

## Recent publication in the field of Synthetic Biology

The list covers some articles published in the period in the period December 2017 – August 2019 and is by no means complete and represents publications in the field of Synthetic biology that I find interesting.

### Macromolecular Design

*De novo* design of tunable, pH-driven conformational changes, Boyken *et al.*, Science 364 (6441), 658-664  
pH-driven conformational transitions with tunable cooperativity and pH set point are created using computational protein design.

Design and evolution of an enzyme with a non-canonical organocatalytic mechanism, Burke *et al.*, Nature 570 (7760), 219-223

An enzyme with a non-canonical organocatalytic mechanism was generated by introducing N $\delta$ -methylhistidine into a designed active site.

Evolution of a designed protein assembly encapsulating its own RNA genome, Butterfield *et al.*, Nature 552 (7685), 415-420

The paper presents the development of synthetic nucleocapsids that can package their own RNA genome. This is an example of *de novo* design of virus-like structures.

*De novo* design of a fluorescence-activating  $\beta$ -barrel, Dou *et al.*, Nature 561 (7724), 485-491

The first demonstration of accurate *de novo* design of  $\beta$ -barrel proteins that can bind small molecule ligands and activate them.

Programmable CRISPR-responsive smart materials, English *et al.*, Science 365 (6455), 780-785  
CRISPR-associated nucleases are used to control multiscale properties of DNA-based materials.

High-Throughput Investigation of Diverse Junction Elements in RNA Tertiary Folding, Knight Denny *et al.*, Cell 174 (2), 377-390

This paper demonstrates the relationships between sequence, structure and energetic in RNA and can provide basis improved design of RNA molecules with specific functions, e.g. switches.

*De novo* protein design by citizen scientists, Koepnick *et al.*, Nature 570 (7761), 390-394

Proteins were designed *de novo* by players of the online protein-folding game Foldit, incl. a protein with entirely new fold.

*De novo* design of bioactive protein switches, Langan *et al.*, Nature 572 (7768), 205-210

A technique for the *de novo* design of switchable protein systems controlled by induced conformational change is presented.

An ultra-stable gold-coordinated protein cage displaying reversible assembly, Malay *et al.*, Nature 569 (7756), 438-442

A stable artificial protein cage with novel non-natural geometry, whose assembly and disassembly can be controlled is presented.

Induction of Potent Neutralizing Antibody Responses by a Designed Protein Nanoparticle Vaccine for Respiratory Syncytial Virus, Marcandalli *et al.*, Cell 176 (6), 1420-1431

The article describes computationally designed self-assembling nanoparticle that displays multiple copies of a trimeric viral protein that induces potent neutralizing antibody responses.

Biotechnological mass production of DNA origami, Praetorius *et al.*, Nature 552 (7683) 84-87

This paper presents a method for scalable productions of large DNA molecules of arbitrary sequence that can be used for production of complex nanostructures.

*De novo* design of potent and selective mimics of IL-2 and IL-15, Silva *et al.*, Nature 565 (7738), 186-191

The paper demonstrates that *de novo* design can be used to develop potent and selective mimics of natural signaling molecules. Such molecules can be completely unrelated to the natural counterpart and might have superior therapeutic properties.

Diverse and robust molecular algorithms using reprogrammable DNA self-assembly, Woods *et al.*, Nature 567 (7748), 366-372

A set of 355 self-assembling DNA 'tiles' is presented that can be reprogrammed to implement many different computer algorithms.

### **Synthetic Circuits and Signaling Pathways**

Cellular checkpoint control using programmable sequential logic, Andrews, Nielsen and Voigt, Science 361 (6408), eaap8987

The paper presents genetic circuits that encode sequential logic to instruct cells to proceed through a linear or cyclical sequence of states.

A universal biomolecular integral feedback controller for robust perfect adaptation, Aoki *et al.*, Nature 570 (7762), 533-539

A synthetic gene circuit implementing an integral feedback topology is shown to achieve robust perfect adaptation in living cells.

Complex signal processing in synthetic gene circuits using cooperative regulatory assemblies, Bashor *et al.*, Science 364 (6440), 593-597

Tunable protein interactions are used to build gene circuits with nonlinear behaviors.

A compact synthetic pathway rewires cancer signaling to therapeutic effector release Chung *et al.*, Science 364 (6439), eaat6982

A rationally designed synthetic pathway specifically detects an intracellular oncogenic state and rewires it for therapeutic outputs.

Programmable protein circuits in living cells, Gao *et al.*, Science 361 (6408), 1252-1258

The paper presents a scalable platform to facilitate protein circuit engineering for biotechnological applications based on orthogonal modular proteases.

Evolutionary Convergence of Pathway-Specific Enzyme Expression Stoichiometry, Lalane *et al.*, Cell 173 (3), 749-761

This paper identifies an important principle for building biological pathways that can significantly facilitate development of new synthetic pathways.

*De novo* design of bioactive protein switches, Langan *et al.*, Nature 572 (7768), 205-210

A technique for the *de novo* design of switchable protein systems controlled by induced conformational change is presented.

Engineering Epigenetic Regulation Using Synthetic Read-Write Modules, Park *et al.*, Cell 176 (1), 227-238  
A synthetic epigenetic regulatory system in human cells using m6A DNA modification that allows construction of regulatory circuits is described.

Programmable RNA-Guided RNA Effector Proteins Built from Human Parts, Rauch *et al.*, Cell 178 (1), 122-134

A general strategy for engineering programmable RNA effectors is presented.

Engineering a Model Cell for Rational Tuning of GPCR Signaling, Shaw *et al.*, Cell 177 (3), 782-796  
Signaling pathway is engineered in yeast that can effectively detect various compounds.

Time-resolved protein activation by proximal decaging in living systems, Wang *et al.*, Nature 569 (7757), 509-513

A general strategy for in vivo protein activation using light-controlled proximal decaging is presented.

Circuit design features of a stable two-cell system, Zhou *et al.*, Cell 172 (4), 744-757

This paper demonstrates the principles on which stable cell-circuits can be formed. Similar principles can be used to design novel cell-circuits that do not exist naturally.

### **Synthetic Metabolic Pathways**

Complete biosynthesis of cannabinoids and their unnatural analogues in yeast, Luo *et al.*, Nature 567 (7746), 123-126

The article presents engineering of a complex biosynthetic pathway in yeast.

Synthetic glycolate metabolism pathways stimulate crop growth and productivity in the field, South *et al.*, Science 363 (6422), eaat9077

The study demonstrates that engineered metabolic pathways can affect and improve the agricultural properties of plants.

Optogenetic regulation of engineered cellular metabolism for microbial chemical production, Zhao *et al.*, Nature 555 (7698), 683-687

The paper demonstrates the use of engineered metabolic pathways to control fermentation with only light.

### **Xenobiology (Non-natural Nucleotides and Amino Acids)**

Design and evolution of an enzyme with a non-canonical organocatalytic mechanism, Burke *et al.*, Nature 570 (7760), 219-223

An enzyme with a non-canonical organocatalytic mechanism was generated by introducing N $\delta$ -methylhistidine into a designed active site.

Hachimoji DNA and RNA: A genetic system with eight building blocks, Hoshika *et al.*, Science 363 (6429), 884-887

DNA and RNA with expanded genetic code from four to eight nucleotide letters that includes synthetic bases is presented.

Genetically programmed chiral organoborane synthesis, Kan *et al.*, Nature 552 (7683) 132-136

A genetically encoded platform for producing chiral organoboranes in bacteria that expands the chemical reactions that can be carried out in cell is presented.

Designer membraneless organelles enable codon reassignment of selected mRNAs in eukaryotes, Reinkemeier, Estrada Girona and Lemke, Science 363 (6434), eaat2644

The article presents the design of an artificial, membraneless organelle into mammalian cells to perform orthogonal translation.

Controlling orthogonal ribosome subunit interactions enables evolution of new function, Schmied *et al.*, Nature 564 (7736), 444-651

An ingenious *in vivo* system that can be used to evolve proteins with new functions, incl. containing non-natural amino acids is described.

### **Synthetic genomics**

Synthetic sequence entanglement augments stability and containment of genetic information in cells, Blazejewski, Ho and Wang, Science 365 (6453), 595-598

Overlapping genes have been synthesized that enhance evolutionary stability and limit lateral dissemination in bacteria.

Total synthesis of *Escherichia coli* with a recoded genome, Fredens *et al.*, Nature 569 (7757), 514-518

*Escherichia coli* with a 61-codon synthetic genome that uses 59 codons to encode all of the canonical amino acids has been generated.

Human Artificial Chromosomes that Bypass Centromeric DNA, Logsdon *et al.*, Cell 178 (3), 624-639

An improved method to construct Human Artificial Chromosomes (HACs) is described.

Karyotype engineering by chromosome fusion leads to reproductive isolation in yeast, Luo *et al.*, Nature 560 (7718), 392-396

Creation of single chromosome yeast is presented. This demonstrates the feasibility of chromosomal engineering.

Creating a functional single-chromosome yeast, Shao *et al.*, Nature 560 (7718), 331-335

Work similar to Luo *et al.*; another demonstration of practicability of chromosomal engineering.

Programmed chromosome fission and fusion enable precise large-scale genome rearrangement and assembly, Wang *et al.*, Science 365 (6456), 922-929

Technologies to split, reorganize, and combine bacterial chromosomes to facilitate highly programmable genome engineering are explored.

### **Minimal and synthetic cells and viruses**

Evolution of a designed protein assembly encapsulating its own RNA genome, Butterfield *et al.*, Nature 552 (7685), 415-420

The paper presents the development of synthetic nucleocapsids that can package their own RNA genome. This is an example of *de novo* design of virus-like structures.

### **Ecosystem engineering**

Small-Molecule Agonists of *Ae. aegypti* Neuropeptide Y Receptor Block Mosquito Biting, Duvall *et al.*, Cell 176 (4), 687-701

Although not utilizing synthetic biology, the paper demonstrates how small-molecule compounds can be used to control disease vectors through altering their behavior.

Super-Mendelian inheritance mediated by CRISPR–Cas9 in the female mouse germline, Grunwald *et al.*, Nature 566 (7742), 105-109

A gene drive system in mammals is described.

Transgenic *Metarhizium* rapidly kills mosquitoes in a malaria-endemic region of Burkina Faso, Lovett *et al.*, Science 364 (6443), 894-897

Transgenically expressing an insect-specific neurotoxin in an insect-pathogenic fungus increases its efficacy against malaria vectors.

Incompatible and sterile insect techniques combined eliminate mosquitoes, Zheng *et al.*, Nature 572 (7767), 56-61

This study demonstrates that mosquito population can be eliminated through inundative mass release of incompatible *Wolbachia*-infected males, which were also irradiated to sterilize any accidentally-released females.

### **Techniques**

*In vivo* CRISPR editing with no detectable genome-wide off-target mutations, Akcakaya *et al.*, Nature 561 (7723), 416-419

A highly sensitive strategy that can robustly identify the genome-wide off-target effects of CRISPR–Cas nucleases *in vivo* is described. The paper shows that appropriately designed guide RNAs can direct efficient *in vivo* editing with no detectable off-target mutations.

VEGAS as a Platform for Facile Directed Evolution in Mammalian Cells, English *et al.*, Cell 178 (3), 748-761  
A system for directed evolution in mammalian cells is presented.

Scalable, Continuous Evolution of Genes at Mutation Rates above Genomic Error Thresholds, Ravikumar *et al.*, Cell 175 (7), 1946-1957

A system for scalable, continuous evolution of user-defined genes *in vivo* is described that allows routine, high-throughput evolution of biomolecular and cellular function to be carried out.

Controlling orthogonal ribosome subunit interactions enables evolution of new function, Schmieid *et al.*, Nature 564 (7736), 444-651

An ingenious *in vivo* system that can be used to evolve proteins with new functions, incl. containing non-natural amino acids is described.

Predictable and precise template-free CRISPR editing of pathogenic variants, Shen *et al.*, Nature 563 (7733), 646-651

The paper presents an approach for precise, template-free genome editing.

RNA-guided DNA insertion with CRISPR-associated transposases, Strecker *et al.*, Science 365 (6448), 48-53  
RNA-guided CRISPR-associated transposase is reprogrammed to achieve efficient and specific DNA insertion into the E. coli genome.

Time-resolved protein activation by proximal decaging in living systems, Wang *et al.*, Nature 569 (7757), 509-513

A general strategy for in vivo protein activation using light-controlled proximal decaging is presented.

Unbiased detection of CRISPR off-targets in vivo using DISCOVER-Seq, Yoshika *et al.*, Science 364 (6437), 286-289

Technique for unbiased identification of off-target sites by CRISPR-Cas nucleases is presented.

## Others

A Synthetic Bacterial Cell-Cell Adhesion Toolbox for Programming Multicellular Morphologies and Patterns, Glass and Riedel-Kruse, Cell 174 (3), 649-658

Genetically encoded synthetic platform for modular cell-cell adhesion in Escherichia coli is reported, which provides control over multicellular self-assembly and allows for quantitative rational design of well-defined morphologies and patterns.

Transposon-encoded CRISPR-Cas systems direct RNA-guided DNA integration, Klompe *et al.*, Nature 571 (7764), 219-225

A programmable transposase integrates donor DNA at user-defined genomic target sites with high fidelity.

De novo protein design by citizen scientists, Koepnick *et al.*, Nature 570 (7761), 390-394

Proteins were designed *de novo* by players of the online protein-folding game Foldit, incl. a protein with entirely new fold.

Mammalian Near-Infrared Image Vision through Injectable and Self-Powered Retinal Nanoantennae, Ma *et al.*, Cell 177 (2), 243-255

Injectable photoreceptor-binding nanoparticles allow mice to develop infrared vision without compromising their normal vision and associated behavioral responses.

Designer membraneless organelles enable codon reassignment of selected mRNAs in eukaryotes, Reinkemeier, Estrada Girona and Lemke, Science 363 (6434), eaat2644

The article presents the design of an artificial, membraneless organelle into mammalian cells to perform orthogonal translation.

Rewritable multi-event analog recording in bacterial and mammalian cells, Tang and Liu, Science 360 (6385), eaap8992

The paper describes a system that allows recording of multiple cellular events in the genome.

Diverse and robust molecular algorithms using reprogrammable DNA self-assembly, Woods *et al.*, Nature 567 (7748), 366-372

A set of 355 self-assembling DNA 'tiles' is presented that can be reprogrammed to implement many different computer algorithms.