3rd International Synthetic & Systems Biology Summer School – SSBSS 2016
8–14 July 2016, Volterra (Pisa) – Tuscany, Italy
www.taosciences.it/ssbss/

	Sat, 9 July	Sun, 10 July	Mon, 11 July	Tue, 12 July	Wed, 13 July
09:00 – 09:50	D. Di Bernardo	Y. Benenson	D. Del Vecchio	M. Herrgard	J. Gootenberg
09:50 – 10:40	S. Itzkovitz	L. Bleris	F. Ricci	J. Cumbers	J. Gootenberg
10:40 – 11:10	Coffee break	Coffee break	Coffee break	Coffee break	Coffee break
11:10 – 12:00	S. Itzkovitz	Y. Benenson	F. Ricci	M. Herrgard	Oral Talks IV
12:00 –12:50	D. Di Bernardo	B. Di Ventura	D. Del Vecchio	M. Guarracino	Oral Talks V
12:50 – 14:30	Lunch	Lunch	Lunch	Lunch	Lunch
14:30 – 15:20	Oral Talks I	B. Di Ventura	Social Tour in Florence	M. Guarracino	Oral Talks VI
15:20 – 16:10	Oral Talks II	L. Bleris		NGS Tutorial	Oral Talks VII
16:10 – 16:40	Coffee break	Coffee break		Coffee break	Coffee break
16:40 – 17:30	Oral Talks III	Free		NGS Tutorial	Oral Talks VIII
17:30 – 18:20	Poster Session I			NGS Tutorial	Poster Session II
18:20 – 19:10				NGS Tutorial	
19:30 – 21:00	Group Photo & Welcome Cocktail	Dinner	Social Dinner in Florence	Dinner	Swimming Pool Cocktail

REGISTRATION — Registration Desk
The registration desk will be located close to the Main Conference Room and will be open during the following hours:

Friday, July 8, 12:30 – 20:30

Saturday, July 9, 08:30 - 17:30

Sunday, July 10, 08:30 - 12:30

Monday, July 11, 08:30 - 12:30

Tuesday, July 12, 08:30 - 17:30

Wednesday, July 13, 08:30 - 17:30

Upon registration at the desk, you will receive your badge, vouchers, and conference materials. To facilitate the process please bring with you your registration confirmation. You are kindly requested to wear your name badge during all events of the conference.

Summer School Venue:
SIAF — The Learning Village in Tuscany
SP del monte Volterrano, Località Il Cipresso,
56048 Volterra (Pisa) Tuscany, Italy
Phone: (+39) 0588 81266 or (+39) 0588 86855
Fax: (+39) 0588 86414
email: info@siafvolterra.eu
http://www.siafvolterra.it/wp/en/how-to-reach-us/
GPS data: Latitude: N 43° 24' 3.99'' Longitude: E 10° 50' 46.78"
Contact:
Giada Ragoni, giada.ragoni@siafvolterra.eu

SSBSS 2016 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:

* **Yaakov (Kobi) Benenson**, Synthetic Biology Group@Department of Biosystems Science and Engineering, ETH Zurich, Basel, Switzerland
Lecture 1: *"The practice of mammalian synthetic biology"*
Lecture 2: *"Mammalian cell classifiers"*

* **Leonidas Bleris**, Bioengineering Department, The University of Texas at Dallas, USA
Lecture 1: *"Genome Editing Technologies and Therapeutic Modalities"*
Lecture 2: *"Benchmark Circuits and Topological Properties"*

* **John Cumbers**, Founder SynBioBeta, Mountain View, CA, USA
Lecture: "*Synthetic Biology: new tools for an industry at an inflection point*"

* **Domitilla Del Vecchio**, Department of Mechanical Engineering, MIT, USA
Lecture 1: *"Modularity in genetic circuits: Dream versus Reality"*
Lecture 2: *"Engineering Modularity in Genetic Circuits"*

* **Diego Di Bernardo**, Dept of Chemical Materials and Industrial Production Engineering University of Naples "Federico II", Naples, Italy
Lecture 1: *"Engineering and Control of Biological Circuits in Yeast"*
Lecture 2: *"Engineering and Control of Biological Circuits in Mammalian Cells"*

* **Barbara Di Ventura**, Synthetic Biology Group, BioQuant/DKFZ, Heidelberg, Germany
Lecture 1: *"Using blue light to control protein localization in living mammalian cells"*
Lecture 2: *"Using split inteins for protein engineering in living cells"*

* **Jonathan S. Gootenberg**, Department of Systems Biology, Harvard Medical School, Harvard University, USA
Lecture 1: *"Discovering and Characterizing CRISPR effectors"*
Lecture 2: *"Probing Biology with CRISPR Screening"*

* **Markus Herrgard**, Technical University of Denmark, Novo Nordisk Foundation Center for Biosustainability, Denmark
Lecture 1: *"Developing an Integrated Cell Factory Design Tool"*
Lecture 2: *"Using Automated Laboratory Evolution to Optimize Cell Factories"*

* **Shalev Itzkovitz**, Department of Molecular Cell Biology, Weizmann Institute of Science, Israel
Lecture 1: *"Single Molecule Approaches for Studying Gene Expression in Intact Mammalian Tissues"*
Lecture 2: *"Systems Biology of Stem Cell-Maintained Tissues"*

* **Francesco Ricci**, Dipartimento di Scienze e Tecnologie Chimiche, University of Rome Tor Vergata, Rome, Italy
Lecture 1: *"DNA Nanotechnology Tools and Reactions for Synthetic Biology"*
Lecture 2: *"Nature-inspired DNA-based Nanodevices"*

Next Generation Sequencing Lectures – July 12th, 2016

* **Mario Guarracino**, CNR, Italy, *"How fast can we align sequences?"*

Next Generation Sequencing Tutorials

* **Ilaria Granata**, CNR, Italy, *"Detection and analysis of contaminating sequences in NGS sequencing data"*

* **Parijat Tripathi**, CNR, Italy, *"Detection and interpretation of circular RNAs in RNA-seq experiments"*

SSBSS 2016 Plenary Speakers & Abstracts

Yaakov (Kobi) Benenson, Synthetic Biology Group@Department of Biosystems Science and Engineering, ETH Zurich, Basel, Switzerland

Yaakov (Kobi) Benenson received his Bachelor and Master degrees in Chemistry from the Technion - Israel Institute of Technology, and a PhD in Computer Science and Biological Chemistry from the Weizmann Institute of Science. There he did pioneering work in autonomous DNA computing. As a Bauer Fellow, he was an independent group leader at Harvard FAS Center for Systems Biology where he initiated a research program in mammalian in vivo computing. He joined ETH Zurich in 2010 as an Assistant Professor and was appointed an Associate Professor in 2015.

Lecture 1: "*The Practice of Mammalian Synthetic Biology*"
I will describe the nitty-gritty details of planning and executing a mammalian synthetic biology project. I will touch upon the early design stages, the choice of the appropriate model system, DNA construct desing and cloning, whole-system modeling, and system characterization methods.

Lecture 2: "*Mammalian Cell Classifiers*"
Cell Classifiers emerged as a major class of synthetic biological circuits, pioneered in 2011 and followed up by multipe groups worldwide. These circuit run classification algorithms in individual living cells to separate, for example, tumor from healthy cells. I will describe the theoretical framework behind these systems and various aspects of their practical implementation in vitro and in vivo.

Leonidas Bleris, Bioengineering Department, The University of Texas at Dallas, USA

Leonidas Bleris is an Associate Professor with the Bioengineering Department of the University of Texas at Dallas. Before joining UTD, Bleris was a Postdoctoral Fellow at the FAS Center for Systems Biology at Harvard University. Bleris earned a Ph.D. in Electrical Engineering from Lehigh University in 2006. He received a Diploma in Electrical and Computer Engineering in 2000 from Aristotle University of Thessaloniki, Greece. Bleris was awarded the Christine Mirzayan Science and Technology Policy Graduate Fellowship from the National Academy of Science (NAS), and served with the Board of Mathematical Sciences and their Applications. During 2009-2010, Bleris was a Visiting Scientist at the FAS Center for Systems Biology at Harvard University, and since 2008 an Independent Expert with the European Commission under the "Science, Economy and Society" directorate. His research has focused on systems biology, mammalian synthetic biology and genome editing, and has received support from the National Institutes of Health (NIH) and the National Science Foundation (NSF) including the NSF CAREER award.

Lecture 1: "*Genome Editing Technologies and Therapeutic Modalities*"
We present results at the interface of mammalian synthetic biology and genome editing towards gene therapy applications. We study a number of network topologies and exploit their properties to engineer tunable and robust systems. Specific topics include the following: Variable gene dosage and noise are major sources of fluctuations in gene product levels in both endogenous and synthetic circuits. To mitigate gene expression variability we designed, simulated, constructed, and tested a range of regulatory circuits. We introduce a methodology to control the copies and residence time of a gene product delivered in host human cells but also selectively disrupt fragments of the delivery vehicle. We introduce a CRISPR/Cas9 based mechanism to target a heterozygous activating mutation of KRAS in cancer cells and show reversal of drug resistance to a small-molecule inhibitor.

Lecture 2: "*Benchmark Circuits and Topological Properties*"
We present results at the interface of mammalian synthetic biology and reverse engineering. We adopt the notions of abstraction, emulation, benchmarking, and validation in the context of discovering topological features. After subjecting benchmark synthetic circuits to perturbations, we study network connections using a combination of nonparametric single-cell data resampling and modular response analysis. Intriguingly, we discover that recovered weights of specific network edges undergo divergent shifts under differential perturbations, and that the particular behavior is markedly different between topologies. Furthermore, using synthetic networks as a benchmark, we find that network inference results can be influenced by changes in the resources allocated to each node. Specifically, we discover nontrivial “ghost” regulation edges which are not explicitly engineered into the benchmark networks.

John Cumbers, Founder SynBioBeta, Mountain View, CA, USA

John Cumbers has a strong background in the synthetic biology industry as founder of SynBioBeta, a global activity hub and community of entrepreneurs, thought leaders and investors. He has earned several degrees, including a PhD in molecular biology from Brown University as well as a masters degree in bioinformatics from the University of Edinburgh in Scotland and an undergraduate degree in computer science from the University of Hull in England. John is passionate about education and on the use and adoption of biological technologies. He has received multiple awards and grants from NASA and the National Academy of Sciences for his work in the field. John has been involved in multiple startups producing food for space and using microbes to extract lunar and martian resources. He worked at NASA for seven years working on the issues of resource utilization, extremophiles and sustainable technologies. He was instrumental in

starting NASA's program in synthetic biology and most recently, the lead for planetary sustainability at the NASA Space Portal. A super connector, community builder and consultant, John has devoted himself to helping those around him improve themselves and gain the resources that they need to break through scientific boundaries and succeed.

Lecture: "*Synthetic Biology: new tools for an industry at an inflection point*"
Since the popularization of the term 'synthetic biology' over a decade ago, a new community of biological engineers has emerged on to the scene. Thousands of practitioners, students, and entrepreneurs have joined the movement to 'make biology easier to engineer' and as a result, both the field and the industry has developed at a rapid pace worldwide. In 2015, over twenty five companies including Twist Bioscience, Zymergen, Ginkgo Bioworks and Bolt Threads have collectively raised over $722 million in funding to scale and propel their tools, platforms and products to market. In this most recent wave, some of Silicon Valley's most prestigious tech investors such as Eric Schmidt, Sam Altman, Paul Graham, Yuri Milner, Jerry Yang and Max Levchin have made significant investments betting on what they think will be the next industrial revolution: the industrialization of biology. John Cumbers has been in the field of synthetic biology for over 10 years working in academia, government, startups and industry. In this talk, he will review the history of the field starting from an academic outreach pursuit to what is now a fledgling industry. He will contend that the latest wave of investment in the field is a positive sign and that the industry is now at an inflection. He will drive home that the fruits from academia coupled with new VC money create the perfect storm for this disruptive technology to unseat incumbents. Specifically, in markets ranging from pharma, biomaterials, chemicals, fuel and food which will allow for the replacing of fossil fuels with more sustainable feedstocks and seeing widespread adoption along the way.

Domitilla Del Vecchio, Department of Mechanical Engineering, MIT, USA

Domitilla Del Vecchio received the Ph. D. degree in Control and Dynamical Systems from the California Institute of Technology, Pasadena, and the *Laurea* degree in Electrical Engineering from the University of Rome at Tor Vergata in 2005 and 1999, respectively. From 2006 to 2010, she was an Assistant Professor in the Department of Electrical Engineering and Computer Science and in the Center for Computational Medicine and Bioinformatics at the University of Michigan, Ann Arbor. In 2010, she joined the Department of Mechanical Engineering at the Massachusetts Institute of Technology (MIT), where she is currently an Associate Professor and member of the Synthetic Biology Center. She is a recipient of the Donald P. Eckman Award from the American Automatic Control Council (2010), the NSF Career Award (2007), the Crosby Award, University of Michigan (2007), the American Control Conference Best Student Paper Award (2004), and the Bank of Italy Fellowship (2000). She is an associate editor for IEEE Transactions on Network Science and Engineering, IEEE Life Science, and ACS Synthetic Biology. Her research interests include analysis and control of networked dynamical systems with application to engineering biology.

Lecture 1: *"Modularity in genetic circuits: Dream versus Reality"*
Modularity is one of the most vexing questions in systems biology and also crucial for the advancement of synthetic biology. In particular, the combination of smaller functional modules to create a larger system is based on the fundamental assumption that the smaller modules retain their functionality once part of a larger system. This crucial property is however not always satisfied when building synthetic biology circuits and, in fact, as the circuit's complexity grows, it is typically less likely satisfied. As a consequence, functional modules start to behave unpredictably once interacting with each other in the cellular environment. Why? In this talk, we review one of the main causes of modularity braking: loading in its various forms. In particular, I will illustrate the use of a system's concept that explicitly captures loading as a signal called retroactivity. We use this system's concept to predict the extent of modularity of modules given a network where they are inserted and to determine the network-level effects of various forms of loading. Experimental results will be shown to support the model predictions.

Lecture 2: *"Engineering Modularity in Genetic Circuits"*
How do we ensure the ability to compose systems modularly in the face of loading? In this talk, I will illustrate how our system's concept allows us to formulate the loading mitigation problem as a disturbance attenuation problem from control theory in which the disturbance to be rejected is the retroactivity signal. By virtue of this formulation, we devised two main mechanisms for load mitigation, which conceptually resemble the design of OPAMPs in electronics but with significant differences. Realizations of insulation devices (the OPAMP-like systems) will be illustrated using a number of different signaling component libraries. Their experimental implementation and performance will be shown in vitro, in bacteria, and in yeast.

Diego Di Bernardo, Dept of Chemical Materials and Industrial Production Engineering University of Naples "Federico II", Naples, Italy

Diego Bernardo was born in Naples on June 26, 1972. He received the "Laurea cum laude" in Electronic Engineering in January 1997 by the University of Naples "Federico II". In 2001, thanks to a single three-year scholarship "Marie Curie" of the European Commission, received the title of Ph.D. (PhD) from the University of Newcastle School of Medicine, UK, in the laboratory of Prof. Alan Murray. Until April 2002 he was postdoctoral researcher at the Wellcome Trust Sanger Center in Cambridge (United Kingdom) in the laboratory of Dr. Tim Hubbard. From May 2002 to December 2002 was postdoctoral researcher in the laboratory of Prof. Jim Collins in the Department of Bioengineering at the University of

Boston, USA. Since January 2003 he is an independent researcher (Principal Investigator) at the Telethon Institute of Genetics and Medicine in Naples (TIGEM) where he directs the Genetics, Genomics and Systems Biology research program. In November 2007 he became Assistant Professor at the University of Naples "Federico II" and in November 2015 Associate Professor in Biomedical Engineering at the Dept. of Chemical, Materials and Industrial Engineering. His research interests are strongly interdisciplinary topics in the field of bioengineering and its applications in the field of biotechnology and biomedicine. He is the author of over 70 publications in international scientific journals and has contributed chapters to several scientific books. He is currently Associate Editor of the IEEE / ACM Trans Comput. Biol. and Bioinform. He has organized numerous workshops and conferences both nationally and internationally. He coordinated national European and international research projects in the field of Systems and Synthetic Biology (including European Union FP6, FP7 and H2020, HFSP, Italian Telethon Foundation and the Italian Ministry of Health).

Lecture 1: ***"Engineering and Control of Biological Circuits in Yeast"***
Lecture 2: ***"Engineering and Control of Biological Circuits in Mammalian Cells"***
A crucial feature of biological systems is their ability to maintain homeostasis in spite of ever-changing conditions. In engineering, this ability can be embedded in devices ranging from the thermostat to the autopilot of a modern plane using control systems which operate via a negative feedback mechanism: the quantity to be controlled is measured then subtracted from the desired reference value, and the resulting error is used to compute the control action to be implemented on the physical system (e.g. switching on or off the heating, changing the position of the rudder). These two lectures will introduce the concept of "negative feedback control" in engineering and show how it can be applied in synthetic biology in order to force a the expression of a gene to be in a desired range, or to change in time with a desired dynamics (e.g. pulsatile expression, sinusoidal expression etc.). Examples on the control of gene expression in yeast and mammalian cells will be shown.

Barbara Di Ventura, Synthetic Biology Group, BioQuant/DKFZ, Heidelberg, Germany

Barbara gained her degree in Computer Science from the University of Rome "La Sapienza" after which she obtained a Ph.D. in molecular biology at the EMBL, Heidelberg. She is currently group leader at the BioQuant center, at the University of Heidelberg. Her team is interested in understanding the importance of protein dynamics for cellular processes. They use an interdisciplinary approach that combines molecular and cellular biology with synthetic biology and mathematical modelling. A special focus of the lab is optogenetics, that is, the use of light to externally control protein function and localization in individual living cells.

Lecture 1: ***"Using blue light to control protein localization in living mammalian cells"***
Intracellular processes are controlled in many ways. One way consists in placing proteins in the right place at the right time. For instance, transcription factors (TFs) are often kept cytoplasmic until an activating signal arrives to the cell. Signal cascade activation leads to the translocation of the appropriate TF into the nucleus where transcription of target genes occurs. Some TFs are known to enter the nucleus with different dynamical patterns dependent on the type of stimulus. The very same TF can enter the nucleus in a single pulse with amplitude and duration proportional to the strength of the activating signal, or in several pulses whose number depends on the strength of the activating signal. There is compelling evidence that different TF dynamics lead to the activation of different gene expression programs. Optogenetics can help elucidate the role of TF dynamics in living cells in the absence of upstream signaling events. Being able to reversibly control the nuclear localization of proteins of interest with light is indeed crucial if we wish to investigate how the same protein activates different sets of genes depending on the temporal pattern of its nuclear localization.
In this lecture we will discuss some recent optogenetic methods that allow importing or exporting a protein of interest in and out of the nucleus of mammalian cells. We will focus on tools based on the blue light-sensing LOV2 domain.

Lecture 2: ***"Using split inteins for protein engineering in living cells"***
Biological processes are carried out by complex networks of interacting proteins that continuously adapt to cellular environment and external stimuli with structural changes, which lead to new functional properties and binding partners. Being able to control protein function to dissect or build cellular networks is one of the fundamental goals of synthetic biology. Expressing a genetically modified protein that carries either mutations that inhibit or activate a certain function or a "handle" that allows switching it on and off, is a powerful way to achieve control over it. Yet, this method implies that the protein is always modified, whenever expressed. In certain applications, it would be advantageous to have the unmodified protein expressed until a certain time-point, after which it should be post-translationally modified to perform new functions or interact with other partners. A universal toolbox that enables post-translational modifications of a protein of interest can be built based on natural enzymes, called inteins, whose action results in protein splicing or, very interestingly, protein circularization. This latter process can render proteins particularly thermostable and resistant towards exopeptidases. Circularization is, therefore, often used in biotechnology to produce protein variants more suitable for in vitro applications. In this lecture we will discuss inteins with a particular focus on how to use them for two interesting applications, namely protein circularization and protein reconstitution.

Jonathan S. Gootenberg, Department of Systems Biology, Harvard Medical School, Harvard University, USA

Jonathan S. Gootenberg is currently a DOE Computational Science Graduate Fellow and a Ph.D. candidate in the Harvard Systems Biology program, co-advised by Feng Zhang and Aviv Regev of the Broad Institute of MIT and Harvard.

Jonathan's research combines computational and molecular approaches to discover and characterize new biological tools, with a specific focus on CRISPR/Cas proteins and genome editing technologies, including Cpf1 and C2c2.

Lecture 1: "*Discovering and Characterizing CRISPR effectors*"
CRISPR-based molecular tools such as Cas9 have been quickly adopted into basic biology due to their re-programmability and ease of use. However, shortcomings with the traditional Cas9 from *S. pyogenes,* such as protein length and PAM constraints, suggest alternative CRISPR proteins may be able to expand the genome editing toolbox. I will discuss methods for discovering and characterizing Cas9 orthologs, such as the smaller Cas9 from *S. aureus*, and other CRISPR effectors, such as Cpf1 and the RNA-targeting effector C2c2.

Lecture 2: "*Probing Biology with CRISPR Screening*"
Genetic screens are a powerful method to tackle the complexity of biological systems, and allow the dissection of genes or elements contributing to a phenotype or pathway. CRISPR, due to its reprogrammable nature, has become a powerful tool for knockout, activation, and inhibition screens. I will discuss how to use new CRISPR tools to perform genome-wide or targeting screens and further developments in CRISPR screening methodology.

Markus Herrgard, Technical University of Denmark, Novo Nordisk Foundation Center for Biosustainability, Denmark

Markus Herrgård is Professor in Data-driven cell factory engineering at the Novo Nordisk Foundation Center for Biosustainability (CFB) at the Technical University of Denmark. He is also the Director of the iLoop Translational Core Unit at the CFB focusing on development of commercialization ready microbial cell factories. Markus has a Ph.D. in Bioengineering from the University of California, San Diego and M.Sc./B.Sc. degrees in Engineering Physics and Mathematics from Aalto University in Finland. From 2006 to 2008, he was a project leader at the University of California, San Diego focusing on systems biology of the yeast S. cerevisiae. From 2008 to 2012 Markus was a senior scientist and group leader at Synthetic Genomics, Inc. in La Jolla, CA managing a group focused on genome mining, synthetic biology design and modeling. He has been at the CFB since 2012 and has been the Director of the iLoop Unit since 2014. Markus is co-author of over 40 peer-reviewed publications with more than 4000 citations and is a co-inventor of several patents and patent applications.

Lecture 1: "*Developing an integrated cellular design tool*"
With the rapid development of synthetic biology methods such as the CRISPR/Cas9 system for genome editing, there is an ever increasing need to design complex non-intuitive manipulations involving simultaneous changes at multiple loci. These designs should ideally be derived based on analysis of omics data used to characterize the systems behavior of the organism being studied. However, existing tools for omics data analysis are not integrated with design tools, design tools at different levels (DNA, genes, pathways, organisms) are not integrated together, and additionally design tools are currently only accessible to specialized computational biologists. I will discuss progress and challenges in developing integrated design tools that allow multi-scale data-driven designs from the level of DNA sequences to whole organisms. I will focus on examples from microbial cell factory engineering, but many of the approaches are extensible to more complex organisms.

Lecture 2: "*Using adaptive laboratory evolution to optimize cellular behaviour*"
Adaptive laboratory evolution (ALE) is emerging as a key method to study the genetic basis of cellular behaviors and to develop improved cell factories. In particular, technological developments in automation, next generation sequencing and genome editing allow performing ALE experiments more rapidly and reproducibly followed by the identification of the detailed genetic changes required for adaptation. I will discuss history of ALE, the anatomy of a typical modern automated ALE experiment, and data analysis challenges related to high-throughput ALE. I will focus on examples from engineering cell factories for substrate or product tolerance, and the production of specific products. I will also discuss other applications of ALE to improve our understanding of genetic basis of cellular behaviors.

Shalev Itzkovitz, Department of Molecular Cell Biology, Weizmann Institute of Science, Israel

BSc in Physics Hebrew University in Jerusalem, Masters in Electrical Engineering at the Technion, PhD with Uri Alon at the Weizmann Institute, Postdoc at M.I.T. with Alexander van Oudenaarden, For the last 3.5 years - Assistant Professor at the department of Molecular Cell Biology at the Weizmann Institute of Science. Here is a link to Shalev Itzkovitz's

Lecture 1: "*Single molecule approaches for studying gene expression in intact mammalian tissues*"
Understanding how single cells cooperate within the context of a tissue requires quantitative techniques to measure gene expression in cells within their natural tissue microenvironment. I will describes approaches based on single molecule Fluorescense In-Situ Hybridization that enable determining the absolute amount of mRNA in individual cells, their rates of transcription and degradation and their intra-cellular localization. Using these approaches we found that gene expression in the intact mammalian liver occurs in transcriptional bursts. These bursts could potentially generate large variability in the mRNA content of neighboring cells, however the liver seems to have developed strategies to minimize this variability. These strategies include coordination of burst frequency and mRNA lifetime, cellular polyploidy and nuclear retention of mRNA.

Lecture 2: "*Systems biology of stem cell-maintained tissues*"
Tissue stem cells need to constantly proliferate to maintain their numbers while generating distinct proportions of differentiated cells. These homeostatic tasks are challenging as stem cells often operate in small compartments and are thus sensitive to biological noise. The intestinal crypt is a classic model system for studying tissue stem cells due to their small sizes, their clear spatially defined compartments and the availability of powerful mouse models that enable quantification of stem cell clonal dynamics. I will describe mechanisms applied by intestinal stem cells to achieve timely and robust production of distinct cell types during adult homeostasis. These two tasks, timely production and robustness, clash when considering the stage in the stem cell hierarchy at which differentiation occurs. I will describe how this tradeoff is resolved through spatially restricted lateral inhibition feedback mechanisms.

Francesco Ricci, Dipartimento di Scienze e Tecnologie Chimiche, University of Rome Tor Vergata, Rome, Italy

Francesco Ricci is an associate professor at the Chemistry Department of the University of Rome, Tor Vergata. His research interests are in the fields of DNA Functional Nanotechnology, DNA-based sensors and DNA-based nanomachines and nanodevices with possible practical applications in clinical diagnosis and drug delivery. After the PhD in chemistry earned in 2006 at the University of Rome, Tor Vergata, Francesco Ricci spent 2 years as a visiting post-doc researcher at the University of California, Santa Barbara in the frame of a Marie Curie International Outgoing Fellowship.
Prof. Ricci holds a 2013 ERC Starting Grant. He is also coordinator of two FP7 Marie Curie projects, a national "PRIN" research grant and a "Young Researcher grant" from the Italian Ministry of Health.
He is author of more than 70 research papers in peer reviewed high impact factor international journals (i.e. PNAS, JACS, Angew. Chem., Nano Lett. etc) with more than 2000 total citations (Scopus source) and a H-index of 29.
More information on the research activity and publications can be found at the lab website: www.francescoriccilab.com.

Lecture 1: "*DNA nanotechnology tools and reactions for synthetic biology*"
DNA nanotechnology uses DNA (or nucleic acids) as a versatile material to rationally engineer tools and molecular devices that can find a multitude of different applications (e.g., in-vivo and in-vitro diagnostics, drug delivery, genetic circuits etc.). With its simple base-pairing code and its nanoscale dimension, in fact, DNA appears as the perfect building block to assemble and engineer complex molecular architectures with unique accuracy and precision.
Similarly, the possibility to quantitatively predict and simulate DNA thermodynamics interactions has allowed to expand the horizons of DNA nanotechnology into the construction of programmable and autonomous DNA-based nanodevices that can be engineered to have different functions.
During this first lecture I will introduce the field of DNA nanotechnology and I will talk about some of the most used reactions in this field. More specifically, I will introduce the toehold-mediated (or toehold-exchange) DNA strand displacement reaction, a process through which two strands hybridize with each other displacing one (or more) prehybridized strands. Because it can allow a specific kinetic control of several reaction pathways, DNA strand displacement has found applications in the construction of DNA-based nanostructures, origami and, recently, genetic circuits (1).
I will show how it is possible to rationally engineer different DNA-based reactions (i.e. strand displacement and other reactions) so that they can be finely regulated by biological inputs (i.e. pH, small molecules, transcription factors, etc.) thus opening the future to new possibilities in the field of synthetic biology.

(1) Green AA, Silver PA, Collins JJ and Yin P. Toehold switches: de-novo-designed regulators of gene expression. Cell 159: 925-939 (2014).

Lecture 2: "*Nature-inspired DNA-based nanodevices*"
During this second lecture I will show how to exploit the "designability" of DNA to fabricate nature-inspired DNA-based nanoswitches and nanodevices that respond to different inputs including pH, antibodies, transcription factors and other clinically relevant targets.
These DNA-based nanodevices are specifically designed so that they undergo a conformational change (switch) upon binding to a specific input (i.e. target). This input-triggered conformational change can be then used for diagnostic, drug-delivery or synthetic-biology applications. I will show how to design different switching mechanisms. The inspiration behind all these mechanisms is derived from nature's sensing systems, which employ nanometer-scale protein and nucleic-acid-based "switches" to detect thousands of distinct molecules (including disease markers) in real time within complex physiological environments.

Next Generation Sequencing Lectures – July 12th, 2016

Mario Guarracino, CNR, Italy

Mario Guarracino is researcher at High Performance Computing and Networking Institute of the Italian National Research Council. He received a PhD in Mathematics defending a thesis on projection techniques for parallel sparse linear algebra and an Ms in Applied Mathematics. His postdoctoral training from National Research Council focused on low cost high performance architectures for scientific computing. He has been collaborating with Center for Applied Optimization at University of Florida since 2005. He has taught various undergraduate courses in both computer science and mathematics. His research interests include machine learning methods for computational biology and planning and development of high performance computational components for parallel and distributed problem solving environments. He is author of publications in the field of high performance scientific computing, computational biology and machine learning.

"How fast can we align sequences?"
Sequence alignment consists in the comparison of two or more strings to find similarities between the sequences. Each symbol of a string is assigned to at most one (maybe none) symbol in another string. These similarities are particularly important when the sequences represent biological molecules, such as DNA, RNA and proteins, because we assume that similar sequences hold a similar function, structure, and there might be an evolutionary relationships. In this lecture, we will address the issue of sequence similarity. We will introduce the concept of sequence alignment, and the concept of sequence similarity in terms of distance between symbols. Given a matrix of similarities between all possible pairs of symbols, the similarity of the alignment is the sum of the similarities between the aligned symbols. The problem is to find the alignment between two sequences having the maximum similarity (minimum distance). A global search in the space of all possible alignments is computationally impractical, and we will see how dynamic programming efficiently solves the problem. We will devote some time to the problem of finding local and local alignments between sequences. Finally we will focus on algorithms where short sequences need to be compared to a reference. This is often the case with next generation sequencing technologies, in which ten of millions of short strings need to be locally matched on a long one. A wide variety of alignment algorithms have been developed over the past few years and we will discuss their properties and applications on different types of experimental data.

Next Generation Sequencing Tutorials

* **Ilaria Granata**, CNR, Italy, *"Detection and analysis of contaminating sequences in NGS sequencing data"*

Reads alignment is an essential step of NGS data analyses. One challenging issue is represented by unmapped reads that are usually discarded and considered as not informative. However, it is important to fully understand the source of those reads, to assess the quality of the whole experiment. Moreover, is of interest to get some insights on possible "contamination" from organisms other than the one under investigation that might be present in the sequenced samples. Contamination may take place during the experimental procedures leading to sequencing, or be due to the presence of microorganisms infecting the sampled tissues. We will present a new pipeline aimed to the detection of viral, bacterial and fungi contamination in human sequenced data. The contaminating sequences can be filtered out from total reads in fastq or fasta formats and detected after the alignment to better understand their origin and correlation to the object of study. To this extend, data are sorted by organism and classified by taxonomic group.
Description of the tutorial:
1) Theoretical explanation of the topic and the state of art (Presentation);
2) Illustration of the new pipeline and workflow (Practical);
3) Application of the pipeline to a case study and discussion of the results (Practical).

* **Parijat Tripathi**, CNR, Italy, *"Detection and interpretation of circular RNAs in RNA-seq experiments"*

Circular RNAs are a large class of animal RNAs with regulatory potency. In the few unambiguously validated circRNAs in animals, the spliceosome seems to link the 5' and downstream 3' ends of exons within the same transcript. There are number of tools available to detect circular RNA such as CIRI, segemehl, find_circ and CIRCexplorer. In this tutorial, we focus on CIRCexplorer tool to identify circular RNA. Basically CIRCexplorer based on combined strategy to identify junction reads from back splices exons and introns lariats. At present it is only a circular RNA annotating tool, and it parses fusion junction information from mapping results of other aligners. In the tutorial, we try to identify these junction reads from unmapped reads after alignment is carried out for normal reads. CIRCexplorer need number of prerequisite steps which should be further carried out before running this tools. We have developed a computational pipeline using CIRCexplorer and all the other dependencies to identify Circular RNA in a given sample of RNA-seq data. We also added some more in house-built script to compare two different samples, for example disease vs. normal condition with respect to the expression of circular RNA and also try to understand the functional importance of Circular RNA harboring regions.

Description:
1) Introduction to mapping strategy to obtain junction reads for circular RNAs;
2) Running in house built wrapper pipeline using CIRCexplorer to obtain the results;
3) Parsing the results for functional annotation and comparative studies between different samples.

If you would like to participate to the NGS Tutorials please register sending an email to ilaria.granata@icar.cnr.it with subject "NGS@SSBSS" by Tuesday 5th.

Please indicate: your name, your topics of interest, the characteristics of your laptop (CPU/memory/storage) and operating system. We will send you the instructions to install the needed software on your local machine.

Oral Talk Sessions

The SSBSS 2016 Talks are exactly 16 minutes long: approximately 13 minutes for the talk + 3 minutes for the questions.

S. Andreas Angermayr, "*A growth–mediated negative feedback loop lowers the sensitivity to antibiotics*" – S. Andreas Angermayr, Guillaume Chevereau, Tobias Bollenbach – Oral Talks I (Saturday July 9th, 2016)

Ilaria Massaiu, "*Evaluation of different constraint–based methods to predict the growth of Escherichia coli in different environmental and genetic conditions*" – Ilaria Massaiu, Simone Maestri1, Susanna Zucca, Lorenzo Pasotti, M.G. Cusella De Angelis and P. Magni – Oral Talks I (Saturday July 9th, 2016)

Adèle Kerjouan, "*Spatiotemporal patterns of src activity reveals new signal transduction encoding to drive cell fate*" – Adele Kerjouan, Christiane Odddou, Edwige Hiriart–Bryant, Sanela Mrkonjic, Corinne Albiges–Rizo, Olivier Destaing – Oral Talks I (Saturday July 9th, 2016)

Jole Costanza, "*Genomics of chemoresistant acute myeloid leukemia*" – Oral Talks II (Saturday July 9th, 2016)

Alberto Giaretta, "*Modeling HPV early promoter gene expression*" – A. Giaretta, E. Bergamo, B. Di Camillo, L. Barzon, G.M. Toffolo – Oral Talks II (Saturday July 9th, 2016)

Jonny Naylor, "*Bioform: an in–silico 3D physical modelling workbench for the design, simulation and analysis of bacterial populations*" – Oral Talks II (Saturday July 9th, 2016)

Massimo Bellato, "*Mathematical model–based prediction of metabolic burden effects in interconnected synthetic gene circuits*" – M. Bellato, L.Pasotti, A. Serra, M.Casanova, S.Zucca, M.G. Cusella De Angelis and P. Magni – Oral Talks III (Saturday July 9th, 2016)

Ning Yin, "*Engineering Prophage to Increase Lysogen Competitive Fitness*" – Ning Yin, Roy Kishony – Oral Talks III (Saturday July 9th, 2016)

Nadège Merabet, "*Mathematical modeling of redox imbalance in Dominant Optic Atrophy Type 1*" – N. Merabeta A. Milleta, P. Belenguera, J. Bordeneuve–Guib eb, N. Davezaca – Oral Talks III (Saturday July 9th, 2016)

Anat Zimmer, "*Prediction of multi–dimensional drug dose–responses based on measurements of drug pairs*" – Anat Zimmer*, Itay Katzir*, Erez Dekel, Avi Mayo, Uri Alon – Oral Talks IV (Wednesday July 13th, 2016)

Kristian Jensen, "*Genome–wide associations between genes and microbial chemical tolerance*" Kristian Jensen, Rebecca Lennen, Nikolaus Sonnenschein, Markus Herrgård – Oral Talks IV (Wednesday July 13th, 2016)

Agnieszka Swiatek, "*Alternative method ontology*" – Agnieszka Swiatek, Malgorzata Nepelska, Ivana Campia, Sharon Munn, Annett J. Roi, Maurice Whelan – Oral Talks IV (Wednesday July 13th, 2016)

Roberta Bardini, "*Using Nets-Within-Nets for Modeling Differentiating Cells in the Epigenetic Landscape*", Roberta Bardini, Alfredo Benso, Stefano Di Carlo , Gianfranco Politano, Alessandro Savino – Oral Talks V (Wednesday July 13th, 2016)

Anna Degen, "*Spotlight on NRPSs – Visualization of Non–Ribosomal Peptide production using a pigment Synthetase*" – Oral Talks V (Wednesday July 13th, 2016)

Julia Zischewski, "*Plant cell packs: a versatile high–throughput screening tool for basic and applied plant research*" – Thomas Rademacher, Markus Sack, Julia Zischewski, Luisa Bortesi, Rainer Fischer – Oral Talks V (Wednesday July 13th, 2016)

Akos Nyerges, "*A highly precise and portable genome editing method allows systematic comparison of mutational effects across bacterial species*" – Ákos Nyergesa, Bálint Csörg_a, István Nagyb, Balázs Bálintb, Péter Biharib, Viktória Lázára, Gábor Apjoka, Kinga Umenhoffera, Balázs Bogosa, György Pósfaia, Csaba Pála – Oral Talks VI (Wednesday July 13th, 2016)

Song Feng, "*Exploring the design principles of cellular information processing*" – Song Feng, Orkun S Soyer – Oral Talks VI (Wednesday July 13th, 2016)

David Wernick, "*Engineering an evolutionary ladder for synthetic carbon fixation*" – Oral Talks VI (Wednesday July 13th, 2016)

Alexander P. S. Darlington, "Modelling the use of orthogonal ribosomes in synthetic gene circuits" - Alexander P.S. Darlington and Declan G. Bates – Oral Talks VII (Wednesday July 13th, 2016)

Daria Gaidar, "*Assosiation kinetics of S. aureus strains to human blood cells*" – Daria Gaidar, Alice Jordan, Ruslan Akulenko, Lutz von Muller, Volkhard Helms – Oral Talks VII (Wednesday July 13th, 2016)

KURSHED AKTAR SHAIKH, "*High yield cellulase production and secretion in E.coli*", Kurshed Aktar Shaikh, Annamma Anil, and Arvind M Lali – Oral Talks VII (Wednesday July 13th, 2016)

Javiera López, "*Production of ß–ionone by combined expression of carotenogenic and plant CCD1 genes in Saccharomyces cerevisiae*" – Javiera López, Karen Essus, Il–kwon Kim, Rui Pereira, Jan Herzog, Verena Siewers, Jens Nielsen, Eduardo Agosin – Oral Talks VIII (Wednesday July 13th, 2016)

Poster Session I – Saturday July 9th, 2016

Poster will be on display in the Poster Session Conference Room. Presenters in Poster Sessions should set up their posters during the lunch, or during the morning of their session, and take them down immediately after their session.

Simonas Marcisauskas, "*Constrain-Based Modelling Approach to Comprehend Thermotolerance of Kluyveromyces marxianus*" – Simonas Marcisauskas, Boyang Ji, Jens Nielsen

Hariharan Dandapani, "*Synthetic biology approach in the assembly of versatile production platforms in cyanobacteria*" – Hariharan Dandapani, Kati Thiel, Edita Mulaku, Natalija Petrova, Csaba Nagy, Pekka Patrikainen Pauli Kallio & Eva–Mari Aro

Sebastian Köbbing, "*Synthetic promoter libraries, a powerful tool for synthetic biology to fine tune expression*" – Sebastian Köbbing, Benedikt Wynands, Lars M. Blank, Nick Wierckx

Christine Skovbjerg, "*Platform for Generating bioactive compounds*"

Tapio Lehtinen, "*Dual sensor for monitoring hydrocarbon metabolism*" – Tapio Lehtinen, Ville Santala, Suvi Santala

Alicia Viktoria Lis, "*Dicarboxylic acid production in non–conventional Saccharomyces cerevisiae strains*" – Alicia V. Lis, Tim Snoek, Tobias Klein, Vratislav Stovicek, Konstantin Schneider, Jochen Förster, Michael Krogh Jensen, Jay Keasling

Mojca Ogrizovi, "*Regulation of lipid metabolism and neutral lipid accumulation in yeast Saccharomyces cerevisiae*" – Mojca Ogrizovi, Toma Curk, Klaus Natter, Uro Petrovi

Angelyn Lao, "*Understanding the Effect of RaphanussativusExtract on the Pathogenesis of Chronic Myeloid Leukemia, Breast and Colon Cancer through Mathematical Modeling*" – Jan Marie Claire J. Edra, Kathleen Dane T. Talag, Angelyn Lao

Sheraz Bhat, "*Modification of chickpea cystatin by reactive dicarbonyl species: glycation, oxidation and aggregation*" – Sheraz Ahmad Bhat, Bilqees Bano

Alberto Ciaramella,"Structural *and Functional Characterisation of CYP116B5: a new class VII catalytically self–sufficient bacterial P450*"

Side Selin Su Yirmibesoglu, "*Synthetic Biology Enabled Biomedical Sensors*" - Side Selin Su Yirmibesoglu**,** Urartu Özgür Şafak Şeker

Federico Tomasi, "*IMMUNOGLUBIN CLONES DETECTION WITH UNSUPERVISED MACHINE LEARNING*"

Hsiao–Chun Huang, "*Organization of Intracellular Reactions with A Heterologous Protein Scaffold*" – Liu Yang, Cheng–Ju Pan and Hsiao–Chun Huang

Tugce Onur, "*Engineered Bacterial Functional Amyloids*"

Gábor Apjok,"*pORTMAGE genome engineering systematically compares mutational effects across bacterial species*" – Gábor Apjok, Ákos Nyerges, Bálint Csörg, Viktória Lázár, Csaba Pál

Anantha Peramuna, "*Compartmentalization of High–Value Compounds in Green Cells*"

Gabriella Galatà, "*Bladder voiding dysfunction due to biallelic CHRM3 variant*"

Andrea Santoro, "*Complex Metabolic Networks*"

Fredy Altpeter Altpeter, "*Precision Genome and Metabolic Engineering for Genetic Improvement of Sugarcane*" – Je Hyeong Jung, Tufan Oz, Baskaran Kannan1, Ratna Karan, Saroj Parajuli, Janice Zale, Jae Yoon, Kim, Bhuvan Pathak, Hui Liu, Jason Candreva, Zhiyang Zhai, John Shanklin and Fredy Altpeter

Hector Arturo Hernandez Gonzalez, "*Epistasis in a development network of Myxococcus xanthus*"

Poster Session II – Sunday July 13th, 2016

Poster will be on display in the Poster Session Conference Room. Presenters in Poster Sessions should set up their posters during the lunch, or during the morning of their session, and take them down immediately after their session.

Miri Adler, "Cell Circuits for Tissue homeostasis"

Anne Pihl Bali, "*ENGINEERING AN ASSAY FOR SCREENING VITAMIN CELL FACTORIES*" – Anne P. Bali, Hans J. Genee, Luisa S. Gronnenberg, Morten O. A. Sommer

Tonja Wolff, "*Development of a conditional protein knock–down strategy by in–depth exploration of the N–end degradation criteria of ClpAP/ClpS in Escherichia coli*" – Tonja Wolff, Virginia Martínez, Ida Lauritsen and Morten H. H. Nørholm

Maja Ilievska, "*Identification of metabolic fluxes leading to the production of industrially relevant products*"

Javier Porcayo, "*Engineered yeast strains for the production of bulk chemicals from algal biomass*"

Jhonatan Hernandez–Valdes, "*Selection of metabolic biosensors for screening of Lactococcus lactis cells with increased product–yield for industrial fermentations*"

Nursyuhaida Mohd Hanafi, "*TRANSCRIPTOME ANALYSIS TOWARDS UNDERSTANDING CARRAGEENAN BIOSYNTHESIS PATHWAY IN KAPPAPHYCUS ALVAREZII*" – Nursyuhaida Mohd Hanafi, Teo Chee How, Norihan Mohd Saleh and Roohaida Othman

Elise de Reus, "*Peer–to–peer evolution: the role of Horizontal Gene Transfer in shaping the secondary metabolism of filamentous fungi*"

SURABHI SONI, "*Designing of Lipase nano–reactors as biocatalysts*" Surabhi Soni, Annamma Anil, Sanjeev K Chandrayan and Arvind M Lali

Roberta Bardini, "*Using Nets-Within-Nets for Modeling Differentiating Cells in the Epigenetic Landscape*", Roberta Bardini, Alfredo Benso, Stefano Di Carlo , Gianfranco Politano, Alessandro Savino

Emil Damgaard Jensen, "*Manipulation of pathway flux by CRISPR–Cas9 in yeast*", Emil D. Jensen, Tadas Jakociunas, Michael K. Jensen, Jay D. Keaslin

Thordis Kristjansdottir, "*A Genome–Scale Metabolic Network Reconstruction of the Thermophilic Bacterium Rhodothermus marinus DSM 4252T*" – Þórdís Kristjánsdóttir, Steinn Guðmundsson, Snædís Björnsdóttir, Edda Olgudóttir, Birkir Reynisson, Ólafur Friðjónsson, Sigurður Brynjólfsson and Guðmundur Óli Hreggviðsson

Giorgio Jansen, "*Metabolic Engineering of Cancer Tissues*"

Andrea Patanè, "*Pareto Optimal Design for Metabolic Engineering*"

Tom Wahlicht, "*A bimodal synthetic expression system controlling hepatic plasticity*" – Tom Wahlicht, Christoph Lipps and Dagmar Wirth

Victor Olariu, "*Oct4 and Tet1 interplay in establishing pluripotency*" – Victor Olariu, Cecilia Lovkvist, and Kim Sneppen

Rodrigo Santibáñez, "*A GoldenGate Library of plasmids based on bidirectional promoters to enhance combinatorial plasmid assembly and combinatorial yeast transformation*" – Rodrigo Santibáñez, Javiera López, Bastián Pérez, Vicente Cataldo, Eduardo Agosín

Internet WI-FI
Internet WI-FI connection is available everywhere inside the SIAF Campus. During the check in, we will assign you a personal passphrase that can be used on every device you have. The network is "**SIAF Guests**" and the password is **siaf3cnjpsep1** Internet WI-FI connection is free for the SSBSS 2016 Participants.

Social Tour and Dinner in Florence
14:30 Departure from SIAF To Florence
Guided tour of Florence (1h30 minutes approximately)
Free time in Florence
19.30 Departure from Florence City Centre to Restaurant for Dinner, live music will be performed during the dinner.

The menu is composed by:
Welcome cocktail
Appetizer (Bruschetta and bread with mixed sauces)
Penne (a kind of pasta) with pork and rosemary sauce
Rice with asparagus sauce
Roasted Pork
Side dish
Tiramisù Dessert
White and red wine
Mineral water
Coffee

Departure from the restaurant to SIAF after dinner.