SynthBio@UNIPD: Greetings & Introduction

Co-organizers: Luca Schenato (DEI), Ignazio Castagliuolo (DMM), Livio Trainotti (DiBio)

DIPARTIMENTO DI INGEGNERIA DELL'INFORMAZIONE

DMM Dipartimento di Medicina Molecolare Università di Padova

DIPARTIMENTO DI BIOLOGIA

DIPARTIMENTO DI INGEGNERIA INDUSTRIALE

Fondazione Cassa di Risparmio di Padova e Rovigo

Support:

Financial support:

Fondazione Cassa di Risparmio di Padova e Rovigo

RICERCA SCIENTIFICA DI ECCELLENZA

Endorsement:

DIPARTIMENTO DI INGEGNERIA DELL'INFORMAZIONE

DMM Dipartimento di Medicina Molecolare Università di Padova

DIPARTIMENTO DI BIOLOGIA

DIPARTIMENTO DI INGEGNERIA INDUSTRIALE

UNIVERSITÀ DEGLI STUDI DI PADOVA

Fondazione Cassa di Risparmio di Padova e Rovigo

Greetings

Pro-Rettore Ricerca : Prof. Fabio Zwirner

Fondazione Cariparo: Prof. Nunzio Cappuccio

RICERCA SCIENTIFICA DI ECCELLENZA

Why SynthBio@UNIPD and why now ?

- **Context**:
  - Synthetic Biology to be one main research driver in the future
  - Spontaneous and uncoordinaterd activities at UNIPD
  - UNIPD international excellence in PE, LS, Medicine,
  - Research centers on Network Medicine and Neuroscience but not Synth Bio …. yet

PCNM Padua Center for Network Medicine

PNC Padova Neuroscience Center

- **Question**:
  - Can we make UNIPD a leading international HUB in Syntetic Biology in next years?

Fondazione Cassa di Risparmio di Padova e Rovigo

UNIVERSITÀ DEGLI STUDI DI PADOVA

RICERCA SCIENTIFICA DI ECCELLENZA

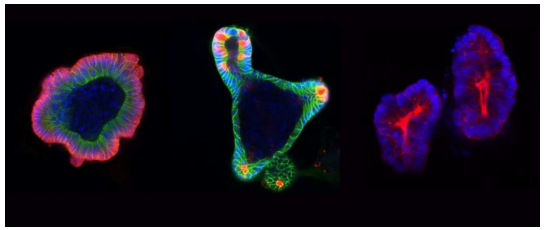
Inception of SynthBio@UNIPD

2017-2020: Department of Informarmation Engineering (DEI)

Proactive Seed grant (200KEuro, 3Y): create new sinergies within DEI

DIPARTIMENTO DI INGEGNERIA DELL'INFORMAZIONE

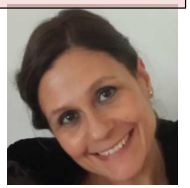
From single-cell to multi-cell information systems analysis



Goal: modeling and analsys of organoids and as multi-agent systems

The Team

Prof. Barbara Di Camillo — Bioinformatics



Prof. Fabio Vandin

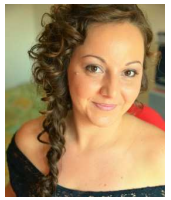
Bioengineering

Prof. Simone Del Favero

PhD. Giacomo Baruzzo

Automatic Control

Prof. Luca Schenato



PhD. Alessandra Dal Molin

Dr. Rita Zamarchi (IOV)

Biology and Clinics

Prof. Nicola Elvassore (DII)

Biotechnology

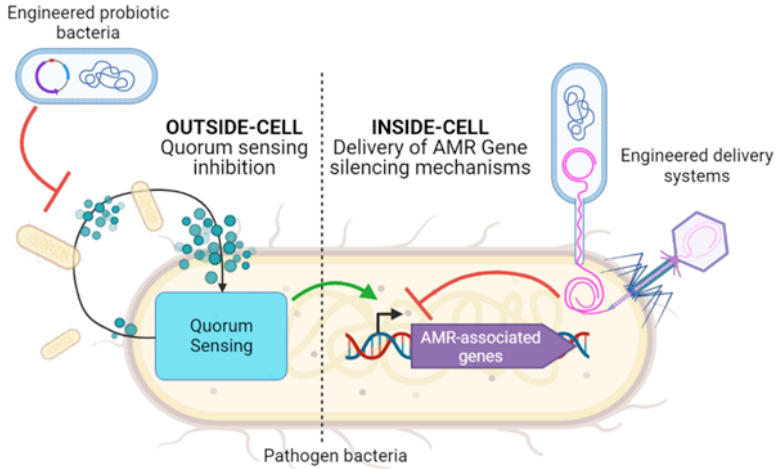
Elisabetta Rossi (DiSCOG)

Fondazione Cassa di Risparmio di Padova e Rovigo

Inception of SynthBio@UNIPD

2021-2025: Progetti di Eccellenza Scientifica CARIPARO
(400K Euro, 3Y)

ReActing: Restoring Antibiotic sensitivity in Bacteria: a synthetic biology approach

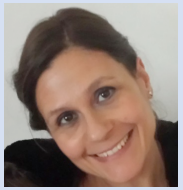


Goal: create engineered bacteria tackling AMR both at single bacterium and at population level

next talk

ENGINEERING

Prof. Luca Schenato (DEI)



Prof. Barbara Di Camillo (DEI)

Prof. Simone Del Favero (DEI)

Dr. Massimo Bellato (DEI/DMM)
Phd. SynthBio @UNIPV
Visiting scholar at SynthBio Lab @MIT

MEDICINE

Prof. Ignazio Castagliuolo (DMM)

Prof. Paola Brun (DMM)

Prof. Stefano Dall'Acqua (dSF)

Inception of SynthBio@UNIPD

ENGINEERING

Prof. Luca Schenato (DEI)

Systems Biology
(6CFU-LM Control Sys. Engineering)

Synthetic Biology
(6CFU-LT Biotecnologie, 5 instructors)

LIFE SCIENCES

Prof. Livio Trainotti (DiBio)

Dr. Massimo Bellato
Phd in Synthetic Biology UNIPV (prof. Lalo Magni)
Visiting scholar MIT (prof. Domitilla Del Vecchio)

Afternoon talk

MUTANS

Student association
(Biology, Engineering, Medicine)

iGEM 2023 iGEM Competition
20th year of iGEM

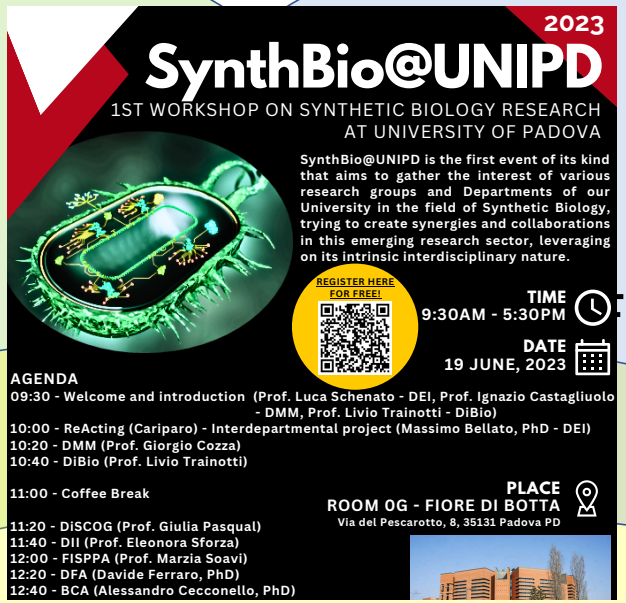
International Genetically Engineered Machine (*iGEM*) competition
(additional faculties)

Inception of SynthBio@UNIPD

Engineering
Physics
Mathematics
Chemistry

Biology
Medicine
Veterinary
Food Science

Humanities
Philosophy
Law

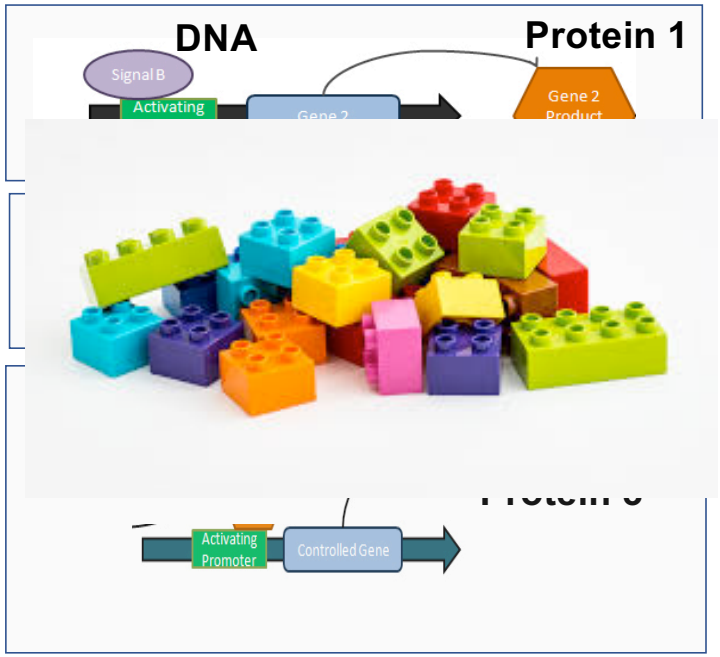


morning talks

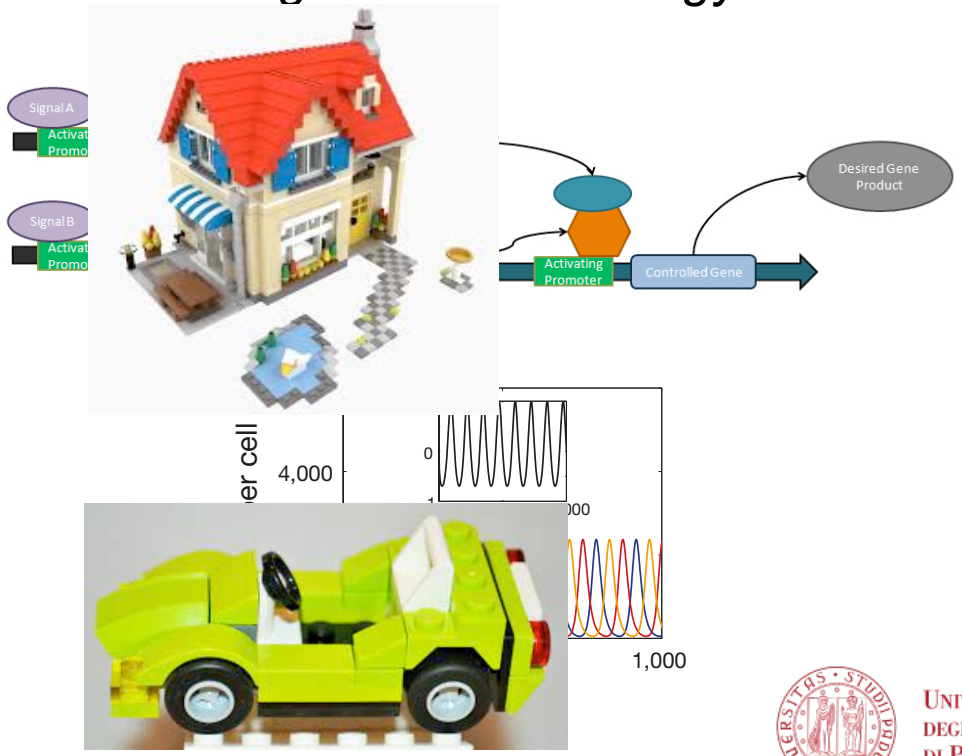
What is Synthetic Biology?

Definition by EU:

Engineering of biologic components and systems that do not exist in nature, *and the re-engineering of existing biologic systems; it is determined on the intentional design of artificial systems, rather than an understanding of natural biology.*



Synthetic Biology



Quick history of Synthetic Biology?

Biological Circuit Definition

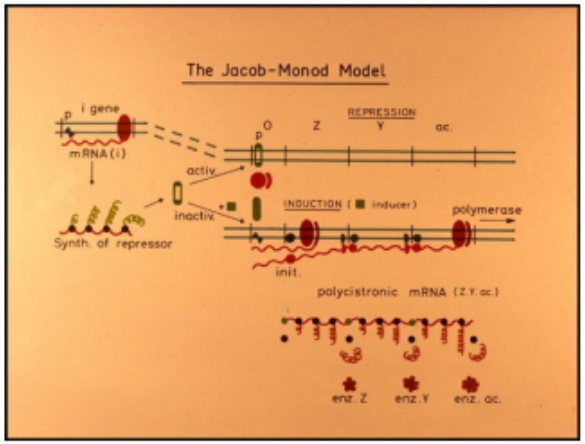
Jaques Monod (1910-1976): Elucidated regulation of gene expression by proteins to create **feedback loops**.

J. Mol. Biol. (1961) **3**, 318-356

REVIEW ARTICLE

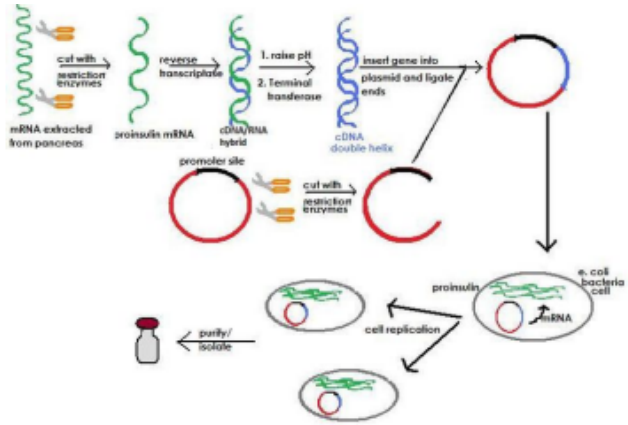
Genetic Regulatory Mechanisms in the Synthesis of Proteins †

FRANÇOIS JACOB AND JACQUES MONOD



Nobel Prize & Philosopher:
bottom-up-approach

Early Genetic Engineering Applications



Insulin Production in E.coli (1978)
Herbert Boyer (b. 1936)
co-founded Genetech

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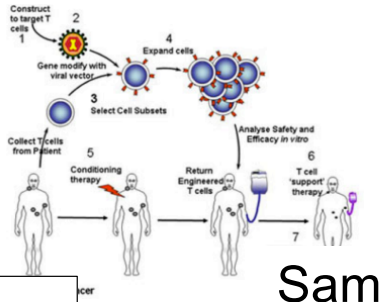
Università degli Studi di Padova

Synthetic Biology vs Genetic Engineering?

Genetic Engineering

Inserting new genes or manipulating DNA

Dolly



R T-cell ther

Biological intuition
Trial&error

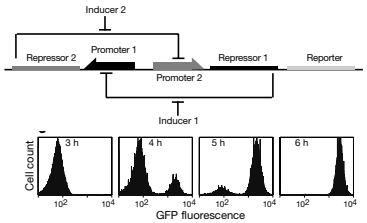
Synthetic Biology

Nature 2000

Construction of a genetic toggle switch in *Escherichia coli*

Timothy S. Gardner*†, Charles R. Cantor* & James J. Collins*†

** Department of Biomedical Engineering, † Center for BioDynamics and ‡ Center for Advanced Biotechnology, Boston University, 44 Cummington Street, Boston, Massachusetts 02215, USA*



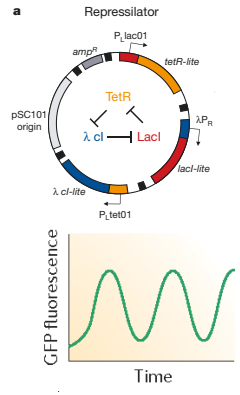
A synthetic oscillatory network of transcriptional regulators

Michael B. Elowitz & Stanislas Leibler

Departments of Molecular Biology and Physics, Princeton University, Princeton, New Jersey 08544, USA

Networks of interacting biomolecules carry out many essential functions in living cells[1], but the 'design principles' underlying the functioning of such intracellular networks remain poorly understood, despite intensive efforts including quantitative analysis of relatively simple systems[2]. Here we present a complementary approach to this problem: the design and construction of a synthetic network to implement a particular function. We used three transcriptional repressor systems that are not part of any natural biological clock[3–5] to build an oscillating network, termed

NATURE | VOL 403 | 20 JANUARY 2000 | www.nature.com

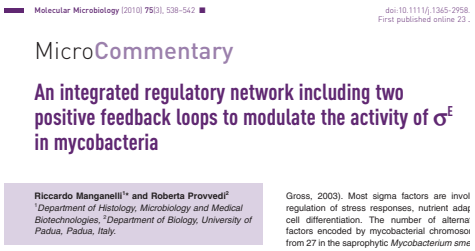


Same molecular biology tools
Conceptually different approach

Bottom-up DESIGN from minimal genetic bricks

Synthetic Biology vs Systems/Quantitative Biology?

Systems/Quantitative Biology


Molecular Microbiology (2010) 75(3), 538–542 ■

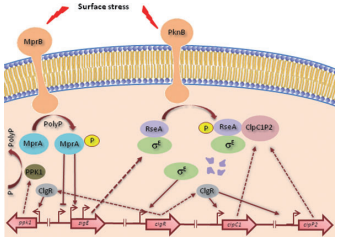
doi:10.1111/j.1365-2958.
First published online 23 .

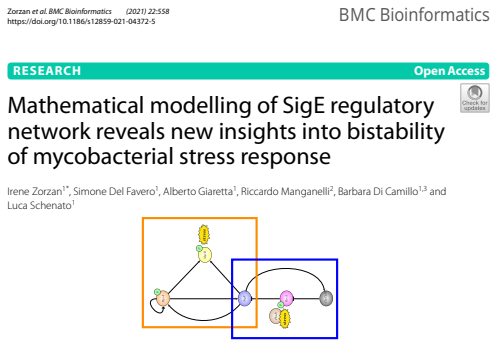
MicroCommentary

An integrated regulatory network including two positive feedback loops to modulate the activity of σ^E in mycobacteria

Riccardo Manganelli[1]* and Roberta Provvedi[2]
[1]*Department of Histology, Microbiology and Medical Biotechnologies,* [2]*Department of Biology, University of Padua, Padua, Italy.*

Gross, 2003). Most sigma factors are invol
regulation of stress responses, nutrient ada
cell differentiation. The number of alterna
factors encoded by mycobacterial chromoso
from 27 in the saprophytic *Mycobacterium sme*




Zorzan et al. BMC Bioinformatics (2021) 22:558
https://doi.org/10.1186/s12859-021-04372-5

BMC Bioinformatics

RESEARCH Open Access

Mathematical modelling of SigE regulatory network reveals new insights into bistability of mycobacterial stress response

Irene Zorzan[1*], Simone Del Favero[1], Alberto Giaretta[1], Riccardo Manganelli[2], Barbara Di Camillo[1,3] and Luca Schenato[1]

Bistability

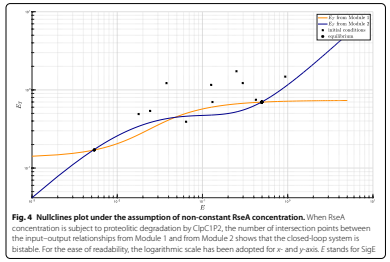


Fig. 4 Nullclines plot under the assumption of non-constant RseA concentration. When RseA concentration is subject to proteolitic degradation by ClpC1P2, the number of intersection points between the input–output relationships from Module 1 and from Module 2 shows that the closed-loop system is bistable. For the ease of readability, the logarithmic scale has been adopted for *x*- and *y*-axis. *E* stands for SigE

Synthetic Biology

letters to nature

Construction of a genetic toggle switch in *Escherichia coli*

Timothy S. Gardner*†, Charles R. Cantor* & James J. Collins*†

** Department of Biomedical Engineering, † Center for BioDynamics and ‡ Center for Advanced Biotechnology, Boston University, 44 Cummington Street, Boston, Massachusetts 02215, USA*

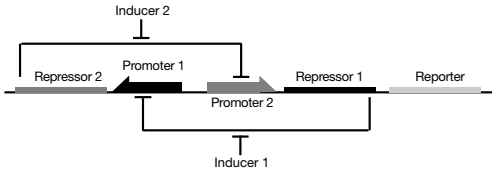
Box 1
The toggle model

The behaviour of the toggle switch and the conditions for bistability can be understood using the following dimensionless model for the network:

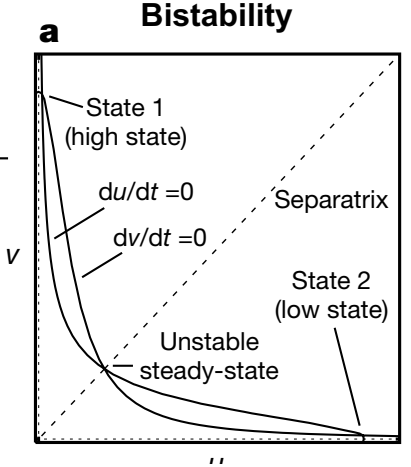
$$\frac{du}{dt} = \frac{\alpha_1}{1+v^\beta} - u \quad (1a)$$

$$\frac{dv}{dt} = \frac{\alpha_2}{1+u^\gamma} - v \quad (1b)$$

where u is the concentration of repressor 1, v is the concentration of



Bistability



ANALISYS
of natural systems

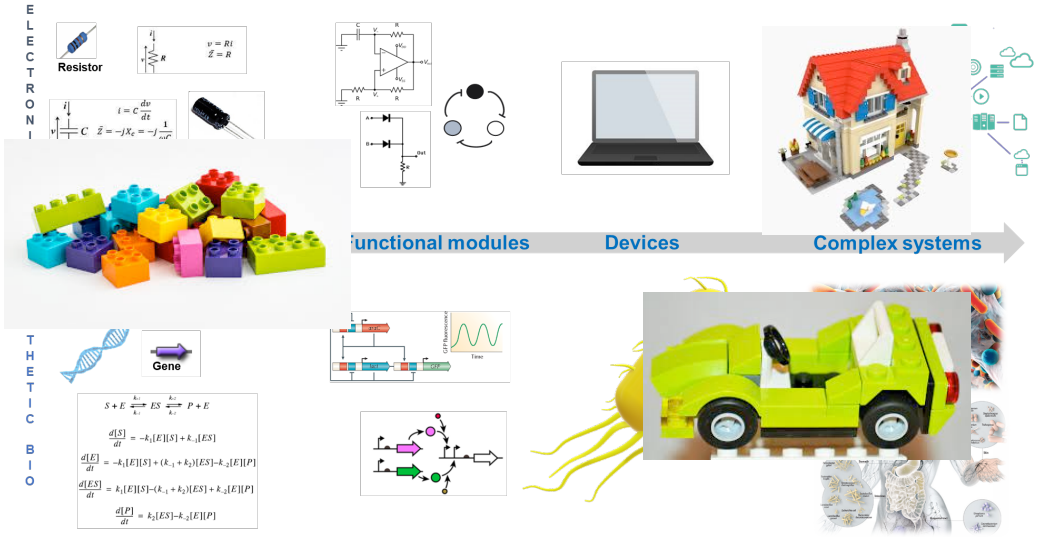
Same mathematical tools
Totally different use

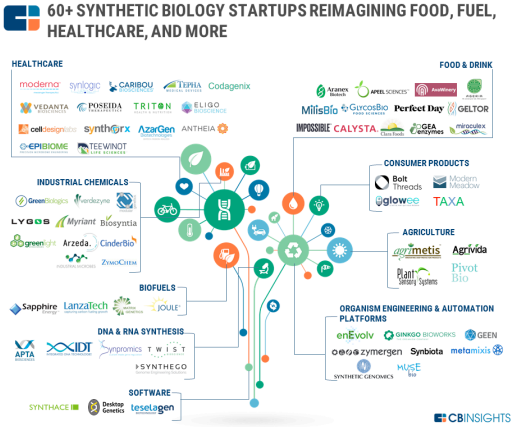
DESIGN
of engineered systems

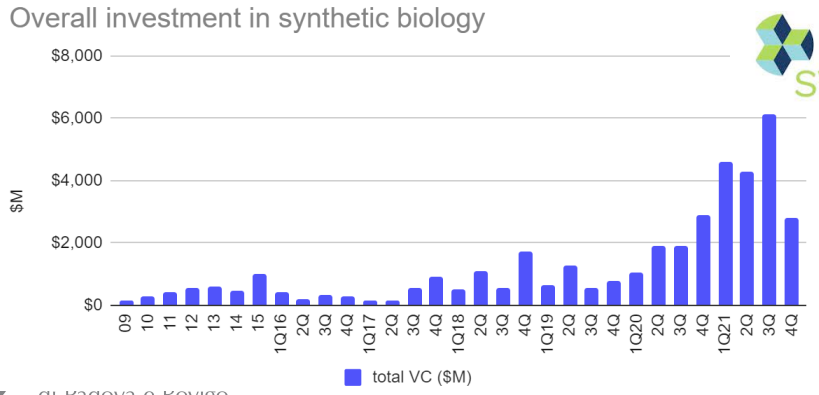
Cassa di Risparmio di Padova e Rovigo

Università degli Studi di Padova

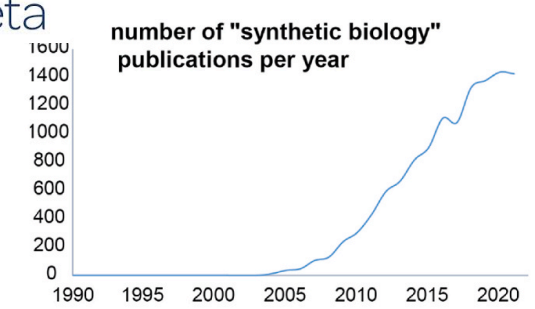
Synthetic Biology: where it is going?



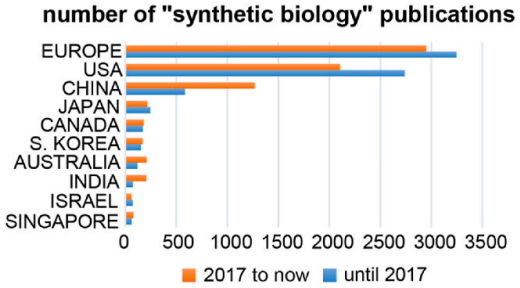




synbiobeta



B



di Padova e Rovigo

RICERCA SCIENTIFICA DI ECCELLENZA

Synthetic Biology: the international context

MIT BE
BIOLOGICAL ENGINEERING

Creating biological technologies from discovery to design.

What is the difference between Biological Engineering and Biomedical Engineering?

The main difference between Biological Engineering and Biomedical Engineering is in scope. BME is focused on using engineering principles for medical problems. BE, on the other hand, uses these engineering principles on the molecular and cellular level for a wide variety of applications - not solely in medicine. Many faculty members are engineering biology for applications in the fields of energy, the environment, and microbial systems.

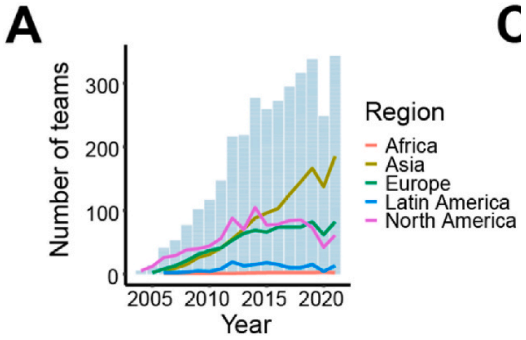
THE UNIVERSITY of EDINBURGH

MSC SYNTHETIC BIOLOGY AND BIOTECHNOLOGY

Synthetic Biology Hub

The Imperial College Centre for Synthetic Biology

iGEM participans



CornellCALS
College of Agriculture and Life Sciences

Biological Engineering Major

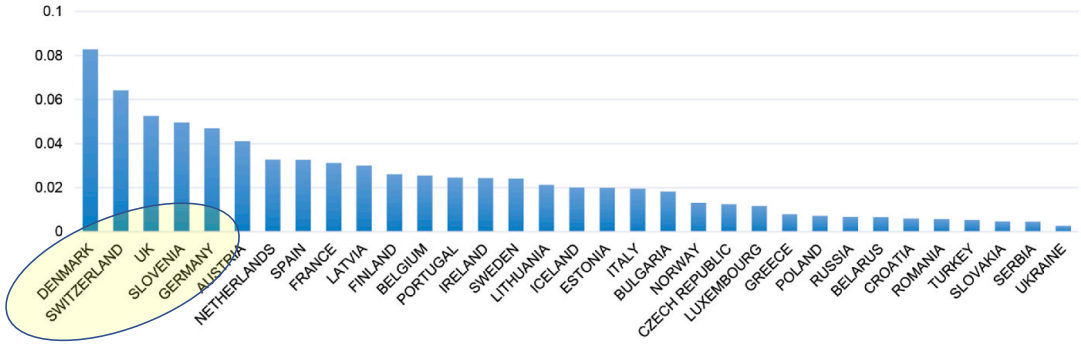
Caltech | Division of Biology and Biological Engineering

Berkeley BIOENGINEERING

Master of Engineering in Bioengineering / Synthetic Biology

SYNTHETIC BIOLOGY
LIFE ENHANCING LIFE
HARVARD MEDICAL SCHOOL

percentage of "synthetic biology" publications over the general scientific output



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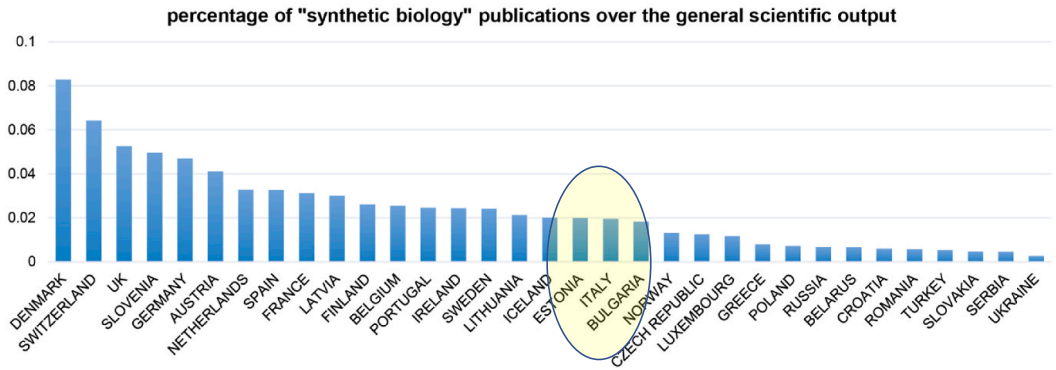
Synthetic Biology: the national context



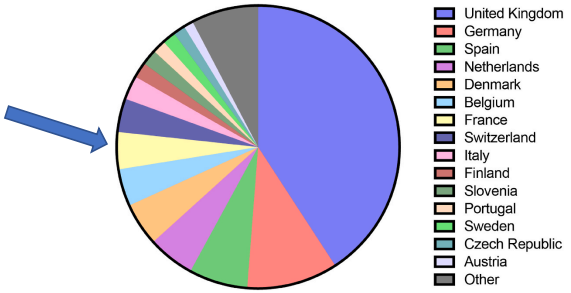


Fig. 3. country of residence of EUSynBioS community members. Under "Other" are included other countries as well as members that did not specify their place of residence.

TELETHON INSTITUTE OF GENETICS AND MEDICINE
igem

iit ISTITUTO ITALIANO DI TECNOLOGIA
Systems and Synthetic Biology
PI: Fabrizio Pirri

BMS bioinformatics mathematical modelling and synthetic biology
Afternoon talk

Università Ca' Foscari Venezia
Dipartimento di Scienze Molecolari e Nanosistemi
Afternoon talk

Several other scattered groups (Catania, Bologna, Pisa, ….)

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Università degli Studi di Padova

RICERCA SCIENTIFICA DI ECCELLENZA

Synthetic Biology: the UNIPD context

10:00 - ReActing (Cariparo) - Interdepartmental project (Massimo Bellato, PhD - DEI)
10:20 - DMM (Prof. Giorgio Cozza)
10:40 - DiBio (Prof. Livio Trainotti)

11:00 - Coffee Break

11:20 - DiSCOG (Prof. Giulia Pasqual)
11:40 - DII (Prof. Eleonora Sforza)
12:00 - FISPPA (Prof. Marzia Soavi)
12:20 - DFA (Davide Ferraro, PhD)
12:40 - BCA (Alessandro Cecconello, PhD)

13:00 - Lunch

14:10 - MUTANS - the iGEM experience @UNIPD
14:30 - SpotLight talks*

PLACE
ROOM 0G - FIORE DI BOTTA
Via del Pescarotto, 8, 35131 Padova PD

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Università degli Studi di Padova

RICERCA SCIENTIFICA DI ECCELLENZA

Synthetic Biology @UNIPD: what's next?

- How do we make UNIPD a leading international HUB in next years?

1. Research Center on SynthBio@UNIPD: aggregator and showcase?
2. Create/modify courses accessible to students across departments?
3. Hiring of new faculty (interdipartimental projects, …)?
4. How to attract interest and funding from industry?
5. ……

15:00 - SB@UniPV: an Engineering perspective (Prof. Paolo Magni)
15:30 - SB@UniVE: a Biology perspective (Prof. Alessandro Angelini)
16:00 - SB@UniFreiburg: an European perspective (Prof. Barbara di Ventura - Zoom)
16:30 - Round Table: A proposal for SynthBio@UniPD

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Università degli Studi di Padova

RICERCA SCIENTIFICA DI ECCELLENZA

Thank you for your attention

Fondazione Cassa di Risparmio di Padova e Rovigo

Università degli Studi di Padova