Synthetic Systems Biology Summer School

2014

Taormina, Italy - June 15-19, 2014

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The organizers would like to acknowledge the
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Leonardo Design Systems

AGENDA: First Annual International Summer School on Synthetic and Systems Biology
Biology meets Engineering and Computer Science
June 15-19, 2014, Taormina – Sicily, Italy

June 2, 2014

Website for the School: http://www.taosciences.it/ssbss2014/

Link to abstracts and posters: http://www.taosciences.it/ssbss2014/ssbss-2014-abstracts.pdf

Email address for the organizers: ssbss2014@dmi.unict.it

Venue: Hotel Villa Diodoro
Via Bagnoli Croci 75, 98039 Taormina, Messina, Italy
T: +39 0942 2 33 12
E: diodoro@gaishotels.com
W: http://www.hotelvilladiodoro.com/
W: http://www.hotelvilladiodoro.com/en/how-to-reach-us.html

Registration: in the hallway outside the Main Conference Room (a.k.a *Ettore Majorana Room*)

Poster will be on display in the Loggia of the Main Conference Room

Wireless Login for School Room Internet:
Networking ID: Taosciences
Password: TBA

List of Restaurants and Bar close to the Conference Venue:

Ristorante Al Giardino
Via Bagnoli Croci, 84
98039 Taormina Messina
0942 23453
http://www.algiardino.net/

Ristorante La Bougainville
Via Bagnoli Croci, 88
98039 Taormina Messina
0942 625218

Minimarket Venuto
Via Bagnoli Croci, 68
Taormina Messina
0942 625556

Al Settimo Cielo del Paradiso
Via Roma, 2
Taormina Messina
0942 23922

International Synthetic & Systems Biology Summer School SSBSS'14
Biology meets Engineering and Computer Science
Taormina - Sicily, Italy, June 15-19, 2014
http://www.taosciences.it/ssbss2014/
ssbss2014@dmi.unict.it

SSBSS 2014 is a full-immersion course on cutting-edge advances in systems and synthetic biology. The school provides a stimulating environment for doctoral students, early career researches and industry leaders.
The school will be lectured by world-renowned experts of synthetic and systems biology including:

- **Uri Alon**, *Weizmann Institute of Science*, Israel
- **Joel Bader**, *Johns Hopkins University*, USA
- **Jef Boeke**, *Johns Hopkins University*, USA
- **Jason Chin**, *MRC - Cambridge*, UK
- **Paul Freemont**, *Imperial College London*, UK
- **Farren Isaacs**, *Yale University*, USA
- **Tanja Kortemme**, *University of California San Francisco*, USA
- **Giuseppe Nicosia**, *University of Catania*, Italy
- **Sven Panke**, *ETH*, Switzerland
- **Rahul Sarpeshkar**, *MIT*, USA
- **Velia Siciliano,** *MIT, USA*
- **Giovanni Stracquadanio**, *Johns Hopkins University*, USA
- **Ron Weiss**, *MIT*, USA
- **Liliana Wroblewska***, MIT, USA*

Industrial Panel:

- **Michael Liss**, *Thermo Fisher – Life Technologies, USA*
- **Carlos Olguin**, *Autodesk Inc., USA*

School Directors:
Jef D. Boeke, *Johns Hopkins University*
Giuseppe Nicosia, *University of Catania*
Mario Pavone, *University of Catania*
Giovanni Stracquadanio, *Johns Hopkins University*

Saturday, June 14, 2014

15:30 – 18:30 Arrival and Registration.

17:00 – 18:30 Poster setup for Poster Session I.

Sunday, June 15, 2014

08:15 – 09:30 Registration

09:30 – 11:00 **Synthetic biology: from parts to modules to systems**
Ron Weiss, MIT, USA

11:00 – 11:30 Coffee Break

11:30 – 13:00 **Synthetic Biology of Cell free Systems**
Sven Panke, ETH, Switzerland

13:00 – 14:30 On own for lunch

14:30 – 15:30 **Mammalian synthetic biology: scientific and therapeutic applications**
Ron Weiss, MIT, USA

15:30 – 16:00 Coffee Break

16:00 – 18:00 Poster Session I

19:30 Concert of "*Klàripian Duo*":
Aria "sulla quarta corda" BWV 106 of *Johann S. Bach*,
Seguidilla from "Carmen" of *G. Bizet*,
Pocket Size Sonata n.1 of *Alec Templeton*,
Three Preludes, Summertime, **It ain't necessarily so,**
and **Rhapsody in Blue** of *George Gershwin*.

21:00 Welcome Cocktail get-to-know

Monday, June 16, 2014

09:00 – 11:00	**Exploiting Engineered Cell-Cell Communications in Large Scale Biotechnology** *Sven Panke, ETH*, Switzerland
11:00 – 11:30	Coffee Break
11:30 – 13:00	**Minimal Genomes: High-Throughput Sequencing, Statistical Methods and Physics Models to Unveil Minimal Yeast Chromosomes Compatible with Life** *Giovanni Stracquadanio, Johns Hopkins University*, USA
13:00 – 14:30	On own for lunch
14:30 – 15:30	**Biosensors and synthetic circuits in mammalian cell - part I** *Velia Siciliano, MIT, USA*
15:30 – 16:30	**Biosensors and synthetic circuits in mammalian cell - part II** *Liliana Wroblewska, MIT, USA*
16:30 – 17:00	Coffee Break
17:00 – 18:00	**Programming Matter across Domains and Scales** *Carlos Olguin,* Autodesk Inc. USA

Tuesday, June 17, 2014

09:00 – 10:00	**Analog versus Digital Computation in Biology** *Rahul Sarpeshkar, MIT*, USA
10:00 – 11:00	**Reprogramming the Genetic Code – part I** *Jason Chin, MRC - Cambridge*, UK
11:00 – 11:30	Coffee Break
11:30 – 13:00	**Computational protein design - principles, challenges and progress** *Tanja Kortemme, University of California San Francisco*, USA
13:00 – 14:30	On own for lunch
14:30 – 15:30	**Reprogramming the Genetic Code – part II** *Jason Chin, MRC - Cambridge*, UK
15:30 – 16:30	**Analog Synthetic and Systems Biology** *Rahul Sarpeshkar, MIT*, USA
16:30 – 17:00	Coffee Break
17:00 – 18:00	**Design of reprogrammed and new functions - from proteins to cells** *Tanja Kortemme, University of California San Francisco*, USA
18:00 – 18:40	Poster setup for Poster Session II
19:00 – 21:00	Poster Session II

Wednesday, June 18, 2014

09:00 – 10:00	**Genome engineering technologies for rapid editing & evolution organisms** *Farren Isaacs, Yale University*, USA
10:00 – 11:00	**Foundational Technologies for Synthetic Biology - from DNA Assembly to Part Characterisation** *Paul Freemont, Imperial College London*, UK
11:00 – 11:30	Coffee Break
11:30 – 13:00	**Combinatorial DNA Assembly methods and their Applications** *Jef Boeke, Johns Hopkins University*, USA
13:00 – 14:30	On own for lunch
14:30 – 15:30	**Design, construction & function of genomically recoded organisms** *Farren Isaacs, Yale University*, USA
15:30 – 16:30	**Genome Design and Synthesis** *Jef Boeke, Johns Hopkins University*, USA
16:30 – 17:00	Coffee Break
17:00 – 18:00	**Computational Tools for Genome editing, Combinatorial Assembly and Workflow Tracking** *Giovanni Stracquadanio, Johns Hopkins University*, USA
18:00 – 19:40	Short Talks Selected From Submitted Abstracts I

Thursday, June 19, 2014

09:00 – 11:00	**Synthetic biology designs for biosensor applications** *Paul Freemont, Imperial College London*, UK
11:00 – 11:30	Coffee Break
11:30 – 13:00	**Network Remodeling during Development and Disease** *Joel Bader, Johns Hopkins University, USA*
13:00 – 14:30	On own for lunch
14:30 – 15:30	**Gene and Pathway Analysis of Genome-wide Association Studies** *Joel Bader, Johns Hopkins University*, USA
15:30 – 16:30	**Writing DNA – Enabling Technologies for Synthetic Biology** *Michael Liss, Thermo Fisher – Life Technologies, USA*
16:30 – 17:00	Coffee Break
17:00 – 19:05	Short Talks Selected From Submitted Abstracts II
20:30	Swimming Pool Party

End of School

Saturday, June 20, 2014

Departure.

Courses

Uri Alon, Weizmann Institute of Science, Israel

Lecture I: **Elementary Circuits in Biology**
To understand biological systems, our lab has defined "network motifs": basic interaction patterns that recur throughout biological networks, much more often than expected at random. The same small set of network motifs appears to serve as the building blocks of the circuitry that processes information from bacteria to mammals. Specific network motifs may be universal building blocks of biological computation. We experimentally studied the function of each network motif in the bacterium E. coli using dynamic fluorescent measurements from living cells. Each network motifs can serve as an elementary circuit with a defined function: filters, pulse generators, response accelerators, temporal-pattern generators and more. Evolution seems to have rediscovered the same motifs again and again, perhaps because they are the simplest and most robust circuits that perform these information-processing functions.

Lecture II: **Evolution and Optimality of Gene Circuits**
Organisms, tissues and molecules often need to perform multiple tasks. But usually no phenotype can be optimal at all tasks at once. This leads to a fundamental tradeoff. We study this using the concept of Pareto optimality from engineering and economics. Tradeoffs lead to an unexpected simplicity in the range of optimal phenotypes- they fall on low dimensional shapes in trait space such as lines, triangles and tetrahedrons. At the vertices of these polygons are phenotypes that specialize at a single task. We demonstrate this using data from animal and fossil morphology, bacterial gene expression and other biological systems.

Joel Bader, Johns Hopkins University, USA

Lecture I: **Network Remodeling during Development and Disease**
Biological networks change in response to genetic and environmental cues. Changes are reflected in the abundances of biomolecules, the composition of protein complexes, and other descriptors of the biological state. Methods to infer the dynamic state of a cell would have great value for understanding how cells change over time to accomplish biological goals. We describe methods that predict the dynamic state of protein complexes in a cell, combining dynamic information from mRNA transcript profiling with underlying protein-protein interaction networks.

Lecture II: **Gene and Pathway Analysis of Genome-wide Association Studies**
While most genome-wide association studies are based on analysis of individual variants, the causal variants often cluster in a small set of genes. We describe Bayesian methods that exploit gene-based and pathway-based clustering to improve the search for disease-related genetic variation.

Jef Boeke, Johns Hopkins University, USA
Lecture I: **Genome Design and Synthesis**
Genome Design and Synthesis strategies vary considerable. Most of the published work on genome synthesis involves resynthesis of the native or near-native genome of bacteria. In this case, the design considerations are rather minimal and the major challenges involved have to do with design of an assembly strategy that is effective. Hierarchical strategies involve going from 10s of bases in oligonucleotides up to several megabases of dsDNA. A wide variety of methods have been described that can be used to assemble DNA and the details of these methods have significant impacts on speed of synthesis, cost of synthesis, and accuracy of synthesis. Innovative methods have been described that operate at all different levels of the assembly hierarchy. When more radical designs that deviate from that of wild-type genomes are considered, appropriate design software tools are needed. Our group has focused on genome editing software which takes advantage of well-developed browser platforms for visualizing genome features, and adapting them to genome editing. A variety of design features were somewhat arbitrarily selected for incorporation into Sc 2.0, the synthetic yeast genome. These, as well as possible future more aggressive designs under consideration will be discussed, as will interesting targets for future genome synthesis projects.

Lecture II: **Combinatorial DNA Assembly methods and their Applications**
A wide variety of pathways are available for engineering to make useful products or encode interesting behaviors in cells and organisms. As more and more complex pathways and gene networks are discovered and dissected, more and more efficient means of assembling pathways are needed. Even more importantly, libraries of these, in which the promoter strength or host of origin for the coding sequences can be systematically varied are especially valuable. Methodologies and strategies for accomplishing this are discussed, incorporating Golden Gate, MoClo, Gateway cloning, and combinations of such methods will be discussed. Examples of pathway optimization will also be reviewed.

Jason Chin, MRC - Cambridge, UK

Lecture I: **Reprogramming the Genetic Code**
The information for synthesizing the molecules that allow organisms to survive and replicate is encoded in genomic DNA. In the cell, DNA is copied to messenger RNA, and triplet codons (64) in the messenger RNA are decoded - in the process

of translation - to synthesize polymers of the natural 20 amino acids. This process (DNA RNA protein) describes the central dogma of molecular biology and is conserved in terrestrial life. We are interested in re-writing the central dogma to create organisms that synthesize proteins containing unnatural amino acids and polymers composed of monomer building blocks beyond the 20 natural amino acids. I will discuss our invention and synthetic evolution of new 'orthogonal' translational components (including ribosomes and aminoacyl-tRNA synthetases) to address the major challenges in re-writing the central dogma of biology. I will discuss the application of the approaches we have developed for incorporating unnatural amino acids into proteins and investigating and synthetically controlling diverse biological processes, with a particular emphasis on understanding the role of post-translational modifications.

Lecture II: **Reprogramming the Genetic Code - part II**
TBA

Paul Freemont, Imperial College London, UK

Lecture I: **Foundational Technologies for Synthetic Biology - from DNA Assembly to Part Characterisation**
Synthetic biology is an application-focused field attempting to apply a systematic engineering approach to the design of new biological systems at the molecular level primarily using DNA. Notable progress has been made in the implementation of synthetic genetic circuits in living-systems that mimic functions such as switches, oscillators, timers, pulse generators, band-pass filters and logic gates (1,2). These genetic circuits are anticipated to enable the engineering of biological systems to a complexity previously unattainable. Over the past decade synthetic biology has aided the development of novel biological systems for a range of applications from bacteria that seek and destroy herbicides to the biosynthesis of valuable drugs (3, 4). To accelerate the development of the field many groups are establishing foundational technologies, which can be used across a wide range of applications. Within the Centre for Synthetic Biology and Innovation at Imperial College London (CSynBI; www.imperial.ac.uk/syntheticbiology) we are developing a series of platform technologies to enable the systematic design assembly and testing of synthetic biology designs including integration into an information system. I will describe recent developments in CSynBI on high throughput in vivo part characterization and the automated production of datasheets as well as new approaches in combinatorial DNA assembly. I will also describe our recent in vitro platform for the rapid characterization of DNA regulatory elements using a cell free system (5).

Lecture II: **Synthetic biology designs for biosensor applications**
Biosensors generally can be used to monitor parameters of interest or target analytes and in part they involve a biological component. Early biosensors started when techniques for immobilising enzymes onto solid supports were first

developed (1). The relatively recent discovery of bioluminescent (e.g. luciferase) and fluorescent (e.g. green fluorescent protein, GFP) proteins has provided a convenient mechanism for visualising gene expression and protein synthesis in cells and has lead to their use as reporter proteins. By utilizing such constructs, whole cell biosensors have been developed for example to specifically detect certain compounds or act as indicators to monitor cell growth and fitness (2,3). Biological organisms naturally monitor their environment and react accordingly with highly evolved detection and sensing systems, which can now be refactored at the genetic level for specific biosensor applications. One overall aim of synthetic biology is to harness nature's toolbox by fusing molecular biology and engineering disciplines and thus the field of biosensor design and construction has been a major focus for synthetic biologists (4-8). In this lecture I will describe the principles behind biosensor design using synthetic biology approaches providing exemplars to illustrate these principles. I will also present recent data from my groups on developing synthetic biology biosensors for healthcare applications and show how additional societal implications can be integrated into biosensor designs.

Farren Isaacs, Yale University, USA

Lecture I: **Genome engineering technologies for rapid editing & evolution organisms**

The growing availability of whole genome sequence data sets generated by massively parallel sequencing permits detection of potential associations between genotype and phenotype. These advances motivate the development of high throughput genome editing technologies to systematically elucidate the causative mutations underlying important phenotypes. Similarly, expanding protein and RNA structure databases provide a valuable resource for researchers seeking to engineer macromolecules with new binding specificities. Finally, as complex metabolic networks controlling the flow of biomolecules through cells are elucidated, efforts to alter native metabolism for engineered biosynthesis of desired compounds are rapidly growing in basic research and industrial biotechnology. I will discuss the development of high-throughput and automated methodologies for precise manipulation of genomes. Multiplex automated genome engineering (MAGE) simultaneously targets many locations on the chromosome for modification in a single cell or across a population of cells, thus producing combinatorial genomic diversity. Conjugative assembly genome engineering (CAGE) facilitates the large-scale assembly of many modified genomes. These methods treat the chromosome as both an editable and evolvable template and are capable of fundamentally re-engineering genomes from the nucleotide to the megabase scale. I will present applications of MAGE to generate combinatorial genomic variants from a complex pool of synthetic DNA to diversify target genes in order to optimize biosynthetic pathways. The growing toolbox for genomic engineering will be discussed.

Lecture II: **Design, construction & function of genomically recoded organisms**

The conservation of the genetic code, with minor exceptions, enables exchange of gene function among species, viruses and across ecosystems. Fundamental changes to the genetic code could significantly enhance our understanding of the origins of the canonical code and reveal new subtleties of how genetic information is encoded and exchanged. Modifying the canonical genetic code could also lead to orthogonal biological systems with new properties. I will discuss the construction of a genomically recoded organism (GRO). In the GRO, all known UAG stop codons in Escherichia coli MG1655 were replaced with synonymous UAA codons, which permitted the deletion of release factor 1 and reassignment of UAG translation function. This GRO exhibited improved properties for incorporation of nonstandard amino acids that expand the chemical diversity of proteins in vivo. The GRO also exhibited increased resistance to T7 bacteriophage, demonstrating that new genetic codes could enable increased viral resistance.

Tanja Kortemme, University of California San Francisco, USA

Lecture I: **Computational protein design - principles, challenges and progress**

Designer proteins with new biological functions have tremendous practical importance; they can also enable us to ask questions about the design principles of function and fitness in new ways. Many applications can be imagined: potent protein therapeutics with minimal side effects; new enzymes and biological synthesis pathways for fuel molecules or compounds that are otherwise too expensive to produce; sensor/actuator devices that can report on cell biological processes in real time; robust signaling systems that can detect specific inputs and generate a precise response; protein machines and new biological materials that can be controlled by specific external inputs such as light.

The first lecture in this two-part series will describe the current state-of-the-art in computational protein design. I will introduce the main conceptual advances and considerable challenges faced in the field: to sufficiently sample the vast space of possible sequences and structures and to accurately distinguish functional from non-functional designs. Work addressing these challenges uses a combination of ideas from computer science, physical chemistry, engineering and protein biophysics. Highlights from work creating designer proteins – new protein folds, specific binding proteins, and large assemblies – will illustrate where we are.

Lecture II: **Design of reprogrammed and new functions - from proteins to cells**

The second part of the series will focus on current and future opportunities and applications. We'd like to engineer new molecules that operate as predicted in biological contexts, and to utilize prediction and engineering to address fundamental questions on the relationship of molecular characteristics and

function. I will describe recent work and new approaches to engineer sensor/actuators that detect and respond to molecules that can currently not be sensed in living cells, and to control the conformational cycle of large protein machines with light.

Giuseppe Nicosia, University of Catania, Italy

Lecture I: **Biological Circuit Design by Pareto Optimality**

Lecture II: **Programming Living Molecular Machines for Biofuel Production**

Sven Panke, ETH, Switzerland

Lecture I: **Synthetic Biology of Cell free Systems**
The use of parts of cells, specifically enzymes, has a long tradition in therapy, diagnostics and particular chemical synthesis. One of the most attractive feature of enzymes as biological catalysts is that they all have been engineered by nature to operate at comparable environmental conditions. This is a major difference to chemistry and enables the coordinated operation of a cascade of enzymes concomitantly in one vessel, opening ways to efficiently conduct complex chemistry and circumventing thermodynamic challenges. Synthetic biology allows constructing such systems with an unprecedented degree of scope and ease. We will illustrate the potential of the approach by discussing the generation of large enzyme systems for the production of fine chemicals. Furthermore, we will discuss an engineering approach to optimizing such systems based on advanced on-line MS-analytics and design of experiments.

Lecture II: **Exploiting Engineered Cell-Cell Communications in Large Scale Biotechnology**
Synthetic biology brings with it a drastic increase in the scope of experimental operations, which it typically accommodated by a tendency to miniaturize and parallelize experimentation. While this is relatively straight forward for in vitro approaches such as DNA assembly, suitable approaches are less clear when interaction of living cells is required. We will discuss recent efforts of our laboratory to develop nanoliter-sized cultivation systems and their resulting applications to high-throughput screening strategies in the fields of fluorescent protein engineering, vitamin production, and engineering of novel antibiotics.

Rahul Sarpeshkar, MIT, USA

Lecture I: **Analog versus Digital Computation in Biology**
The fundamental laws of noise in gene and protein expression set limits on the energy, time, space, molecular count, and part-count resources needed to compute at a given level of precision in the cell. Based on these laws, we

conclude that analog computation is significantly more efficient in its use of resources than deterministic digital computation in the cell. Hence, synthetic and natural circuits in cells must use analog, collective analog, probabilistic, and hybrid analog-digital computational approaches to function; otherwise, even relatively simple computations in cells like addition will exceed energy and molecular-count budgets. We present schematics for efficiently representing analog DNA-protein computation in cells. A deep connection between analog circuits and cell biology enables us to also engineer synthetic analog computation in cells efficiently.

Lecture II: **Analog Synthetic and Systems Biology**
The deep connection between analog circuits and cell biology arises because there are astounding similarities between the equations that describe noisy electronic flow in sub-threshold transistors and the equations that describe noisy molecular flow in chemical reactions, both of which obey the laws of exponential thermodynamics. Based on these similarities, we have engineered logarithmic analog computation in living cells with less than three transcription factors, almost two orders of magnitude more efficient than prior digital approaches. In addition, highly computationally intensive noisy DNA-protein and protein-protein networks can be rapidly simulated in mixed-signal supercomputing chips that naturally capture their noisiness, dynamics, and loading interactions at lightning-fast speeds. Such an approach may enable large-scale design and analysis in synthetic and systems biology that is faithful to how messy analog biology works, quite different from clean, well-defined digital design.

Velia Siciliano - MIT, USA

Workshop on "Biosensors and Synthetic Circuits in Mammalian Cells" – part I
Synthetic biology aims at engineering systems from characterized genetic parts to perform complex coordinated tasks for pharmaceutical and industrial applications. Mammalian synthetic biology slowly enters the phase where proof-of-concept designs move closer to therapy. Engineered networks are designed to sense clinically relevant molecules, integrate signals from the various sensors and finally produce a clinically relevant output. A key feature is the ability of such synthetic circuits to "sense" intracellular states or exogenous cues. We will discuss designs of sensory circuits for metabolites of human body, proteins, mRNA and microRNA.

Giovanni Stracquadanio, Johns Hopkins University, USA

Lecture I: **Minimal Genomes: High-Throughput Sequencing, Statistical Methods and Physics Models to Unveil Minimal Yeast Chromosomes Compatible with Life**
A central problem in biology is the identification and characterization of the fundamental genetic components required by a living cell. The concept of minimal

genome has been motivated by the fact that only a subset of genes are essential for life, while others are completely dispensable. However, the iterative deletion of non-essential genes will lead to an inviable system due to the accumulation of fitness defect and genetic interactions.
The Synthetic Yeast Genome (Sc2.0) aims at finding the minimal eukaryotic genome compatible with life by using an inducible evolutionary system (SCRaMbLE), which causes systemic structural variations by Cre recombinase. The availability of the first synthetic chromosomes opened the way to the first genome minimization experiments.
In this lecture, I will present the algorithms designed to reconstruct and analyze minimal yeast genomes from sequencing data. I will go through the steps of i) variant detection; ii) copy number estimation and iii) sequence reconstruction. I will show how to use statistical methods to track fitness defects and analyze changes in genome structure.
Finally, I will present a polymer physics model to predict minimal genomes and validate experimental results.

Lecture II: **Computational Tools for Genome editing, Combinatorial Assembly and Workflow Tracking**
DNA synthesis technologies are improving faster than Moore's law, allowing the synthesis of genes, pathways, bacterial genomes, and eventually entire eukaryotic genomes. Many projects rely on the assembly of individual, well-characterized, and standardized 'biological parts'. Parts such as promoters, coding domains, and transcriptional terminators provide granular biological function and can be designed for interoperability and combinatorial library screens.

In this lecture, I will present the BioParts framework for combinatorial assembly, tracking and inventory of biological parts. I will go through the steps required to retrieved biological sequences from multiple sources, prepare the DNA sequence for combinatorial assembly using Golden-Gate and prepare fabrication plans. I will also present our system to track every experiment of DNA synthesis and how to store this information in our inventory system.

Ron Weiss, MIT, USA

Lecture I: **Synthetic Biology: From Parts to Modules to Systems**

Lecture II: **Mammalian Synthetic Biology: Scientific and Therapeutic Applications**

Liliana Wroblewska MIT, USA

Workshop on "Biosensors and Synthetic Circuits in Mammalian Cells" – part II

Another critical aspect on the way of mammalian synthetic biology towards therapy is safety of the engineered systems. We will discuss different approaches undertaken to ensure the minimal negative footprint of the engineered systems on the host organism including cell-based therapies, and circuits encoded exclusively on RNA. Additionally we will discuss development of platforms for easy prototyping of genetic circuits that can be used to test their long term behavior and reliability.

Industrial Panel

Writing DNA - Enabling Technologies for Synthetic Biology

Michael Liss, *Thermo Fisher – Life Technologies, USA*

Biotechnology has enabled us to render the adaptation of living natural resources from a top-down approach (breeding) to a bottom-up process (designing). Common modern cloning techniques allow for the rearrangement of genetic building blocks, the removal of cross-species boundaries and minor modifications of the DNA sequence itself. The availability of *in silico* gene optimization and *in vitro* gene synthesis from synthetic oligonucleotides has ushered a new era by conferring independency of natural templates. The fast development of this technology during the last decade has dramatically advanced the availability of this service to a present level that by now outperforms classical cloning techniques in terms of flexibility, speed and costs. The exponential increase of biological sequence database contents and the growing need for genes designed for industrial applications, rather than natural function, further drives this market. With the emerging field of synthetic biology the requirements for gene synthesis expand particularly in terms of synthesis speed and construct size to allow for the construction of pathway operons or even complete genomes. This challenges the engineering of novel techniques to assemble and manipulate synthetic DNA building blocks in concert with natural genomes to large molecular entities efficiently to provide the necessary tools for tomorrows biotechnology.

Programming Matter across Domains and Scales

Carlos Olguin, *Autodesk Inc., USA*

Scientists in emerging fields such as synthetic biology and 3D bioprinting are inevitably headed to revolutionize established industries including biotechnology and pharmaceuticals. Other emerging fields such as 4D printing aim to transform manufacturing and by implication, eventually, the building industry too. However, the software tools used in these new fields are in many cases non-existent. When they do exist they are often disconnected, repetitive, and manually intensive—making standardization, collaboration, and complex projects more difficult than they should be. Powerful techniques like multi-objective optimization and multi-physics simulation are rarely exploited and the interoperability amongst different lab-developed tool makers has been limited at best. To address this gap, at Autodesk Research we are building a new design platform called Project Cyborg. We will describe its use in collaboration with world-class researchers in industry and academia as we co-envision and co-implement the design paradigms and applications needed to program matter across scales and domains, from the design of new molecular transports, to the 3D bioprinting of micro-slices of tissue, to the design of the self-assembly of non-biological human-scale manufactured devices.

Contributed Talks

Oral Session I – Wednesday, June 18, 18:00 – 19:40

The integration of stochastic events and their effect on gene regulation
Daphne Ezer and Boris Adryan
University of Cambridge, UK

Genotypic Diversity of a Pathogen Across Spatial Locations in the Human Lung
Hattie Chung[*], Tami Lieberman[*], Sara Vargas[**], Kelly Flett[**], Alexander McAdam[**], Gregory Priebe[**] and Roy Kishony[*]
* Harvard University, USA ** Children's Hospital Boston, USA

Strategies for synthetic chemotaxis of DNA self-assembled devices
Ibon Santiago
University of Oxford, UK

The Genome Engineering of a Xylose-Utilising Synthetic Yeast: SCRaMbLE-ing in Novel Genes into SC2.0
Dejana Jovicevic, Ben Blount, Tom Ellis
Imperial College London, UK

Oral Session II – Thursday, June 19, 17:00 – 19:30

Layered Analysis for Biochemical Reaction Networks
Thomas P. Prescott and Antonis Papachristodoulou
University of Oxford, UK

Challenging Issues in Synthetic Biology Design Cycle
Peyman Gifani[*], Ye Yuan[*] and Jorge Gancalves[*,]**
* University of Cambridge, UK ** Université de Luxembourg, Luxembourg

Exploiting the Yeast Genome for DNA Pathway and Library Assembly
Andy (Yao Zong) Ng[1], Alessandra Eustaquio[2], Jeffrey Janso[2], Nathaniel Jaffe[1], Millicent Olawale[1], Dean Deng[3], Maddy Jones[1], Estefania Chavez[1], Kevin Vo[1], Jingkang Chen[1], Yu-Wei Chang[1], Matthew Wilder[1], Frank Koehn[2], and Virginia Cornish[1]
1 Columbia University, USA 2 Pfizer Inc, USA 3 Hunter College High School, NY, USA

Predicting Polymerase Chain Reaction Efficiency using Physico-Chemical Sequence Properties
Eleni Karamasioti[1,2,3], Ellis Whitehead[1,2], Fabian Rudolf[1,2] and Jörg Stelling[1,2]
1 ETH Zürich, Department of Biosystems Science and Engineering, Basel, Switzerland
2 Swiss Institute of Bioinformatics, Basel, Switzerland
3 PhD Program Systems Biology, Life Science Zurich Graduate School, Zurich, Switzerland

Quantitative multi-layer stress regulation analysis of yeast
Petri-Jaan Lahtvee and Jens Nielsen
Chalmers University of Technology, Sweden

Satellite Meeting

3rd International Synthetic Yeast Genome (Sc2.0) Meeting

Taormina, Hotel Villa Diodoro Congress Center
Friday, June 20, 2014 From 9:00 to 20:00

Jef D. Boeke, Giuseppe Nicosia & Giovanni Stracquadanio

https://www.eventbrite.com/e/3rd-international-synthetic-yeast-genome-sc20-meeting-tickets-11284703853

The Synthetic Yeast Genome Project (Sc2.0) is synthesizing and constructing a modified version of the S. Cerevisiae genome to test biological questions and give new functions. For this one day meeting we will be bringing those around the world involved in the Sc2.0 project together in beautiful Taormina to discuss progress on the synthetic S. cerevisiae genome and opportunities to use the strains and tools of the project. Related topics in synthetic and systems biology will also be discussed. This meeting is open to all interested in Sc2.0 and we encourage you (and your colleagues) to register if you'd like to attend.

Previous edition: The 2nd International Synthetic Yeast Genome (Sc2.0) Consortium Meeting Johns Hopkins University and Imperial College London Friday, July 12, 2013 from 9:00 AM to 8:00 PM (GMT) London, United Kingdom, co-located event at SB 6.0.

UNESCO World Heritage sites in Sicily

The UNESCO compiled its first list in 1978: in year 2013, the listed sites are 964. They are divided into cultural, natural and mixed properties. Actually, the main part of the sites is in Italy, which boasts *49 sites*, followed by Spain and China, both with 44.

Sicily, with its treasures of historical, cultural and natural importance, boasts *6 sites* listed in the *World Heritage List*.

1) Archaeological Area of Agrigento, listed in 1997
Founded in the 6th Century B.C., the ancient city of Agrigento was one of the greatest Mediterranean centres. The remains of the Doric Temples which dominates the city are well preserved and are one of the most terrific monuments of Greek art and culture. They testify the magnificence and supremacy of the ancient city.

2) Villa Romana del Casale, listed in 1997
Late Roman Villa located in "Contrada Casale" (Casale district), at the foot of Mont Mangone. Villa Romana has been built around III – IV century B.C. and represents a great example of luxury Roman villa. The exceptional beauty and quality of the mosaics which decorate the villa illustrate the greatness and underline the importance of the Villa.

3) Isole Eolie (Aeolian Islands), listed in 2000
The Aeolian Islands are located north of the coast of Sicily.
The 7 islands which compose the archipelago of Lipari (Panarea, Stromboli, Vulcano, Alicudi, Filicudi, Lipari and Salina, more 5 small islets) are all of volcanic origins and are separated from the land of Sicily by 200 m deep waters. Over the centuries, the Aeolian Islands have provided two different kinds of eruption (Vulcanian and Strombolian) and have given to the science of vulcanology the chance to enrich their education and improve their knowledge.

4) Late Baroque Towns of the Val di Noto (South-Eastern Sicily), listed in 2002
The Baroque towns listed by Unesco were rebuilt in 1693 after a terrible earthquake. The cities of south-eastern Sicily (Caltagirone, Militello Val di Catania, Catania, Modica, Noto, Palazzolo, Ragusa and Scicli) represent the result of a great collective undertaking, and are the expression of a high-quality architectonical and artistic achievement. Linked to the Baroque style of the period, they also boast important improvements in town planning as well as in urban building.

5) Syracuse and the Rocky Necropolis of Pantalica, listed in 2005

The last site listed by Unesco is composed by two different parts, containing remains of both Greek and Roman origins: the Necropolis of Pantalica and the Ancient Syracuse. The Necropolis contains more than 5,000 tombs, mainly dating back from the 13th to 7th centuries B.C. The second part, the Ancient Syracuse, includes Ortigia, the first centre of this city founded by Greeks in the 8th century B.C. The Ancient Syracuse contains, among other things, the rests of the Temple of Athena, a Greek Theatre and a Roman amphitheatre.

6) Mount Etna, listed in 2013

Last gem of the Italian UNESCO Heritage, Mount Etna has been listed for its huge geological, scientific and cultural value. Mount Etna is the most active and the highest volcano in Europe and has been recognized World Heritage Site on basis of its intense and persistent volcanic activity, as well as for the fundamental role within the Mediterranean bio-geographical region.

Notes