Any embarrassing moments? Yes. In my first year as an assistant professor I was asked to give a talk in a neighboring department. They had just moved to a new building and I was the first speaker in their new auditorium. As I started my talk, we discovered that the auditorium was so new there weren't any light switches. I couldn't turn off the lights, and my slides were invisible. All those hours spent preparing my talk were for naught, and instead I gave a chalk talk with a lot of fuzzy sketches!

Any good advice you can pass on to young scientists? As a graduate student I met Ira Herskowitz, and he said this: "as you think about your data, keep your foot on the ground. But only one foot!" That saying reminds me of the movie *Brazil* and the idea of being grounded, but also letting your ideas take flight. I also remember what a lonely time it was when I started my own lab. The silver lining was that I had a lot of time to myself to think about my science and to do experiments. So my third piece of advice, especially to struggling junior faculty, is to focus on the biology. If you do good science, everything else will work itself out.

What do you see as an issue for the sciences in future years? One area that I'm concerned about is the organization of our labs. The idea of a lab filled with graduate students and postdocs was born at a time when we wanted the sciences to expand rapidly. It was an effective way to train young scientists and to get work done at low cost. But today, we are at a steady state, and we don't need to generate hundreds of new labs. Instead we should consider how to balance the need for job opportunities and funding for students and postdocs with the need for a vibrant workforce in the lab. Some of those challenges we've met with better support for postdocs, different review processes for junior faculty at the NIH. Maybe we also need to train fewer students and postdocs and to increase the number of permanent positions in our labs. The problem is not solved yet and will probably require some creative thinking.

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Quick guides

Cyanobacteria

Robert Haselkorn

What's in a name? Before 1960, the organisms we know today as cyanobacteria were called blue-green algae. They were classified along with the green algae, the red algae, and the brown algae as photosynthetic microbes. It was universally agreed that all of these carried out green plant photosynthesis, fixing CO_2 and generating O_2 from water. But in the 1960s it became apparent, from new biochemical evidence, that the blue-green algae, unlike the other algae, are really bacteria: they are sensitive to penicillin because of their peptidoglycan cell walls; they have bacterial-sized ribosomes sensitive to the usual antibiotics; and they do not contain organelles such as chloroplasts and mitochondria. A major consequence of the name change was to remove this vast array of organisms from the realm of botany and to put them into the microbial world (Bergey's Manual). Figure 1 shows an electron micrograph of a section through a cyanobacterial cell, revealing the photosynthetic membranes and numerous ribosomes.

Are they really old? This is still an open question. There are certainly ancient rocks, say 1.5 billion years old, that contain tracks of connected objects which look as though they could be cell-wall ghosts of contemporary cyanobacteria. Unfortunately there is no chemical trace associated with these objects,

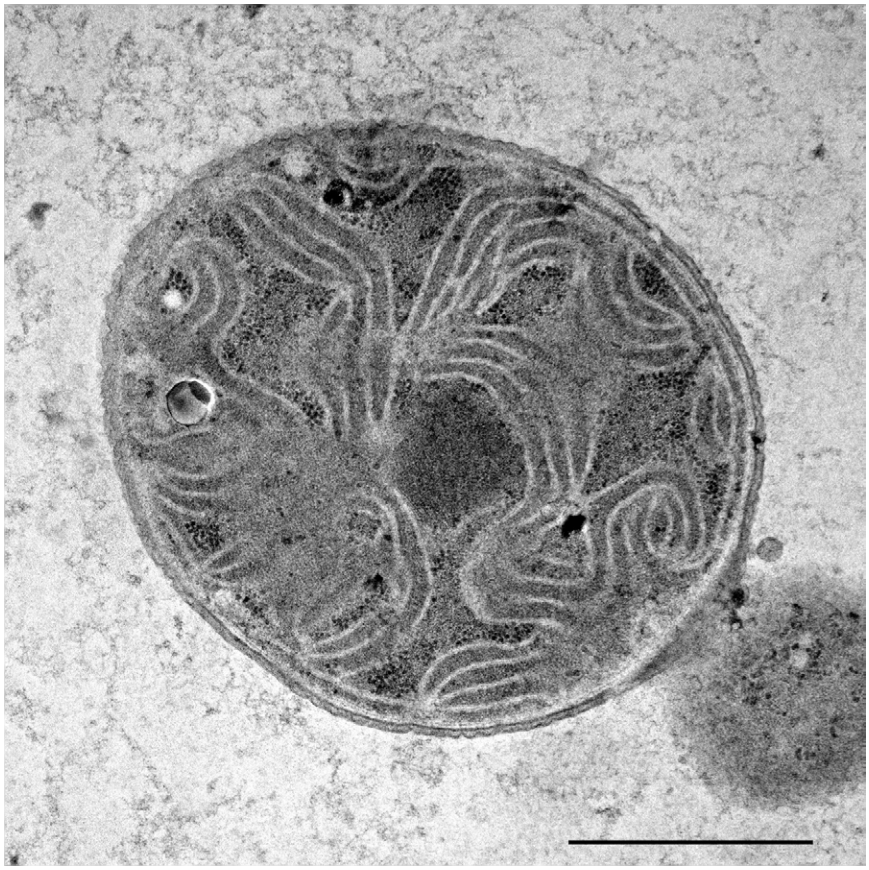

Figure 1. Electron micrograph of a section through *Anabaena*.

The sample was prepared by high-pressure freezing, freeze-substituted, stained and sectioned as described in: Plastoglobules are lipoprotein subcompartments of the chloroplast that are permanently coupled to thylakoid membranes and contain biosynthetic enzymes. Austin II, J.R., Frost, E., Vidi, P.A., Kessler, F., and Staehelin, L.A. (2006). Plant Cell *18*, 1693-1703. The bar represents 1 micron. (Figure courtesy of J.R. Austin and Z. Ye.)

so other than their appearance it is not possible to guess what they might have been. But if they really were cyanobacteria, then they could be credited with putting oxygen into the atmosphere and making aerobic life possible. And from modern genomic analysis, in particular the sequences of the proteins that make up the core of the photosynthetic apparatus, it is possible to conclude with some confidence that a cyanobacterium provided the ancestor of the chloroplast.

Did cyanobacteria really originate altruism? Well, yes, in a way. Many species of cyanobacteria grow in long filaments, containing hundreds of cells. Cells along the filaments communicate by way of slender cytoplasmic channels. Through these channels they can exchange nutrients, particularly in those species that are capable of fixing atmospheric nitrogen, reducing it to ammonia. Nitrogen fixation is found only in bacteria; many instances of higher organisms apparently able to fix (reduce) nitrogen are due to symbiotic bacteria or cyanobacteria that actually do the work. N_2, which comprises 80% of air, has a triple bond that is difficult to reduce. The enzyme nitrogenase transfers three pairs of electrons and protons successively to N_2, creating two molecules of ammonia. The ammonia is added immediately to glutamic acid to make glutamine, which provides its amide nitrogen for the synthesis of all the other amino acids and nucleotide components of DNA and RNA.

The reducing power generated from carbohydrates and funneled to nitrogenase flows through a system of enzymes that are extremely sensitive to oxygen. Any nitrogen-fixing system requires a way to sequester the enzymes and to keep them from oxygen. The filamentous cyanobacteria do this by differentiating specialized cells, called heterocysts, in which the oxygen-evolving photosystem is inactivated and all the reducing power from photosynthate is used to fix nitrogen. Here are the beginnings of society: the heterocysts provide fixed nitrogen for all the other cells in the filament, while the other cells continue to fix CO_2 and to provide carbohydrate (probably sucrose) to the heterocysts.

The photosynthesizing vegetative cells continue to divide. The heterocysts, originally spaced about every tenth cell along the filament, do not divide. As the vegetative cells divide, the space between two heterocysts doubles and eventually one cell in the middle differentiates into a new heterocyst, keeping the spacing of these cells more or less constant. The vegetative cells are immortal, in the sense that as long as there is light and CO_2 and fixed nitrogen from the heterocysts, they will continue to grow and divide. The heterocysts are terminally differentiated, however, and after six or seven generations of vegetative cells they will die. We don't know why. Among the approximately 7,000 genes that comprise the genome of the species just described, about 1,500 are expressed differentially to make a heterocyst. Whether any of these can be directly associated with aging remains to be seen.

What about the symbioses mentioned above? Many nitrogen-fixing symbioses have been studied for years, for example, the association of nitrogen-fixing bacteria called *Rhizobium* with the roots of legumes, and the more recently described association of nitrogen-fixing bacteria in the gut of termites, which allow the termites to survive eating only carbohydrate (wood). Cyanobacterial symbioses have been described for several groups of plants: cycads, which have filamentous cyanobacteria in their roots; hornworts, which have packets of nitrogen-fixing cyanobacteria on their leaves; and the floating fern *Azolla*, which has a filamentous cyanobacterium in packets embedded in their leaves. In the latter case, the symbiont differentiates a very high proportion of cells, reducing severely the number that can provide photosynthate. The host plant makes up for that. In turn, the symbiont fixes N_2 but it does not add the ammonia to glutamate. Instead, it secretes the ammonia, which is taken up by cells of the surrounding host and incorporated into glutamine in those cells.

Cyanobacteria can adapt to different light regimes? Indeed. All of them are rather good at catching rays: they have accessory pigments called phycobiliproteins that absorb energy throughout the visible spectrum and transfer the energy to chlorophyll in the reaction centers. But some species go further: they adjust the amount of specific pigments according to the light being experienced. The results are dramatic: cells grown in red light become green, while cells grown in green light become red. These color changes are controlled at the level of transcription of genes encoding the respective pigment proteins, the transcription regulated by (of course) another pigmented protein.

Don't cyanobacteria make some nasty toxins? Yes they do — many. The most interesting are cyclic peptides containing seven amino acids or amino acid-like constituents. They are called microcystins because the first ones were found in *Microcystis*, but many species make them. They are synthesized by very large enzyme complexes, non-ribosomally. The complexes bind each of the seven units using seven different domains, each of which activates the amino acid with ATP and attaches it using thioester chemistry. The bound element is modified — racemization, methylation and hydroxylation — and then all seven are joined by peptide bonds. The finished product is a powerful toxin for metazoa, binding tightly to protein phosphatases. In a mouse, inhibition of protein phosphatase in cells of the microcirculation prevent dephosphorylation of the subunit of intermediate filaments, leading to collapse of those cells and leakiness of the blood vessels. The mouse dies quickly. The same toxins can kill fish, insect larvae, and corals.

Where can I find out more?

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