The team projects at this year’s iGEM World Championship Jamboree featured a huge range of tools, approaches, and potential applications of synthetic biology. From DNA modified to conduct electricity to bacteria that play minesweeper to engineered moss that cleans polluted water, iGEM teams use standardized genetic parts and a lot of imagination to come up with new and unexpected designs. iGEM teams must develop holistic projects that engage with the applications and implications of synthetic biology. But while iGEM projects often start with the broad themes and application areas of synthetic biology—fuels, food, and medicine—they typically end up exploring many new creative directions that look far beyond current industry paradigms.

This year’s teams competed for dozens of awards in 9 tracks, but I want to highlight some of the emerging themes coming from iGEM beyond the official judging results. I’ve clustered the 71 projects into 8 broad themes: 1.) control over gene expression and novel molecular biology tools, 2.) cellular computation, 3.) projects related to metabolic engineering for the production of chemicals or proteins, 4.) bioremediation 5.) diagnostic tools or biosensors, 6.) drug delivery and therapeutics, 7.) applications in food or medicine that use living cells as probiotic therapies, and 8.) projects that focus on engineered symbiosis or cell-cell communication. While some teams can be classified into multiple categories, and some projects resist classification altogether, what follows is a comprehensive look at this year’s iGEM championship and the projects defining a new generation of synthetic biology.
1.) Controlling Gene Expression

Synthetic biology seeks to put “engineering” into genetic engineering through the tight and predictable control of gene expression. While all teams must engage with molecular biology tools and attempt to control gene expression in some way, this year 12 of the teams made these tools central to their project goals. From the design of tandem promoters by Wuhan University and the University of Ottawa’s fold-change detector to the University of Lethbridge’s ribosome frame-shifter and UANL-Monterrey’s RNA thermometers, these teams approached a wide range of molecular biology tools and devices.

Many teams working in this area developed toolkits that could be used by teams in the future to build their own genetic designs. These included work on novel transcription factors, like Freiburg University’s mammalian CRISPR/Cas9 system or the University of California, Davis’s RiboTALs, new riboswitches by Fudan University, and a system for epigenetic control by the University of Pennsylvania. Other teams focused on controlling multiple genes simultaneously, such as Shanghai Jiao Tong University’s “metabolic gear box,” NCTU Formosa’s E. colightuner, or Hokkaido University’s designs for a recombination system to shuffle promoters and RBS’s and tune pathway expression. Purdue University went “back to the basics” of synthetic biology, focusing on strong characterization of parts, circuit robustness, and promoter design for more predictable control of gene expression.

2.) Biocomputation

Gene expression and other molecular tools can be used to design cellular logic and memory, devices that have been used to design cellular “computation.” Many teams use the language of computers and concepts from biological logic, but 4 teams this year focused primarily on projects about logic and biocomputation in populations of engineered cells. Tsinghua University A designed a gene switch that adapts to DNA copy number, and the University of Michigan team worked on designing recombinase systems that could be used to flip DNA segments and perform computations. Such recombinases could be used, for example in projects like the 2006 iGEM project on the burnt pancake problem.

This year, the team from the University of Alberta took on a different computationally challenging problem, using combinatorial plasmid assembly to compute the traveling salesman problem. Such problems are difficult to solve with computers because they require sampling many possible routes, something that is easier to do in parallel using a population of cells. ETH Zurich designed populations of cells that don’t solve computational problem but play a computer game: identifying the AHL-secreting “mines” in a game of Colisweeper.

3.) Making Cellular Factories

The molecular tools and computational switches from the previous sections have many potential applications, including the tuning and timing of enzymatic expression in engineered metabolic pathways. Metabolic engineering of cells for the production of chemicals is a significant focus of
synthetic biology. At the World Championships, there were 13 teams who focused on tools, techniques, or new pathways for producing chemicals in engineered microbial cells. From small molecules to large polymers and complex proteins, these teams sample a wide range of biological chemistry and address many biotechnological applications.

Many of these teams considered the environmental impacts of the processes they were trying to replicate and replace, in addition to the potential environmental impacts of their own proposed process. For example, the University of Manchester’s E. c(oil)i project focused on producing fatty acids that could offer an alternative to the environmentally damaging harvesting of palm oil. The team also worked on a detailed impact analysis of synthetic palm oil, from an economic and environmental perspective. Environmental concerns were on the mind of several other teams that worked on the production of plastic, such as Yale University and Imperial College, or the production of rubber, like the team from the University of Southern Denmark. Cornell University also focused on environmental issues related to synthetic materials, partnering with the sustainable design company Ecovative to develop biological tools to aid in the production and disposal of biodegradable packaging.

Other teams designed pathways to produce a range of small molecules and unique bioprocesses. The University of California, Berkeley worked on a biological pipeline for dying blue jeans, from the production of indigo to its solubilization and subsequent incorporation into dyed fabric. The University of Trento developed a pathway in B. subtilis to produce ethylene, a molecule that is used to ripen fruits. Inspired by the gold-capturing peptides form Delftia acidovorans, the University of Heidelberg worked on porting the non-ribosomal peptide synthetase systems that produce these peptides to E. coli.

Two teams worked on projects to develop cellular “factories” to produce protein molecules instead of chemicals. Phillipps University Marburg’s “phaectory” project aimed to use the microalgae Phaeodactylum tricornutum as a platform to produce therapeutic antibodies. The University of Colorado-Boulder focused on methods for fast and easy production and purification of restriction enzymes to enable DIY approaches to molecular biology.

Somewhat surprisingly, none of the teams focused directly on producing biofuel molecules, which has been a major focus of much synthetic biology attention in metabolic engineering. Several teams, however, worked on developing tools for optimizing biofuel production or fermentation processes, like Tianjin University’s alkane biosensors or Beijing Institute of Technology’s heat tolerant fermentor cells. Others focused on a different approach to energy, like Bielefeld University’s microbial fuel cells.

4.) Cleaning up pollution

Along with “cleaning up” polluting industries by designing new bioprocesses, synthetic biology aims to clean up polluted environments using engineered cells to perform bioremediation—breaking down dangerous pollutants and toxins through microbial metabolism. This year teams designed engineered metabolic pathways that can break down polycyclic aromatic hydrocarbons (The Chinese University of Hong Kong), atrazine (Nanjing University), or dichloroethane (Sydney University). The University of Dundee team’s “Toximop” project was designed to clean up microcystin toxin released by cyanobacteria during algal blooms. The
Technical University of Munich also focused on water pollution, engineering the tiny moss *Physcomitrella patens* to break down antibiotics.

Like all iGEM projects, teams working with bioremediation have to worry about safety and environmental consequences of their work. However, bioremediation faces a unique challenge because the goal of many of these projects in environmental release and ecological consequences. Projects like those from the Ben-Gurion University team focus on other potential safety concerns, limiting the lifetime of engineered cells used in an environmental contexts.

5.) Biosensors

From the outside environment to the inside environment of the human body, synthetic biology has a lot of potential for medical applications in the diagnosis and treatment of disease. This year, many projects approached aspects of human health, including 10 that created biological diagnostic tools or sensors. Teams like Zhejiang University, BGI Shenzhen ATCG, or Georgia Tech worked on basic sensing tools that could be applied in many applications. Other teams worked on designing tools for testing for environmental pollutants, like the team from the University of Buenos Aires water Arsenic sensor and Peking University’s “Aromatic Scout,” or for potential dangers in food and dairy, like the Beijing Institute of Technology team’s sensor that detects antibiotics in milk. Clemson University and the University of Calgary worked on sensors for dangerous microorganisms in industrial food production that can cause food-borne illness. Tsinghua University worked on detecting pathogens for mobile health diagnostics. Other teams designed sensing systems to detect health problems in the body as well, like the UFMG Brazil team’s work on detecting biomarkers for Acute Coronary Syndrome.

6.) Therapeutic applications

After diagnosis, the projects that focused on medical application of synthetic biology approached drug delivery, or novel therapies using genetically engineered pathways. Many of these teams focused on antibiotics, developing projects to target bacterial infections. Paris-Bettencourt worked on a range of projects related to tuberculosis, designing systems to detect, target, infiltrate, and sabotage the bacteria that cause TB. In addition, intrigued by the gender bias in TB infection rates around the world, the Paris team did a comprehensive study of gender diversity on iGEM teams. The Technical University of Delft designed antimicrobial peptides that target Methicillin-Resistant Staphylococcus aureus (MRSA). Students from the University of Göttingen and Brigham Young University also were interested in novel antimicrobials, identifying new antibiotic targets and developing phage systems to target and kill cholera.

Other teams looked further into future applications, such as Sun Yat-Sen University’s work on induced pluripotent stem cells or the work of the Hong Kong University of Science and Technology team, working on an engineered pathway to burn excess energy in the body and lose weight through genetic engineering.

Targeted delivery of medicines is crucial to avoid side effects and create more effective therapies. NJU China designed exosomes, small vesicles secreted by mammalian cells, filled with targeted siRNAs as a “biomissile” against virus infected cells. The University of Virginia had
a similar approach, developing tools for the design of bacterial minicells as cell-targeting drug delivery systems, with a goal of specifically targeting cancer cells.

7.) Probiotics and living medicines

Many teams took drug delivery and targeted therapeutics one step further, focusing on medical applications that would involve live engineered cells targeting specific sites in the body. Teams developed live cell vaccines (University of Science and Technology of China), bacterial cancer therapies (Tec de Monterrey), bacteria that could be used to help visualize tissues in MRI (Eindhoven University of Technology), or bacteria that can protect bees from fungal pathogens linked to colony collapse disorder (National Yang Ming University, Taiwan). Living therapies like these require thinking about many complex aspects of environments, ecosystems, safety concerns, in addition to the work of designing and building genetic networks inside the cell.

The complexity of microbial communities, and the human gut microbiome in particular has seen significant recent attention for its role in many different aspects of human health, and this year many iGEM teams sought to target gut bacteria as a method of preventing or treating disease. Probiotics—like the bacteria in yogurt—interact with the microbiome in many complex ways, and two teams focused on yogurt production: The University of British Columbia worked on systems to protect large scale yogurt production from phage infection, while Uppsala University worked on engineering yogurt bacteria to produce vitamins and other nutritional supplements.

Other teams focused on particular therapeutic applications of engineered gut microbes rather than general use yogurt probiotics. The University of Illinois-Urbana Champaign designed a gut resident bacteria that digests L-carnitine, a molecule found in red meat and associated with the development of atherosclerosis. The team from the University of Evry also designed gut bacteria that digest potentially harmful molecules, specifically to chelate iron and decrease the dangerous levels of iron in the blood of thalassemia patients. Huazhong University of Science and Technology students created a gut bacterium with an oscillating gene network, to time the release of blood pressure releasing molecules. EPF Lausanne’s team took a different approach to “probiotic” therapies in the gut, designing “Taxi.Coli” cells that transport medicinal nano particles on the cell surface that can be released in the digestive tract. The University of California, San Francisco team was also interested in the human microbiome, focusing not on adding new strains to the microbiome but targeting delivery of RNA interference to specific strains in a complex community.

8.) Cell-cell communication and symbiosis

Teams working with living therapies and probiotics have to consider the ecosystem effects of their projects, and how their microbes will interact with other cells in the body and in the microbiome. 9 teams this year developed projects focused in particular on cell-cell communication and symbiosis. These projects work on biological communication broadly construed, at many scales, and often at many scales at once, like the Stanford-Brown team’s collection of projects related to communication through time and space, from bionanowires to engineered cells sent to space onboard a satellite.
Microbial cells communicate with each other in nature through chemical quorum sensing signals. Many teams used quorum sensing molecules and sensors as part of their projects, to coordinate the behavior of cells, including ETH Zurich’s colisweeper mentioned earlier. Other teams used quorum sensing to create synchronized oscillations of gene expression across a population of bacteria (Xiamen University), switch between different biological states (Tokyo Tech), or create a microbial consortium with three cell types interacting (Braunchweig Technical University). Other teams worked on designing new systems of cell-cell communication, expanding on the work of the Endy lab to engineer DNA-based communication. Both Stanford-Brown and the University of Waterloo worked on these M13 phage based DNA signals. The team from MIT designed a system for cell-cell communication between mammalian cells using exosomes as signal carriers.

Artificial symbiosis and synthetic ecosystems played a role in several other creative projects with different approaches and goals. Students from Newcastle University worked with “naked bacteria” without a cell wall, exploring their interactions with plants. Plant-microbe interactions also were central to the project of KU Leuven, who designed microbial pathways to block aphids from attacking plants. Students from the University of Valencia also developed a unique and creative synthetic ecosystem, designing a system where the nematode worms C. elegans transport bacteria living on their surface to sites of increased nutrients in the soil.

**Conclusion: The iGEM Experience**

During the closing ceremonies of this year’s world championship jamboree, MIT synthetic biology professor Ron Weiss eloquently described the emotional ups and downs of the iGEM experience.
experience. From the first rush of excitement that comes with the thought that you can use synthetic biology to change the world to the first devastation of a failed experiment, to the emotional oscillations of the experimental grind to the final excitement of presenting a project at the jamboree, the iGEM experience is an intense and emotional educational experiment, where students learn much more than synthetic biology lab techniques.

The projects that the students presented at the jamboree and highlighted here in this report are all exceptional for their complexity and creativity. The students are all working to learn but also to define the future of synthetic biology. But the projects themselves are not the most important outcome of iGEM as a learning experience. The students themselves emerge from the iGEM experience as creative and holistic thinkers and engineers, understanding very deeply the technical aspects of synthetic biology, but also the emotional and subjective aspects of life in the lab, the cultural and political aspects of synthetic biology’s “human practices,” and the ways that all of these factors are important to building the future of synthetic biology.