Abstractions

SENIOR AUTHOR

In 2002, Roger Brent, director and president of the Molecular Sciences Institute in Berkeley, California, secured a US$15.5-million grant to define every chemical reaction in yeast's biochemical pathways. The paper published online this week (doi:10.1038/nature03998) presents the first results of this 'Alpha Project'. Brent took some time out to talk to *Nature* about his work.

Where does this finding fit in with the total goal of the Alpha Project?

In some sense, it's equivalent to an electrophysiology experiment in the 1930s. We're establishing baselines to how the gears in the cell work. This is kind of like the first electrode.

Isn't there some controversy about whether your approach, which measures small variations between similar cells, is useful or just a detection of 'noise'?

There has been a great deal of noise about noise in the scientific literature over the past five years or so. In this work, we're trying to distinguish between how one cell transmits more than another. It's important to make that distinction between pre-existing cell-to-cell variation and noise in the gear work.

How different is your approach to other methodologies in systems biology?

I only use the term 'systems biology' with great reluctance. I dislike the phrase because the waters are very muddy. You don't just pile up an inventory of things and the waters became clear. But the Alpha Project, at the end of the day, is looking at a system.

How difficult was it to establish the multidisciplinary environment for this work?

The country is being run by biologists. The biologists outnumber the immigrants (mathematicians, computer scientists, chemists and physicists). The immigrants will enrich us. We will all be better for it. The biologists can't be xenophobes; the biologists can't ghettoize. The lingua franca is English. On good days there aren't riots.

You teach an undergraduate course, aimed primarily at non-scientists, called 'Genomics and citizenship'. What's its aim?

The course is about four things. Here's what you need to know about molecular biology; here's something you need to know about how you know that — how experiments are done; here's what you need to know about the structures of the places where this stuff plays out; and here are some ways you can think about these things. What we ideally want to do is teach people enough so that they can make informed political opinions, or so that they can ask the right questions. ■

MAKING THE PAPER

David Stahl

On the trail of nitrification among marine microorganisms.

The hunt for conclusive evidence that Archaea turn ammonia into nitrites took David Stahl's research team more than 11 years. The search began with water samples from Chicago's Shedd Aquarium, led to a New England estuary, then to the Seattle Aquarium, and concluded at the lab bench with a rigorous process of purification and characterization, before turning into a paper (see page 543).

Stahl had been interested in marine nitrification of ammonia for about 15 years and knew that bacteria account for a great deal, but not all of it. "We had the suspicion, as have others, that the key marine ammonia oxifiers had not been discovered," Stahl says.

Eleven years ago, when he was studying water samples from the Shedd Aquarium, he noticed that ammonia was being purged from the system. He couldn't find any sign of the usual bacteria that do this, but was unable to see what was doing the job.

Some seven years later, Stahl's group collaborated with John Waterbury at the Woods Hole Oceanographic Institute in Massachusetts to look at nitrification in the Plum Island Sound estuary. After Stahl examined the results that his postdoc, Anne Bernhard, had obtained from the field, he experienced deja vu. "It was the same observation as at Shedd," he says. "We weren't seeing the bacteria associated with nitrification."

Archaea became the number one suspects, but to confirm their guilt, Stahl needed to culture them and see them in action. But culturing Archaea is difficult: the microorganisms grow slowly, and bacterial by-products tend to linger for a long time, which makes getting a pure sample a challenge.

Stahl and his team decided to maximize their chances of success by taking samples from a setting where the population would be 'enriched' because of a high ammonia content. They went for the Seattle Aquarium. "With an aquarium full of fish poop, we thought our opportunities of isolating Archaea would be better than from a cold marine system," Stahl says.

David Stahl's postdoc Anne Bernhard hunts for Archaea samples at the Plum Island estuary.

Bernhard set up cultures using samples from the aquarium and, after many months, was finally able to get them to grow. She also developed a method to quantify the microorganisms and determined that the production of nitrite from ammonium coincided with the growth of the Archaea. But without a pure culture, she couldn't be certain.

But then a paper appeared in *Science* on a genomics screen of the Sargasso Sea ecosystem. One paragraph in the article noted that a gene in Archaea was similar to one in bacteria that are known nitrifiers. "That was when we started to worry that the cat was out of the bag," Stahl says. But rather than publish quickly, Stahl decided to continue until the Archaea culture was virtually pure.

Stahl expects to face more competition as his research continues. Other groups are looking at nitrification in soil Archaea and he expects that some are also looking at those in fresh water. Stahl says that he is keen to learn which genes are responsible for nitrification in the Archaea, and wonders if different genes are responsible in different kinds. But he hopes that finding out doesn't take as long as pinpointing the process to Archaea in the first place. ■

QUANTIFIED **JAPAN**

A numerical perspective on *Nature* authors.

So far this year, only the United States has submitted more papers to *Nature* than Japan. A good publication record can be important when trying to secure funding in Japan, says Jun Yamamoto of Kyoto University, whose recent work on a new liquid-crystal phase is described on page 525. But a strong and interesting research programme is also important, he adds.

Ichiro Terasaki of Waseda University agrees. In addition, he says, it is a good thing to allow individuals freedom to perform experiments, follow their own leads and direct their own research agendas. This policy led Fumiaki Sawano, one of Terasaki's co-authors and an undergraduate at the time, to discover an organic material that can intrinsically act as a d.c. to a.c. current converter (see page 522).

786 submissions have been made to *Nature* from Japan this year (which represents 7.9% of total submissions).

201 authors of papers published in *Nature* so far this year are working in Japan (total number of published authors = 4,155).

5 is the median number of authors per paper for published papers submitted from Japan.

21 authors working in Japan present research in this week's issue of *Nature*.