Synthetic Biology-

ANDREW E. BLANCHARD



Andrew E. Blanchard

Current Position: Ph.D. Candidate, Department of Physics, University of Illinois at Urbana–Champaign. Advisor: Dr. Ting Lu. Education: M.S. in Physics at University of Illinois at Urbana–

Champaign, B.S. in Physics and Mathematics at University of Arkansas.

Nonscientific Interests: Running, hiking, reading, playing guitar.

My research focuses on quantitative studies of microbial communities by combining mathematical modeling with computer simulation. My overarching goal is to determine the relationship between social interactions and spatiotemporal structures. The current paper investigates the outcome of competition between two strains capable of employing different nutrient utilization strategies in fluctuating environments. Both analytical and computational approaches are utilized to understand how fluctuations in environmental cues can impart an advantage to a certain competitive strategy. (Read Blanchard's article; DOI: 10.1021/sb4002008).

MIHAILS DELMANS



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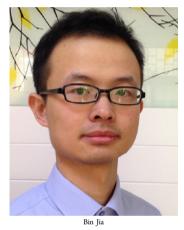
Current Position: Ph.D. student, Department of Plant Sciences, University of Cambridge. Advisor: Dr. Jim Haseloff.

Education: B.Eng. Biomedical Engineering, Imperial College London.

Nonscientific Interests: Traveling, cycling, hiking.

My general scientific interest is studying and designing biological systems by exploiting mathematical, computational and engineering tools. My ambition is to master both dry and wet lab skills. In this paper we tried to bring synthetic biology a step closer to a natural environment by presenting a possible design for a biosafe cloning vector. I believe that we managed to create a robust solution, and I hope that more supporting evidence is coming soon. In my Ph.D. project I am going to study patterns of cellular division and proliferation and their relation to a shape of a plant tissue. The ultimate aim of the project is to develop a computational tool that would help explain existing plant morphology and give some insight into designing novel plant shapes. (Read Delmans' article; DOI: 10.1021/sb500234s).

BIN JIA



Current Position: Ph.D. Candidate, School of Chemical Engineering and Technology, Tianjin University, China. Advisor: Prof. Yingjin Yuan.

Education: Undergraduate in Biochemical Engineering, Tianjin University, China.

Nonscientific Interests: Ping-pong, basketball, running and cooking.

My research is focused on developing new tools and methods for synthetic biology. The emergence of the field of synthetic biology has put an ever-increasing demand on developing more accurate, efficient, convenient and economical cloning technologies. In this paper, we developed a method termed Rapid Assembly of DNA Overlapping Multifragments (RADOM), which can assemble designed DNA fragments up to 10 kb long. This protocol has proved to be very robust and reliable in the synthetic yeast genome project, Sc2.0. Currently, I am working on constructing larger metabolic pathways of *Escherichia coli* with this method. In the future, RADOM will be widely used in construction of synthetic biological systems in a rapid and effective manner. (Read Jia's article; DOI: 10.1021/sb500241e).

Received:March 5, 2015Published:March 20, 2015

HANSON LEE



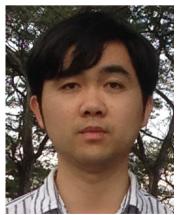
Current Position: Staff Scientist, Cambrian Genomics, San Francisco, CA (2013–present).

Education: Postdoctoral fellow (2010–2013) at Energy Biosciences Institute, University of California, Berkeley. Advisor: John Dueber. Postdoctoral fellow (2007–2010), Molecular and Cell Biology, University of California, Berkeley. Advisor: Ehud Isacoff. Ph.D. Molecular and Cell Biology, University of California, Berkeley (2007). Advisor: Ehud Isacoff. B.S. Life Sciences, National Tsing Hua University, Hsinchu, Taiwan (2001).

Nonscientific Interests: Digital animation, cooking, and traveling.

My general scientific interest lies in creating tools that enable better abstraction for genetic engineering, such that scientists can save time and energy by not worrying about procedures to construct the underlying DNA sequences or the unintended consequences they can cause. In this work, we examined undesired protein truncation when porting protein coding sequences from eukaryotes to prokaryotes. Furthermore, potential solutions to circumvent these problems were proposed and demonstrated. In my current position at Cambrian Genomics, we combine next generation sequencing techniques and microarray DNA synthesis to produce genes in a massively parallel fashion so production costs can be dramatically reduced and the overall manufacturing capacity can be significantly increased. (Read Lee's article; DOI: 10.1021/sb500003x).

JIAZHANG LIAN



Jiazhang Lian

Current Position: Ph.D. candidate, Department of Chemical and Biomolecular Engineering, University of Illinois at Urbana–Champaign. Advisor: Huimin Zhao.

Education: B.S., Bioengineering, Zhejiang University, Hangzhou, China. Advisor: Zhinan Xu.

Nonscientific Interests: Ping-pong, music, reading, and playing cards.

My research is focused on the engineering of yeast cell factories for efficient production of fuels and chemicals *via* enhanced supply of precursor metabolites, such as pyruvate, acetyl-CoA, and acyl-CoAs. In this paper, we showed that the β -oxidation cycle could be functionally reversed in *Saccharomyces cerevisiae*, a versatile platform to produce n-butanol, medium-chain fatty acids, and medium-chain fatty acid ethyl esters. Currently, I'm trying to further boost the titer of the desired products by increasing the intracellular concentration of acetyl-CoA, a precursor of the reversed β -oxidation pathway. Synthetic biology approaches are used to introduce alternative acetyl-CoA biosynthesis routes from bacteria (pyruvate dehydrogenase) and oleaginous yeasts (ATP-dependent citrate lyase). (Read Lian's article; DOI: 10.1021/sb500243c).

JOANNA LIPINSKI-KRUSZKA



Sarah Deragon

Current Position: Founder, fPrime Analytics.

Education: Ph.D. Bioinformatics, UCSF, Advisor: Hana El-Samad. M.S. Physiology and Behavioral Biology, San Francisco State University, Advisor: Megumi Fuse. B.S. Computer Science, University of Illinois at Urbana–Champaign.

Nonscientific Interests: I love traveling, road biking and ballroom dancing. However, at the moment my hobbies are taking a backseat to crafty projects and tea parties with a Power Ranger and a princess.

I am interested in developing methods elucidating information flow and decision making in cellular pathways. In order to gain a system-level understanding of how such programs are executed it is necessary to map the structure of the underlying generegulatory networks. Traditionally, prediction and modeling of such networks are done using mean gene expression data of the entire population of cells. However, data averaging can lead to significant information loss and, hence, can result in nonunique solutions. In order to improve these predictions additional information is needed. To this end, in my Ph.D. work I focused on understanding and learning how to utilize data that is often discarded such as molecular noise. Since finishing my Ph.D., I turned my passion for science into a business. I am a cofounder of a consulting firm, fPrime Analytics, focusing on mathematical modeling, algorithm development and analysis of complex biological data. (Read Lipinski-Kruszka's article; DOI: 10.1021/sb5000059).

JUERGEN MAIRHOFER



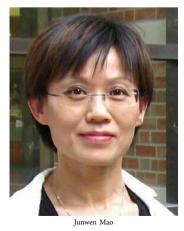
Current Position: CEO of enGenes Biotech GmbH.

Education: Ph.D. in Biotechnology, University of Natural Resources and Life Sciences (BOKU), Vienna. Supervisor: Prof. Reingard Grabherr.

Nonscientific Interests: Traveling, photography, skiing, hiking, fermented foods.

I am generally interested in genetic and bioprocess engineering with the overall research goal to substantially improve current state-of-the-art production regimes for recombinant proteins in microbial systems. The T7 RNA polymerase is a powerful tool in the field of synthetic biology used for the overexpression of genes. Our paper published in this issue deals with improving the commonly used major late T7 terminator (that was intended to be a leaky terminator by nature since the T7 promoter also drives expression of two genes downstream of this terminator by read-through transcription). Using an improved, synthetic terminator had major influence on the overall output of the T7 expression system used in an industrial-relevant fed-batch production process. We believe that our findings will have major implication on the design of genetic circuits that employ the orthogonal T7 RNA polymerase for gene expression. (Read Mairhofer's article; DOI: 10.1021/sb5000115).

JUNWEN MAO



Current Position: Professor in the Department of Physics at Huzhou University, Zhejiang, China.

Education: Ph.D. Physics, Zhejiang University, China (2006). Advisor: Dr. Youquan Li. B.S. Engineering Thermophysics, University of Science and Technology of China (1992).

Nonscientific Interests: I enjoy walking and traveling. The combination of both is the best—walking in a new place to explore its landscape and culture.

My research interests involve statistical physics and systems biology. Specifically, I am interested in quantitative modeling of biochemical reaction kinetics and cellular stochastic dynamics, with the goal of advancing the understanding of complex cellular functionality. Our recent work includes the development of a three-component model for the analysis of horizontal gene transfers based on natural transformation as well as the exploration of bacterial exploitative competition strategies that maximize cellular survival. (Read Mao's article; DOI: 10.1021/sb4002008).

RYO MIZUUCHI



Current Position: Graduate student at the Department of Bioinformatic Engineering, Graduate School of Information Science and Technology, Osaka University. Advisor: Prof. Tetsuya Yomo.

Education: B.S. in Biotechnology, Department of Biotechnology, School of Engineering, Osaka University.

Nonscientific Interests: Badminton, running, cycling, and scifi movies.

My primary research interests are the origin of life and early evolution. I have addressed these puzzles by reconstituting lifelike properties. To date, although several cellular functions have been reconstituted *in vitro* from biological molecules and deep insights have been given, it is still challenging to reconstitute the same level of evolutionary ability as natural organisms. In our project, we focused on adaptive evolutionary ability, which allows living things to survive in various environments; we were able to partially reconstitute the adaptive ability in a simple artificial genome replication system. Currently I am trying to understand how life has continued to evolve while obtaining new components and functions. (Read Mizuuchi's article; DOI: 10.1021/sb5000884).

MORTEN NØRHOLM



Gustav Nordlund

Current Position: Senior Scientist and Academic-Entrepreneurial Research Group Leader at the Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark.

Education: M.Sc. in Biochemistry from University of Copenhagen, Advisor: Gert Dandanell. Ph.D. in Molecular Biology from University, Advisor: Barbara Ann Halkier. My PhD studies included a stay in Matthias Hediger's lab at Harvard Medical School. Postdoc with Gunnar von Heijne, Stockholm Center for Biomembrane Research.

Nonscientific Interests: Long-distance running. Skiing.

My research at the Center for Biosustainability is focused on developing molecular tools for synthetic biology and optimizing expression of complex pathways and membrane proteins in microbial cell factories. During my Ph.D. studies, I was part of a research group that developed the uracil excision DNA assembly technology (AKA USER cloning), and throughout my research career I have been fascinated with the challenge of difficult-to-express membrane protein encoding genes. (Read Nørholm's article; DOI: 10.1021/ sb500055u).

TONG SI



Wenjia Ma

Current Position: Postdoctoral fellow, Carl R. Woese Institute for Genomic Biology, University of Illinois at Urbana– Champaign. Advisor: Huimin Zhao, Jonathan V. Sweedler.

Education: Ph.D. Chemical Engineering, University of Illinois at Urbana–Champaign (2014). Advisor: Huimin Zhao. B.S. Chemistry and Biology, Tsinghua (2009). Advisor: Yanmei Li.

Nonscientific Interests: Marathon runner, singing, reading books.

I am interested in developing high-throughput approaches to understand and engineer biological systems. Given our limited knowledge of complex biological systems, directed evolution often out-competes rational design in improving desirable phenotypes. However, the success of directed evolution is mostly confined to individual proteins and pathways, due to the lack of tools to introduce mutations globally and iteratively into a genome. In this paper, we harness the simplicity and effectiveness of RNAi screening to enable continuous evolution of the Saccharomyces cerevisiae genome by accumulating beneficial knockdown mutations. Whereas the current ability to manipulate a genome in multiplex is limited to bacterial hosts, our work has expanded the genome-scale engineering practice to yeast. Looking forward, we are trying to include more types of genetic mutations, as well as to introduce automation technology to improve and accelerate the directed genome evolution effort. (Read Si's article; DOI: 10.1021/ sb500074a).

GERALD STRIEDNER



Current Position: Assistant Professor of Bioengineering, Department of Biotechnology, University of Natural Resources and Life Sciences, Vienna.

Education: Ph.D. in Biotechnology, University of Natural Resources and Life Sciences (BOKU), Vienna.

Nonscientific Interests: Running, yoga, singing.

My scientific interest is to a large extent driven by the motivation to put basic research results into practice and application. Our success in achieving this goal is based on an integrated systems approach in bioprocess engineering, which equally considers biology and engineering aspects. Detailed characterization of host cells under production conditions revealed that inefficient transcription termination of T7 RNA polymerase is a serious problem in T7 based expression systems with significant influence on host metabolism and product yield. The clear cause and effect assignment allowed for a systems modification on a rational basis—the dedicated goal in bioprocess engineering. (Read Striedner's article; DOI: 10.1021/ sb5000115).

MAULIK THAKER



Charul Jani

Current Position: Research Investigator II, SynBio Group, Global Discovery Chemistry, Novartis Institutes for Biomedical Research, Cambridge, MA.

Education: Postdoctoral research: Institute for Infectious Disease Research, McMaster University, Hamilton, Canada. Advisor: Prof. Gerry Wright. Ph.D. in Biochemistry from Maharaja Sayajirao University of Baroda, India. Advisor: Dr. Jayashree Pohnerkar. MBA in Healthcare Services from Sikkim Manipal University, India. M.Sc. in Botany from Maharaja Sayajirao University of Baroda, India.

Nonscientific Interests: I am a nature enthusiast and love to travel. I like to watch documentaries and enjoy informal debates on current affairs.

My broad interest is in studying natural product biosynthesis pathways in Actinomycetes and employing synthetic biology approaches to replace the classical "discovery" based approaches with more directional "invention" oriented methods. In this paper, we use the example of glycopeptide antibiotic scaffolds to describe the scope for expanding the chemical space using synthetic biology approaches and creating synthetic natural molecules. The device or minimal set of genes required for biosynthesis of the core molecule can be loaded on a chassis represented by a suitable heterologous host, collectively providing a platform. Various scaffold decorating enzymes that serve as parts, when supplied in different combinations to the platform, create new bioactive molecules. The approach is beneficial in creating diverse chemical matters of choice with limited efforts. (Read Thaker's article; DOI: 10.1021/ sb300092n).

NANXI WANG



Nanxi Wang

Current Position: Graduate Student, Department of Chemistry, University of Nebraska–Lincoln. Advisor: Dr. Jiantao Guo.

Education: B.S. in Pharmaceutical Science, China Pharmaceutical University, China.

Nonscientific Interests: Anime, reading, and travel.

My research is focused on developing a nonsense codon suppression system and utilizing the system for biochemical investigations. In this system, a nonsense codon (e.g., amber codon) is reprogrammed into a sense codon to encode unnatural amino acids using a suppressor tRNA and aminoacyl tRNA synthetase pair. In this work, by optimizing anticodon recognition of tRNA by aminoacyl-tRNA synthetase, we identified a number of aminoacyl-tRNA synthetase variants with significantly enhanced activity for the incorporation of unnatural amino acids into proteins, in response to the amber nonsense codon. Currently, I am applying this nonsense codon suppression strategy to the development of HIV-1 vaccine. I am also working on a quadruplet codon decoding system and utilizing it as a tool to study how the ribosome maintains its reading frame. (Read Wang's article; DOI: 10.1021/ sb500195w).

WESTON WHITAKER



Weston Whitaker

Current Position: Postdoctoral fellow. Department of Microbiology and Immunology, Stanford University. Advisor: Justin Sonnenburg.

Education: Ph.D. Bioengineering, University of California, Berkeley (2012). Advisors: John Dueber and Adam Arkin. B.S. Biomedical Engineering, Columbia University (2005).

Nonscientific Interests: My hobbies are home-brewing beer and tinkering with electronics—I am currently attempting to automate much of my brewing process. I also enjoy reading history and hiking.

Here we examine the potential problem of translation initiation at unintended sites. During my graduate work, I focused primarily on engineering signal transduction in *E. coli*, and it was necessary to produce low concentrations of proteins. We noticed that at these low concentrations, achieved primarily by reducing the ribosome binding site strength, the relative amount of translation initiation beginning within the open reading frame at unintended sites is often substantial and problematic. We investigate this phenomenon and how it may be avoided by recoding to introduce RNA secondary structure and balancing transcription and translation rates. My current work applies synthetic biology to develop genetically encoded probes for studying the human gut microbiota. (Read Whitaker's article; DOI: 10.1021/sb500003x).

OLIVER WRIGHT



Oliver Wright

Current Position: Founder, Tutorly.

Education: Ph.D. Biotechnology, University of Cambridge. Advisor: Alan Tunnacliffe. B.App.Sc. Molecular Biotechnology, University of Otago, New Zealand.

Nonscientific Interests: I dabble in business start-ups, and am currently taking time away from the bench to fully indulge.

Biosafety issues relating to proposed environmental deployments of genetically modified microbes are nothing new. Over the past ~25 years, several groups have experimented with various approaches (some more sensible than others) in attempts to ameliorate concerns, and this ground is being raked over again during the rise of synthetic biology. In this paper we combined what we considered to be the soundest approaches (reviewed by us in 2013) into a single plasmid-based biosafety system (aka "GeneGuard"). While refactoring entire genomes (*e.g.,* Lajoie *et al.,* 2013, DOI: 10.1126/science.1241459) represents, in my opinion, the next advance, our platform can be retrofitted to existing projects as they stand. Which biosafety approach will prove publicly acceptable (if any), however, awaits a suitable pilot application to act as a standard-bearer. (Read Wright's article; DOI: 10.1021/sb500234s).