

**PROFESSOR:** If you're a teacher and you're inventing a course for the first time, or revising it a lot, you sit down with your teaching partners and you put on the table all the ideas. Teaching, you've got an ever-expanding universe of knowledge out there, and you have to cherry-pick the things that are going to be important. It has to hang together.

One of the strategies JoAnne and I thought, when we went into the current iteration of teaching 5.07 biological chemistry, was to abandon completely, higher eukaryotes, namely us, because genome sequencing projects had sequenced so many bacteria that one could create an entire course in biochemistry that would be very meaningful, just focusing on microorganisms.

We spent a couple of days reading and thinking about it. That would be the course JoAnne and I would teach, if it weren't for the fact that we actually have-- feel as though we have a commitment to students that are going to go on to medical school and therefore, if we avoided mammalian biochemistry, students wouldn't know anything about the mitochondria and organelles, and things like that that are associated with eukaryotes. We wouldn't be able to make these connections to disease, the physiological scenarios.

Nevertheless, why were we so interested in bacteria? What would be an interesting story, that I might be able to tell you, if we had taken that path. So we have a fellow in biological engineering, named Eric Alm. And he is an informaticist and an engineer, and an extremely good chemist. He really knows his pathways. When he looks at a cell, he thinks about what it is, but also where it came from, in terms of how it evolved from precursors, its family tree, so to speak.

One of the most interesting organisms that he's published on, not too long ago, is an organism called, *Desulforudis*. And this would be a wonderful biochemistry course in itself. He wondered, if he went out and dug up a cubic meter of dirt-- and outside MIT-- and if he did 16S RNA sequencing, how many living things would be there, many thousands, maybe 10,000.

Then he asked the question, what if you went down 100 meters, you know, maybe you see 1,000. But what if you go down until there's really only one thing there. And that's what he did, going down two miles into the ground. And there was a single, species ecosystem called, *Desulforudis*.

And I remember seeing this paper, and I brought it over to JoAnne. I was so excited because the last picture showed its metabolic network, its metabolic pathways. It had everything. And it makes sense. It can't rely on other things.

For example, we can't make all of our amino acids. We got to get them from food that we eat, or in our co-factors, some of our vitamins are made by the bacteria in our gut. So, if all the bacteria disappear, we would too.

So we rely on other things, but *Desulforudis* doesn't rely on anything. So when you look at its biochemical networks, what you see is that it can fix nitrogen. It can take  $N_2$  and convert it  $NH_3$ , and then put that into amino acids, and it can make all of its amino acids. It has a really good pentose phosphate pathway.

It actually uses radiation in a strange way to generate some of the energy that it needs. It uses it to generate carbon monoxide. Ultimately, that CO is going to form an acetyl group that will be able to generate all of the organic material inside the *Desulforudis*.

It's got all kinds of electron transport pathways. So it's developed enormous versatility by being a single-species ecosystem. So, again, this was a course where we had to make a compromise because of our clientele. Teachers have to think about that. We have to teach to what the people need in order to go on to the next step.

But as sort of a closing thought, I think that it would be wonderful for next-generation biochemists to really turn their attention to the microbial world, to teach this vast biochemistry and understand how bacteria effortlessly, swap biochemical pathways, pick-up entire biochemical pathways without even breaking a sweat. Whenever they find themselves stressed, they just pick up a new pathway and they survive.