Podcast Interview: Bernhard Palsson

PNAS: I'm your host Ann Griswold, and welcome back to Science Sessions. Photosynthetic bacteria have attracted considerable attention for their potential to provide sources of renewable energy. But researchers must first unravel the organisms' complex metabolic maps before the bacteria can be used to create new types of industrial materials. In a 2012 paper, Bernhard Palsson collaborated with a team of researchers to produce one of the most comprehensive metabolic reconstructions of a photosynthetic organism to date. Palsson recently explained to PNAS how the work has helped researchers design bacterial cell factories capable of producing economical and sustainable materials.

Palsson: These reconstructions in general are a critical part of systems biology, and bottom-up systems biology, that were enabled by whole-genome sequencing in the late 90s.

PNAS: Palsson and his team dug through the annotated genome of the organism *Synechocystis* and fished out each metabolism-related gene, eventually reconstructing an entire metabolic map along with a network model to illustrate how nutrients flow into the bacterium and eventually exit the cell as metabolic byproducts.

Palsson: We had inputs and outputs into this network and we could formulate very elementary flux balance models that balance the flux throughout the network. And these are called genome-scale models, or GEMs, because they're so valuable. And what they really represent is a mechanistic genotype-phenotype relationship. So for the first time in the history of life sciences, we have this fundamental relationship that can be put into a quantitative form.

PNAS: Palsson has spent the last 10 years using these relationships to reconstruct the phenotypic traits of various bacteria. The result could potentially change how bacteria are used in industry.

Palsson: We now have true genome-scale science for microbial metabolism and we can calculate these things. We can have in silico cells that compute the properties of real cells. Not all, but many.

PNAS: While most models have been built for single organisms, researchers are focused on building metabolic models for microbial communities containing several different types of bacteria. Such models could provide the chemical industry with sustainably produced versions of the standard compounds that make up many of the products we use today.

Palsson: Ten percent of the oil that comes out of the ground goes into chemical synthesis. It’s the main feedstock for the entire chemical industry. The chemical industry today is about a $3 trillion industry a year, with a “T,” in a world that has a GDP, global GDP, of about $60 trillion. So this industry is literally 5% of the world’s
GDP. But it is now clear that most of that industry can probably be replaced using biomass foodstock in an economically feasible manner. So we can get sugars, cellulosic biomass, or potentially one carbon sources, feed them to metabolically engineered microbial cells, and they will make a product for you.

**PNAS:** Palsson founded a company called Genomatica in 2000 to do just that. And in 2013, their first engineered product—1,4, butane-diol, or BDO, is expected to hit the market.

**Palsson:** Most people are familiar with Spandex, for instance, that’s a popular polymer that has BDO in it. I understand that a large fraction of the plastics found in a car right now come from BDO. So there are many, many products that are derived from BDO. Many polymers with many applications.

**PNAS:** The difference is that Palsson’s version of BDO is entirely engineered.

**Palsson:** That is not a natural metabolite, so you have to make synthetic enzymes in a synthetic pathway, place it in *E. coli*, engineer *E. coli* so it becomes what’s called a microbial cell factory, and you can make this compound, BDO. And there will be many more. And the interesting thing about this is unlike biofuels, this is both economically feasible and also in terms of feedstock size and demand for biomass, it’s also feasible. So using these genome-scale models of metabolism to design, engineer, and build microbial cell factories becoming real, and it is expected that over the next 10, 15, 20 years that this technology, this approach, will have a big impact on the chemical industry.

**PNAS:** Thanks for listening. You can find more Science Sessions podcasts at PNAS.org.