# Ben Engel

Ben Engel is an Assistant Professor at the Biozentrum of the University of Basel, Switzerland. He leads the Cell Architecture Lab (www.cellarchlab.com), which uses cryo-electron tomography to visualize molecular complexes inside native cells, providing new insights into how organelles are built.

*What is your lab working on currently?*

Cryo-ET remains my lab's central method. We investigate many types of cellular organization, from classical membrane-bound and cytoskeletal organelles to more recently discovered phase-separated condensates. We have a strong focus on organelles that perform photosynthesis. These include thylakoids, membrane-enclosed compartments that harvest the energy of sunlight, and pyrenoids, condensates of Rubisco that capture carbon dioxide to produce sugar. Recently, we started a project called "cryOcean", where we will explore the thylakoids and pyrenoids of diverse and globally-important marine algae.

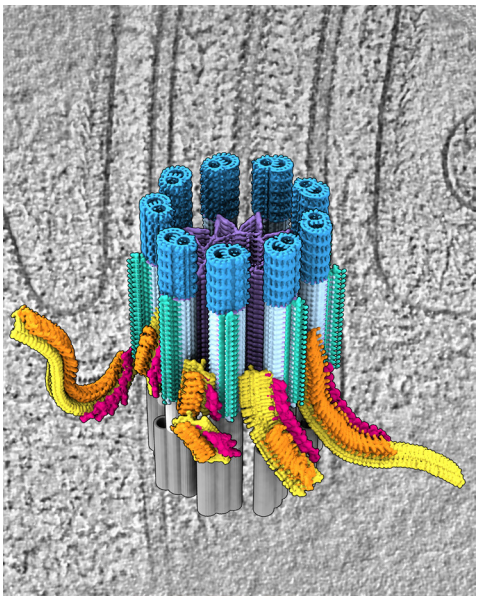
*What does a typical day look like for you?*

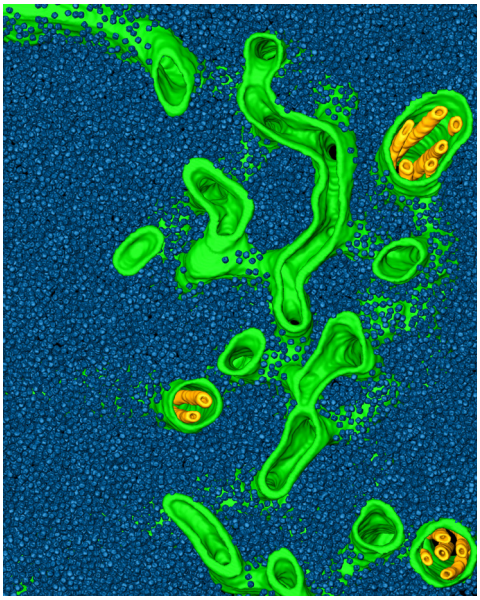
Every day brings new challenges and fun surprises. But one routine is how I start my day by getting my kids ready for school. Science can be really demanding, but I try to maintain some balance and spend as much time as I can with my family.

> "I love how every cryo-ET imaging session feels like a voyage into the unknown"

*Tell us about your background. How did you first become interested in cell architecture?*

I've always been a visual person, so it's fun to think about organelle shapes and the molecular organization inside cells. My PhD mentor at the University of California San Francisco, Wallace Marshall, remains a huge influence on my scientific thinking. He introduced me to the idea of how cells count, measure, and do geometry. I then moved to Munich and was very fortunate to work with Jürgen Plitzko and Wolfgang Baumeister, who pioneered the use of cryo-electron tomography (cryo-ET) to image the insides of frozen cells in three dimensions. Cryo-ET reveals native cell architecture at the resolution of single molecular complexes. The detail is absolutely stunning. Once I started to explore cells with cryo-ET, there was no turning back.





*Left:* Cryo-ET reveals a molecular train station inside algae cells. Intraflagellar transport trains (yellow/orange/red) assemble at the ciliary base (blue/aqua/purple) before driving into the cilium. Image credit: Hugo van den Hoek. From van den Hoek *et. al.* 2022, Science, DOI: 10.1126/science.abm6704.
*Right:* Molecular organization of the pyrenoid, a phase-separated compartment inside algal chloroplasts that enhances the efficiency of carbon fixation. $CO_2$ is generated by an enzyme in the central membranes (green/orange) and then fixed into sugar by the many Rubisco protein complexes (blue). Image credit: Ben Engel. From Freeman Rosenzweig *et. al.* 2017, Cell, DOI: 10.1016/j.cell.2017.08.008.

*What do you most enjoy about your work?*

I love how every cryo-ET imaging session feels like a voyage into the unknown. There is so much potential for new discoveries. It's a fairly regular occurrence that we point to an unexpected structure in a tomogram and exclaim: "what is that!?". I also really enjoy working with my team of postdocs and students. They're an incredibly talented and creative group, and also a lot of fun.

*What do you find most challenging?*

The field of "visual proteomics" is moving very quickly. This is super exciting, and I can't wait to see the new discoveries that will be enabled in the coming years by the combination of cryo-ET, mass spectrometry, and AI structure prediction. This also means that it is challenging (and fun) to keep up with the advancements in methodology. Fortunately, we have a fantastic group with complementary skills and two amazing senior scientists who push our methods forward: Wojciech Wietrzynski and Ricardo Righetto. It's so cool to see new ideas and approaches brewing in our team. Other than that, time management and work-life balance are also big challenges of course!

> "Follow your curiosity...There is so much out there to discover if you are willing to look in new places"

*What is your lab hoping to work on in the future?*

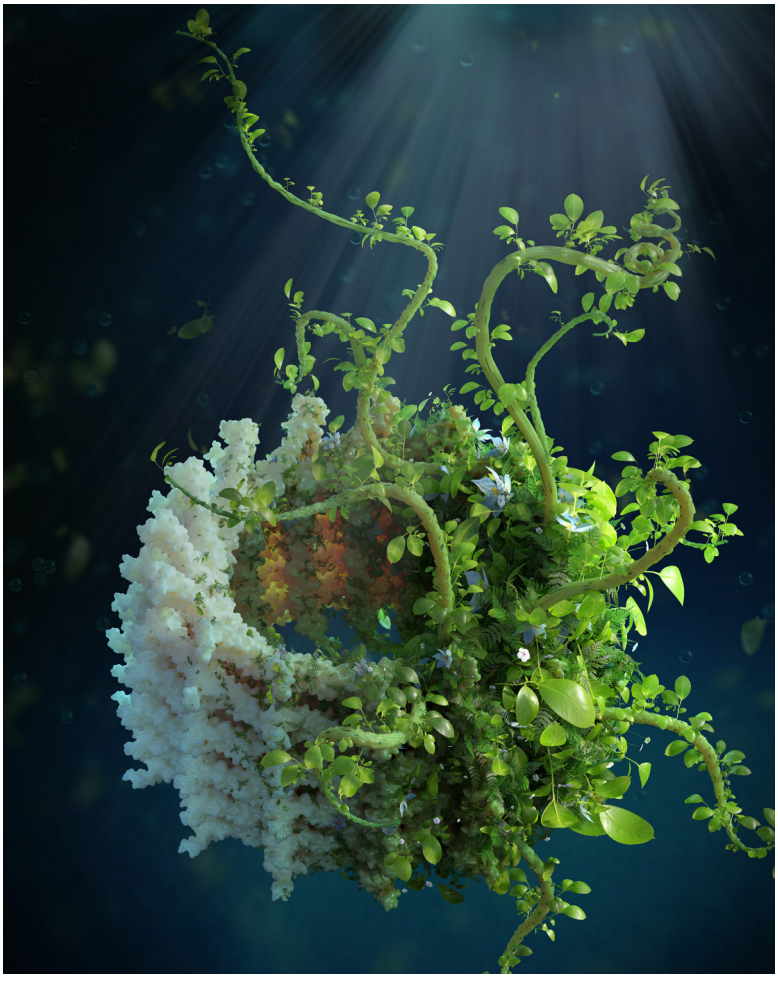
One new adventure our lab is currently embarking on is to directly sample marine algae from the ocean before freezing them on site for cryo-ET (#WeFreezeOnTheBeach). This year, we teamed up with the European Molecular Biology Laboratory (EMBL) to participate in their Traversing European Coastlines (TREC) expedition (www.embl.org/about/info/trec/). The idea of combining high-resolution structural biology with field sampling is quite new, so there's a lot to work out. The long-term goal is to enable researchers to acquire atomic-scale structural information on basically any organism on the planet, directly sampled from its natural environment.

*What advice would you give to aspiring scientists in this area?*

Follow your curiosity! When picking a biological topic, don't be afraid to wander off the well-trodden path. There is so much out there to discover if you are willing to look in new places. And remember to "look through the microscope with your eyes open".

*Who are your scientific heroes?*

I am inspired by classical electron microscopists such as George Palade, Ursula Goodenough, and Andrew Staehelin, who revealed the inner architecture of cells for the first time. We are absolutely standing on their shoulders and just fortunate to have access to these powerful new microscopes. For the current generation of scientists, I greatly admire my colleague at EMBL, Yannick Schwab, who is really paving the way for environmental structural biology with the TREC expedition. I am lucky to work with him.



*Left:* The interwoven ring structure of VIPP1, an ESCRT-III family membrane-remodeling protein found in cyanobacteria and the chloroplasts of algae and plants (see also cover of collection). VIPP1 is required for the biogenesis and maintenance of thylakoid membranes, which use light to produce the biochemical energy and oxygen that sustain most life on Earth. The VIPP1 structure is decorated with growing plants to illustrate the protein's essential role in building photosynthetic membranes. Image credit: Verena Resch (luminus-lab.com). From Gupta *et. al.* 2021, Cell, DOI: 10.1016/j.cell.2021.05.011. *Right:* Hand-drawn illustration depicting bundles of hydrogen-dependent $CO_2$ reductase (HDCR) nanowires inside an anaerobic bacterium. These enzyme-decorated nanowires strip electrons from hydrogen, which they then use to power carbon fixation with high efficiency. Image credit: Ricardo Righetto and Ana Paula Barros. From Dietrich *et. al.* 2022, Nature, DOI: 10.1038/s41586-022-04971-z.