iGEM TÜBINGEN

A competition aiming
to inspire the
development of
innovative
and intelligent
solutions
in the field of
synthetic biology

Content

Prof. Dr. Dr. h.c. Detlef Weigel

Director at the Max Planck Institute for Developmental Biology

The major problems of our time - including the inevitable global warming, the environmental pollution caused by the extraction of raw materials or the scarcity of agricultural land - urgently require inventive and effective solutions. This is the only way to ensure a dignified life for all people on earth, even if the world's population continues to grow. Biotechnology, in particular Synthetic Biology, offers a multitude of efficient solutions that have become an integral part of our lives. Just two examples are the production of human insulin in *Escherichia coli* and yeasts or recombinantly produced enzymes that can be used to effectively clean laundry even at low temperatures.

As the director of the Max Planck Institute for Developmental Biology, I am particularly pleased about the highly motivated, creative young minds who are committed to tackle current problems that affect us all. The iGEM competition not only offers an opportunity to gain important practical experience, but also contributes to the international exchange of young researchers and each year produces a variety of innovations and suggestions for improvement. That is why I am very happy to support the iGEM team in Tübingen. The Tübingen interdisciplinary team has excellent chances of successfully completing its original project. I wish the team a successful year, a lot of endurance and many new insights.

The international Genetically Engineered Machine (iGEM) competition offers a unique opportunity for students to translate their knowledge from class to a real world problem in an applied fashion. The iGEM competition provides the students with invaluable experience in soft skills, such as project management, team communication, public outreach, along with the chance to work at the lab-bench early in their undergraduate studies. The project is self-chosen by the iGEM team which clearly motivates the students to put all their efforts into the successful realization of their ideas. This has so far paved the way for the iGEM team Tübingen to bring home several Medals and Awards from the iGEM competition in the past years.

In the aftermath of the iGEM competition, past participants have built on the ideas they pursued with their iGEM teams and turned them into scientific publications or even start-up companies, and more generally embarked on successful careers in academia as well as industry.

In recent years, the field of synthetic biology is getting a lot of public attention and is increasingly moving into the limelight of the media. With game-changing technologies, such as CRISPR/Cas, it is important to support highly motivated students in their desire to use these technologies to change the world for the better, and to guide students to participate in an evidence-based but controversial discussion about the benefits and risks of these technologies. This year, the iGEM team Tübingen devised a project around the CRISPR/Cas technology. The team will design, build, and test an innovative microbial chassis as a concept for increased biological safety when handling genetically modified organisms. With your support you can contribute to the success of this year's iGEM team Tübingen to once again represent not only the University of Tübingen but the entire region at outreach events, in the media, and last but not least at the influential concluding conference (Giant Jamboree) at the Massachusetts Institute of Technology in Boston, USA.

Dr. Bastian Molitor

Junior group leader Environmental Biotechnology Group University of Tübingen and mentor of the iGEM Team Tübingen 2019

Theresia Bauer

Minister of Science, Research and Art State of Baden-Württemberg

The iGEM Competition, in which several hundred student teams from all over the world take part every year, is undoubtedly the most prestigious international competition in synthetic biology. I am delighted that teams from Baden-Württemberg regularly take part in the competition and that they continue to represent our state very successfully.

However, the competition does not only offer the opportunity to network internationally during one's studies. It also provides initial insights into research and, above all, into interdisciplinary and international cooperation, without which science is no longer imaginable today.

The iGEM Competition is also dedicated to synthetic biology, a field in which the opportunities and risks of modern biology become obvious. The fascinating possibilities of modern biology are also accompanied by an ever-increasing responsibility. Therefore, the examination of bioethics, as well as communication with the general public, is an important aspect of the competition. Through their involvement in the iGEM team, students can gain experience in this field early in their scientific careers.

I wish the iGEM team in Tübingen and all other Baden-Württemberg teams every success and above all much joy and valuable impressions at this year's competition.

What is iGEM

iGEM (International Genetically Engineered Machine) is an international competition in the field of synthetic biology, which was initiated by the Massachusetts Institute of Technology (MIT) in Boston. The competition aims to inspire the development of innovative and intelligent solutions for relevant and recent problems through genetic modifications. By participating in the iGEM competition, our team will be able to utilize the theoretical background attained during our studies in an interdisciplinary and self-reliant manner. Often, the projects initiated through iGEM are published or lead to the foundation of Start-ups.

For the duration of the competition, the iGEM team Tübingen will represent the Eberhard-Karls-University of Tübingen, as well as the faculty of mathematics and natural sciences on multiple occasions, such as conferences on an international level, within and outside of Europe. We will also participate in public events and discussion rounds to make a useful contribution to our society. The iGEM competition will close with a congress, the Giant Jamboree, which annually brings thousands of contestants to Boston.

The iGEM team Tübingen itself participates since 2011, successfully representing the Eberhard-Karls-University of Tübingen, Baden-Württemberg and Germany.

2019-2020

Giant Jamboree

Traveling to Boston to present our project at the Giant Jamboree. Meeting all the other teams and finishing the intensive but awesome year.

Start of the Team

Formation of a new interdisciplinary iGEM-Team with diverse expertise. Finding supervisors, PIs, lab rooms...Teambuilding.

Did you Know ?
The founder of GINKGO Bioworks also was a former iGEM member and won the grand prize

Did you Know ?
In 2018 over 300 teams from around the world participated in the iGEM competition

iGEM

Preparation for Boston and project revision:

Collect and compile results, development of the project and the team, evaluate future steps and possibilities. Wrap-up of the project and preparation for the final presentation at the Giant Jamboree in Boston.

Projectfinding & Fundraising

Finding a promising topic to work on for the rest of the year. Start fundraising, networking and public presentation.

Human Practices

Get in touch with other iGEM-Teams, authorities, researchers, companies and local communities to discuss and present our project.

Laboratory

Extensive time spent in the lab to complete our project with impactful results. Combination of wet and dry lab to overcome obstacles and to improve the experiments and results.

Who WE ARE

We, the iGEM-Team Tübingen 2019, are a group of 16 students spanning the fields of biochemistry, bioinformatics, biotechnology, chemistry, nano-science and molecular medicine. With our diverse and interdisciplinary team, we plan to pursue an interesting and forward-looking research project once again. The expertise of our competent lab-team and past experiences from former projects combined with great motivation and the support of research groups as well as companies will help us to achieve our goal of a successful project. The safety of genetically modified systems and their risk-free use in clinical applications is of great importance for us.

With this year's project we do not only aim at winning one of the prices at the 'Giant Jamboree' in Boston, but also strive to contribute to the progress and development in synthetic biology.

Instructors

Patrick Schweizer
Environmental Biotechnology PhD

Sarah Schulz
Environmental Biotechnology PhD

Dr. Pengfei Xia
Post-doc. Env. Biotechnology

Faculty advisors

Dr. Bastian Molitor
Junior group leader

Prof. Dr. Largus Angenent
Environmental Biotechnology

The Team

Katharina Czik
Molecular Medicine B.Sc.

Eva Kunzelmann
Biochemistry B.Sc.

Patrick Müller
Molecular Medicine B.Sc.

Marie Evers
Molecular Medicine B.Sc.

Antonia Binder
Biochemistry B.Sc.

Jonas Steinwender
Nano-Science B.Sc.

Zoe Kentischer
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Marco Kögel
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Bioinformatics M.Sc

Mirna Maalouf
Pharmaceutical Sciences M.Sc

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Jakob Keck
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Famke Bäuerle
Nano-Science M.Sc

Luzia Hamma
Cognitive Science B.Sc..

Carolin Schwitalla
Biochemistry B.Sc.

Lina Widerspick
Molecular Medicine B.Sc.

Past Projects

2013

Development of a **yeast-based sensor for progesterin**, a contaminant in wastewater, by activating the expression of ucieferin. This allows quantitative spectrometric measurements.

2014

Construction of the **T-ECO system** (Tuebingen erythrocyte converter to 0), which modifies the glycoproteins of erythrocytes responsible for the blood groups, in order to **change the cells to** the rarer **blood type 0.**

2015

Development of a **light-inducible expression system**, based on the dimerizing capabilities of the fluorescent protein Dronpa.

2016

Design of a **fructose processing lactobacillus** to be integrated in the microbiome of fructose intolerant people.

Production of a pipetting robot able to perform simple cloning experiments.

2017

Development of a **novel antibiotic** that only targets ß-lactam resistant pathogens without affecting other bacteria resident in the body.

2018

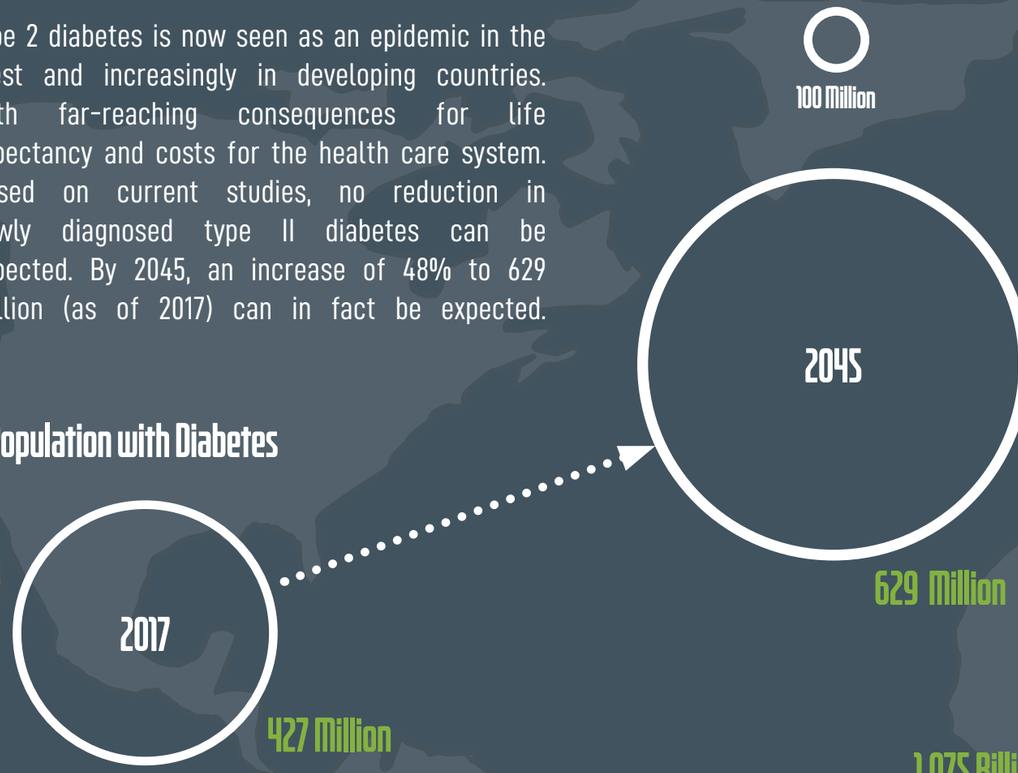
Detoxification of Botulinum toxins by coupling it to different substances for therapeutic utilization and specific neuronal targeting. Also, **homology modeling** algorythms, **Molecular dynamics** simulations and a **deimmunisation workflow.**

2019
Wetlab

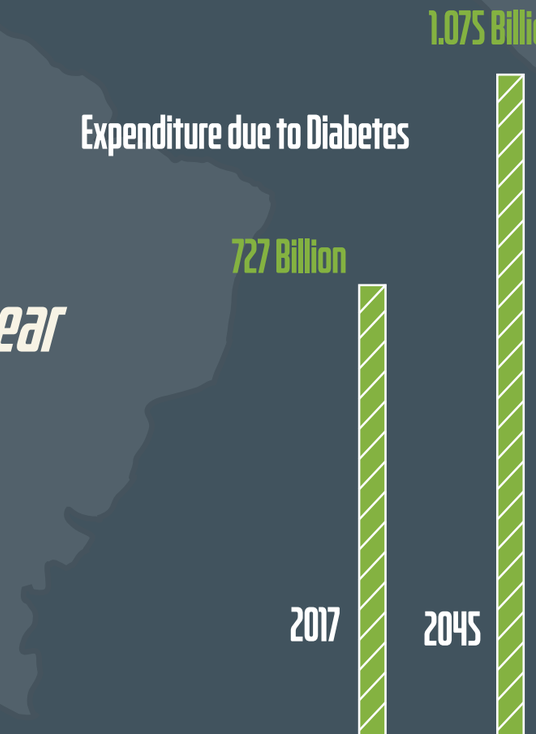
Probiotic for the therapy of Type II Diabetes Mellitus

Type 2 diabetes is now seen as an epidemic in the West and increasingly in developing countries. With far-reaching consequences for life expectancy and costs for the health care system. Based on current studies, no reduction in newly diagnosed type II diabetes can be expected. By 2045, an increase of 48% to 629 million (as of 2017) can in fact be expected.

Population with Diabetes



Expenditure due to Diabetes



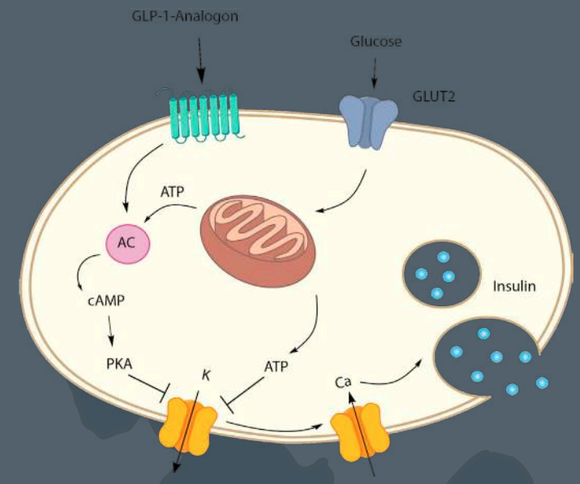
„4 Million deaths per year in 2017“

All information on this page is taken from IDF Diabetes Atlas 8th Edition

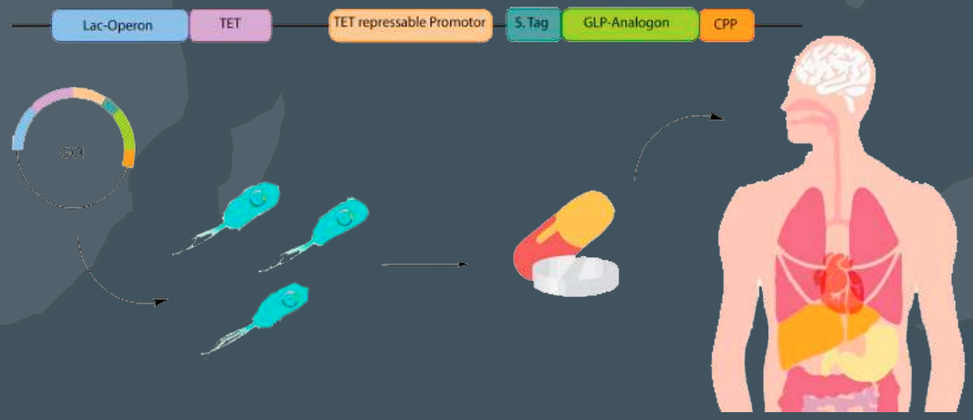
Diabetes Mellitus is caused by a relative lack of sensitivity to insulin, which leads to the decreased uptake of glucose into the cells, resulting in a cellular energy crisis. In type 2 Diabetes mellitus, the body tries to compensate this relative lack by secreting more insulin. This leads to increased stress levels in the insulin-producing beta cells of the pancreas,eventually resulting in cellular death..

As Glucagon-like peptide (GLP-1) is downregulated in diabetes type 2 patients, GLP-1 analogues are used to mimic the “incretin” effect. GLP-1 itself is rapidly degraded by the enzyme dipeptidyl peptidase 4 (DPP4), therefore its potential as a drug is limited. Thus,our goal is the synthesis and secretion of a metabolically stable GLP-1 analogue by the probiotic E.coli Nissle 1917.

The binding of the GLP-1 analogue to the GLP-1 receptor activates the coupled adenylate cyclase,initiating the production of cAMP. The elevated cAMP levels result in the activation of protein kinase A (PKA). Overall, this will lead to the stimulation of insulin secretion, mediated through an increased calcium ion influx into the pancreatic cells.



Simplified representation of our project. The plasmid encoding the GLP analogue and signalling molecules for the uptake into the blood circulation, is introduced into a probiotic E. coli strain, which subsequently secretes the peptide in the patient‘s intestine. This peptide can be absorbed through the intestine to increase insulin secretion in the pancreas. To prohibit extracorporeal survival of the organism, we will introduce a kill switch system with regulators based on the intestinal environment.



2019
Bioinformatics

Creating a data analysis pipeline for GUIDE-Seq and CIRCLE-Seq experiments to identify off-target sites in CRISPR/Cas9 experiments

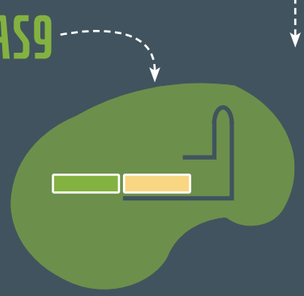
While our biocontainment system relies on a Class I Type I CRISPR system, we will utilize CRISPR/Cas9 technology for the construction of the chassis. CRISPR/Cas9 (or similar) technology has become a versatile toolkit for gene editing in all domains of life. Despite of the successes, off-target activities can be observed in many cases. A modern way of determining off-target effects is via the GUIDE-Seq assay. Hence, our goal is to generate a reproducible and parallelizable GUIDE-Seq data analysis workflow based on the bioinformatics workflow management system Nextflow.

What is CRISPR ?

Clustered, regularly interspersed short palindromic repeat

CRISPR can be considered as a quasi adaptive immuno risponce of bacteria. After „defeating" an viral attack its DNA is cut and Build into the Genome.

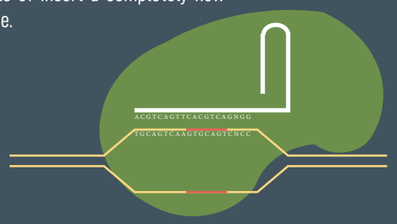
After the DNA has been anchored in the CRISPR-locus, (a region on the bacterial DNA) it is transcribed and cut into small pieces, the so-called crRNA.



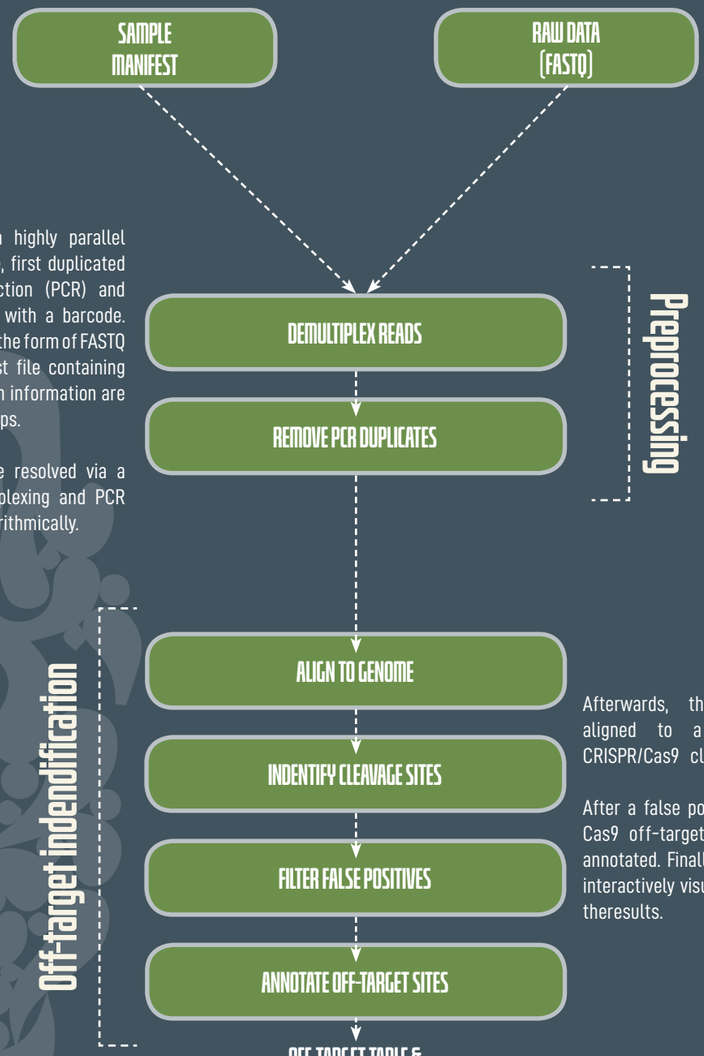
This complex recruits another RNA strand and additionally the CAS9 complex. Together, they are now able to recognise and cut the DNA of a new viral infection, which makes the virus harmless.

For everyday use, crRNA and tracerRNA were combined to form sgRNA. It is now easily possible to recognize and cut DNA sections in organisms with 24 bp length.

Usage of sgRNA is not limited for cutting out indivuidal gene segements. It also offers the possability to introduce mutations, switch off specific segments of insert a completely new sequence.



Despite the high specificity it can happen that the CAS9 complex binds to so-called homologous sequences which have a similar motive as the target sequence. These false sequences are called off targets. With the help of bioinformatics it is now possible to predict which these off-target sequences are.

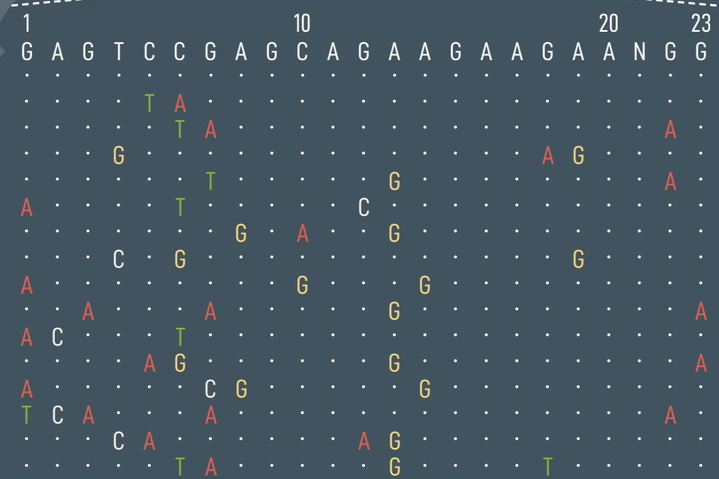


Sequencing nowadays is a highly parallel process, where samples are, first duplicated via polymerase chain reaction (PCR) and second individually labeled with a barcode. Raw sequencing read data in the form of FASTQ files and a sample manifest file containing required experimental design information are first preprocessed in two steps.

The individual barcodes are resolved via a process known as demultiplexing and PCR duplicates are removed algorithmically.

Afterwards, the sequencing reads are aligned to a reference genome and CRISPR/Cas9 cleavage sites are identified.

After a false positive filtering step, CRISPR/Cas9 off-target effects are identified and annotated. Finally, the off-target effects are interactively visualized for easy inspection of theresults.



WHY YOU should support us

The iGEM team Tübingen is an independent research group of motivated students and is therefore responsible for the organization and financing of the project. In order to realize a successful iGEM project and achieve our goals in this competition, we need the support of companies, institutions, associations and private individuals. Not only financial support, but also the provision of materials and resources help us.

iGEM offers each of us a unique and valuable training opportunity that is hard to find anywhere else. Not only are the practical skills deepened, expanded and improved within the framework of a large project, but it also gives the opportunity to expand one's knowledge and skills in other areas. This enables the participants to learn useful skills in the areas of project organization, implementation, presentation, financing and public relations. These are also essential skills for your later career, which make iGEM participants stand out from the crowd. Since iGEM is an international competition and new contacts are established through cultural exchange.

iGEM's intensive experience gives us the opportunity to continue their education outside of their academic career and, by networking with professors, companies, researchers and former participants, it draws on a large pool of knowledge and experience.

The iGEM team Tübingen has always been able to successfully realize its goals and projects thanks to the support it has received in recent years. Through the iGEM team Tübingen, sponsors come into contact with capable and motivated young scientists and are associated with an innovative scientific project. In return for a sponsorship of our project, have the opportunity to advertise and represent themselves in public, at presentations, on our website and in many social networks.

Social Media: Banner
Poster: Standard size representation
Portfolio: Standard size representation

Social Media: Banner
Poster: Standard size representation
Portfolio: Standard size representation
Press: Mention at interviews Print/Digital.

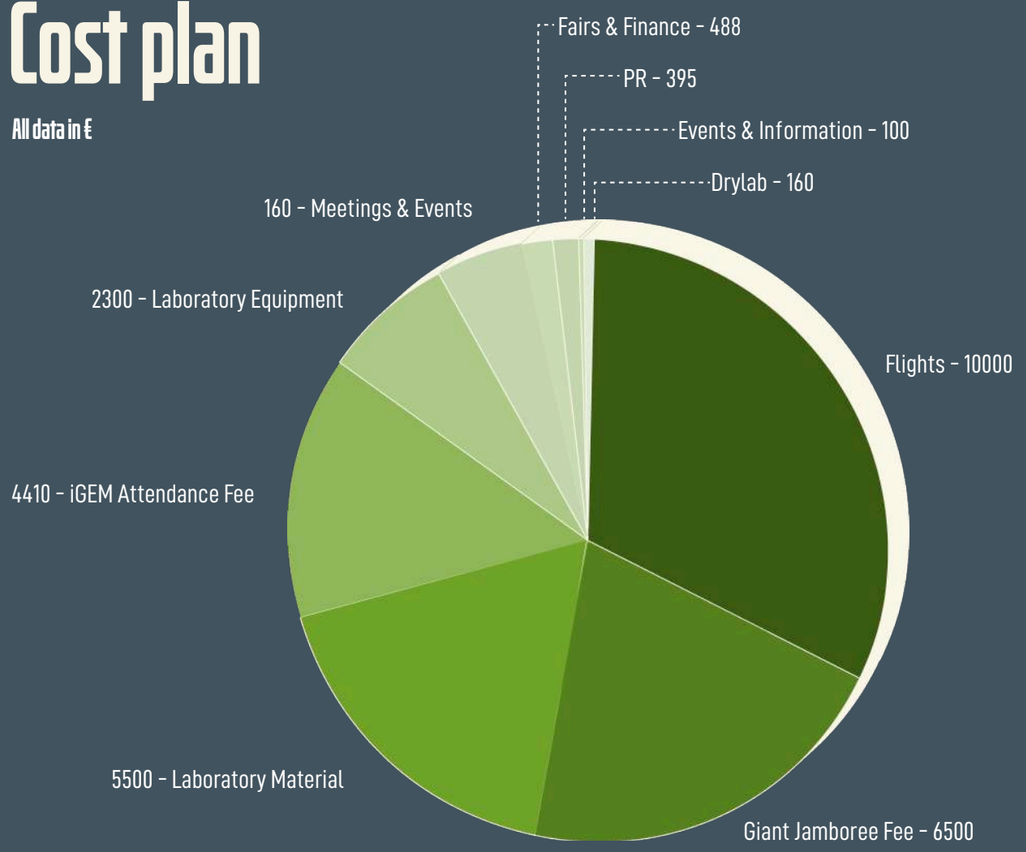
Social Media: Banner & Videos
Poster: Header
Portfolio: Representation on the front page
Press: Mention at interviews print/digital.
T-Shirts: Logo on the back
E-Mail: Header
More: Representation on standard - products

Sponsoring

One major part of an iGEM project is the funding. The costs that arise during one year of intensive research on one's own topic are immense and have to be balanced. Below you find an exemplary list of the expenses of our iGEM project.

Cost plan

All data in €



Sponsors 2018/2019

With the generous support of our sponsors in the past, we have been able to successfully take part in the iGEM competition. Our sponsors have contributed to our success and enabled the completion of professional research projects, through financial support and by providing us with materials and training. Since we are an autonomous student team responsible for project organization, funding, and public representation, our participation at the iGEM competition would not have been possible without our sponsors. Despite paving the way for a promising project, our supporters could also connect with highly motivated studentsand contribute to the intercultural exchange of young scientists. We are immensely grateful for your support and help!

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