

Essentials of Life

In the course of evolution, cells have acquired a lot of redundancy. Many processes are probably more complicated than they need to be. **Petra Schulle** from the **Max Planck Institute of Biochemistry** in Martinsried wants to find out what constitutes the bare essentials of a cell. By concentrating on what's important, the biophysicist also manages to reconcile her career and family life.

TEXT **CATARINA PIETSCHMANN**

Petra Schulle's small corner office is crammed with books and scientific journals. There are no personal items on the desk – nothing to distract from the research. Two large photos in the vestibule are the only concessions to personal interests. They show the picturesque Elbe Sandstone Mountains shrouded in autumn mist – a reminder of Dresden, and of hikes in the area. As a climbing enthusiast, that is what she misses the most. Although the Alps are visible from her new workplace, she has yet to find the time to go mountain climbing. Petra Schulle has only been working as a scientist at the Max Planck Institute of Biochemistry on the Martinsried campus on the southern outskirts of Munich since the summer of 2012.

Those who don't know her might easily mistake this small, slender woman – dressed in jeans, T-shirt and a striped blouse – for one of her students. She wears no adornments, save for her

warm, friendly smile. Petra Schulle speaks fast and succinctly, as if she had no time to spare. And yet she has achieved much already. She wrote her Ph.D. under a Nobel laureate, became a professor at 34, then had three daughters and received several prestigious scientific awards, including the Gottfried Wilhelm Leibniz Prize of the German Research Foundation (DFG) in 2010. She is now Director of the Cellular and Molecular Biophysics Department at the Max Planck Institute in Martinsried.

A TOOLKIT FOR CUSTOMIZING CELLS

Petra Schulle is working on an ambitious project: she wants to develop synthetic cells. More precisely, a toolkit for customizing cells for any conceivable purpose. If she succeeds, it will mark a milestone in cellular biology, in biotechnology and maybe even in medicine. But she still has a long way to go.

So where did she get this idea, with her background in physics? And how did she become a physicist in the first place?

It was definitely not something she dreamed of while growing up; more an act of rebellion. Born in Sindelfingen, Petra Schulle grew up near Stuttgart, and later, Heilbronn. Though she liked animals as a young girl, biology held little interest for her at school. "I accepted and learned scientific relationships, but I never challenged them," she says.

Instead, she specialized in physics and mathematics. They were "easy subjects" in which she got good grades. A career in chemistry was out of the question. "That was unthinkable, since my dad was an industrial chemist." This left physics, the only subject her father struggled with. Daddy's girl? "Definitely," she says. "Basically, I wanted to prove myself to him."

Nevertheless, at Stuttgart University, she soon started to doubt her choice of physics. She was used to getting top



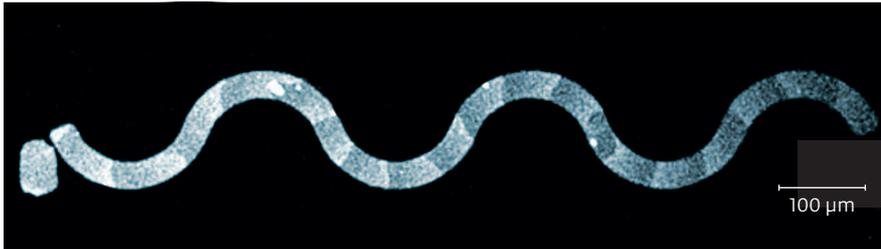
KINONVYKID

LA SPORTIVA

LA SPORTIVA

Aiming high, in her research and elsewhere: Petra Schwille is a passionate climber. Since she started to work in Martinsried, she has had no time for Alpine excursions. Instead, she practices on the climbing wall.

»» The physics lectures had quickly become dry and tedious, but Immanuel Kant fascinated her from beginning to end.



Min proteins play an important role in the cell division of *Escherichia coli*. They oscillate inside the cell and tell the bacterium where its center is, and thus where it should divide. Similar dynamic patterns can be created on synthetic membranes. Using different membrane shapes – in this case, waves – the scientists investigate the effect of the geometry on the oscillations (above) and compare their observations with theoretical models (below).

grades, but failed to stand out at her university, where “some people just juggled with complicated integrals in their heads.”

Not her. It looked like she wasn’t destined to become the great theoretical physicist (nothing less would be acceptable) she had hoped to, after all.

The career advisor in Göttingen told her about the Max Planck Institute for Biophysical Chemistry, where a certain Dr. Eigen worked – Manfred Eigen, the first German of the post-World War II generation of scientists to receive the Nobel Prize for Chemistry. Throughout her childhood, her dad had raved about this man. So, she transferred to Göttingen.

THE PLAN: A PH.D. IN PHILOSOPHY OF SCIENCE

Here she met a student of protestant theology who would play a pivotal role in her life. “I cared little about religion, but we discussed philosophy at great length.” They became an item and Pe-

tra Schulle started attending lectures on “The Critique of Pure Reason” in the philosophy department’s auditorium. The physics lectures had quickly become dry and tedious, but Immanuel Kant fascinated her from beginning to end. Spellbound, she listened and then scrutinized what she had learned. “I found it genuinely interesting.”

She was writing her thesis at the Institute of Medical Physics, and in the afternoons, she’d cross the street to attend philosophy lectures. She even planned to do a Ph.D. in philosophy of science. In the end, her plans were thwarted by a lack of vacancies in the field.

Instead, there was her father’s hero, Manfred Eigen, soon to retire. She wanted to study evolutionary theory under him, but Eigen suggested something different: fluorescence correlation spectroscopy (FCS), a highly sensitive optical method for investigating the dynamics of molecules. The method consists of labeling the molecules with a fluorescent dye, which is then heavily diluted. A focused laser beam is

used to excite the dye, which starts to glow. This allows sensitive photon-counting instruments to record the movements of the tiny dye dots.

Manfred Eigen’s laboratory was strongly involved in the development and application of this method. Petra Schulle expanded it by studying the reactions between two types of molecules using two different dyes.

In 1997, half a year after she received her doctorate, Petra Schulle went to work at Cornell University in the US, under Watt W. Webb, in the very laboratory where the original form of FCS had been invented.

LEADING HER OWN TEAM, A PERSONAL GOAL

This is also the lab that developed two-photon excitation. Firing two low-energy photons at a molecule in quick succession will excite it as much as a single photon with twice the energy. This can be used to circumvent problems in the observation of cells. Petra Schulle combined the method with FCS.

She was finally lured back to Germany by the Federal Research Ministry’s call for applications for “BioFuture,” because this program would allow her to establish her own research group in Germany. “It was a dream of mine,” she says. In 1999, Petra Schulle returned to the Max Planck Institute of Biophysical Chemistry in Göttingen as the head of a junior research group. “I was able to move into Manfred Eigen’s old laboratory premises, equipment included.”

Things went well in Göttingen – so well that she applied to become a professor at Dresden University of Technology (TUD) soon after. She had never experienced the GDR, but shortly after the wall had come down, Petra Schulle had spent a week in Dresden with her mother and grandmother. The city had fascinated her. “When I got the call from that university, there was no doubt in my mind.”

That was in 2002, thirteen years after reunification. The Frauenkirche was just being rebuilt, and one could still find bomb-damaged sites between beautifully renovated old buildings. The university's biomedical campus, however, was brand new.

The former theology student – her husband since 2002 – was working as a pastor in Göttingen. They commuted back and forth for two years, until he finally moved to Dresden. Petra Schwille's research was just getting going again when the couple had their first child. Dresden was the ideal place for it, with adequate daycare centers and nannies.

One thing came as a complete surprise to the scientist. "It's well known that your brain changes radically in puberty, but no one tells you that the same thing happens when you're pregnant. The boost in hormones tries to program you for motherhood and staying at home. The brain probably doesn't relax again until the kids finally move away from home. "But particularly in the early years, biology is simply working against us. The choice is to conform or do it your own way." Petra Schwille chose the latter: she found a dedicated nanny for her daughter and went back to the institute eight weeks after giving birth.

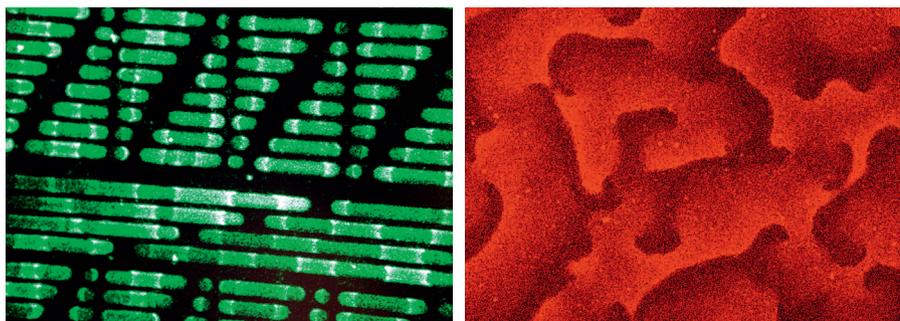
In the end, she had two more children. She laughs. "Once your brain has changed, you might as well go on with it." However, she didn't experience any professional drawbacks. "Of course, there were sleepless nights, but apart from that, there was no downside."

Combining motherhood with a career – few female scientists can pull it off. Many have children as students and postdocs, and often the biological trap snaps shut, so mom gives up her



Team meeting: Petra Schwille discusses the design of a new measuring chamber for model membranes with Ph.D. student Grzegorz Chwastek and postdoc Ariadna Martos.

» Her first goal is to use individual cellular building blocks to build a structure that looks like a cell and can self-divide under controlled conditions.



Biomolecular clocks: Depending on the length of the test chambers – visible as rod-shaped structures – different oscillations are generated in the cell division proteins MinD and MinE (left). By isolating Min proteins from bacteria, the scientists can study their behavior in the lab. For example, wave-shaped patterns can be generated on flat membranes (right).

career to care for the children. Others concentrate on their research and choose to postpone starting a family, but that doesn't always work out.

CAREER AT LIGHTNING SPEED – AND THEN MOTHERHOOD

No doubt about it, Petra Schwille is an exception. She attained her professional goals at lightning speed and then had children. “I couldn't have done it any other way. At Cornell University, I spent 80 hours in the lab every week. I enjoyed it, and back then I didn't yet feel the need to start a family.” She encourages young women to do the same. She doesn't think that a strict quota for women in science is easy to implement. “Rather, we should look for young, talented women and create positions specifically for them. It may seem unfair to talented men, but we also have to compensate for biological unfairness.”

It wouldn't have been possible without a partner who didn't mind fitting

his career around hers. Petra Schwille's husband has had to make some sacrifices. He left his ecclesiastical office in Göttingen and started over in Dresden – in medical ethics. He isn't opposed to his wife's plans to create cells in the laboratory. “He's no dogmatist. Prenatal diagnosis and end-of-life care are ethically challenging issues. Whether we should be allowed to create life as such, on the other hand, is an academic discussion. You have to be deeply religious to take issue with that.”

After all, Petra Schwille isn't planning to create artificial human beings; she's simply looking to understand how life as such actually functions, in its most basic form. “The structure of the first synthetic cell will be much simpler than that of a bacterial cell.”

In 2010, Craig Venter claimed to have produced synthetic cells in his lab, but that is the subject of some debate, since what he really did was to reverse engineer the genetic makeup of a bacterium and transplant this to an empty bacterial cell envelope.

Petra Schwille is taking a different approach. Her first goal is to use individual cellular building blocks to build a structure that looks like a cell and can self-divide under controlled conditions. She aims to achieve this within five years. “Self-organization is the decisive principle that creates order. Hopefully it will allow us to use just a few different types of molecules.”

An example of self-organization is the cellular membrane and its ability to change shape. This double layer of lipid molecules forms structures that resemble soap bubbles. Simply shaking them can cause them to divide. However, random division isn't sufficient. A cell envelope has to divide exactly in half to produce two viable daughter cells. The scientist is thus looking for molecules that can be used to exactly regulate division.

COMPLICATED, ALTHOUGH THERE ARE SIMPLER SOLUTIONS

“Some of nature's solutions to problems are superb, but others seem very circuitous at first glance.” The uncontrolled splitting of membrane vesicles, for instance, is essentially very straightforward, but nature has come up with a complicated machinery for vesicle budding and fusion. “I'm astonished at the degree of complexity with which this is realized in the cell. There are certainly reasons for it, but is there really no easier way of doing it?” Her approach is different, Platonic: What would be the purest physically possible form of cell division?

We already know a few principles. The signal to divide is given by a molecular clock through a chemical reaction. Once this reaction has produced a suffi-



Petra Schuille has already received many awards for her work in the field of fluorescence spectroscopy, including the Gottfried Wilhelm Leibniz Prize from the German Research Foundation in 2010. This photo was taken at the award ceremony for the Brunswick Research Prize the following year.

cient amount of a certain substance and has distributed it in the cell, division starts. Schuille has already identified a suitable timing reaction for this purpose. “We now want to link it to the mechanical impulse for division.”

Millions of years of evolution have produced a lot of molecular “excess baggage.” Petra Schuille wants to eliminate it all and keep only the bare necessities.

She works like an engineer: Engineers don’t really want to know exactly how a bird flies. They understand the physical laws of flight and simply build something that can fly as well. “That’s probably the reason I didn’t become a biologist – biologists always want to describe what they see as precisely as possible. I don’t need to know every detail. I’m only interested in what is necessary and what isn’t.”

Some biologists are convinced that everything is important; that perhaps life formed in a primordial soup of countless different molecules and produced complex structures from the beginning. “I don’t think so. There are surely molecules or classes of molecules that are more important than others.”

THE CONTENT OF THE TEST TUBES POSES NO THREAT

The scientist has no fear that life in the test tubes will acquire a will of its own and manage to escape. “Cells are so complex because they have to be able to compete with other cells. Our synthetic cells won’t have any defense mechanisms. Such a defenseless organism will constitute no threat.”

Petra Schuille likes to concentrate on what is important, both in the cell and in her professional life, which is quite full: she is a member of the boards of advisors and trustees of eight renowned scientific journals. She is also a peer reviewer for the German Research Foundation (DFG) and sits on the board of several professional societies. In addition to her own research, she has to write reviews and attend conferences.

At the same time, she has a private life: her three daughters are now three, six and eight years old. She likes to play music and practice for future trips to the mountains on the climbing walls in Munich.

A career and family life – it is possible to have both, but only if you know what is really important. ◀