50 Years of Cyanobacteria and Photosynthesis

Wim Vermaas

School of Life Sciences and Center for Bioenergy and Photosynthesis, Arizona State University, Tempe, AZ 85287-4501, wim@asu.edu

Cyanobacteria have been part of the biosphere for billions of years, and are thought to be a main contributor to the transition from an anoxic to an oxic atmosphere during the Great Oxidation Event that occurred over two billion years ago. They still are an important part of global photosynthetic productivity, particularly in the oceans.

Fast forward to about 50 years ago, when the idea arose to genetically modify photosynthetic organisms to learn more about them, with in the back of scientists' mind to perhaps improve agricultural production over time. The first study on transforming a cyanobacterium was published by Sergey Shestakov in Moscow in 1970. Around the same time the first plant transformations were performed by Rob Schilperoort in Leiden and other groups in Belgium and the US. It became clear that the genomes in some cyanobacteria and chloroplasts (derived from cyanobacteria long ago) could undergo double-homologous recombination, a process that allows for insertion of markers into genes, thus interrupting them, or for exact gene replacement. With this approach in the 1980s the donor to P680 in PSII was identified as a Tyr residue in the D1 protein, with the equivalent Tyr in D2 serving as Y_D. Similarly important residues and subunits were identified in the photosystems of cyanobacteria and other photosynthetic bacteria. Guidance was provided by the crystal structure of the purple bacterial reaction center (earning Hartmut Michel, Johann Deisenhofer and Robert Huber a Nobel Prize), which was recognized to be homologous to PSII.

When the gene for the homodimeric heliobacterial reaction center was sequenced and analyzed, the idea arose of the two photosystems in plants and cyanobacteria to be homologous, with the PSI reaction center protein having been split in an antenna and reaction center component in PSII.

In the 1990s genomic sequencing of prokaryotic genomes became feasible, and the *Synechocystis* genome was sequenced by Satoshi Tabata and coworkers in Chiba (near Tokyo) even before that of *Escherichia coli*. This led to a flurry of activity to determine the function of open reading frames in the *Synechocystis* genome using double-homologous recombination knock-out and insertion strategies, and provided a way to understand not only the function of individual genes but also metabolic pathways, regulation of gene expression, and the role of photosynthesis in this all.

Now with the major functional components of the cyanobacterial "blueprint of a cell" known, it has become more feasible to start viewing the cyanobacterial cell as a chassis that can be modified to make products for human use. Indeed, strains producing and excreting biofuels (ethanol, fatty acid esters, alkanes) have been developed and grown at pilot plant scale; their productivity per acre far exceeds that of plants. However, fossil fuels are still too cheap for cyanobacterial biofuels to be fully price-competitive, and valuable co-products typically are needed to make the economics work. Phycocyanin is an example of a valuable co-product from cyanobacteria, and work has been ongoing to improve its thermostability in order to develop it as a natural food dye, replacing blue chemical dyes that have toxicity issues.

A 2022 Executive Order on the Bioeconomy from President Biden has invigorated the microbial biotechnology field. In the years and decades ahead, the use of cyanobacteria and other living systems for production of compounds currently made from fossil fuels or even by non-sustainable agriculture hopefully will become a lasting and sustainable part of the social fabric globally.