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Abstract

In the framework of the 24 Month Meeting of the project CADMAD, a Minisymposium on Synthetic Biology is been organized by the Mathematics and Computer Sciences Faculty of the Weizmann Institute.
This Sympoisium sponsored by CADMAD, a FET-Open Consortium, is being held on March 19 at the Weizmann Institute of Science Faculty of Mathematics and Computer Science
The speakers are 3 members of the CADMAD consortium and one speaker outside CADMAD consortium.
Invitations to this Symposium were sent to the scientific community in Weizmann with special emphasis to the biological departments, and to the other Universities in Israel.

Keywords[7]

Symposium, Synthetic Biology, CADMAD

Speakers :

Frank Edenhofer -
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Programming transcriptional networks for reprogramming cells

Recent advances in transcription factor-driven reprogramming of somatic cells have opened up attractive interfaces between synthetic biology and cell biology. Seminal studies by Yamanaka and co-workers demonstrated that retroviral transduction of the transcription factors Oct4, Sox2, Klf4, and c-Myc is sufficient to induce pluripotency in somatic cells. Such artificially induced pluripotent stem (iPS) cells are functionally equivalent to embryonic stem (ES) cells and provide fascinating prospects for biomedical applications. More recently it has been shown that cellular reprogramming can yield neurons, cardiomyocytes, neural as well as hepatocyte progenitors. We demonstrated the direct derivation of neural stem (NS) cells from fibroblasts employing a modified Yamanaka-type reprogramming paradigm. Retroviral transduction of Sox2, Klf4, c-Myc and timely restricted activation of Oct4 was used to initiate dedifferentiation of fibroblast cells and 19 days post infection we observed neurosphere-like colonies that could be readily isolated and clonally expanded both as sphere and adherent cultures. Such induced NS (iNS) cells are able to differentiate into all three neural lineages, neurons, astrocytes as well as oligodendrocytes. Fibroblast-derived iNS cells exhibit clonal growth and maintain their marker expression profile and differentiation capability over prolonged expansion (>50 passages). Putative reprogramming mechanisms and therapeutic value of reprogrammed cells will be discussed demonstrating that direct cellular conversion of somatic cells is to develop into a new paradigm for both regenerative medicine and disease modeling.

Natalio Krasnogor
Applied Interdisciplinary Computing, School of Computer Science, University of Nottingham

Computational tools for rapid model prototyping in synthetic biology

The conceptual cornerstone of Synthetic Biology is that methodologies commonly used to design and construct non-biological artefacts (e.g. computer programs, airplanes, bridges, etc) might also be mastered to create “designer” living entities. In particular, and notwithstanding that a biological substrate is very different than electronic computers, one would like to be able “program” the former with the same ease as one programs the later.
This talk presents progress being made in trying to develop an integrated computer aided design (CAD) suite for programming cellular behavior via rapid biomodel prototyping. Biomodels are formally specified using a domain specific

[7] Keywords that would serve as search label for information retrieval

programming language (InfoBiotics) that captures several layers of biological organization (colony level, cellular level, sub-cellular processes) and permits models reuse. An InfoBiotics program (i.e. a prototype biomodel exhibiting a designer phenotype) can be executed with state-of-the-art stochastic simulators and analysed via model checking techniques. Once the target phenotype is achieved in silico, the InfoBiotics program must be converted into well-defined DNA sequences ready for synthesis. Currently, this process is knowledge-intensive; our methodology automates (part of) this process by compiling the formal specifications into a detailed list of biological DNA parts. Usually, a compiled list of parts requires substantial optimisation (e.g. strengthening/weakening of binding sites, degradation rates, etc) in the wet lab. To formally capture this process, a domain specific programming language, DNALD, is used to program combinatorial DNA libraries.
Time permitting, I will briefly mention challenges and opportunities for computer scientists working in Synthetic Biology.

Ido Bachelet
Institute of Nanotechnology & Advanced Materials
Bar-Ilan University

Natural user interfaces for controlling molecular machines

Computers and robots augment our ability to perceive and control reality. However, implementing them for controlling molecules inside living organisms has not been feasible so far. We are developing and studying solutions to this challenge based on biocompatible, nanomechanical robots made from DNA molecules. Our recent research focuses on designing user interfaces for nano-robots that control therapeutic molecules using natural outputs such as motion and EEG patterns. These techniques could be applied to other settings such as scientific research and industry, where precise control over molecules in nonlinear media is highly desired.

Udi Shapiro and Tuval Ben Yehezkel
Depts. of Applied Math and Computer Science and Biological Chemistry
Weizmann Institute of Science

Computer aided design and manufacturing of DNA for synthetic biology

DNA programming is the DNA-counterpart of computer programming. The basic computer programming cycle is to modify an existing program, test the modified program, and iterate until the desired behavior is obtained. Similarly, the DNA programming cycle is to modify a DNA molecule, test its resulting behavior, and iterate until the goal (which is either understanding the behavior or improving it) is achieved. One key difference between the two is that unlike computer programming, our understanding of DNA as programming language is very far from being perfect, and therefor trial and error are the norm rather than the exception in DNA-based research and development. Hence DNA programming is more efficient if multiple variants of a DNA program, also called a DNA library, are created and tested in parallel, rather than creating and testing just one program at a time. Hence the basic DNA programming cycle, when operating in full steam, takes the best DNA programs from the previous cycle, uses them as a basis for creating a new set of DNA programs, tests them, and iterates until the goal is achieved.
The CADMAD consortium aims to deliver a system and method for DNA processing that will support DNA programming. The talk will review the goals, plans and achievements to date, as well as challenges for the future.