ACS SyntheticBiology

In This Issue

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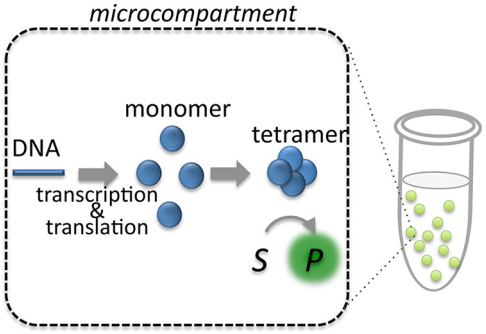
COMPARTMENT SIZE AND MULTIMERIC PROTEIN SYNTHESIS

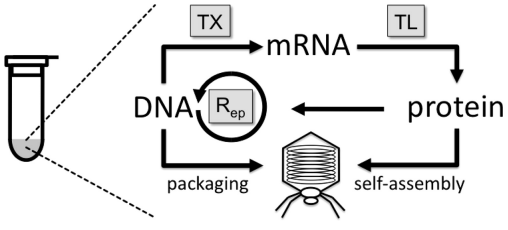
All chemical reactions in the cell take place inside a compartment, whose volume is typically in the range of a micro- to femtoliter. While the volume of the compartment is a fundamental physical parameter in such reactions and can affect intracompartmental reaction kinetics, there have been few studies to elucidate the effects of changes in volume. Here, Matsuura et al. (DOI: 10.1021/sb300041z) investigate how changes in compartment volume regulate the cascade reaction of transcription, translation, and tetramer assembly.



Using prepared artificial cell-like compartments with different volumes, but identical constituents, the authors show that compartment volume alone can have a measurable effect on multimeric protein synthesis. Additionally, the kinetic mechanism underlying the volume dependency is also identified.

TEST TUBE SYNTHESIS OF THE BACTERIOPHAGE T7

The bottom-up synthesis of living systems in the laboratory is a standing challenge to biology, chemistry, and physics. Although many experimental approaches to synthesize complex biological systems *in vitro* have been proposed, there has been no demonstration to date of natural genome-sized DNA programs being entirely replicated and expressed *in vitro* into a self-assembled functioning whole. Here, Shin et al. (DOI: 10.1021/sb300049p) show, for the first time, that a viable biological entity, the bacteriophage T7, can be entirely synthesized in a single test tube reaction from the expression of its DNA genome.

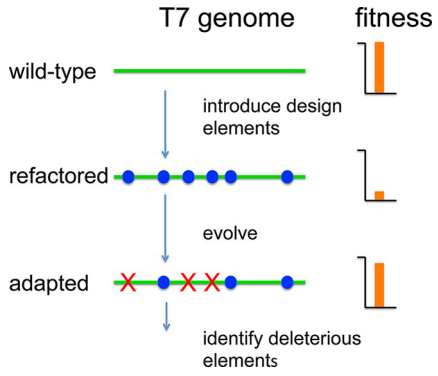


Using a transcription-translation cell-free reaction, the authors demonstrate that the DNA genome is replicated concurrently with phage gene expression and self-assembly. Their work recapitulates the entire biological process from DNA replication, transcription, and translation to assembly, in a test tube.

The authors also show that the phage φX174 can be synthesized *in vitro* with the same system, indicating that this approach is not limited to the phage T7 alone.

EVOLUTIONARY STABILITY OF A REFACTORED PHAGE GENOME

When engineering a genetic system, only those genetic elements whose functional properties are entirely known are used. This enables elements from diverse genetic backgrounds to be put together to create new pathways and functions. While it is often assumed that the functional properties of the linker sequences used to tie these genetic elements together are insignificant, these sequences may sometimes have regulatory effects that diminish fitness.



Here, Springman et al. (DOI: 10.1021/sb300040v), using the refactored bacteriophage T7, suggest that experimental evolution along with alternative engineering can identify potential design issues and lead to improved genetic engineering.

UNSATURATED LIPIDOIDS FOR EFFICIENT INTRACELLULAR GENE DELIVERY

Intracellular gene delivery or gene therapy has long been viewed as a method of treatment for genetic disease. However, there is a lack of safe and efficient gene delivery vehicles. Here, Wang et al. (DOI: 10.1021/sb300023h) describe an efficient combinatorial strategy to synthesize a library of lipid-like materials, called lipidoids, that facilitate *in vitro* gene delivery.

Using EGFP encoding plasmid DNA and mRNA as model gene drugs for preliminary screening, the authors determined that unsaturated lipidoids were superior transfection agents compared to saturated lipidoids under the same conditions. They further demonstrate the potential application of these lipidoids for gene delivery and therapy by investigating their ability to transfect fibroblasts in addition to different cancer cell lines. This combinatorial strategy to construct nanoparticles for gene delivery has potential applications in the programming of

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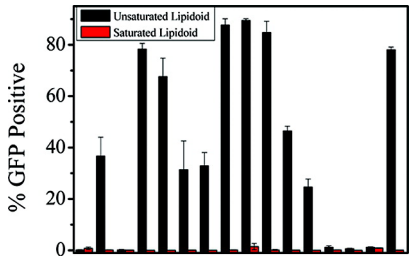
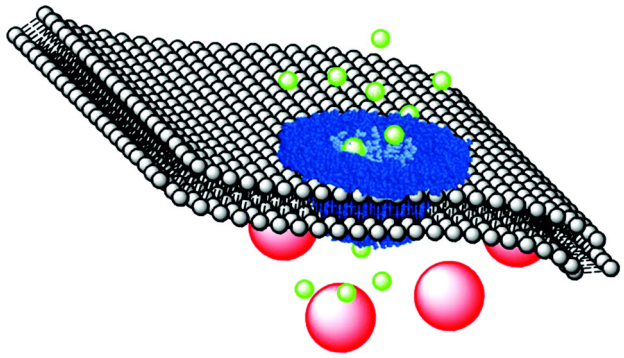


therapeutic cells and in medical applications, such as cancer vaccines and immunotherapies.

ENGINEERING FUNCTIONAL DNA TRANSLOCATION

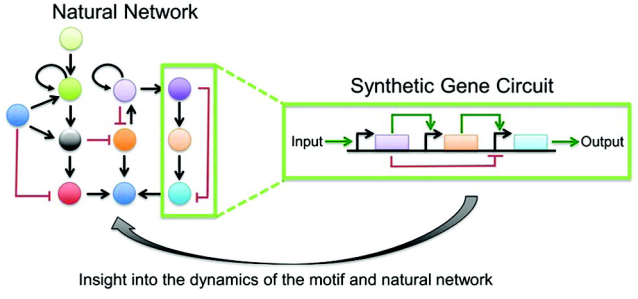
The "portal connector" of bacteriophage viruses is a pore-like structure that allows for DNA translocation. The high specificity of this connector along with its well-defined structure makes it attractive for use as a DNA-nanopore in synthetic tools. Previous studies have described the integration of the bacteriophage ϕ29 connector into lipid bilayers. Here, Moleiro et al. (DOI: 10.1021/sb3000063) propose a new reconstitution method based on the specific surface reactivity of the native viral connector protein with functional lipids.



The authors employ a synthetic route based on chemical modification of the lipid bilayer and devise an approach for optimal insertion of the ϕ29 connector in an orthogonal orientation. This method is potentially interesting for nanotechnological applications such as gene delivery requiring high integration rates with optimal orthogonal insertion.

SYNTHETIC BIOLOGY TO EXPLAIN CELLULAR INFORMATION PROCESSING

Appropriate responses to environmental signals are essential for the survival of all cells and organisms. These responses are regulated by cellular networks that process these environmental cues. Here, Riccione et al. (DOI: 10.1021/sb300044r) describe recent developments in synthetic biology that aim to understand cellular information processing.



In this Review, the authors provide a survey of recent efforts in using engineered gene circuits to examine dynamic properties commonly encountered in biological systems. These include different input/output responses, generation of nonlinear dynamics (bistability, adaptation, and oscillation), as well as the impact and modulation of cellular noise.

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