Engineering synthetic nanofactories

This group of projects is centered around cyanobacteria, a prodigiously productive photosynthetic organism formerly known as “blue-green algae.”

We seek to understand the fundamentals of how energy capture and conversion work in this single-cell organism and apply that knowledge to engineer improvements in productivity.

Our approach embodies an iterative process of *learn, design, build, text, and learn* in order to build a new body of knowledge incrementally towards synthetic biology solutions.

The challenge: Looking at Photosynthesis from an engineering perspective

We are addressing key questions in photosynthetic energy capture and storage from a unique perspective, using concepts borrowed from engineering, especially **modularity**.

Modules in engineering are semi-autonomous functional units or components that function strongly together in the context of larger systems. Some of the hallmark features of modularity include division of labor and the requirement for communication among modules in order for complex functions to emerge.

In biology, modules can be seen on multiple scales, including protein domains, genes and operons, molecular pathways, and molecular compartments.

Biological modules each usually have unique functions, but they cannot always be predicted by studying each individual module. Connections between modules can be physical (ex: protein domains or protein-protein interactions) or the connections can be metabolic (ex: metabolites or electron carriers).

Photosynthesis in cyanobacteria can be seen as a connection of functional modules. For example, the distinction between electron transport and carbon reactions is one such view.

We can also look at photosynthetic modules under finer subdivisions. For example, carbon reactions involve different types of modules, both structural and functional: the inorganic carbon uptake systems in the cell membrane, the carboxysome, and the remainder of the Calvin-Benson cycle.

The solution: Understanding natural modules and creating synthetic ones for application

We want to apply “modular thinking” across the biological continuum, from the protein domain to the concept of a cell as a module within a community in the environment.

Interestingly, biological modules have the potential for “plug and play” into new contexts, which makes them useful to understand both evolutionary processes and engineering principles.

Currently, we are emphasizing research on the features and interconnectivity of two modules in cyanobacteria:

* Light harvesting and the **carboxysome**
* The light-sensitive protein, the **Orange Carotenoid Protein (OCP)**.

Carboxysomes are the center of carbon fixation in cyanobacteria, and their importance to cyanobacteria’s photosynthetic efficiency is very high. But we still need to understand the carboxysome’s regulatory connections with other photosynthetic modules, including light reactions.

The OCP is a modular protein that controls photosynthetic efficiency by attaching to the phycobilisome. The OCP senses and responds to changes in light quality and intensity in order to protect the cell from damage.

Both modules are prominent components of photosynthesis and possess features useful for bioengineering applications.

The three projects here are aimed at fundamentally understanding the structure and function of these two modules, revealing how they communicate, and then using the knowledge to engineer and recombine modules to improve photosynthesis, create new renewable energy sources, or devise new compounds for medical or industrial uses.

* We want to understand the relationship between light perception and carbon fixation within cyanobacteria, focusing on the carboxysome (Ducat, Kerfeld, Montgomery, Sharkey).
* This project builds on the first by using that knowledge to design and construct new types of compartments and scaffolds for engineering purposes (Ducat, Kerfeld).
* We want to draw on our understanding of the OCP to repurpose it as a light-responsive protein that can be used to connect or activate engineered photosynthetic modules for specific applications (ex: Optogenetics).