iGEM COMPETITION

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ABSTRACT

iGEM, the International Genetically Engineered Machine competition, is an initiative from MIT and has become the premiere undergraduate Synthetic Biology competition. The competing teams consist of students who work on a synthetic biology project. They design and build novel biological systems and operate them in living cells. In November, the results of their project are presented at the iGEM Jamboree in Boston, Massachusetts. The first iGEM competition in 2004 featured teams from 5 Universities. Last year, 110 teams from were participating with over 1200 participants taking part in the competition. In 2010, 6 students from the University of the Witwatersrand will compete as the first team from Africa. These students are supported by scientists from the University of Witwatersrand and the CSIR.

BACKGROUND

Origins of iGEM competition

iGEM stands for international Genetically Engineered Machines. This competition is an initiative derived from the new scientific field of Synthetic Biology. The competition has been formulated by MIT (Massachusetts Institute of Technology) in the USA to promote Synthetic Biology and encourage young researchers to become actively involved in this area of research. iGEM first started in 2003 as a course run at MIT. This soon grew into a

national and then an international competition starting off with 5 teams competing in 2004 to the expected 2010 participation of 180 teams. Teams from North and South America as well as Europe and Asia are involved. 2010 is also the first year that a team from an African University has participated. All participating teams are required to build a genetically engineered machine under academic supervision and document the progress online (2010.igem.org).

Synthetic Biology – origins/development/ top down – bottom-up, Biobricks

Synthetic biology as a distinct scientific discipline has only been recognised quite recently. The term synthetic biology was used in the 1980's by Hobom (1980) when describing genetically engineered bacteria. Synthetic Biology can be loosely defined as biology meets engineering. The EU NEST report (2005) defined synthetic biology as 'the design and construction of novel biologically-based or inspired parts, devices and systems and the re-design of existing, natural biological systems for useful purposes'. Unlike the conventional approach used within the life sciences, synthetic biology is focused not on discovery but rather on engineering. Various concepts and working practices have been adopted from the engineering discipline of amongst others the idea of having components with well defined technical specifications, modularity and interchange ability of parts.

Part of the drive for this research is the production of functional nanoscale systems. This requires the ability, at the nanoscale, to assemble interconnecting components into a working mechanism. It is a major challenge to achieve this and be commercially viable (Siegel 1999). The technologies for fabricating man-designed nanodevices are still in their infancy when compared to biological counterparts (Endy 2005). In many cases analogous nanoscale biological components already exist ( ). Cells and cellular structures are functional units which contain an energy supply, regulatory and repair systems, and possibly most significantly assembly and reproduction systems ( ). All these components work in precise synchrony ( ). Hence, there is a strong interest in investigating the potential offered by biological systems (Jelinski 1999).

The field of synthetic biology became possible with the development of micro- and nano-scale imaging (Patil et. al 2007, Chan et. al 2008) as well as nano-scale manipulation

(Gimzewski 1998, Garab et. al 2005, Neuman and Nagy 2008) and fabrication (Benner and Sismour 2005) of materials. There are two different approaches to synthetic biology. One is referred to as the top down approach and the other a bottom up (EU 2010) approach. The bottom up approach is the typical engineering approach and revolves around assembling a device at a modular level into a more complex system using biological parts. The top down approach is a biologist's approach starting with a whole organism and removing unneeded genes leaving the minimum required for the designed purpose. In both approaches the existing protein synthesis machinery of an organism is used to manifest the activity of the device. Protein coding regions are assembled together in a plasmid and inserted into an organism. The organisms own genetic mechanisms are then used to read, express and regulate the activity of the device (Andrianantoandro et. al 2006). From this developed the concept of BioBricks™. A BioBricks™ is defined by iGEM as 'a standard for interchangeable parts, developed with the view to building biological systems in living cells'. Each BioBrick™ part has standard BioBrick™ prefix and a suffix. As each BioBrick™ is flanked by the same prefix and suffix then they can both be cut out of its supporting plasmid in the same manner. This produces the same complementary linking regions and thus two, or more, BioBrick™ parts can easily be linked together to form a more complex and useful system. This process is called 'standard assembly'. The same assembly process can be repeated almost endlessly. In this manner a complex system using standard BioBricks™ can be produced (Figure 1). It is the bottom-up approach that is used in the iGEM competition. All BioBricks™ which were created in the course of the iGEM competition have been submitted to the Registry of Standard Biological Parts (parts.mit.edu).

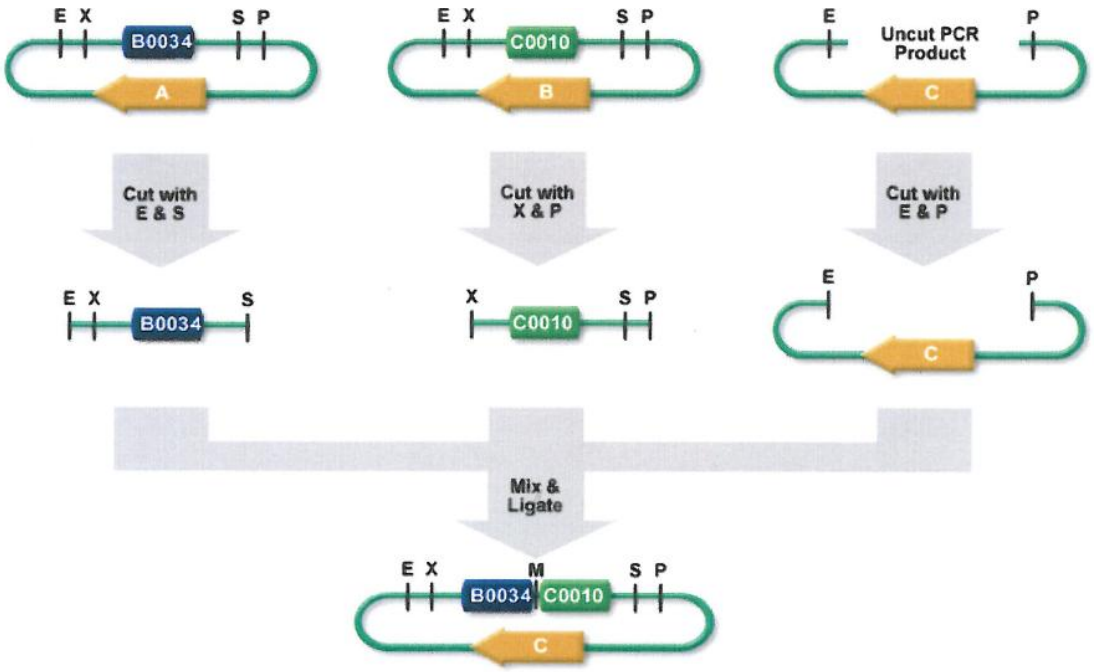

Figure 1. Diagram showing standard BioBricks™ and standard assembly of BioBricks™. (taken from parts.mit.edu)

THE WITS – SOUTH AFRICA TEAM

Competition criteria

The competition requires that the team which enters is composed of under graduate students. The students are then responsible for coming up with a design for a machine which is genetically engineered to perform a specific function or set of functions. The team then needs to construct and characterise at least one aspect of the machine. The data needs to be fully documented and added to the iGEM website. Each team has a WIKI based website into which they can add their data and ideas. Each team is encouraged to present their work at a Jamboree held at the MIT laboratories in the USA in November.

The research undertaken for this competition is not discovery orientated research; here the emphasis is on engineering. The concepts are to construct a device or system using standard parts and assembling the system using systematic standard molecular biology techniques. Once the components have been constructed ideally they need to be well characterised and documented. This also encompasses the idea of technical specifications for parts which are

interchangeable producing a variety of designs based around specific components. An analogy commonly used is viewing these biological components as there equivalents in an electrical circuit. In an electrical circuit there are components such as resistors, capacitors and switches. Biological systems have components which have essentially analogous functions to those in electrical circuits.

Each team is encouraged to use the experiences and parts that teams from previous years have contributed. Each team is, in turn, expected to contribute new or improved parts to a data base of components. As mentioned above, these are added to a 'registry of standard parts'. This registry is a repository of data relating to components with known functionalities that can be used to make new devices. iGEM has a WIKI based website one for each team as well as the repository of standard parts. These are areas where a team documents their team details, the project and the new part(s) they have produced. The competition is judged based on the information presented on the team website. The competition organisers emphasise that the whole machine does not need to work. They would rather the team focus on one or two key aspects of the machine and ensure that these operate and are well characterised. The emphasis is on the quality of the parts and not the quantity of parts produced.

As part of the competition the team is required to raise the funds for registering the team, constructing the device and participating in the Jamboree organized at the MIT in Boston.

Collaboration with CSIR & Support from University / CSIR

The University of Witwatersrand and the CSIR (Council for Scientific and Industrial Research) Synthetic Biology ERA (Emerging Research Area) are collaborating together to support a team from South Africa. This is the first team from an African University to register as a team in the iGEM competition. The students on the team are all undergraduates studying at the University of Witwatersrand. The University is also providing the daily scientific and academic supervision of the team. The CSIR is acting as a supporting institution providing scientific, administrative and financial support for the team.

Establishing and recruitment of team

The initiative to enter a team from South Africa came from the Research Leader of the CSIR – Synthetic Biology ERA after meeting the iGEM organisers at a conference in the USA. A collaboration was becoming established between the Gene Expression and Biophysics group of the ERA and scientists at the University of Witwatersrand. The initiative was taken up by Dr. Rumbold of the School of Molecular and Cellular Biology at the University of Witwatersrand. Then, various departments were contacted and invited to participate. The first step was to identify supervisors within each of the participating departments. The first meeting of the Wits iGEM organising committee in South Africa took place in December 2009. During this meeting it was agreed that the supervisors for each department would recruit one student towards the team. At this meeting it was requested that the CSIR act as the administrative co-ordinating arm of the team. Following from this meeting a brochure was produced advertising the iGEM competition inside Wits and for Honours student nominations to be team members. The academic year in South Africa commences in February. By late February 2010 student nominations had been received from which the supervisors selected the team members. The first team meeting was held on 5th March 2010. After which the team was registered for the competition and the team was established under the name of Wits – South Africa.

Team members

The Wits South Africa team consists of six Honours students from the University of Witwatersrand.

The team members are as follows:

Michelle Robinson is from the School of Pathology studying antiviral gene therapy with Dr. Weinberg.

Gregory Meyer is from the School of Engineering and Information Engineering studying Biomedical Engineering and supervised by Professor Rubin.

Byron Jacobs is from the School of Computational and Applied Mathematics studying Biomathematics under the supervision of Prof. David Sherwell.

Shaun Burd is from the School of Chemical and Metallurgical Engineering supervised by Mr.

Madigoe studying Food processing Technology.

Langelihle Ntloko is a student of Dr. Rumbold from the School of Molecular and Cell Biology studying Industrial Biotechnology.

Liam Wilson is being supervised by Dr. Kowalenko from the School of Social Sciences studying the Philosophy of Science and Metaphysics.

Supervisor

Six departments from the University are involved and a supervisor with a student from each is part of the team.

The team is supervised by a member of each department that has student within the team. The supervisors are:

Dr. Robert Kowalenko is a lecturer in the School of Social Sciences in the department Humanities and Philosophy.

Dr. Marco Wienberg is a Senior Lecturer in Pre-clinical Medicine in the School of Pathology in department Molecular Medicine and Haematology at the Medical School of the University.

Professor David Sherwell is the Head of the School of Computational and Applied Mathematics.

Professor David Rubin is Adjunct Professor in the School of Engineering and Information Engineering.

Mr. Ezekiel Madigoe is an Associate Lecturer in the School of Chemical and Metallurgical Engineering.

Dr. Karl Rumbold is a lecturer in the School of Molecular and Cell Biology.

The team is also supported by Dr. Musa Mhlanga the Research Leader of the CSIR – Synthetic Biology ERA and Dr. Raymond Sparrow the Skills Development Manager of the CSIR – Synthetic Biology ERA.

In addition a number of PhD students are also acting in an advisory capacity. Two are from the CSIR – Biosciences and these are Dr Robyn Brackin who has a background in Electrical Engineering and Ms Laura Millroy with a background in Biotechnology and Genetics. Then, from the University of Witwatersrand is Mr Youtaro Shibayama who specialises in micobial genetics.

The practical experimental aspects of building and characterising the parts and device of the project will be carried out in the laboratories of Dr. Weinberg at the Medical school of the University. This will be supported by the laboratories and equipment available in the laboratories of Dr. Rumbold and that available within the laboratories of Dr. Mhlanga at the CSIR – Biosciences.

The Project

The organisers suggest that a team chooses a project that addresses a local or a global challenge. To this end the Wits – South Africa team chose to develop an *in vivo* whole cell biosensor for the detection and neutralisation of Human Papillomavirus (HPV). The machine is designed to detect the virus, inform neighbouring bacteria in the immediate vicinity as well s the host. In this case the signal is the production of a coloured dye which will be visible in the infected individuals' urine. Thus providing an impetus for the infected person to seek medical intervention and inform their partner. In formulating the mechanism there were several design parameters, outside the strictly scientific field, with which the team wished to consider. These were, that the device needed to be safe, low cost, robust, easy to administer, obtain and use without the need for clinical intervention. The primary target for the device is women in resource-poor settings.

The students making up the team have a skills ranging from molecular biology, chemistry, engineering, mathematical and social sciences. Making use of the combination of skills the team developed their conceptual ideas for the design of their machine. With the guidance of

the supervisors and advisors the ideas crystallised into a finalised blueprint for the mechanism as a whole.

The molecular biologists, chemists and engineers then have the task of constructing the machine and providing experimental data for performance characterization. The role of the engineer and the mathematician is, also, to model the performance of the individual components of the device and of the integrated machine. The experimental data mathematical research is essential for the accurate modelling to predict the parameter under which the device can operate and response of the device under these conditions.

The role of the social science constructs the ethical framework within which the development, deployment and use of the device is being undertaken. This will also provide the philosophical platform with which this project, the research and broader impact on the community can be debated. Team Wits South Africa will employ the ethical theory of Ubuntu (ref). In simple terms this is how the perceptions of community in which one lives effects decision making.

Fund raising and promotion

Part of the remit of the CSIR – Synthetic Biology ERA is to encourage the establishment of Synthetic Biology in South Africa. The ERA also has a focus on developing students. These two aspects match both the ideals of the iGEM competition and that of the ERA. Thus the CSIR – Synthetic Biology ERA was able to cover the costs of specific items such as the team registration and the costs associated with the attendance of a supervisor at the European Spring Workshop from its own funds.

However, additional money is required for the students and any supervisors who are to attend the iGEM Jamboree. Here the emphasis is on the team to source funding. The team members prepared a funding proposal document which included information relating to the iGEM competition, the project description, methods, outputs, the team members and a budget. This was presented to the executive of the University of Witwatersrand. A meeting was also held between the team and the of the University executive. The first target for funding is the University itself where the team will lobby the Deans of Faculty for

sponsorship. To this end, the Dean of Engineering, Professor Beatris Lacquet, is the lead donor for Team Wits South Africa.

The research and educational perspectives of competing in the iGEM competition

The iGEM competition provides students with the opportunity to see a research project from start to end. The average student starts a project with funding organised and provided with a framework in which to understand their project. The iGEM competition allows for the freedom of choice in the selection of the project topic. Guided by their supervisors, the students develop and nurture their own ideas while facing the realities of finding funding and selling their ideas. The educational benefit of iGEM goes beyond the textbook teachings of their field. The multidisciplinary team structure promotes free flow of ideas allowing problems to be tackles from many different angles. This method of instruction prepares the learner for the realities of the research field.

iGEM is changing the way biology is taught and understood. This is achieved by taking the learning-by-doing approach into an interdisciplinary setting. Participation in the iGEM competition is focused on the students and the development of students as research scientists. The developmental philosophy is a heuristic approach of learning by doing. Thus the emphasis is very much on the whole team to drive their own project to come up with the design concept, funding and perform the practical experimental work. Constructing the device including performing relevant experimental measurements to ensure the components are functional for the parameters in which they operate is delegated to the relevant members of the team. The iGEM philosophy is one of open source and open communication. Thus, iGEM does not claim any IP that may result from the research that has been pursued during this completion by the teams.

This type of research requires the close collaboration of a variety of disciplines. Each team member brings ideas, experience and techniques from their own specific discipline to the project. It is the mix and interplay of the different perspectives, when applied to the project, which can produce unique solutions. This requires consistent and effective communication

between all the participants. It is quite possible that this aspect of participating in the competition that is of most value to the students.

Other aspects of the competition are that the students acquire a realisation that managing inter-personal working relationships are important. There is inter-dependency between the team members required to ensure the successful pursuit and conclusion of the project. Time management and delegation of tasks are also required for the competition.

As a condition of participation the team is responsible for raising the funds for conducting the project and attendance at the Jamboree. As a result of this they gain appreciation of the cost of conducting research and of the value and effort required to enable research and the ancillary activities such as travel to be possible.

With a number of teams they include a member who evaluates the philosophical perspective of their research and the project. It is important that scientists appreciate that they are not conducting research in isolation from the community at large. The community in question is being either, the immediate local community, the national or the international global community. The public is increasingly becoming more aware and vocal with regards research and products developed as a result of scientific research. The public often has quite a distinct opinion as to what it is willing to accept. Therefore an assessment of how to obtain acceptance by the public of new developments is becoming increasingly important.

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