



***INTERNATIONAL WORKSHOP ON  
ENGINEERED CROPS***

**NSF EPCoR Supported**

**Susanne von Bodman BIO/MCB  
Friedrich Srienc ENG/CBET**

DIVISION OF  
MOLECULAR & CELLULAR BIOSCIENCES

*Predictive Biology through Interdisciplinary Research*





# National Science Foundation

EMPOWERING THE NATION  
THROUGH DISCOVERY AND INNOVATION.

- **An Independent Agency of the US Federal Government**
- **Established in 1950 to promote and advance scientific progress in the United States by sponsoring fundamental research and science education (does not support disease-related research)**
- **Does not conduct research itself.**
- **Receives over 50K proposals each year and funds about 10K.**
- **Supported research of 204 Nobel Laureates so far.**



# NSF Core Values and Strategic Goals

## ■ Core Values:

- Visionary
- Dedicated to Excellence
- Learning and Growing
- **Broadly Inclusive**

## ■ Strategic Goals:

- Transform the Frontiers
- Innovate for Society
- Perform as a Model Organization



# Divisions in the Directorate for Biological Sciences

**MCB**

DIVISION OF  
MOLECULAR &  
CELLULAR  
BIOSCIENCES

Predictive Biology through Interdisciplinary Research

**IOS**

**Integrative Organismal Systems**

**DEB**

**Environmental Biology**

**DBI**

**Biological Infrastructure**





# Directorate for Biological Sciences

## Division for Molecular and Cellular Biosciences

### Clusters:

**Molecular Biophysics**

**Cellular Dynamics and Function**

**Genetic Mechanisms**

**Systems and Synthetic Biology**





# Plant Genetic Engineering



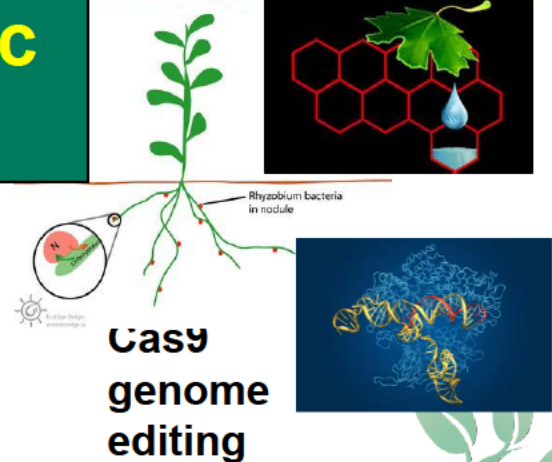
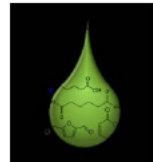
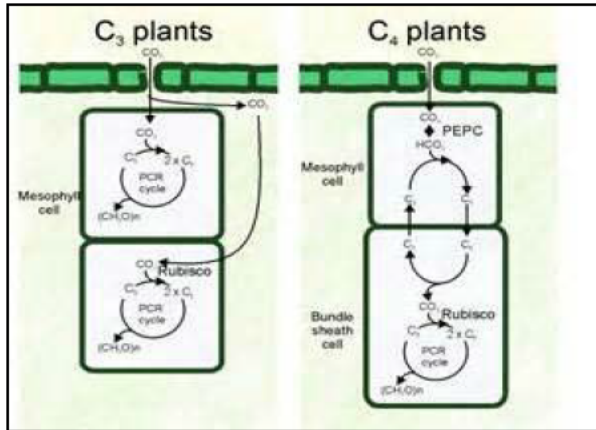
## Molecular Breeding and Marker Assisted Breeding

SSYy	SSyY	SsYY	SsYy
SsYy	SSyy	SsYY	Ssyy
sSYy	sSyy	ssYY	ssYy
sSyy	sSyy	ssYY	ssyy

## Genome to Phenome



## Plant Synthetic Biology



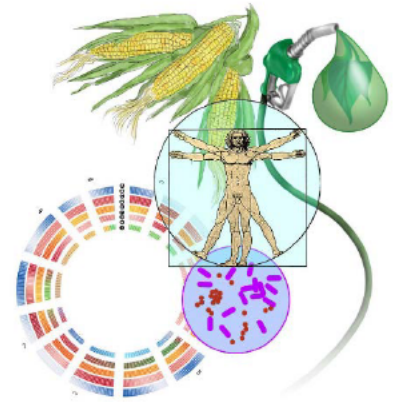
# New Initiatives and Funding Opportunities

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# GENOME TO PHENOME



**CORE Programs    BIO - MCB IOS DBI DBE**

**Genomes -> Phenomes - Grand Challenge Home Page**

<https://extwiki.nsf.gov/display/gpgc/Genomes+-+Phenomes+Grand+Challenge+Home>

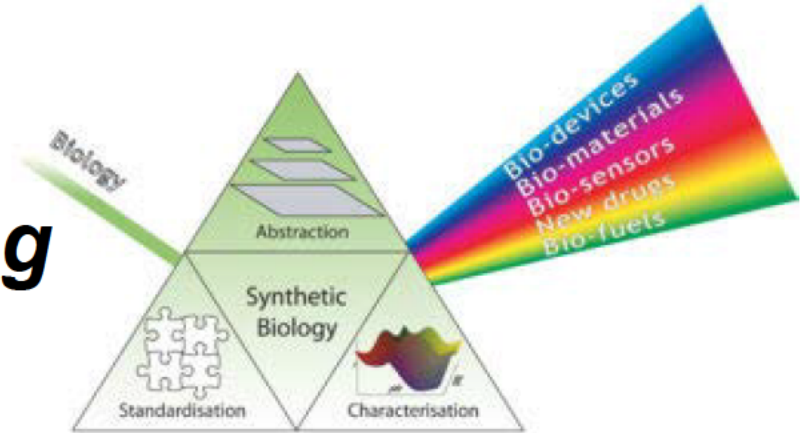
*Outcome from Phenomics: Genotype to Phenotype: A report of the Phenomics workshop sponsored by the USDA and NSF in 2011*

*([http://www.nsf.gov/bio/pubs/reports/phenomics\\_workshop\\_report.pdf](http://www.nsf.gov/bio/pubs/reports/phenomics_workshop_report.pdf))*





# ***Synthetic Biology and Advanced Manufacturing***

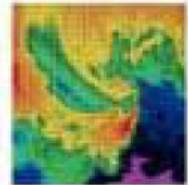


## **CORE Programs**

**BIO MCB SSB**

**ENG CBET**

- Complex Engineered and Natural Systems
- Energy and the Environment
- Innovation
- Manufacturing Frontiers
- Nanotechnology



# ***Joint Activities***

- **Workshop on Advanced Biomanufacturing**  
Aug. 2013; [www.nsf.gov/CBET](http://www.nsf.gov/CBET)
- **NRC consensus project on Industrialization of Biology**  
A Roadmap to Accelerate Advanced Manufacturing of Chemicals  
<http://nas-sites.org/synbioroadmap/>
- **Ecological Implications of Synthetic Biology**  
(MCB/DEB/ CBET) Ken Oye MIT; Todd Kuiken Wilson Center  
*Creating a Research Agenda; Jan. 2014; to be published shortly*
- **Dear Colleague Letter: Submission of I/UCRC Proposals in Response to NSF 13-594 in Areas Related to Engineering - Biology and Cellular Biomanufacturing**



# ***Other Initiatives in SynBio***

## **International Engagement**

EU ERASynBio, EU-US Biotechnology task force SynBio WG

UK BBSRC& EPSRC ideas labs, science & innovation workshops

Germany - DFG-NSF joint workshop (2011)

India joint workshop (2014)

**SAVI- yeast genome engineering** (UK, China, India, UK, France, Australia)

## **Interagency Engagement**

National Science and Technology Council (NSTC) working group (2012-2013)

Informal SynBio WG to share information

## **Applications & Industry Partnerships**

SBIR and STTR programs

Exploring opportunities to reduce barriers to commercialization

National academies workshop – Industrialization of Biology



# Activities of Interest

## ***First International Workshop on Plant Synthetic Biology***

May 17-18, 2014 at MIT Stata Center, Cambridge, MA USA

<http://plantsynbio.org>

**Organizers: Chris Voigt MIT and June Medford Colorado State Univ.**



## **ERASynBio 2<sup>nd</sup> Joint Call for Transnational Research Projects: *Building Synthetic Biology capacity through innovative transnational project***

[http://www.erasynbio.eu/lw\\_resource/datapool/\\_items/item\\_50/erasynbio2\\_call\\_announcement\\_140319\\_final.pdf](http://www.erasynbio.eu/lw_resource/datapool/_items/item_50/erasynbio2_call_announcement_140319_final.pdf)

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# Dear Colleague Letter: Special Guidelines for Submitting Collaborative Proposals under the US NSF/BIO - UK BBSRC Lead Agency Pilot opportunity



## NSF/BIO Solicitations

Division of Molecular and Cellular Biosciences Solicitation NSF 13-510  
Division of Biological Infrastructure Solicitation NSF 12-567

<http://www.nsf.gov/pubs/2014/nsf14034/nsf14034.jsp>

## BBSRC Strategic Research Priorities, Responsive Mode

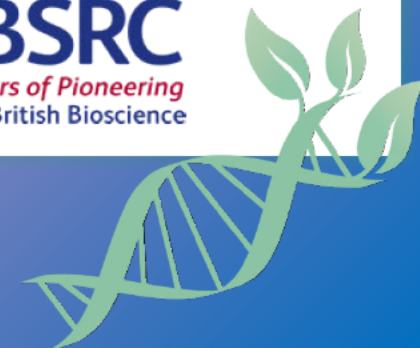
Data Driven Biology Systems Approaches to the Biosciences Synthetic Biology (Fall 2015 submissions only)

<http://www.bbsrc.ac.uk/funding/internationalfunding/nsfbio-lead-agency-pilot.aspx>



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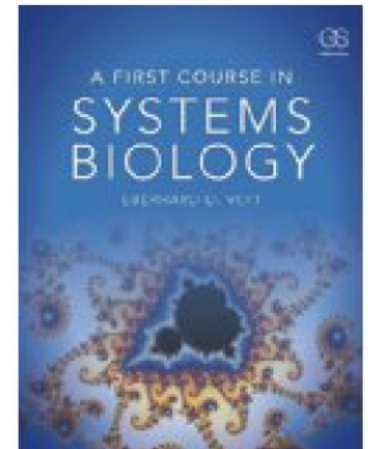
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## TAKE HOME LESSONS

- ◆ **Biotechnology – globalization**
- ◆ **Interdisciplinary, theory-driven research**
- ◆ **Interdisciplinary training of students**
- ◆ **More collaboration with Industry**





# NSF Directorate for Engineering (ENG)

Office of the Assistant Director

Emerging Frontiers in Research and Innovation (EFRI)

Engineering Education and Centers (EEC)

- Engineering Centers
- Engineering Education
- Engineering Workforce

Chemical, Bioengineering, Environmental, and Transport Systems (CBET)

- Chemical, Biochemical, and Biotechnology Systems
- Biomedical Engineering and Engineering Healthcare
- Environmental Engineering and Sustainability
- Transport and Thermal Fluids Phenomena

Civil, Mechanical, and Manufacturing Innovation (CMMI)

- Advanced Manufacturing
- Mechanics and Engineering Materials
- Resilient and Sustainable Infrastructure
- Systems Engineering and Design

Electrical, Communications, and Cyber Systems (ECCS)

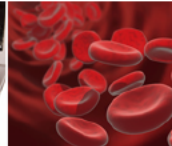
- Electronics, Photonics, and Magnetic Devices
- Communications, Circuits, and Sensing Systems
- Energy, Power, and Adaptive Systems

Industrial Innovation and Partnerships (IIP)

- Academic Partnerships (GOALI, I/UCRC, PFI AIR, and PFI BIC)
- Small Business Partnerships (SBIR, STTR)



WHERE DISCOVERIES BEGIN



National Science Foundation | Directorate for Engineering  
**Chemical, Bioengineering, Environmental,  
and Transport Systems Division (CBET)**



Deputy Division  
Director (Acting)  
**Susan Kemnitzer**



Division Director  
**JoAnn Lighty**

**Chemical, Biochemical  
and Biotechnology  
Systems**



1491 Biotechnology,  
Biochemical, and  
Biomass Engineering  
**Friedrich Srienc**



1401 - Catalysis  
and Biocatalysis  
**George Antos**



1417 - Chemical  
and Biological  
Separations  
**Rose Wesson**



1403 - Process  
and Reaction  
Engineering  
**Maria Burka**

**Bioengineering  
and Engineering  
Healthcare**



5345 - Biomedical  
Engineering  
**Thanassis  
Sambanis**



7236  
Biophotonics  
**Leon Esterowitz**



7909  
Nano-Biosensing  
**Alex Revzin**



5342 - General  
and Age Related  
Disabilities  
Engineering  
**Ted Conway**

**Environmental  
Engineering and  
Sustainability**



7644 - Energy for  
Sustainability  
**Gregory Rorrer**



1440 - Environmental  
Engineering  
**William Cooper**



1179 - Environmental  
Health and Safety  
of Nanotechnology  
**Barbara Karn**



7643 - Environmental  
Sustainability  
**Bruce Hamilton**

**Transport, Thermal,  
and Fluid  
Phenomena**



1407 - Combustion,  
Fire, and Plasma  
Systems  
**Ruey-Hung Chen**



1443 Fluid Dynamics  
**Dimitrios  
Papavassiliou**



1414 - Interfacial  
Processes and  
Thermodynamics  
(Acting)  
**Eddie Chang**

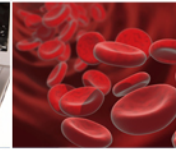


1415 - Particulate  
and Multiphase  
Processes  
**William Olbricht**



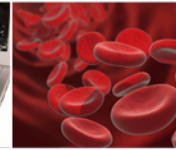
1406 - Thermal  
Transport  
Processes  
**Sumanta Acharya**





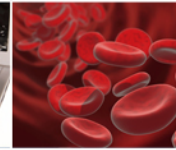
# CBET Vision

- **Humans will live sustainably on earth**
  - Drinking water, food
  - Energy, biofuels
  - Advanced manufacturing
- **The quality and length of life will be maximized**
  - Synthetic biology
  - BRAIN, Opto-genetics



# Current Activities in Systems at NSF

- Systems is a common theme in all divisions in ENG
  - CBET, CMMI, ECCS, EEC, and IIP
- Systems oriented work is supported in CISE:
  - CNS
- Systems in other directorates:
  - Social and Behavioral Sciences
  - Biological Sciences
  - Mathematical and Physical Sciences
  - Geological Sciences



# Many ENG programs invest in systems science and engineering:

- **Bio-process Systems (CBET)**
- **Chemical Process Systems (CBET)**
- **Environmental Systems (CBET)**
- Operations Research (CMMI)
- Engineering Systems and Design (CMMI)
- Control Systems (CMMI)
- Dynamical Systems (CMMI)
- Civil Infrastructure Systems (CMMI)
- Communications, Circuits, and Sensing Systems (ECCS)
- Energy, Power and Adaptive Systems (ECCS)
- Engineering Research Centers (ERC)



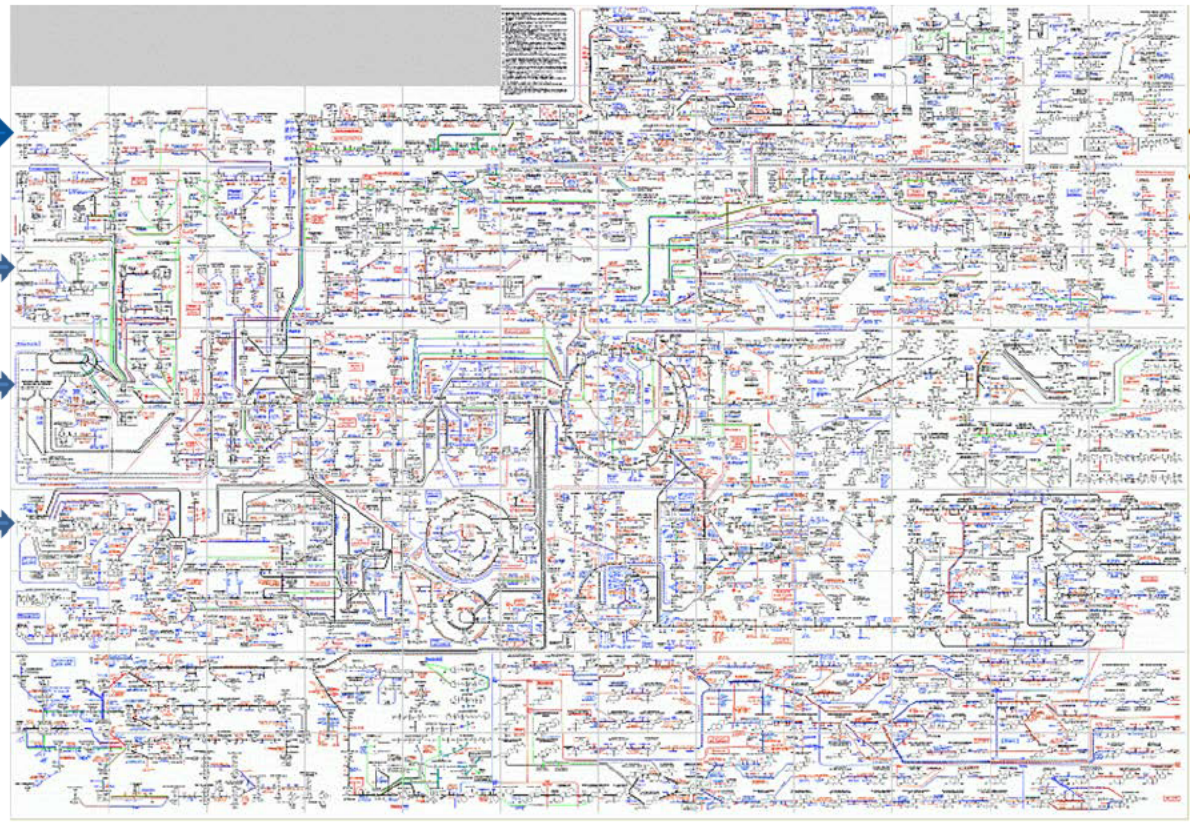
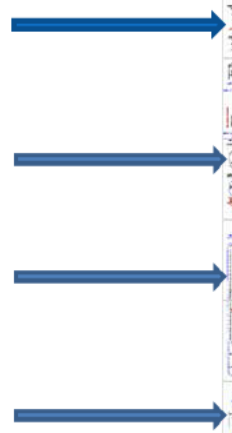
WHERE DISCOVERIES BEGIN



# Re-design of natural biological systems for useful purposes

State-of-the-art for designing bio-production of chemicals: **Systems Metabolic Engineering**

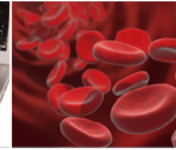
**Input**  
(nutrients)



**Output/Products**

(biofuels,  
amino acids,  
antibiotics,  
drugs, chemicals, etc.)





# Engineering Models for Metabolic Design

## Step 1: Sequence the DNA and annotate the DNA sequence

- DNA sequence contains all information of a cell
- coding genes and corresponding enzymes are identified using bioinformatics tools
- Each enzyme catalyzes a specific reaction  
→ all reactions of a cell are known

## Step 2: build the metabolic map

- The reaction network is reconstructed based on the reactions that are present

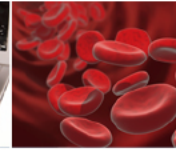
## Step 3: build the mathematical model

- A mass balance is set up for each metabolite in a cell resulting in a system of ODE's describing the change in metabolite concentration as a function of reaction rates

## Step 4: simplify the model

- A steady state assumption is applied to the **system of ODE's** recognizing that metabolite concentrations remain almost constant and that the system expands at a much longer time scale
- This results in a **system of algebraic equations** representing the **stoichiometric model** of the reaction network





# Design Questions

## Design Objectives:

### (1) The highest selectivity/yield

- the highest yielding pathway can be identified from the set of elementary modes
- Knowledge of the set of elementary modes permits identification of elimination targets of reactions that forces cells to operate according to most efficient pathways

### (2) High reaction rates

### (3) Robust, stable systems

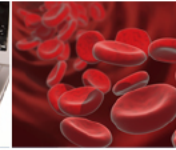
- Biological systems may change due to natural evolution and selection

Realization of (1) – (3) will typically result in the smallest and most economical equipment needed for the process

## Uncertainty, human behavior:

- the main uncertainty is related to the correctness of the model; this has to be validated by experiment and adjusted as needed
- The approach is not affected by human behavior as it is completely rational





# NSF Investments in Synthetic Biology

NSF investments in Synthetic Biology have been predominantly driven through unsolicited proposals by the research community

- |  |   |
|--|---|
| SynBERC  | Largest investment from NSF; established in 2006  |
| EFRI – IDEAS lab                                 | Joint NSF/EPSRC ‘Sandpit’ on Synthetic Biology  |
| CBET/BBBE  | Unsolicited proposals   |
| MCB/Systems and Synthetic Biol. Cluster          | Unsolicited proposals   |
| SBIR/STTR  | Unsolicited proposals   |
| INSPIRE – SAVI Science Across Virtual Institutes | Yeast Chromosome Synthesis and Analysis; partnership between The US, China, Europe, and India |

