

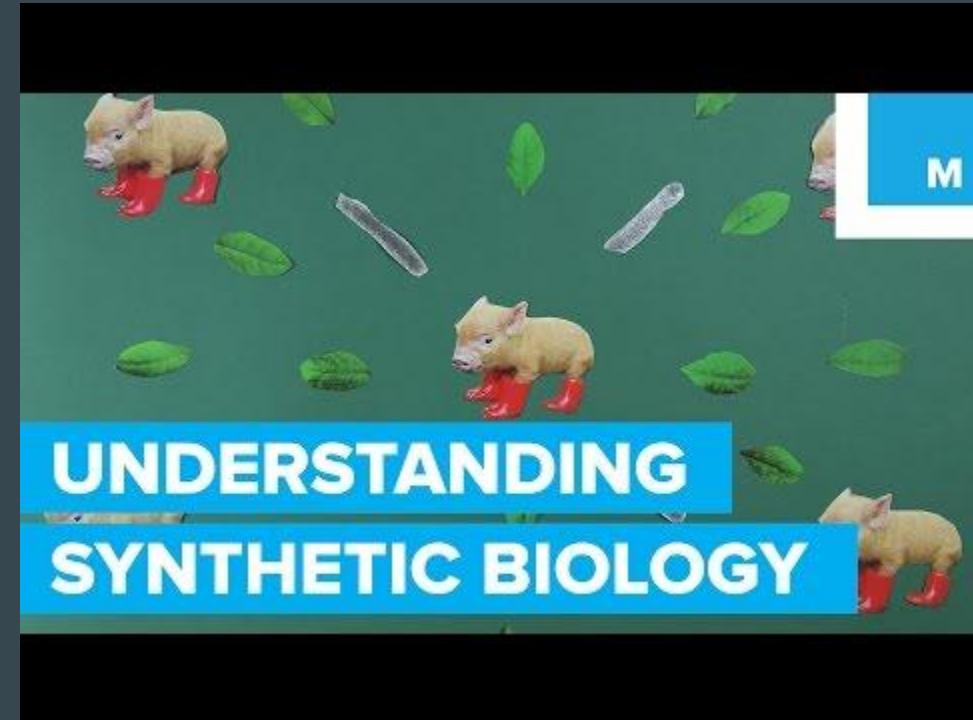
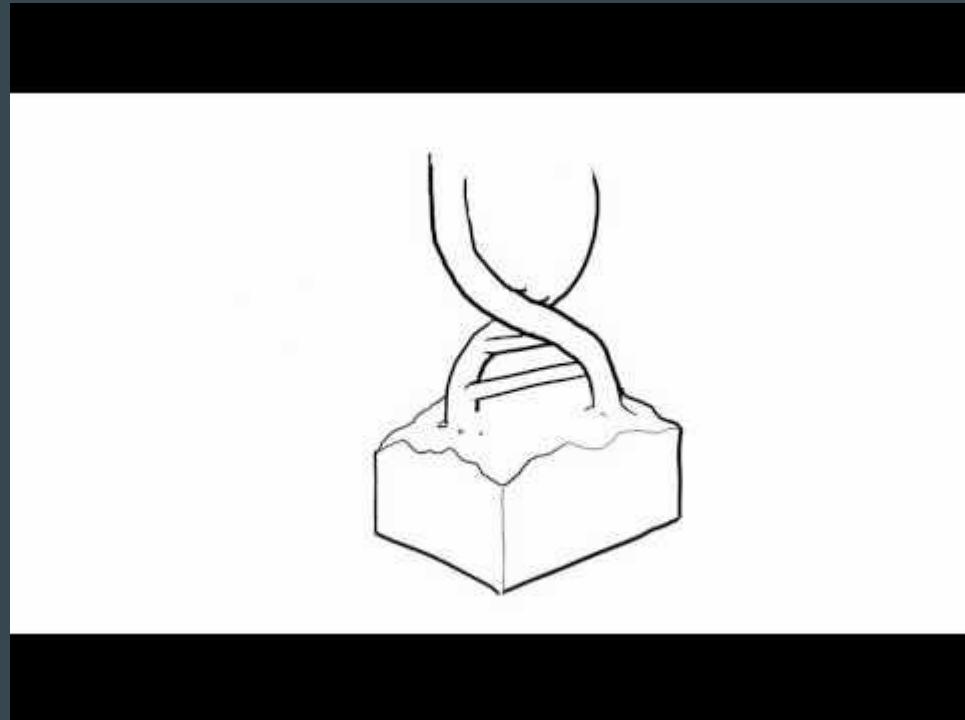
iGEM Winter 2019 Info Session



Agenda

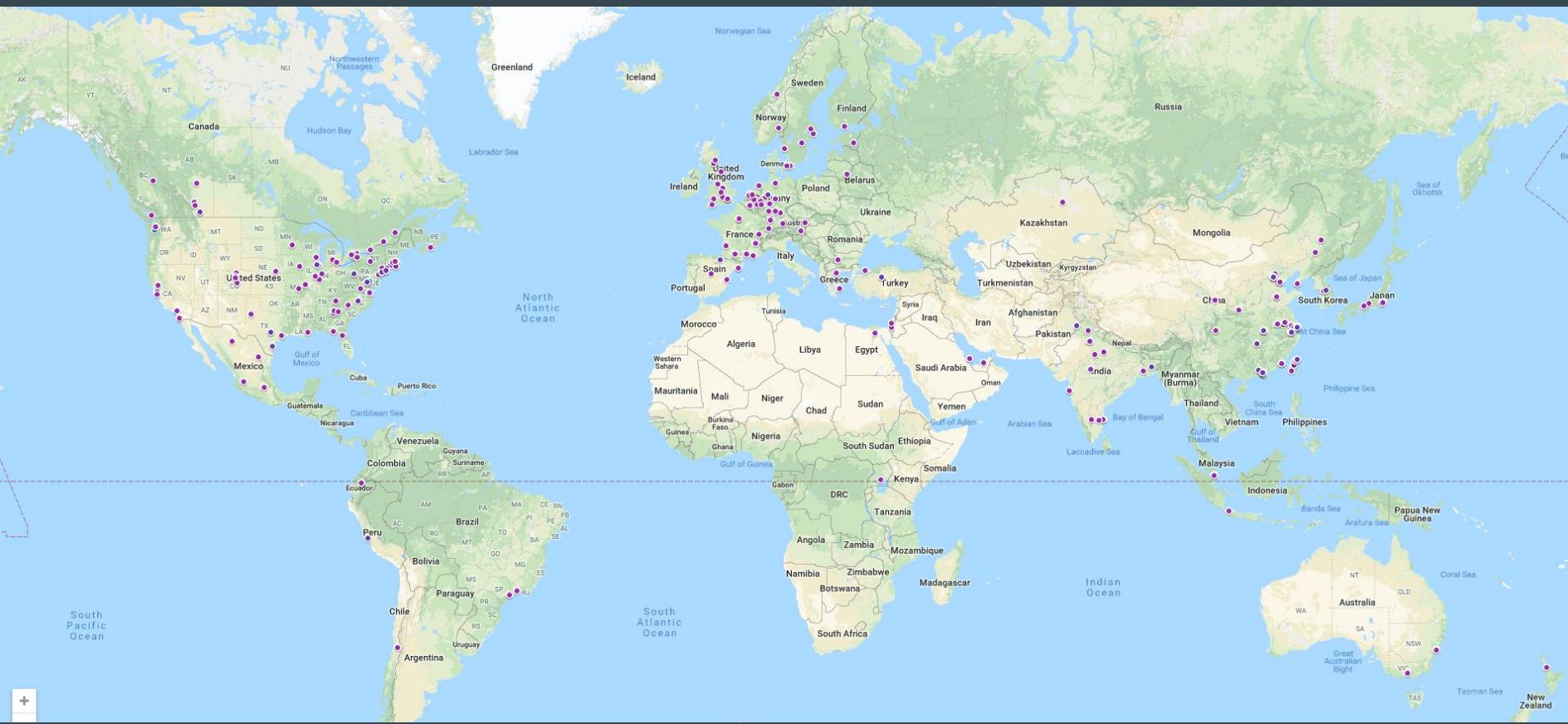
1. Introduction to iGEM
 - a. Synthetic Biology
 - b. What does every team need to do?
 - c. Previous Projects
2. Subteams of iGEM
3. iGEM as a class
4. Preparing for the Competition
5. Funding
6. Q&A

Videos Explaining SynBio



International student team competition in Synthetic Biology

Mission: We aim to solve **real-world challenges** by building
genetically engineered biological systems



316 teams

41 countries

What do we do?

Spring

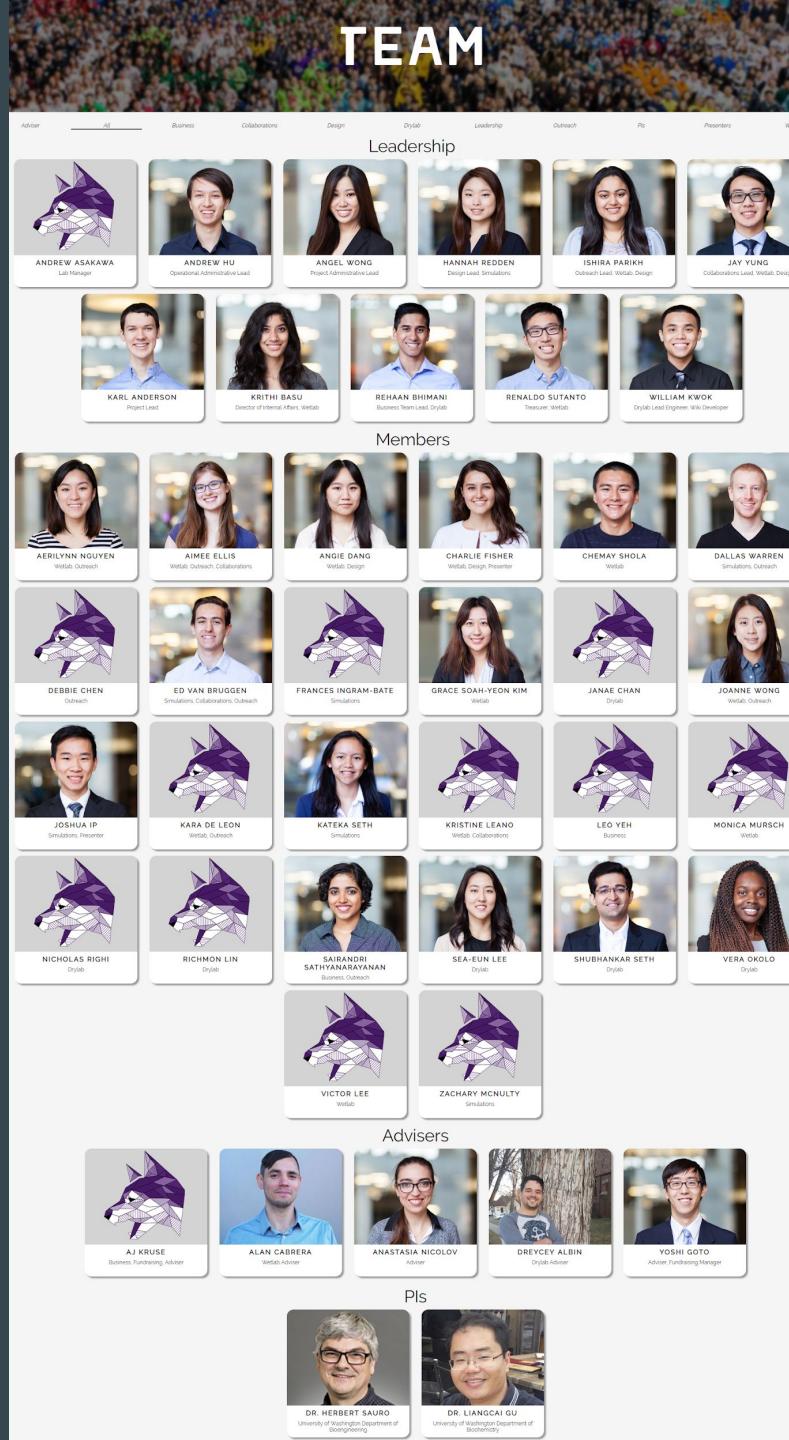
- Training
- Getting to know each other + being certified

Summer

- Bulk of development, research, and lab

Autumn

- Finishing touches (this is not a calm process)
- Fly to Boston to present findings!



iGEM is Interdisciplinary!

Biochemistry

Electrical Engineering

Bioengineering

ACMS

Biology

Informatics

Education

Math

Physics

Computer Science

(Intended and Declared!)

Team (Professors)



Prof. Liangcai Gu
(Biochem,IPD,Genome)

Chemically Induced
Dimerization



Prof. Herbert Sauro
(BioE,EE)

Systems Biology
Software + Biological
Control Systems

iGEM Requirements

All teams have...

- Project
- Website
- Poster
- Presentation
- Biobricks

Good teams have...

- Relevance to the real world
- Engagement with stakeholders
- Modeling
- Business and policy considerations
- Much more...

Website!

- Showcases the project in a complete and comprehensive way
- #Aesthetic

<http://2018.igem.org/Team:Washington>

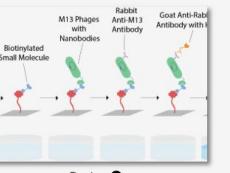


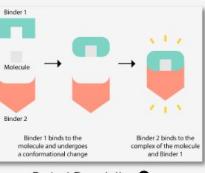
STRONGER TOGETHER
An efficient, generalizable approach to design biosensors for small molecules

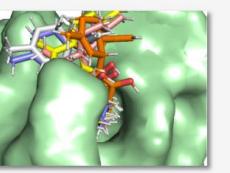
[OVERVIEW](#)

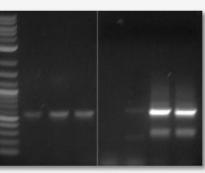
Washington iGEM 2018
Chemically induced Dimerization of Nanobodies for the Development of Versatile Biosensors

Chemically induced dimerization (CID), in which two proteins dimerize only in the presence of a small molecule, has been widely used to control cell signaling, regulatory, and metabolic pathways, and used as logic gates for biological computation in living mammalian cells. However, few naturally occurring CID systems and their derivatives are currently available. Creating a CID system with desired affinity and specificity for any given small molecule remains an unsolved problem for computational design and other protein engineering approaches. To address this challenge, we have used a novel strategy to select CID binders from a vastly diverse combinatorial nanobody library. We have created new CID systems that can sense cholecalciferol and artemisinin. We are validating CID biosensors by a yeast three-hybrid system and built structural models to understand the small molecule-induced dimerization. Our work is a proof-of-concept that can be generalized to create CID systems for many applications.

Design 

Project Description 

Model 

Results 

Collaborations 

Entrepreneurship 

Education & Engagement 

Integrated Human Practices 

Team 

Poster + Presentation!



BioBricks!

DNA parts in a standard format

Open source → available to all scientists!

Figure 7: HA-tag fused to different dCas9-fusion proteins encoded on the RFC25 pSB1C3 backbone.

Sequence and Features [edit]

Subparts | Ruler | SS | DS Length: 5409 bp

Assembly Compatibility: 10, 12, 21, 23, 25, 1000

References [edit]

- [1] WEIR, J. (2001). Regulation of herpes simplex virus gene expression. *Gene* 271: 117-130.
- [2] GREAVES, R., O'HARE, P. (1969). Separation of requirements for protein-DNA complex assembly from those for functional activity in the he 63: 1641-1650.
- [3] TRIEZENBERG, S. J., KINGSBURY, R. C., MCKNIGHT, S. L. (1988). Functional dissection of VP16, the trans-activator of herpes simplex vir 718-729.
- [4] HIRAI, H., TANI, T., KIKYO, N. (2010). Structure and functions of powerful transactivators: VP16, MyoD and FoxA. *Int. J. Dev. Biol.* 54: 1589-
- [5] WALKER, R., GREAVES, R., O'HARE, P. (1993). Transcriptional activation by the acidic domain and involves additional determinants distinct those necessary for TFIIB binding. *Molecular and Cellular Biology* 13: 5233-5244.
- [6] THOMPSON, R., PRESTON, C., SAWTELLI, N. (2009). De Novo Synthesis of VP16 Coordinates the Exit from HSV Latency In Vivo. *PLoS F*

Parameters
None

Categories

Registry of Standard Biological Parts

main page design experience information part tools edit

Part: BBA_K1150020

Designed by: M. Scheidmann Group: iGEM13_Freiburg (2013-09-17)

uniCAS Activator (CMV promoter)

The Freiburg iGEM team 2013 designed a fusion protein consisting of dCas9 and VP16 [1-6] for sequence-specific transactivation of a desired target locus ([more information](#)). Therefore, we used our double mutated dCas9 (BBA_K115000) impaired in its cleavage activity and fused it to the 5' end of the sequence coding for the transactivation domain of VP16 (BBA_K115001). To ensure nuclear localization of the construct a nuclear localization signal (NLS) was fused to both ends of dCas9-VP16. For detection of expression the fusion protein was tagged with a HA-epitope coding sequence (BBA_K1150016) and its expression was set under control of the CMV promoter (BBA_K747096) and BGH terminator (BBA_K1150012). Figure 1 illustrates the detailed design of the whole device.

CMV:Ha-NLS-dCas9-Linker-VP16-NLS:BGH

Function	gene activation
Use in	Prokaryotic cells
RFC standard	RFC 10, RFC 10 compatible
Backbone	pSB1C3
Submitted by	[1] edit

Promoter → HA-Tag NLS dCas9 Linker VP16 NLS Terminator

Figure 1: Construct design. dCas9 was fused via a 3 amino acid linker to VP16. The resulting fusion construct was flanked by NLS sequences and tagged by a HA epitope. The CMV promoter and BGH terminator were chosen to control gene expression.

By co-transfected our RNA plasmid (BBA_K1150034) which includes the tracrRNA and the separately integrated, desired crRNA, the dCas9 specifically binds to the targeted DNA sequence. With the help of the transactivation domain of VP16, transcription factors are recruited and the pre-initiation complex can be built. By placing this construct upstream of a promotor region any gene of interest can be activated.

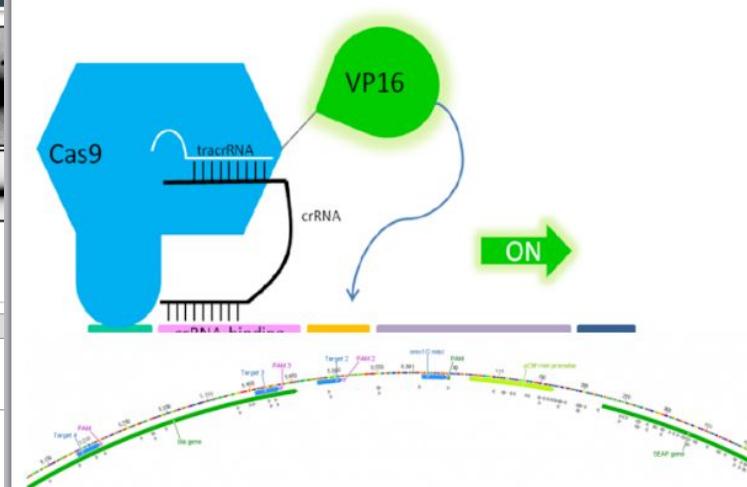


Figure 3: Position of the target loci on the SEAP plasmid.

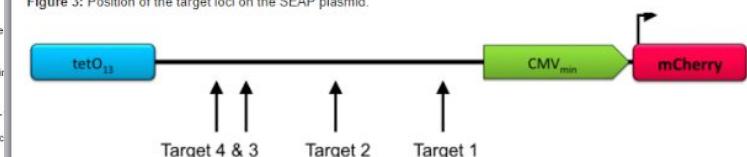


Figure 5:Position of the target sites in front of the mCherry reporter construct.

Figure 6: Results of mCherry activation via dCas9-VP16 using different crRNAs. Scale bar = 200μm.

Student responsibilities + expectations

- Have an attitude to **learn** and **willingness** to participate!
- Ability to **work in a team** in a fast-paced environment
- Be available during **Summer** (if you have to juggle an internship and lab...talk to us)
- Dedicate **5-10 hr/wk** in winter/spring, **10 - 20 hr/wk** in summer/fall*
- Stay **up to date** on communications & contribute your own thoughts!

Previous Projects

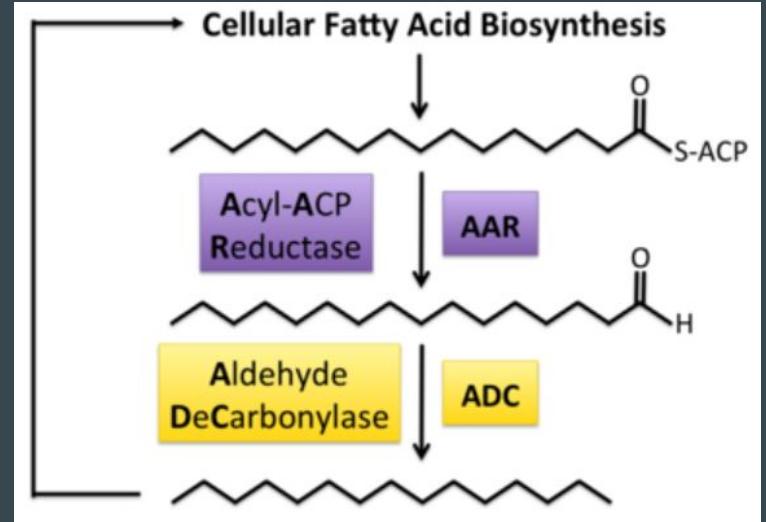
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Boundless Possibilities!

Washington 2011 - Make It or Break It

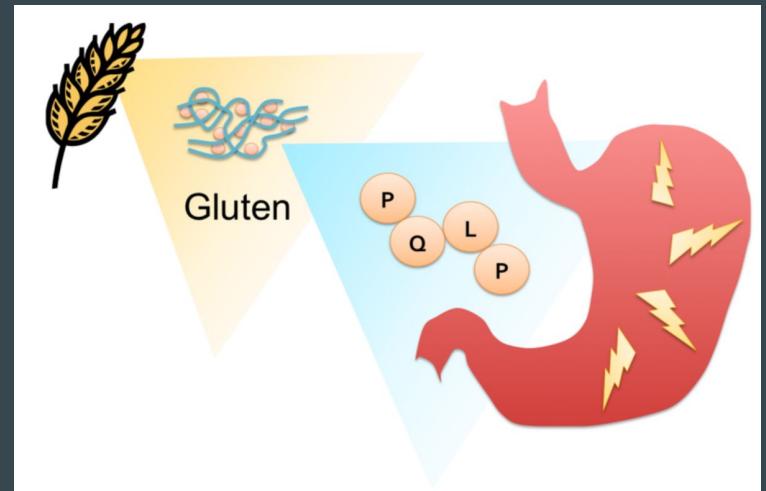
Diesel Production

- E. coli produce alkanes by introducing a pair of genes that convert fatty acid synthesis intermediates into alkanes.



Gluten Destruction

- Reengineered a gluten-degrading protease enzyme to have increased gluten-degrading activity, allowing for the breakdown of gluten in the digestive track for patients with gluten intolerance.





PvP Biologics is in Phase 1 Clinical Trials with KumaMax
45 people have been dosed to date with KumaMax (liquid) for Phase 1

Phase 1 Clinical Progression

- Two clinical studies
 - Univ. of Michigan
 - Anaheim, CA
- Safety and Tolerability
- Proof of Mechanism



Tablet Development for Phase 2

KumaMax pills
Concept for iGEM
2011

Actual Tablets
with KumaMax
2018



Washington 2018 Project

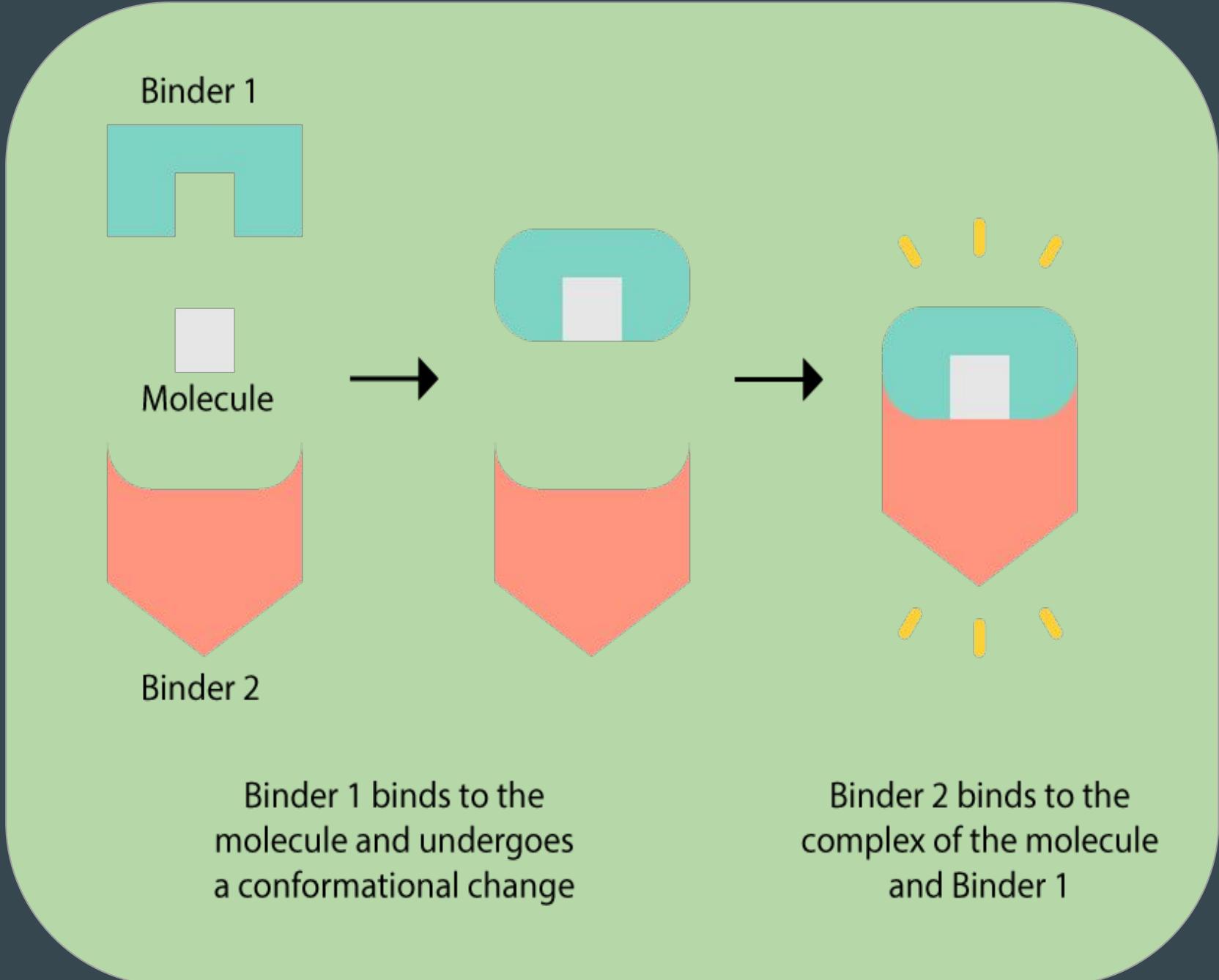
Stronger Together

An Efficient, Generalizable Approach to Designing Biosensors

Background

Chemically Induced
Dimerization

Simple mechanism with
promising applications

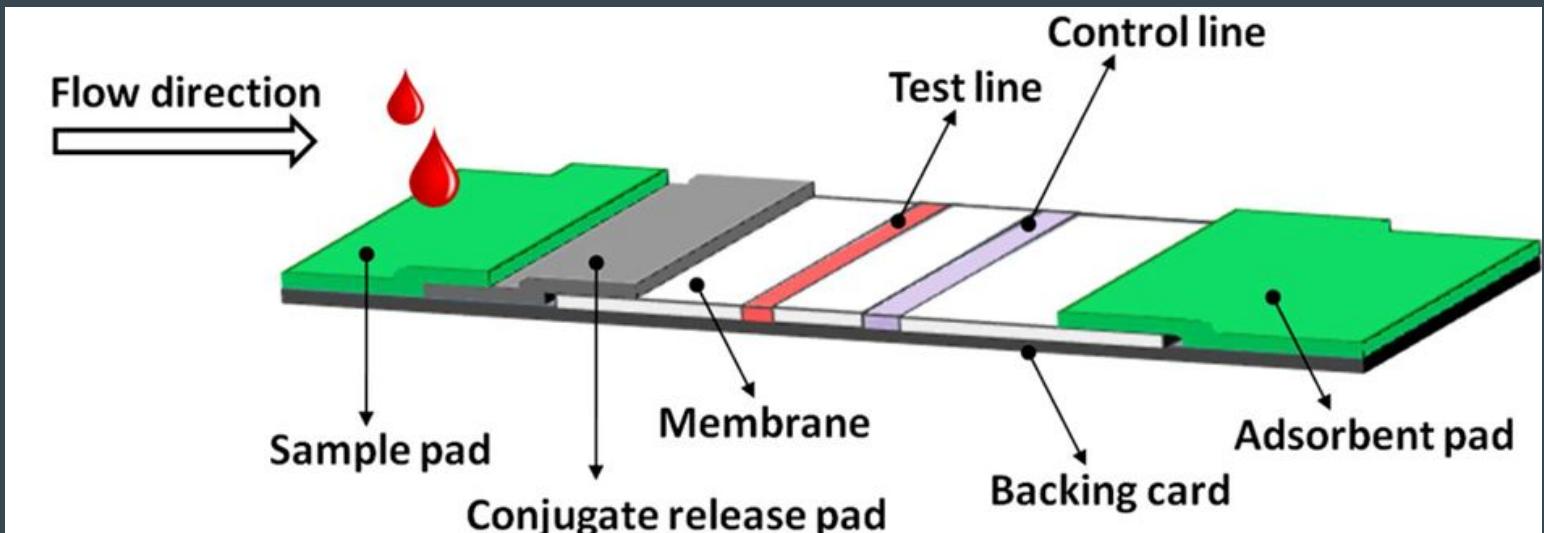
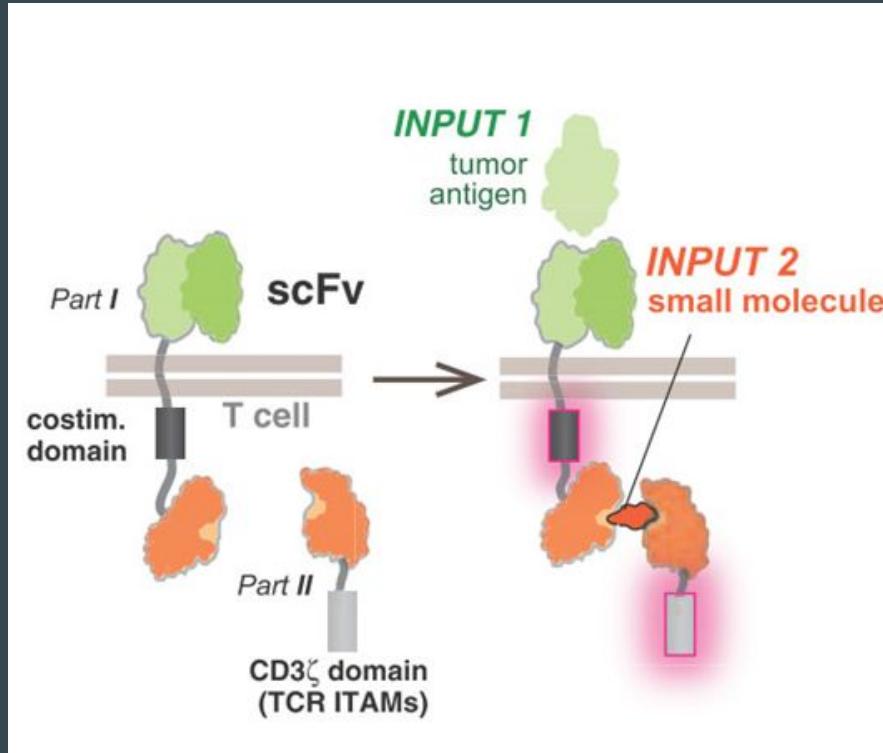


Background

Chemically Induced Dimerization

Simple mechanism with promising applications:

- CAR T-cell Therapy
- Point of Care Diagnostics
- Metabolic Engineering



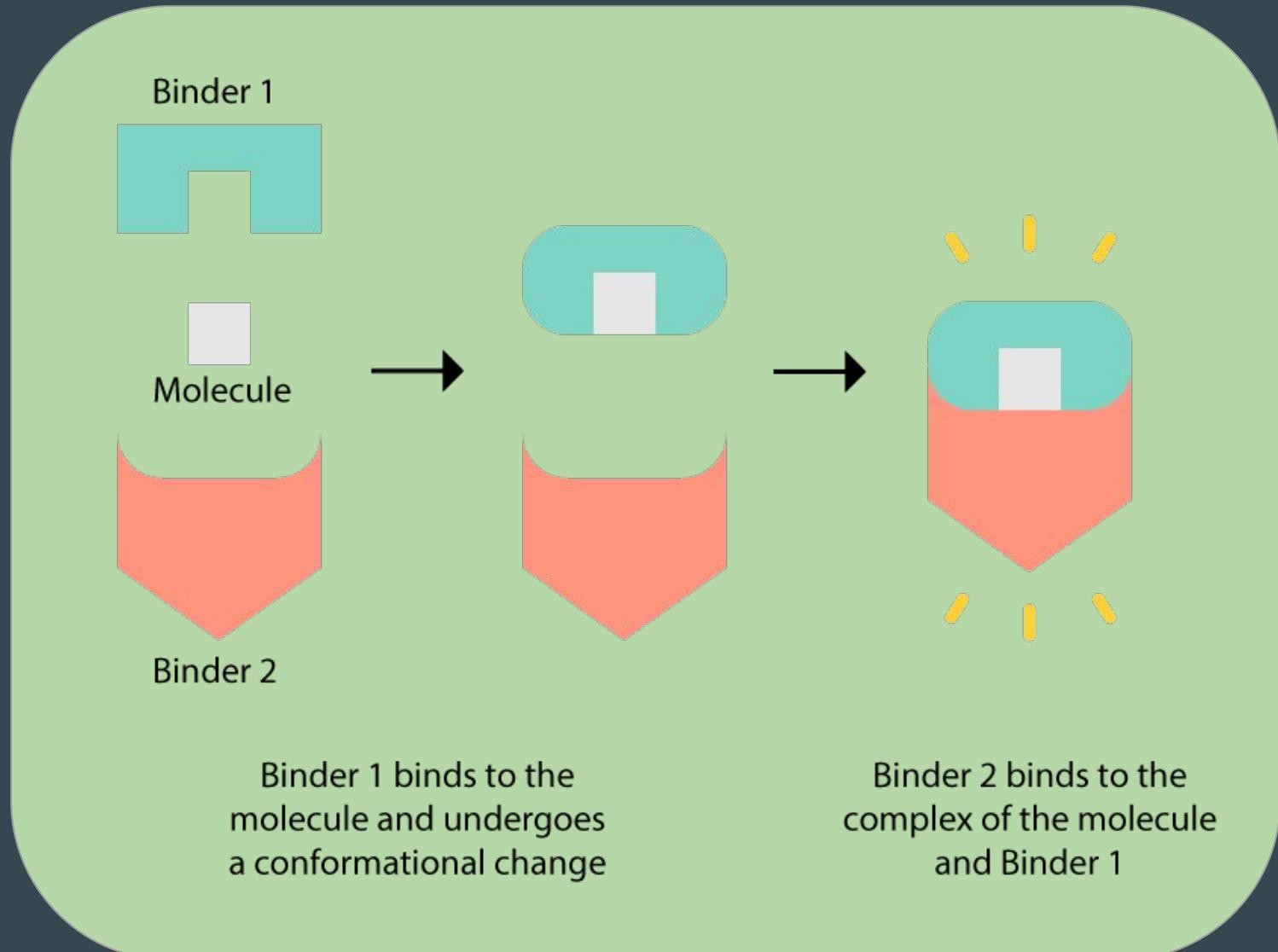
Background

Few CID systems are available:

- Hard to find
- Currently unfeasible to engineer

Solution: antibodies

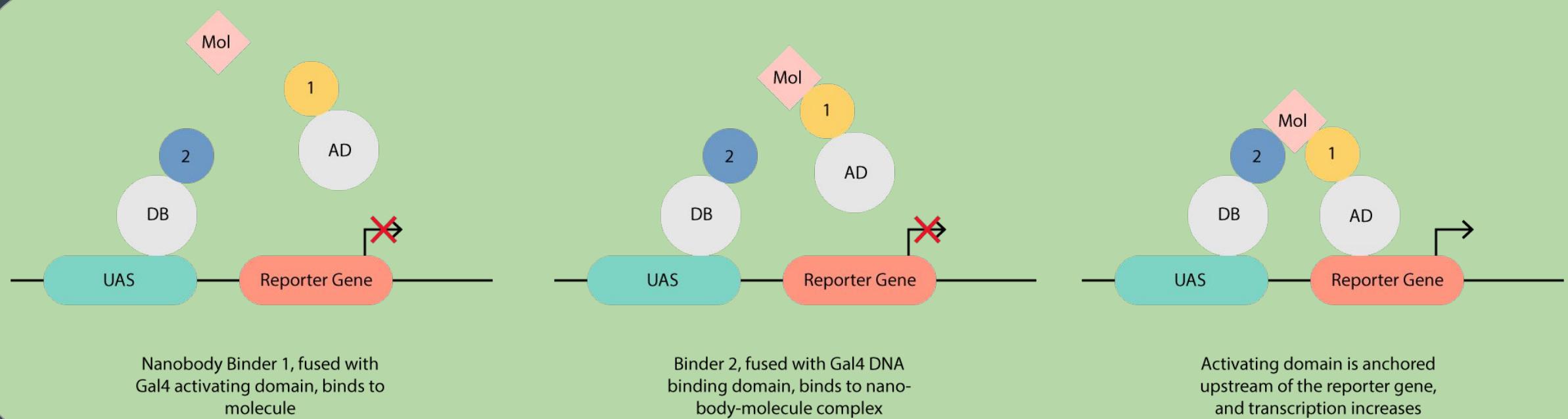
- Screen large library of antibodies to find binders
- Method: Phage Display



Washington 2018 Project- Application

Biosensor: Adapted Yeast 3 Hybrid system

- Create novel biosensors for small molecules
 - Vitamin D3
 - Artemisinin

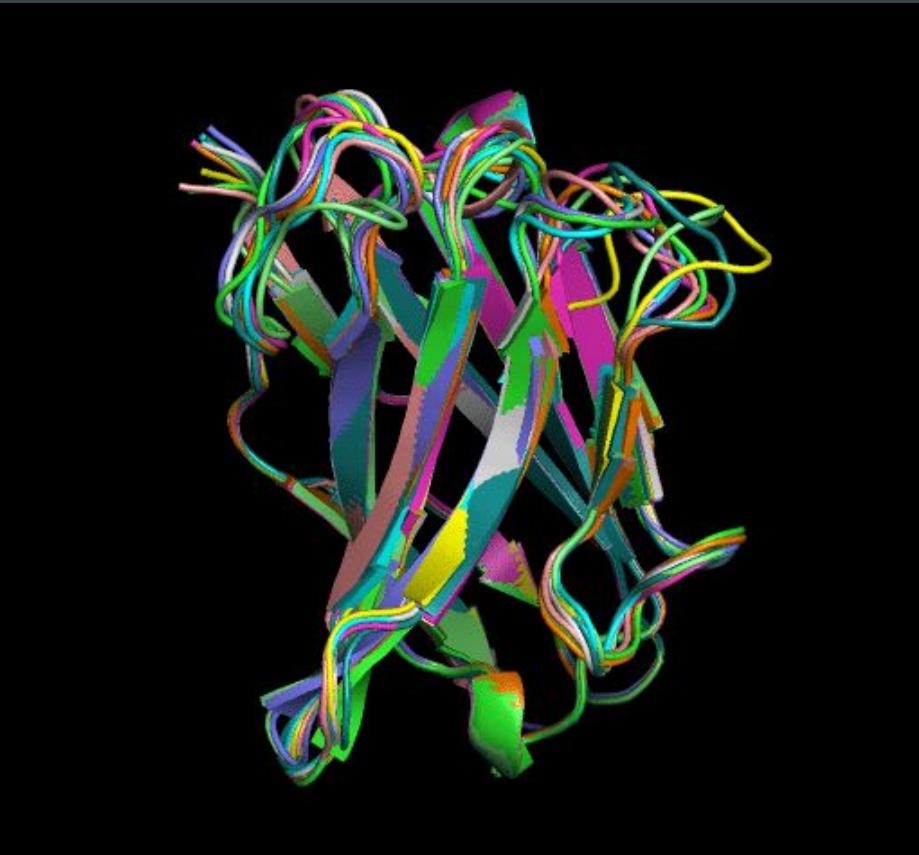


Washington 2018 Project- Future Work

The Need for Optimization

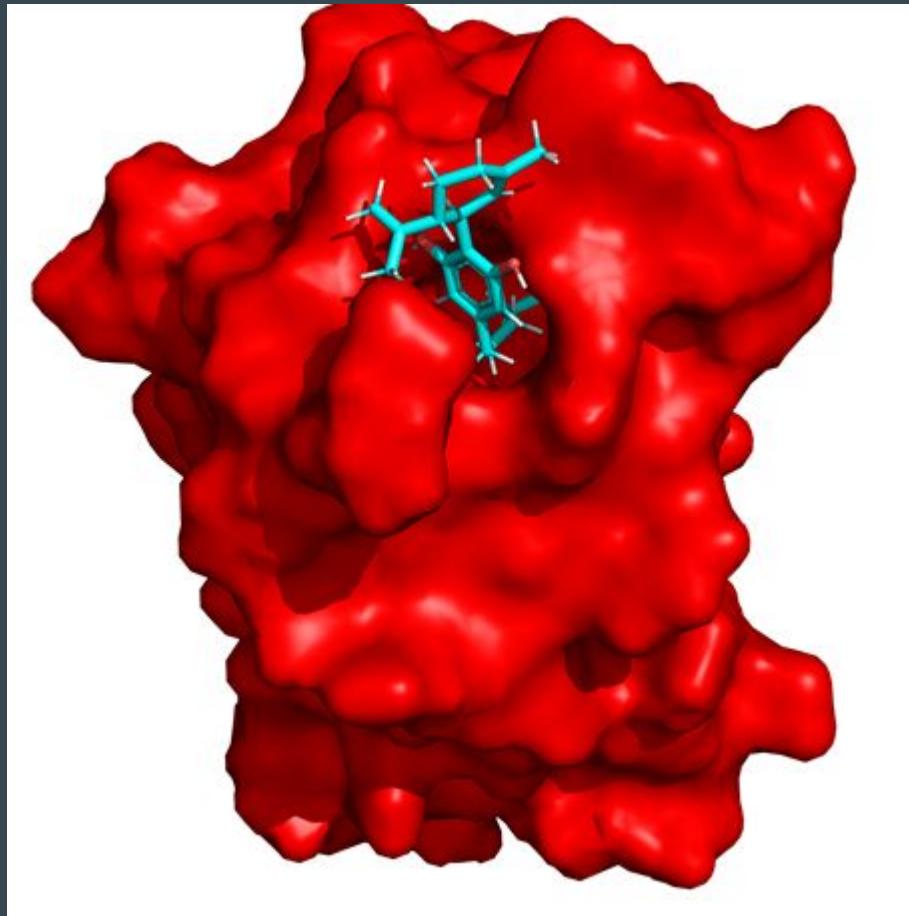
- Poor binding inadequate for applications
- Insufficient specificity leads to false positives

Washington 2018 Project- Future Work



- Simulations goals:
 - Determine antibody structure
 - How do they bind to target molecules
- Ultimate goal: engineer stronger binders

Washington 2018 Project- Future Work



- Simulations goals:
 - Determine antibody structure
 - **How do they bind to target molecules**
- Ultimate goal: engineer stronger binders

Wetlab

• • •

Our Project

- Identifying nanobody binders for specific small molecules
 - Working in close collaboration with the Gu Lab in the department of Biochemistry
- Goal for this year: To identify all nanobodies necessary and create a biological detection system

Interlab

- Have previously analyzed reproducibility
- Largest interlaboratory study
- A chance to get published! And...
- A chance to lead a project!



RESEARCH ARTICLE

Reproducibility of Fluorescent Expression from Engineered Biological Constructs in *E. coli*

Jacob Beal^{1*}, Traci Haddock-Angelli², Markus Gershater³, Kim de Mora², Meagan Lizarazo², Jim Hollenhorst⁴, Randy Rettberg², iGEM Interlab Study Contributors¹

¹ Raytheon BBN Technologies, Cambridge, MA, United States of America, ² iGEM Foundation, Cambridge, MA, United States of America, ³ Synthace, London, United Kingdom, ⁴ Agilent, Santa Clara, CA, United States of America

What do we want from you?

- Your address, credit card number, SSN, soul, and all your waking hours from now until eternity
- Initiative, Good nature, Endurance, Motivation
- ~10 hours a week, often more (in summer)

What do you get out of all this?

- Molecular Biology Lab Techniques
 - DNA – PCR, Gel Electrophoresis, Miniprep, Transformation, etc.
 - Protein – Isolation, Purification and characterization
- Research Skills
- Communication and Leadership

Outreach/Human Practices

•••

Talking to non-scientists/children

Education & Public Engagement

- 120-paged multilingual curriculum
 - Used across the world!
- Sit Down with Synbio



Versión Traducida: iGEM TEC CEM



Integrated Human Practices

- Establish communication with our project's stakeholders and use insight to shape our project's future directions
- Shape the narrative of our project and communicate why our work is important
- How can our project be implemented practically?
- How does it benefit the community?



Collaborations

Collaborations

- Working with other teams around the world!
- Pacific Northwest iGEM Meetup
- Outreach Booklet Language Translations
 - Spanish, French, Hindi, Vietnamese



Design & Animations

...

Design

“If a picture paints a thousand words, the motivation behind the design team is to paint our project as clearly as possible.”



WHAT IS SYNTHETIC BIOLOGY?

Synthetic biology is an interdisciplinary branch of biology and engineering. The subject combines disciplines from within these domains, such as biotechnology, genetic engineering, and molecular biology.

WHY IS SYNTHETIC BIOLOGY IMPORTANT?

Due to our ability to manipulate DNA, an essential part of every living organism, we can use synthetic biology to solve a wide range of issues. In medicine, the synthetic biology community is pushing the boundaries by designing microbes that will seek and destroy tumors in the body before self-destructing. Synthetic biology also provides us a way to clean up our environment. We can build organisms to consume toxic chemicals in water or soil that would not otherwise decompose, for example. It can also help us to better understand flu strains and create vaccines. Synthetic biology will even help us feed the world. The applications are limitless.

By agreeing to come to this event, you are giving iGEM permission to photograph you. If you would not like your pictures to be used in social media, please let the photographer know.

STAY IN TOUCH

Follow us on...
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[@ washington_igem](#)

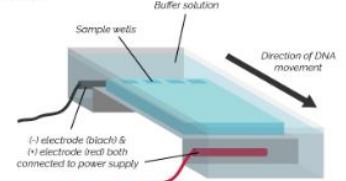
Join our mailing list!
[bit.do/UWIGEMMail](#)



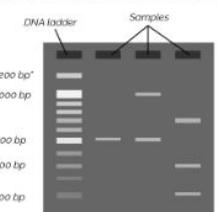
Gel Electrophoresis Bunny Activity
Washington iGEM

HOW DOES GEL ELECTROPHORESIS WORK?

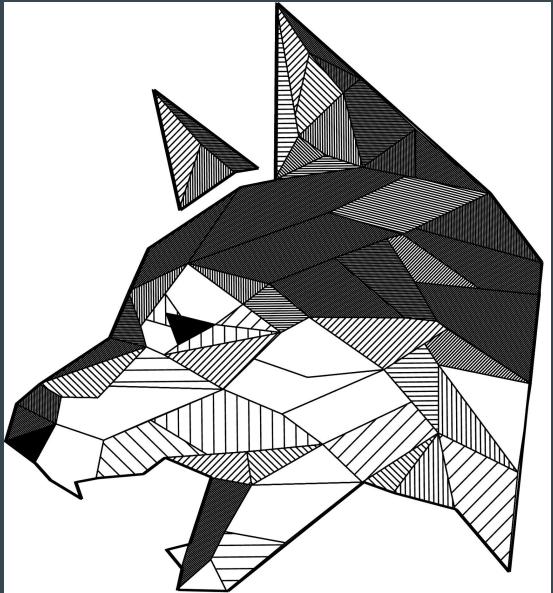
- A gel is prepared that has **wells**. The DNA will be placed into the gels & travel through the gel
- After turning on the power supply, the DNA "swims" through the gel towards the **positive** charge of the box



- Usually, the first well is loaded with **DNA ladder**
 - A ladder is used as a marker for known lengths of DNA fragments
 - DNA fragments show up as bands on the gel, which can be seen with UV light
 - The more negative and **shorter strands** travel through the gel **faster**

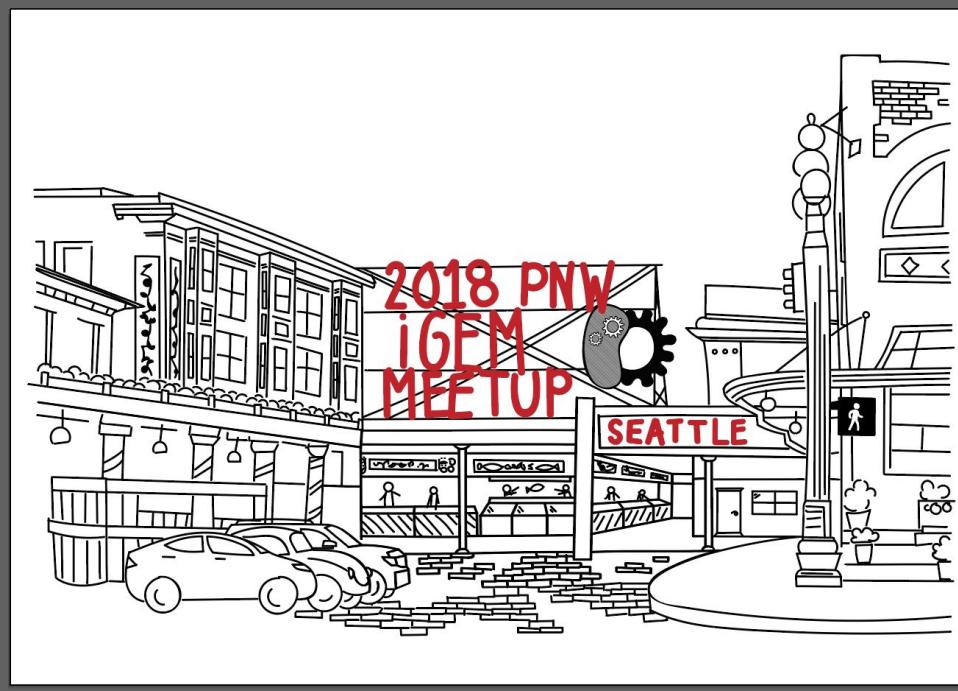


Now that you have learned all about gel electrophoresis, it is your turn to solve a crime!



i G E M
WASHINGTON

What we've accomplished so far



- Logos
- Pamphlets
- Booklets
- Educational Materials

Projects to undertake

Design posters, flyers, and a website

- Team and Project logos
- Outreach informational flyers
- Competition material
 - Project Poster
 - Presentation Slides
 - Wiki figures and animation

Develop a project storyline and introductory animation video

Think up of and tackle fun projects

- Creative introductory pictures

Social Media

- Help us increase our reach through Facebook, Twitter, and Instagram
- Write content highlighting our team members & project for social media
- Work with design team to market our team and ideas!
 - Videos
 - Animations
 - Art



Business, Policy, & Social Media

...

Help us sell our ideas!

Synthetic Biology Funding



\$2,000,000,000

\$1,500,000,000

\$1,000,000,000

\$500,000,000

\$0

2009

2010

2011

2012

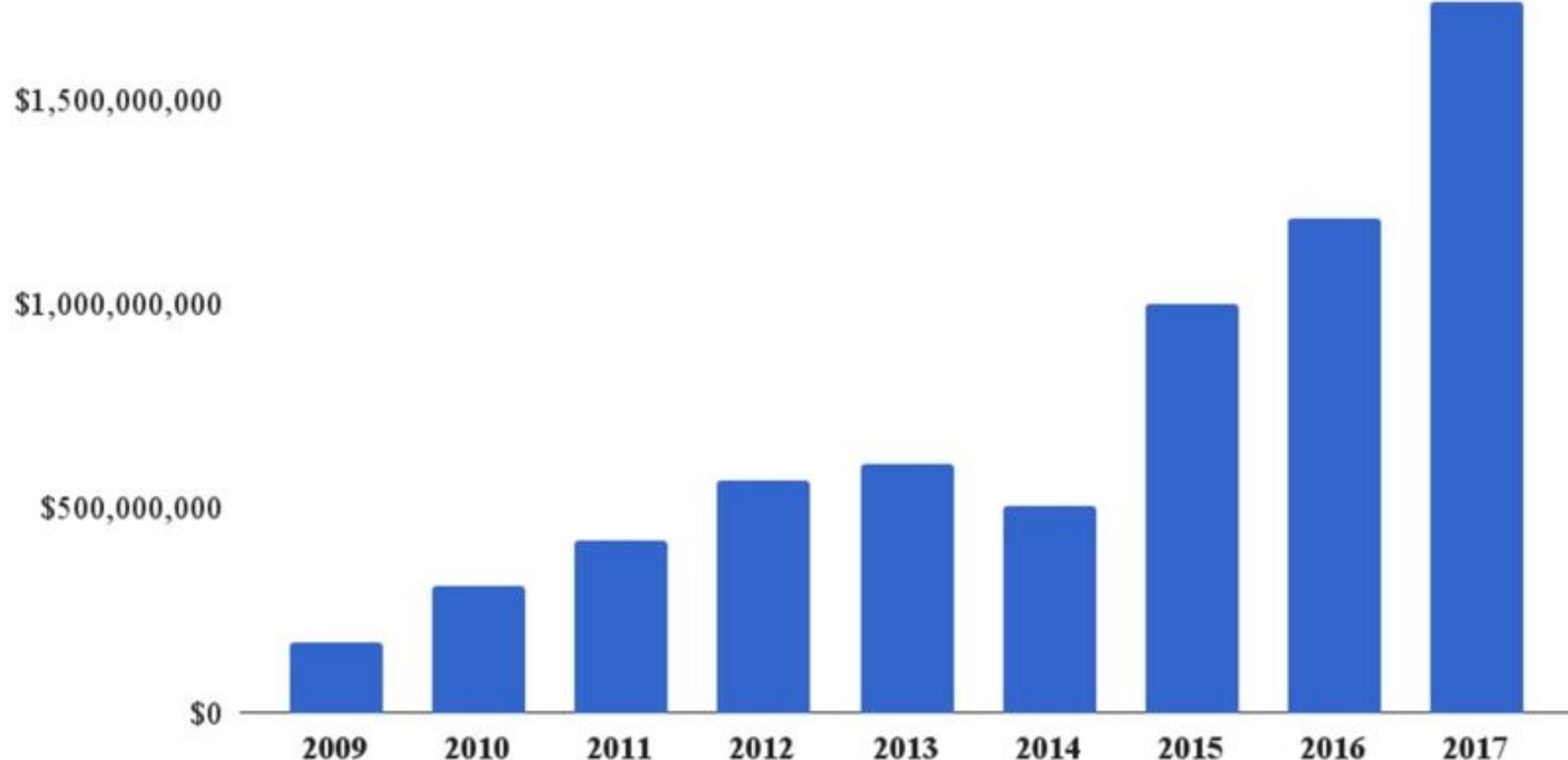
2013

2014

2015

2016

2017





Companies now focus on high-value products



And are getting traction with larger companies

Business & Entrepreneurship

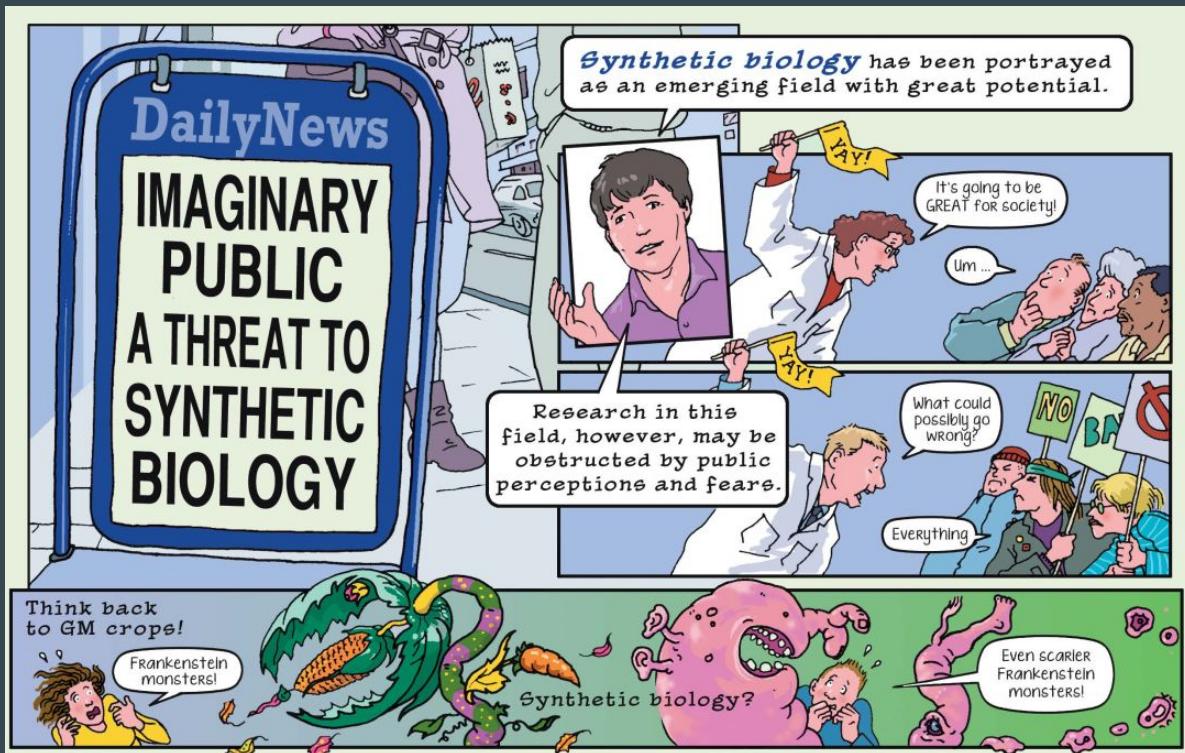
Filling a need (market demand) should inform design decisions in our project

- Engage with biotech industry professionals
- Perform market/industry research and SWOT analysis
- Practice technical writing and business skills
- Fulfill requirements for iGEM entrepreneurship awards



Public Policy & Ethics

Regulation and government policy plays a significant role in our research.

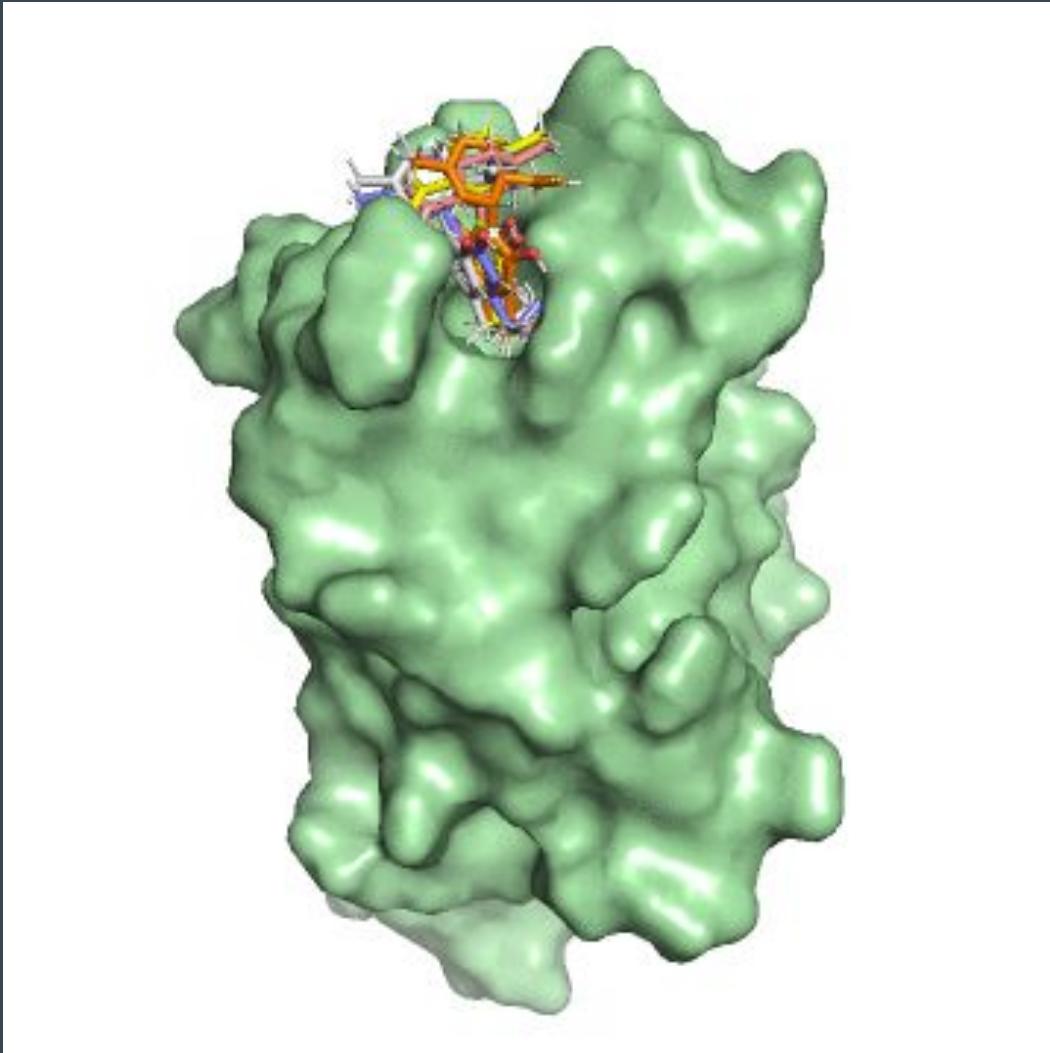


- Learn about policies related to synthetic biology, GMOs, and biotech research
- Research project-related ethical issues
- Interact with local experts and government officials regarding our project
- Write policy briefs related to our project
- Help us make a positive impact in our community!

Simulations

...

What is Simulations?

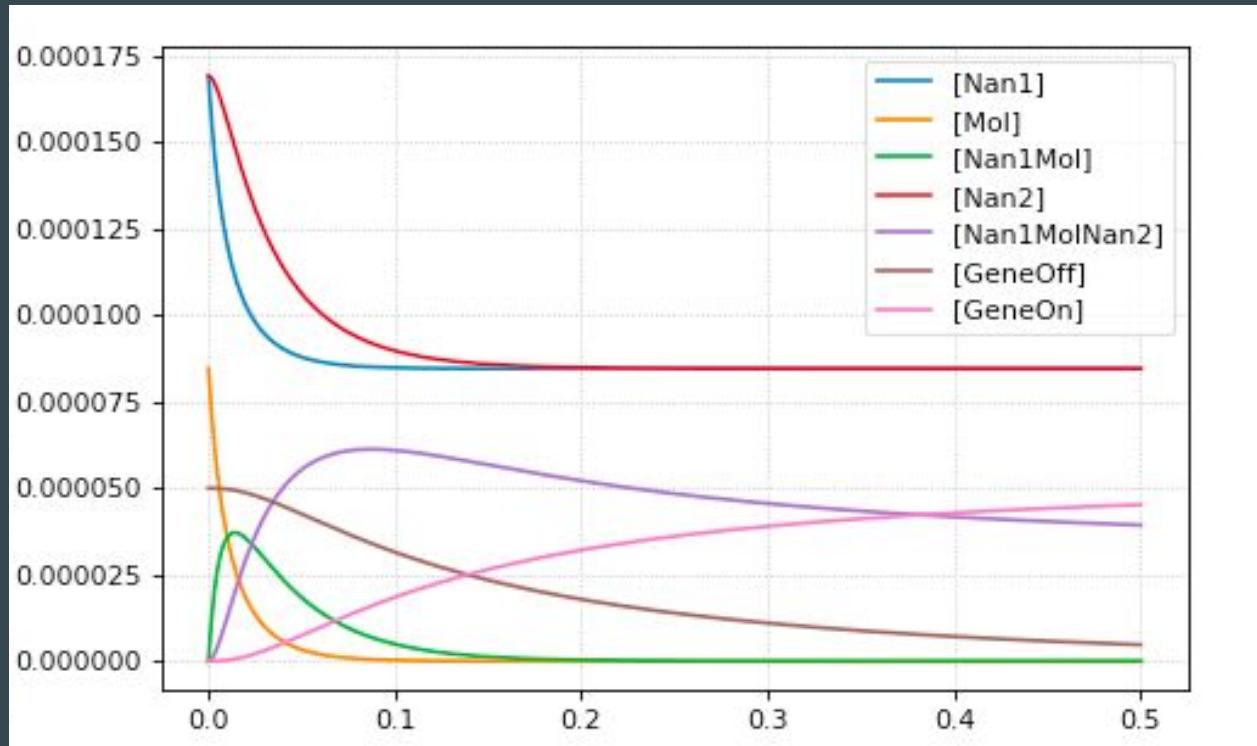
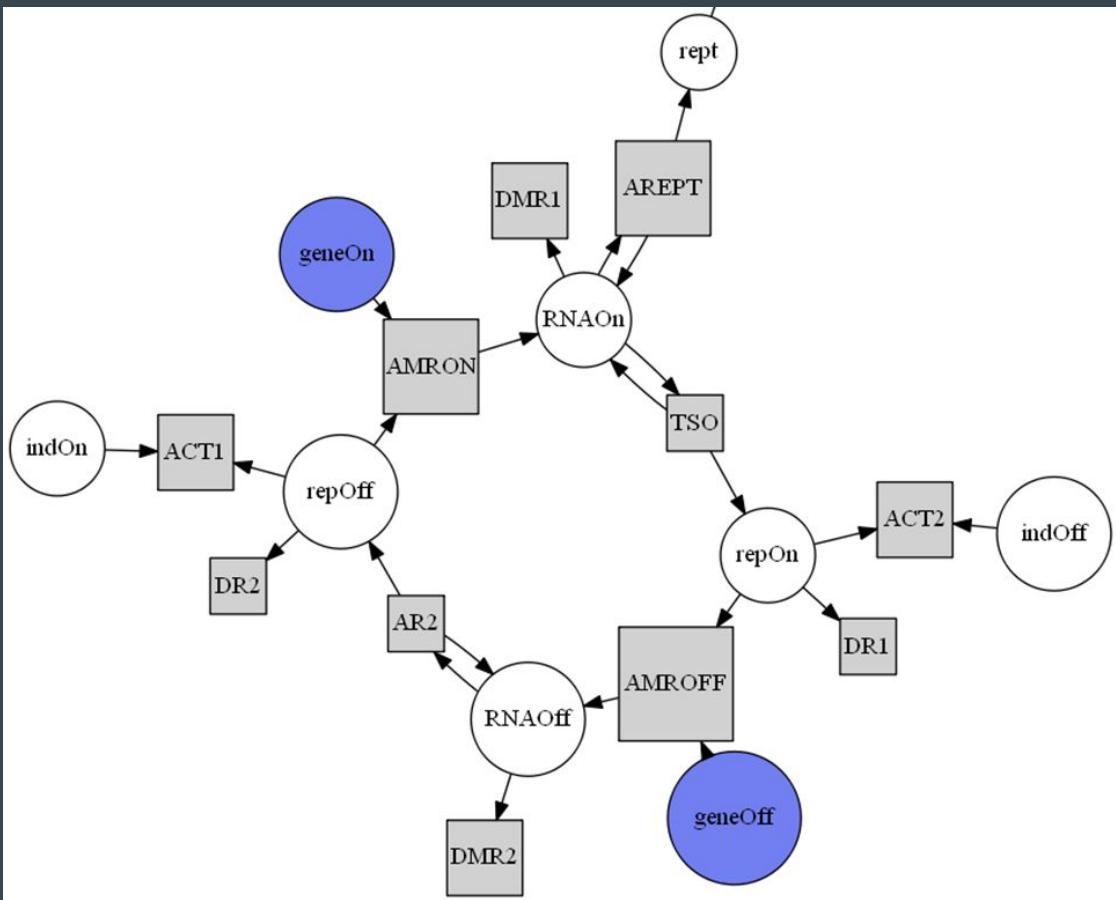


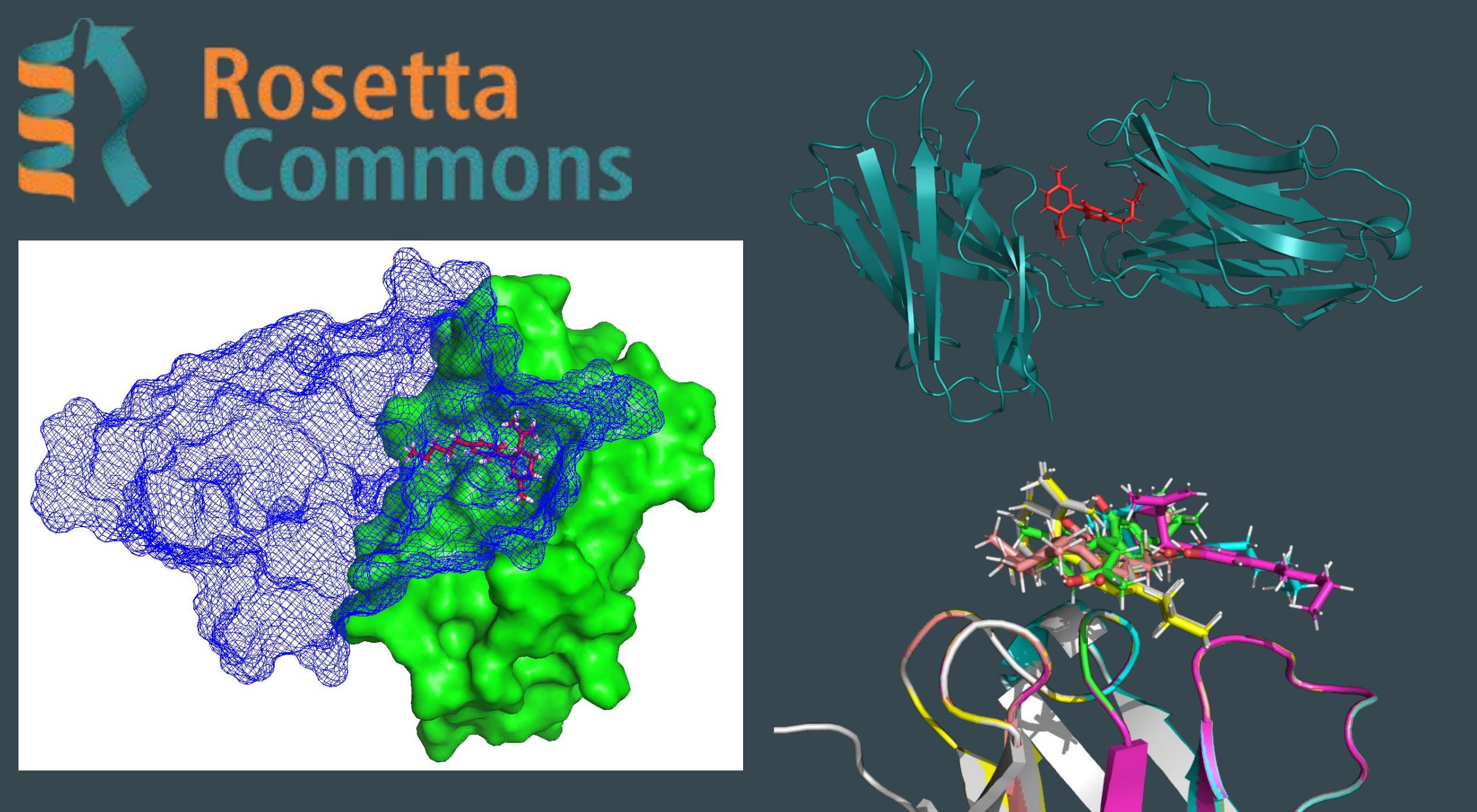
- We construct **computational models** in order to **simulate real systems**, allowing us to *gain insight* and *collect data* on otherwise expensive wetlab experiments
- Simulations are never perfect, only approximations





Tellurium





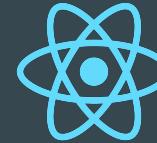
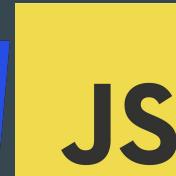
WT

Web Development Team - Intro

- About me
 - William Kwok - Informatics 2020
 - Been with iGEM since freshman year
 - Enjoy building stuff, programming stuff, and playing PC games
 - TA, Research with Code and Cognition Lab, INFO Tutor
 - Interning at Qualtrics as a SDE Summer 2019
- Build a website <http://2018.igem.org/Team:Washington>

The screenshot shows the homepage of the Washington iGEM 2018 website. The top navigation bar includes links for iGEM, wiki tools, search, team Washington, login, Home, Project, Human Practices, Safety, People, and Judging. The main content area features a title "Washington iGEM 2018" and a subtitle "Chemically Induced Dimerization of Nanobodies for the Development of Versatile Biosensors". Below this is a detailed description of the project, mentioning chemically induced dimerization (CID) and its applications in biological computation. Two diagrams are present: one showing the experimental setup with biotinylated small molecules, M13 phages with nanobodies, rabbit anti-M13 antibody, and goat anti-rabbit antibody; and another illustrating the CID process where Binder 1 binds to a molecule, undergoes a conformational change, and then Binder 2 binds to the complex, leading to a signal. To the right, there is a photograph of students working at desks, labeled "Education & Engagement".

Web Development Team - Duties



- Build a performant, mobile friendly website using HTML, CSS, JavaScript ES6, and React
- Ideally, you should know HTML, CSS, JavaScript, and DOM manipulation fundamentals, will teach React if you don't know it
- No need to know any biology
- You will gain experience with:
 - Common React patterns
 - Creating a content management system using Firebase
 - React execution order
 - iGEM MediaWiki quirks
 - working on a mission critical front end aspect of a project with time constraints
- Time commitment: Flexible, on a github issue basis

Web Development Team - Recruitment Process

- Fill out the general recruitment form
- Resume
- Technical project/interview yet to be determined
- Short interview
- 3-5 members.
- More details coming in the email later.

Individual Cost Break Down

3 Main Categories make up the itinerary:

- Airplane Tickets - \$300 (July)
- Hotel or Airbnb Stay - \$150 (Aug)
- Individual Registration Fee - \$700 (Aug)

Est. total:
\$1,150



URP Grant + HUB Grant

URP Conference Grant:

“We encourage all students who have a paper, **poster**, or scholarly creative work that has been accepted for presentation at a professional conference to apply for an award.” – URP

Every member is eligible to apply! SO
APPLY

Last year, every person who applied received the award.

HUB Travel Grant:

\$1500 that the iGEM RSO applies for
- Pending availability

**Together: potentially about
\$250-300 of travel grant
per person.**

Open Leadership Positions

- Fundraising Lead
- Operations Manager
- Director of Internal Affairs
- Treasurer
- Collaborations Lead
- Public Engagement Lead

Question Time!

- General questions now
- Specific/personal questions to relevant people after we break up

