How to build an artificial nano-factory to power our futures

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Marching to the future, one shell at a time. Credit: Mysticsartdesign, Public Domain

Many bacteria contain little factories for different purposes. They can make sugars from carbon dioxide to fuel life, or digest certain compounds that would be toxic for the cell, if the digestion took place outside of these factories.

Manuel Sommer is studying how the factories building sugar from carbon dioxide through photosynthesis, called carboxysomes, are built and work.

This is a step toward designing new kinds of factories, based on their natural cousins, that could produce synthetic materials, like fragrances, or the building blocks for green fuels or products used to diagnose diseases.

The thing is, bacteria are incredibly diverse, found in every environment, from polar ice to hot springs, and carboxysome-based structures can be just as diverse in what they can do.

Part of the problem in building synthetic carboxysomes has been identifying the essential building blocks. And, for the first time, Manuel and the Kerfeld lab have analyzed over 200 sets of genes from different cyanobacteria, also known as blue-green algae that contain carboxysomes, taking us closer to understanding these essentials.

The study is published in the *Journal of Experimental Botany*.

An inventory of miniature factories

Recent studies have made hundreds of new cyanobacteria genomes (a complete blueprint of organisms' DNA) available for study.

"Only five years ago, there were under 50 cyanobacterial genomes available. With the latest analysis we've done, we have over 350, with many species we haven't looked at yet," Manuel says.

Why cyanobacteria?

"Carboxysomes, which are found in cyanobacteria, specialize in photosynthesis. And there is so much research on cyanobacteria already, which makes them easy to study."

"This flood of information makes such carboxysomes a good target for producing a complete inventory of factory parts. Then we can devise strategies to re-engineer them into synthetic factories."

The idea is to use the synthetic carboxysome copies to create renewable materials, stuff they don't usually make (see below), inside of bacteria that have been tamed for biotech use.

The Grand Prismatic Spring of Yellowstone National Park showing steam rising from hot water, which is surrounded by huge mats of brilliant orange algae and bacteria. Credit: Brocken Inaglory (Own work) [CC BY-SA 3.0 or GFDL], via Wikimedia Commons

Building blocks, like legos

Carboxysomes are made of shells, each made up of about 7 different types of proteins that fit together like legos.

"The shells are both filters and barriers, controlling what raw materials come in and what finished product – like sugar precursors – comes out. The chemical reactions happen inside that protected shell. That is why understanding the shell structure is an important step towards building our own systems."

The first major finding was to discover two new variations on these shell proteins that had never been seen before.

"We're thinking that the whole reason why the carboxysome needs a handful of proteins in the first place is that it gives the organism a lot of flexibility to grow under different conditions."

For example, Manuel adds, some viruses need one protein for creating a shell encasing their damaging DNA, but cyanobacteria included in the study have 4 to 9 of these shell proteins.

"It is possible that each protein lets specific substances in. The more proteins available, the more the shell can fine tune what comes in and out."

Evolution of the factories: "Calling ground control"

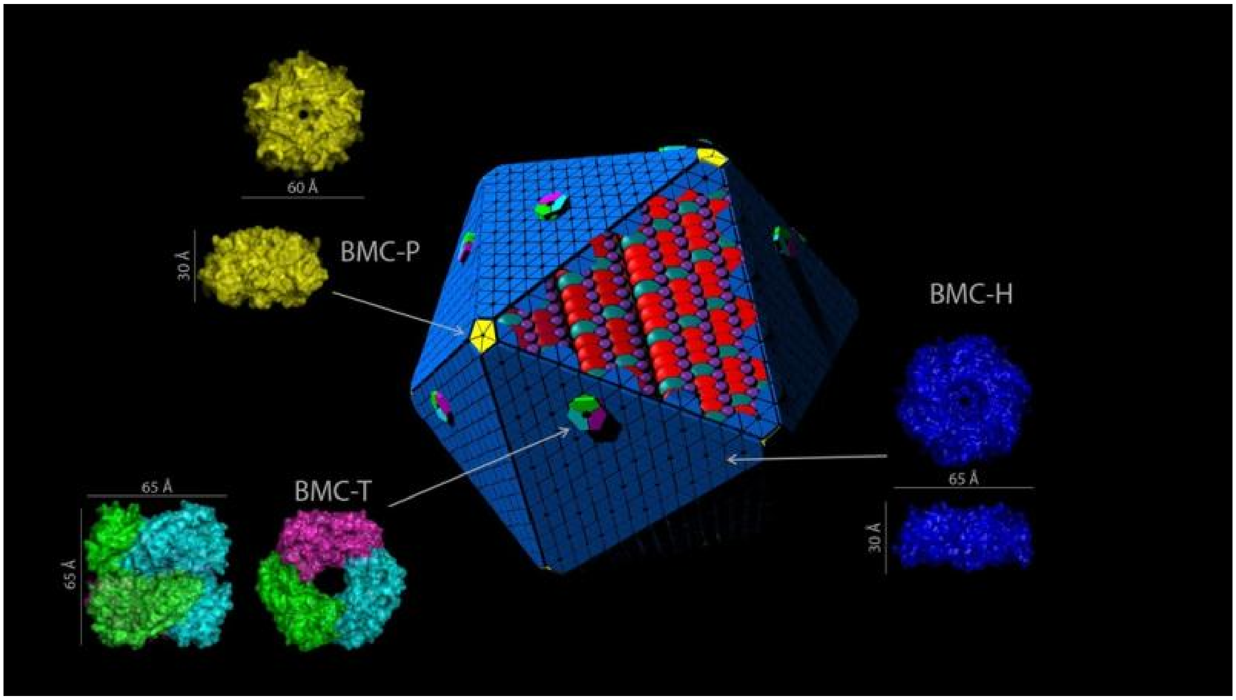
If DNA is like a book, genes are the words. And speaking the words aloud – or 'expressing' the gene – brings their meaning to life.

Manuel found that the genes for the carboxysome shell proteins were expressed differently, depending on how close or far they were located from each other.

"One type of carboxysome (alpha carboxysome) clusters all the genes in one location. The advantages are many. Being closer makes it easier to build the shell, or easier for the genetic code to transfer from one organism to the other, which is one way evolution happens. That probably explains why these types of compartments are found in evolutionarily diverse bacteria."

But while alpha carboxysomes have one control unit, the type of carboxysomes analyzed in the study (beta carboxysome) makes use of extra genes on other locations in the DNA.

"We think that makes those carboxysomes more sophisticated. As long as a gene is found in the main unit, it is expressed at the same time with its neighboring genes."



Different types of proteins, such as the three pictured here (BMC-T, BMC-P, and BMC-H), fit together like legos to build the shell structure, located in the center of the image. Credit: Seth Axen, Markus Sutter, Sarah Newnham, Clement Aussignargues, and Cheryl Kerfeld [Creative Commons Attribution-ShareAlike 4.0 International License], via Kerfeld lab

"But as soon as it moves to a satellite location, it becomes completely independent."

And, the thought goes, this diversity helps cyanobacteria navigate different environments.

"These types of cyanobacteria are quite sophisticated. Each has at least one satellite locus away from the main genes. It makes sense, since they live in dramatically different environments, like alpine lakes, hot springs, salt water, Antarctic waters. They are global citizens."

If light or water quality change, or if the current takes them to different environments, the satellite genes would provide backup or alternative options, without messing with the main shell genes.

"That is the whole reason we believe the evolutionary solution has been to disperse the genes so they are expressed separately, as needed."

Synthetic cousins that could do a lot

Tapping into that natural factory might unlock some amazing technology someday, Manuel says.

The Kerfeld lab wants to build artificial carboxysomes that can be custom fit with enzymes. That would allow them to create renewable materials that could eventually replace industrial products, such as petroleum for example.

Manuel suggests another angle: importing carboxysomes into crop plants.

"One of the biggest problems for crop plants is that they are very inefficient with how they process carbon dioxide to form organic molecules. The result is lower yield."

"Carboxysomes are much better at processing carbon dioxide because the process takes place inside an isolated shell, impermeable to undesirable molecules."

The potential is promising, but scientists have struggled to make cyanobacterial carboxysomes work in land plants.

Manuel thinks that, perhaps, tapping into the recently discovered wealth of the cyanobacteria genome will clear the way.

"Essentially, we're learning how cyanobacteria have survived and evolved over time. And that knowledge is getting us much closer to understanding the basic building blocks needed to build our own artificial nano-factories."

More information: Manuel Sommer et al. β-Carboxysome bioinformatics: identification and evolution of new bacterial microcompartment protein gene classes and core locus constraints, *Journal of Experimental Botany* (2017). DOI: 10.1093/jxb/erx115

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