Exploring synthetic biology: The art of building new things

by iGEM Tongji-Software China

True disruptive technology has two commonalities: solid scientific principles, not a myth or fantasy, but an innovative application of scientific principles; the second is interdisciplinary and cross-disciplinary integration of innovation and design.

Artemisinin, once known to the world through a Nobel laureate, was extracted from the plant Artemisia annua. However, extraction of compounds from plants has problems such as occupying cultivated land, relying on climate, and cumbersome extraction processes. At the beginning of the 21st century, Jay Keasling introduced the artemisinin gene into “artificial yeast”. In other words, as long as the yeast is fed with starch and then shaken evenly with the fermenter, the artificially modified yeast can be fermented like “wine” to produce large amounts of artemisinin. The implications cannot be underestimated;
to solve the problem of the production of artemisinin, in a sense, is to solve the problem of the production of malarial drugs. Jay Keasling used a controllable 100 cubic meter industrial fermenter, enough to replace 50,000 acres of traditional agricultural cultivation.

As an emerging biological discipline in the 21st century, synthetic biology is the product of multidisciplinary intersections in molecular and cellular biology, evolutionary systematics, biochemistry, informatics, mathematics, computers, and engineering. It has made remarkable achievements in many fields such as bioenergy, biomaterials, medical technology and exploring the laws of life. In 2014, the US Department of Defense listed it as one of the six disruptive technologies for priority development in the 21st century; the UK Business Innovation Skills Division listed synthetic biotechnology as one of the eight technologies of the future. In the technical forecast, synthetic biotechnology is listed as one of the ten major breakthrough technologies. In its 13th five-year plan for scientific and technological innovation, China has listed synthetic biotechnology as a strategic, forward-looking development.

**Synthetic biology in "building knowledge"**

Richard Philip Feynman, winner of the Nobel Prize in Physics, once said, "I can't understand what I can't
create." Synthetic biology is the fundamental problem in life sciences that can be solved by artificial biological systems. It has two purposes: the first is to use the artificial cell factory “made for use” for efficient production, the second is to “create and understand” the biological basic rules through artificial life.

The main research contents of synthetic biology are divided into three levels: to build a regulatory networks using existing biological modules and to engineer new functions; the second is to synthesise genomic DNA by de novo synthesis; the third is to create a new biological chassis itself. The accelerated development of genetic sequencing, gene synthesis and gene editing technology has laid a solid foundation for the research in the field of synthetic biology; and the technologies of computer, big data, advanced manufacturing and automation are the wings that carry synthetic biology.

**Synthetic biology is leading the "third biotechnology revolution"**

Synthetic biology is an important breakthrough in the theoretical study of biological sciences, enabling humans to understand evolutionary processes and structural mechanism of living things from by “playing God”.
The discovery of the DNA double helix in 1953 was called the first biotechnological revolution, which brought life science research into the era of molecular genetics and molecular biology. The successful sequencing of the human genome in 2003 marked the arrival of the second biotechnology revolution, which enabled us to “read” genetic information on a large scale and lead life science research into the era of “omics” and systems biology. Synthetic biology is based on systems biology, combined with engineering concepts, using new technologies such as gene synthesis, editing, and network regulation to "write" new life or change existing living bodies. The human understanding of the nature of life has been qualitatively enhanced, leading to the third biotechnology revolution.

Synthetic biology, on the other hand, has biological properties. Biological manufacturing has undergone two revolutions. The first revolution occurred in the 1950s and 1960s via large-scale fermentation and industrial production of antibiotics, amino acids, vitamins and other pharmaceuticals, foods and nutrients. Today, this has become traditional biotechnology. The second revolution occurred in the 1980s, when the development of molecular genetics led to the production of genetic manipulation technology, via gene cloning, expression, modification or transfer, to achieve a variety of high value-added biological products - "one gene, one industry "- developed into today's biotechnology strategic emerging industries.
As previously mentioned, synthetic biology is the use of systems biology knowledge, with the help of engineering science concepts. From genetic recombination, gene regulatory networks and signal transduction pathways to the manual design and synthesis of cells, to accomplish tasks that are difficult to achieve with single gene operations that greatly enhance the capabilities of genetic biotechnology and expand its range of applications. Therefore, there is reason to believe that synthetic biology is giving birth to a third generation of biotechnology tools and techniques.

The concept of synthetic biology has received wide attention, dating back to the 2004 Synthetic Biology 1.0 conference at the Massachusetts Institute of Technology. The biggest highlight of the conference was that venture capital institutions were very excited about the progress of synthetic biology, and they saw the significance of research in this field for biology, especially in bioenergy.

In the following years, many synthetic biology startups were established and received immense funding. However this was a setback as research results of synthetic biology in bioenergy did not have economic benefits, and it was impossible to compete with traditional fossil energy in terms of scale. In the five years that followed, the companies closed down, ergo losing five years in the commercialisation of synthetic biology. In recent years, with the continuous innovation of genome editing, technologies such as CRISPR, and the equally rapid development of big data, artificial intelligence and robotics, the prospects of synthetic biology are clearer and the industrialisation of synthetic biology has improved. The worldly updates on synthetic biology are in bio-
energy, bio-based materials, microbial robotics, food, agriculture, biomedicine, disease treatment, rare resource production, environmental restoration, and the development of bioengineering technology platforms. Japanese scientists have transferred the genes of actinomycetes to E. coli, and by designing new metabolic pathways, they produce bioplastics that can withstand temperatures of 400 °C. The entire production process saves energy and reduces carbon dioxide emissions. The bioplastics used as products are naturally degradable and help to protect the environment. Ginkgo Bioworks, the largest synthetic biology startup in the United States, has achieved the use of yeast to produce expensive rose oils by integrating the genes of the rose into the yeast genome. The company has established a cooperative relationship with famous French perfume companies, and the market prospects are promising.

The number of startups have increased substantially, and the amount of financing has continued to grow. According to the US SynBioBeta data, Global Synthetic Biotech has invested a total of 650 million US dollars in the first quarter of this year, twice the size during the same period last year. The investment in the second quarter reached 925 million USD, a four-fold increase over the same period last year. The funding companies are mostly located in Silicon Valley, USA and the Northeastern United States. The global synthetic biotechnology industry is expected to raise 3 billion USD in 2018. In addition, the British Synthetic Biology Industrial Transformation Center (SynbiCITE) released the "2017 British Synthetic Biology Start-up Survey" on July 12th, showing that the United Kingdom established 146 synthetic bio-enterprises during the period 2000-2016.
The number doubled every five years; during the five-year period of 2010-2014, the company received a total investment of 220 million pounds, 5.5x that of the previous five years. The company gained further investment during the period of 2015-2017, and raised more than 400 million pounds of investment in the three years.

Top scientists are engaged in the tide of entrepreneurship, and the industrialization process of scientific research results is accelerating. Synlogic, founded by James Collins, a professor of bioengineering at the Massachusetts Institute of Technology and a pioneer in synthetic biology, was listed on NASDAQ in August 2017. Ginkgo Bioworks’ founder Tom Knight has received $429 million in financing and is valued at more than $1 billion. Synthetic Genomics is a pioneer in synthetic biology in the United States. Craig Venter - who has publicly challenged the International Human Genome Project- and Nobel laureate Hamilton Smith founded. enEvolv, founded by George Church, director of the Genomics Research Center at Harvard Medical School.

**Interdisciplinary, fusive and innovative biology**

In the Center for Synthetic Biology Engineering of the Shenzhen Institute of Advanced Technology of the Chinese Academy of Sciences, there is a team focusing on research in microbiology and synthetic genomics, theoretical physics and even specializations in microfluidic
chips, led by all of 12 members. Such a "miscellaneous army" with less than four years of establishment and an average team age of only 36 years has achieved great research results in the field of synthetic biology. So far, several papers in Science have been published, attracting the American Academy of Sciences. The Shenzhen Institute of Advanced Technology also received a collaborative visit from Jay Keasling, a leader in synthetic biology, to establish a joint laboratory. As an emerging interdisciplinary subject, traditional biological research methods have failed to meet the developmental requirements of synthetic biology. The deep integration of computer science, engineering, theoretical physics, mathematics and other disciplines and biology can bring impressive results.

Large nations like China have made breakthroughs in the field of synthetic biology. According to reports, on August 2, 2019, the internationally authoritative academic journal Nature published a major breakthrough in the field of synthetic biology: Chinese scientists created the first “minimal genome organism”. Eukaryotes are cells that contain multiple chromosomes, in contrast to prokaryotes that usually possess one circular chromosome. The team fused the 16 chromosomes of baker’s yeast, or Saccharomyces cerevisiae, into one with a single chromosome.

Synthetic biology bids farewell to research within traditional biology and opens up new frontiers in interdisciplinary research. It convinces us that natural and complex life systems can be broken down into its essential elements via human intervention, and the boundaries of natural life can be artificially broken, and even artificially create new life that do not exist in nature.
“It all started with Hurricane Maria:” The birth of an iGEM journey

by iGEM RUM

This is the story of the first year of Team iGEM RUM 2018-2019. Written as experienced by Nathan Gonzalez Cordero, a native Puerto Rican industrial biotechnology undergraduate student who became the Co-founder and CEO of Team iGEM RUM 2018-2019.

Team iGEM RUM (UPRM) is the first and only iGEM Team of Puerto Rico, and the Caribbean region, registered to attend the iGEM Giant Jamboree 2019 Competition. The mission of Team iGEM RUM is to develop an original interdisciplinary undergraduate research project using Synthetic Biology to provide cutting-edge solutions that help resolve long-standing societal problems. We aspire to empower our members and collaborators towards synthesizing a better world while maintaining a sense of bioethics, economic and societal implications. This is the unifying concept behind our objectives and overall team culture.

On May 13, 2019, we celebrated our first year as a student association and research team under the Deanship of Students at the
University of Puerto Rico at Mayagüez (UPRM / RUM). We are sharing our story so other young people, students, and adults may become inspired to pursue their dreams and have hope while facing uncertainty.

You, the reader, are probably aware of the struggles and destruction caused by the passage of Hurricane Maria in the Caribbean region, especially Puerto Rico, during September 2017. We bore witness to all the chaos and uncertainty Maria brought. The economy took a hit, our routine abruptly changed and many of our loved ones either became homeless or died because of health-related complications. We will be forever grateful for all the solidarity and selflessness of the people that helped our island recover from this natural event. The spirit of resilience of our fellow citizens blossomed and for many people, including myself. Maria was a wake-up call into taking action over their life, future, and dreams.
Although this project was assigned and "managed" by another UPRM engineering student association, the conceptualization of the team was developed by the joint work of Claudia M. Mañán Mejías (co-founder, and COO of Team iGEM RUM 2018-2019) and myself during the beginning of February 2018. After developing a series of work plans, each more ambitious and complete than the last, we reached out to some of the best professors of our University. By April 2018, we already had our mentors: Dr. Carlos Ríos-Velázquez, Ph.D. (Professor of Biology) and Dr. Patricia Ortiz-Bermúdez, Ph.D. (Professor of Chemical Engineering). Under their guidance, we developed preliminary objectives, a basic team member recruiting profile and began working in our recruitment process, which was held in May 2018 (before ending the semester).

The date was May 8, 2018. Our day revolved around the expectations of having a successful and crowded information session. Over 40 people showed up, on the notorious “Hell Week”, and even Dr. Rios-Velazquez presented briefly the project to everyone present. Our attendees were a diverse group, ranging from all years of study and various study programs across the UPRM. Interestingly, most of the attendees of the information session were young women from STEM programs. We were surprised and relieved, the information session resulted better than expected and all went great. The interview process was the next big event for our team.

The interview process for selecting the team members began on May 10, 2018. We must admit that it was a chaotic process, but it was the first time any of us participated in such an event from the recruiter's
perspective. It was certainly a fun and critical experience that we ought to complete in the best way our capacities could manage. Being on the other side of the table helped us to realize how this project was going to be one of the most influential and best formation experiences of our college journey. After the interview, we felt humbled, we surely had many great candidates among the interviewed. In the following days, we studied the candidates and our interview notes. By May 13, 2019, we had selected and congratulated our fellow team colleagues. Team iGEM RUM was born.

First, for the members of our executive branch, we appointed Reyna, Elba, Amanda, Edwin, Claudia and myself. Second, for the research and development branch, we appointed Diego, Gustavo, Alondra, Paula, Natalia, Andrea Flores, Esteban, Lucia, and Luis. Finally, for the collaborative branch, we appointed Andrea Guilloty, Ricardo, Raquel, Miguel, and Eryka.
Each branch of our team was designated a specific task, the executive branch was tasked with all the administrative work of the team, the R&D branch with researching and developing our team project and the collaborators branch with providing support to any of the other branch members. The journey was about to start!

It was June 2018, our team had two types of tasks at hand: administrative tasks and personal development and enrichment. The Executive Branch was tasked with planning, developing and proposing a set of documents and directives for the adoption of the team and official recognition at the UPRM as a Student Association/Research Team. Among the authored documents were Team iGEM RUM Constitution, individual work contracts, non-disclosure agreements, branding and marketing material, semester work plan. Completion of a
selected list of MOOCs were recommended for each team member according to their work description and skills.

In July 2018, we began the brainstorming phase of our project. Each member was tasked to bring a topic that they thought could become a great project idea and discuss it with their colleagues. In the last weeks of July, a small vacation period was granted.

Fast Forward to October 2019

Our team has undergone a marvellous journey of many ups and downs. It can be said with confidence that the experiences we had will be forever in our hearts and minds. As we prepare the final touches to our project SynBio101: Road to Coli CTRL, we see our dreams becoming real.

Without further ado, dear reader, I have the honour to present to you the iGEM RUM 2018-2019 Team Delegation:
I'm forever grateful to our team, including those who are not part of the team anymore. This experience has helped me to get out of my comfort zone and get to know a little bit more of each and every one of you, your points of view and your dreams. I am extremely proud of you and really hope you can achieve your dreams. We are now due to experience the iGEM Giant Jamboree 2019 Competition. Our team has what it takes to be successful. I have the feeling we will experience many good surprises at the event! Thank you all for helping me to leave an awesome and positive legacy at our university!
This document provides an overview of the 3G assembly, a hybrid method that utilizes Golden Gate and Gibson Assembly to allow for modular assembly of multi-part circuits in a single day. It is straightforward, and works well in the hands of both experts and novices in the field of synthetic biology. The technique showcases the ability to create modular parts libraries (using Golden Gate and type IIS restriction enzymes) and the ability to create complex multigene circuits in a single pot reaction (using Gibson isothermal assembly). 3G is simpler and more efficient than many other current methods of complex circuit assembly. The full description of this effective technique can be found in Halleran et al. “Single Day Construction of Multigene Circuits with 3G Assembly.”

3G Assembly can be broken down into three basic steps:
- Golden Gate assembly
- PCR
- Gibson assembly
Golden Gate Assembly

In the Golden Gate step, the goal is to create a transcriptional unit consisting of modular parts. These parts typically fall into four categories:

- Promoter
- 5’ Untranslated Region (UTR)/RBS
- Coding Sequence (CDS)
- Terminator

Each of these parts must be flanked on both sides with a restriction site for the Type IIS restriction enzyme BsaI and a set of sticky ends that enables assembly in the appropriate order. For example, if one wants the coding sequence to be followed by the terminator, the 3’ end of the coding sequence must have the same sticky end as the 5’ end of the terminator. In the example below this would be Sticky End D. [Note that Type IIS restriction enzymes have a restriction site that is different from their cutting site. While BsaI does have recognition site specificity, it does not have cutting site specificity. Therefore, there are 256 possible combinations of sticky ends]. The letter designations for these Sticky Ends are derived from Iverson et al., “CIDAR MoClo: Improved MoClo Assembly Standard and New E.coli Part Library Enable Rapid Combinatorial Design for Synthetic and Traditional Biology”, ACS Synth. Biol. 2016, 5, 99-103].

<table>
<thead>
<tr>
<th>Part Type / Sticky Ends</th>
</tr>
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<tbody>
<tr>
<td>Part Type Left (5’)</td>
</tr>
<tr>
<td>Sticky End Right (3’)</td>
</tr>
<tr>
<td>Sticky End</td>
</tr>
<tr>
<td>Promoter</td>
</tr>
<tr>
<td>Sticky End A: GGAG</td>
</tr>
<tr>
<td>Sticky End B: TACT</td>
</tr>
<tr>
<td>5’ UTR</td>
</tr>
<tr>
<td>Sticky End B: TACT</td>
</tr>
<tr>
<td>Sticky End C: AATG</td>
</tr>
<tr>
<td>Coding Sequence</td>
</tr>
<tr>
<td>Sticky End C: AATG</td>
</tr>
<tr>
<td>Sticky End D: AGGT</td>
</tr>
</tbody>
</table>
Terminator Sticky End D: AGGT Sticky End E: GCTT

However there is one more aspect to the Golden Gate step that is necessary to make a transcriptional unit that will be used in the next step. The “ends” of the unit must have a UNS (Unique Nucleotide Sequence) adapter. In the example below, Sticky End A and Sticky End E need to have a UNS adapter – each have a different adapter (in the example shown below, UNS 1 and UNS 10). This will allow for this entire transcriptional unit to be inserted into a vector/backbone with compatible UNS adapters in a subsequent step (Step #3 below, the Gibson step). It also allows transcriptional units with overlapping UNS sequences (e.g. a transcriptional unit with UNS1/UNS3 and a transcriptional unit with UNS3 and UNS10) to be combined in the subsequent Gibson Assembly step. The use of UNS sequences is described in Torella et al., “Unique Nucleotide Sequence (UNS)-guided Assembly of Repetitive DNA Parts for Synthetic Applications,” Nat. Protoc. 2014, 9, 2075-2089.

Example with UNS Sequences Attached
Example: “Universal” Backbone
UNS 1 Biobrick
Prefix
Backbone Sequence Biobrick
Suffix
UNS 10

PCR

The second step entails PCR of the transcriptional unit(s) that was/were assembled via Golden Gate in the preceding step; the PCR uses the UNS specific primers at each end of the transcriptional unit to amplify the DNA. The PCR should be performed on each of the transcriptional units. This generates
a sufficient amount of material for the Gibson Assembly in Step #3.

UNS
1 /Sticky End
A
Sticky End
E/UNS 10

**Gibson Assembly**

Gibson Assembly is then performed using the overlapping sequences present in the UNS adapters. This can be used to insert the transcriptional unit into a backbone/vector, or to assemble multiple transcriptional units into a backbone/vector using overlapping UNS sequences.

UNS 1 Tx. Unit
1
UNS 3 UNS 3 Tx. Unit
2
UNS 5 UNS 5 Tx. Unit
3
UNS 10

3G allows for flexible assembly of circuits and circuit variants in a single day. It also allows for the generation of variant libraries that can be assessed for different circuit architectures without having to construct each circuit individually. It is ideal for use in iGEM.

An interesting side note: the technique was developed by Andy Halleran, a member of the William and Mary 2014, 2015, and 2016 iGEM teams. Andy is currently a Ph.D. student in the CalTech. Bioengineering Program.
Background

Dr. Feng-Yih Yu is a professor at the Department of Biomedicine at Chung Shan Medical University who specializes in screening tests, protein chemistry, food microbiology and toxicology and immunochemical techniques. We interviewed him on April 2, 2019.

After deciding our project topic on the rapid screening of influenza, we began looking for a better way to enhance the feasibility and accuracy of rapid screening and promoting the convenience of its usage. Later, we found several papers which concern aptamers, which have a function similar to antibodies. We hence came up with the idea that it would be possible to develop our influenza rapid screening with aptamers. Therefore, we visited Dr. Yu to ask if our idea is feasible. We drafted the following questions.

Are aptamers able to act as antibodies in screening tests?
How to select aptamers and to apply them to our rapid test paper?

Executive Summary

Dr. Yu was developing screening tests with aptamers. Through his insight, we discussed the possibility of using aptamers that can perform the function of protein antibodies. In fact, their performance is even better than antibodies owing to their small size. We apply SELEX (Systematic Evolution of Ligands by
EXponential enrichment) to select the aptamers that have high affinity with our target proteins. Since Dr. Yu specializes in the screening tests of toxic molecules, smaller than our targeted influenza proteins, he wasn’t very sure whether aptamers would fit the protein or not. However, Dr. Yu indicated that since the principle is the same and encouraged us to pursue our work. Aptamers are easier to process. If we want to have the color changed we can add nanogold or other substrates to the tails of aptamers.

After the interview, Dr. Yu confirmed that applying aptamers to screening is highly possible. Therefore, we decided to develop our influenza rapid screening test with aptamers.
Background

Dr. Babuskin Srinivasan was the Secondary Principal Investigator of REC Chennai for iGEM 2017. It was our college’s first attempt at a synthetic biology competition. We wanted to know what piqued the pioneering team’s curiosity to take part in this initiative.

About iGEM

1. Which aspect of iGEM fascinated you?
The single aspect of iGEM that differentiates it from other competitions is that it is a student-driven. Aside from this, iGEM project not only focuses on laboratory work and generation pertaining to the project, but also encourages other facets like biosafety, biosecurity and public outreach, making it the perfect place to begin a student’s scientific career.

2. What is your perspective on the iGEM competition? Any suggestions on how it can be improved?
I am particularly impressed with the criteria for judging at iGEM, which is based on the fulfilment of medal criteria by the students. These are designed in such a way that they are judged based on their overall performance in all facets.
mentioned above. This also means that the teams only compete with themselves and strive to push their project to perfection. I would still wish for more stringent judging involving relevant experts to evaluate scientific results.

3. Kindly walk us through your iGEM experience.
I was a Principal Investigator of the 2017 REC-Chennai team from Rajalakshmi Engineering College, Chennai, India. We were a team of budding iGEMers, new to the competition. We had to familiarize ourselves with the structure of the iGEM project and had a lot of doubts during the process. We also had questions related to the safety issues of our project, which is the novel use of an antimicrobial peptide in food wrappers, thus enabling long term food preservation. All our queries were briefly and promptly answered by the iGEM Headquarters during the course of our project. This made things easier for us and we had a great iGEM season.

About iGEM REC’s Project

1. You were the Principal Investigator (PI) of iGEM REC-Chennai 2017. What motivated you to take up this role?
I feel the iGEM competition serves as a platform for the students to achieve work experience and to learn and grow, both as a team member and an individual. I was extremely interested to provide valuable support and guide the young minds in this multifaceted competition using my research experience.

2. How has being a PI benefitted your academic career?
Being a PI in iGEM enabled me to learn how to efficiently tap the team’s potential and assess everyone’s strengths. Being part of iGEM has given me a fresh perspective on research. The public engagement activities have shed light on the importance of including the potential of the project throughout the developmental processes. Managing a team of fifteen and
making sure they strictly adhere to the internal deadlines was another aspect that I learnt.

3. What were the barriers encountered in your iGEM season? We faced the same problems usually faced by overseas teams, delay in the shipping of our parts. Our institution was to be made aware of the requirements of the iGEM competition outside the laboratory. According to me, it was a test of my time management, as I had classes to teach as well as other research projects to attend to.

About Synthetic Biology

1. The field of synthetic biology is gaining momentum now. How do you think it is different from genetic engineering? Synthetic biology is an interdisciplinary field which focuses on the engineering aspect of biology akin to biotechnology. The engineered biological systems form the building blocks of synthetic biology. The discovery of tools like CRISPR, which made gene editing easier, has led to a phenomenal growth in the field. While genetic engineering is the modification of the genes of a single organism, synthetic biology involves rewriting the genetic code of an organism to integrate the behaviour of multiple organisms into a singular whole.

2. Although synthetic biology involves genetically engineered circuits, people have certain misconceptions towards the term synthetic biology and not with genetic engineering. Could you explain why it is so? The idea of reconstructing the genome or the term ‘Engineered Microbes’ has sparked the imagination of non-biologists to consider it as unethical, might be due to the term “synthetic” as well. While they believe genetic engineering will enhance human health, the concept of redesigning the genome has made the public think of synthetic biology as capable of creating organisms detrimental to human existence, leading to serious concerns about the biosafety and biosecurity of the field.
3. What do you expect would be the impact of synthetic biology 10 years from now?
A synthetic biology revolution is taking place now. Recent advancements in data processing has made the study of the behaviour of complex genetic circuits feasible. The ‘cellular factories’ created by the aid of synthetic biology could tremendously reduce the cost of medical and agricultural products when compared to conventional manufacturing techniques. In addition, the biomonitoring by microbial sensors can be applied to improve health and track environmental pollutants. To sum up, synthetic biology will be integrated into every aspect of our lives.

About Safety and Ethics

1. Albeit expeditiously growing, synthetic biology has its own safety and ethical issues. Could you enlighten the students on ways to deal with them?
Ethics in synthetic biology points towards an entirely new branch of bioethics, as it is geared towards creating, rather than manipulating the genetic code of living organisms. As students, it is highly advised to take expert suggestions from the biosafety committee of their institution while screening their project design for issues for safety issues. The safety and security hub of iGEM will also be of help in the same. This process should go hand-in-hand with the wet lab work. And care should be taken not to release any Genetically Modified Organisms into the environment. As far as iGEM is concerned, I would recommend to appoint a person from your team as the biosafety in-charge who will be reporting to your PI and biosafety committee.

2. What are your suggestions on making the student community mindful of the safety and ethics associated with a project?
I will always tell my students to think of the community that will directly benefit from their research project. This will automatically lead to the identification of the issues that deter potential customers from opting for this synthetic biology product vis-à-vis the safety. The academic institutions should incorporate courses on biosafety and bioethics as compulsory subjects in the curriculum which will be a big step towards creating a future generation of scientists who vouch for ‘responsible innovation’.

3. Do you find the safety and the check-in forms provided by iGEM to contain relevant questions that serve their purpose? If not, any ideas to improve the same?

The safety and check-in forms provided by iGEM are a source of information to check if the iGEM teams have adhered to the safety and security policies during their project. Although the safety forms demand detailed descriptions of the probable risks that could arise from their engineered organisms and parts, I would recommend that the final safety forms of iGEM should ask for the submission of the Safety Analysis and Report (SAR) forms submitted by the safety committee involving experts who are not part of the iGEM team. It would be great if they are specifically allotted for iGEM by the institution.
Decoding the ban on colistin

by VIT iGEM

On July 19th, Union Ministry of Health and Family Welfare of the Indian Government issued a ban on the sale, manufacturing and distribution of an antibiotic named ‘colistin’. This ban implied that colistin, an antibiotic considered by the World Health Organisation to be amongst the highest priority critically important antimicrobials for humans will not be used in food-production, animal farming, poultry, aqua farming and animal feed supplements. The ban was warmly welcomed by the scientific community in India.

From the outside, prohibiting the use of perhaps the most powerful antimicrobial does not really fit the rationale of science or business. It isn't glaringly obvious as to why the use of colistin in treating livestock would affect the human health. However, if we dig deep into the reason behind the ban, the term ‘antimicrobial resistance’ comes up.

Described by the World Health Organisation as one of the most critical threats to mankind, antimicrobial resistance is not just a scientific issue, but a multi-faceted problem having economical and political implications. It has now come to public knowledge that resistant microbes originating from livestock can be transmitted to humans via various means, including consumption of meat and contaminated water. Recent research work conducted across the globe has proven this time and again. Taking an example in the Indian context, research done by Dr. Abdul Gaffur and his team helped the
movement pick up pace and the promote the ban on colistin for treating livestock.

A major lesson learnt from critically examining the colistin ban is that battling the conundrum of antibiotic resistance requires a combined effort made by scientific study, tackling social pressure and keeping in mind the paramount decisions made by policy makers.
Microbe Art

Shared by iGEM UAAAN
Synthetic biology: Are we missing out on something?

by Shankar Mahesh, SASTRA Deemed University

Engineering is about solving problems, but at the metaphysical level it is about solving problems by providing better solutions and synthetic biology is geared towards that very goal. Starting with the basics, DNA is essentially the code of life that has every minute detail that we see in an organism. It is no surprise that it is known as the blueprint of life. The objective of SynBio is to alter this blueprint effectively in such a way that it has more profound effects than natural selection. SynBio is a developing field which uses computational techniques to alter/construct the DNA of an organism. It is analogous to computer science in a number of ways. The DNA and cell itself are the biological analogs of a computer’s operating system and the hardware it runs on. Biological technologies have always frightened the non biologist because of the misconception that something you can’t see has the ability to kill you. The uncertainty of the biological experiments and their proclivity to be vulnerable to a lot of errors until you get to see the results is what makes SynBio even more frightening.

The term SynBio could almost immediately elicit a strongly negative response to someone who believes in the beauty of naturally created DNA. Mankind has always altered nature’s
way of doing things without a comprehensive knowledge of what is being done. This habit can be substantiated with the examples of cattle domestication, cross breeding and other situations which mankind has exploited for his own benefits. People tend to ask the to anything they are unfamiliar with. I write this piece to shed some light on some of the potentially destructive usages of SynBio.

These are some of the pressing questions posed to the synthetic biology community.

**It is ethically right to have unrestrained control over nature?**
Quoting this with evidence [1], mankind has always tried to modify nature to its own needs; in the past cross breeding and domestication were experiments in biology, albeit not synthetic ones, without an understanding of what was happening. Here, we are trying to emulate the same, but with complete process control of what is being performed.

Won’t scientific advancements lead to the rise in the number of bio-terrorists?
Strengthening the verification provisions of the Biological Weapons Convention would greatly reduce this anxiety.

**How can we ensure that genetic pollution won’t happen?**
Replacing the backbone of DNA with Threose Nucleic Acid, Glyco Nucleic Acid, Hexitol Nucleic Acid will help in preventing gene pollution between synthetic organisms and the natural organisms. [2]

**Fear of lab accidents: What if a lab accident created a “syn virus” that could plague the earth?**
Picking the appropriate level of lab containment and rigorously training lab personnel is essential, but if preventing all lab accidents were mandatory, all research would come to a halt. A news item relevant to this context: “A research at a German lab pricked herself with a needle contaminated with the deadly Ebola virus.” [3] Fortunately, she didn’t die and was
saved by being injected with an experimental vaccine forty hours after she was exposed to the virus.

The best way to deal with these issues is to pursue projects that benefit society. For instance, Jonathan Eisen of the University of California in Davis, said the community can make a positive contribution to biological defence by engineering ways to tag and track DNA. This might help pinpoint the source of biological attacks. Such efforts could “win public support for the technology”, and this will be “crucial for the field and its future”, said David Baltimore, president of the California Institute of Technology in Pasadena. We have to remind everyone that we are working towards a greater good.

Benefits of synthetic biology:
- **Organic synthesis of chemicals for such as biofuels and spider silk.**
- **Information processing**
- **Combating environmental degradation using synthetic organisms.**
- **Customized medication to treat ailments.**

Historians one day would explain how synthetic biologists created life from scratch. It is in our hands whether this story would be a tragedy or a shining story of success.

**Article references:**
Thank you for reading! :) 

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