virtual world where they could collect and mix bacteria to create novel products. Both of the graphics would be structural and highlight the different working aspects of our genetic circuitry in order to co-culture bacteria.

We employed our rules of visual hierarchy, colour and shape continuity, and overlaid spacial information to develop three infographics in Inkscape as well as our game in Unity. These are the sample infographics we created, which were then further critiqued by faculty and students at the Royal College of Art.
Sample Graphic 1

ecolibrium

iGEM 101

1. Communicate
2. Compare
3. Downregulate Growth

Create a co-culture of cells with an artificial population ratio.

Our System

Our DNA!

Insert technology into different microorganisms.

Model Organisms

- e. coli
  - fast growing
  - easy to cultivate
  - does not interact strongly
  - functionally for longer periods of time

- yeast
  - slow growing
  - easy to interact
  - good at secreting substances

- bacillus

Materials

- metals
- ceramics
- polymers/plastics
- composites

Applications

- Using co-culture to create custom pigments.
- Altering the human microbiome to cure diseases.
- Space colonization!
Sample Graphic 2

Different microorganisms form sophisticated networks of interactions

- A co-culture is when more than one cell type is grown together

- Cells growing at different rates can overtake one another leaving a single cell type

We aim to create a technology that can maintain stable ratios of different cell types

- There are more microorganisms in your body than stars in the Milky Way
- There are 1000 species in the human gut alone

Obesity has been associated with poor combinations of microbes in the gut.
A less diverse gut microbiome is associated with Type 1 Diabetes

**eco**

**librium**

Co-cultures allow us to study and exploit these interactions so long as the ratios are kept constant.

**Principles of Synthetic Biology**

- Biobricks are the standard, interchangeable building blocks of synthetic biological circuits
  - Putting these biobricks together in a cell allows us to create new cell-based devices that have a novel combination of traits

**Application Areas**

- Biofuels
- Food & Drink
- Pharmaceuticals
- Industrial Enzymes
- Space Colonisation

**Our Solution**

1. Cells count their own population

2. Compare via communication

3. Stop growth of the larger population so the other can catch up

**What Will We Do With It?**

- We are making biological printer ink and using different ratios of cells to make different shades
In nature, microorganisms exist in communities and maintain stable ecosystems through intricate interactions. Different species exist in the human gut.

Microbes living in ecosystems known as biofilms are estimated to make up 80% of microbial infections.

**Principles of Synthetic Biology**

A library of parts (known as BioBrick parts) is being developed as a toolbox for genetic modification of microorganisms. It is always expanding.

Each species has a different growth rate resulting in one species outcompeting the others. This is a PROBLEM!!!

Groups worldwide wish to artificially engineer such systems.

**Applications**

- Dye Production
- Financial modelling
- Desktop Bioreactors

Much to the delight of the synthetic biology community, we are developing a genetic circuit that will overcome this problem.
Synthetic Biology is the design and construction of new biological parts, devices and systems. It is the redesign of existing, natural biological systems for useful purposes. The final goal is to be able to design biological systems in the same way engineers design electronic or mechanical systems.

Microorganisms exist in communities where they form sophisticated networks of interactions.

Co-cultures allow us to study and exploit these interactions through creating synthetic microbial communities.

Application Areas:
- Biofuels
- Food & Drink
- Pharmaceuticals
- Industrial Enzymes
- Diagnostics
- Space Colonisation

1. Communicate
2. Compare
3. Downregulate growth
4. Create a co-culture of cells with an artificial ratio

Insert technology into different microorganisms.

Co-culture is when more than one types of cells are grown together.

Cells growing at different rates can overtake one another leaving a single cell type in the culture.
The artists and designers we met with suggested that some of the content on our posters was too detailed for people at the New Scientist Live event. They did not think that an entire background to iGEM was necessary in the posters. They also felt that the concepts of transcription and translation for protein synthesis were unnecessary additions. They told us to focus on the ratiometric control in our system. They thought that the visual hierarchy, or flow of information to observe in the posters, was not strong enough in all three cases. They felt that the last two posters had too much text that people would have a hard time reading, and it was not very clear how it related to our idea generation. The artists liked the suggestion of a few applications on the first two posters. After taking all of this into consideration, our group created our final infographic.

At the New Scientist Live we tested our graphics on the public. We had three educational objectives from lowest to highest on Bloom’s taxonomy:

• Recognize what a co-culture is and how they can be beneficial.
• Explain where they occur in nature and how they can be useful to people.
• Produce their own ideas for novel applications of co-cultures

Qualitatively, most people were able to answer questions relating to the first two levels of Bloom’s taxonomy. Some people were able to produce their own ideas for novel applications of co-cultures. For example, a young girl proposed a co-culture where different bacteria produced different coloured pigments.
Of the two visualisations, the game we created was better for educating the public about co-culture. People enjoyed playing and pretending to mix bacteria to make yogurt and magnetic infinity lamps among other things. Full control of the educational medium left people feeling more satisfied with their understanding of the project.

Overall, people felt that they had a better understanding of co-culture. People commented that the visualisations helped to make abstract concepts like the existence of bacteria, and co-cultures more relatable. We would like to conclude that our techniques we employed were a success which could be employed by future foundational iGEM teams and researchers who would like to do more science communication.
Conclusions

“I think and think for months and years. Ninety-nine times the conclusion is false. The hundredth time I am right.”
– Albert Einstein
Overall, visualisation can be an effective tool for communicating with non-specialists more efficiently about synthetic biology. From conception to delivery, we believe the methods and tools we have outlined in this guide will help future iGEM teams and researchers create more effective visualisations. Thank you so much for reading, and good luck!


