From photosynthesis to new compounds for eye diseases

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Credit: Swiss National Science Foundation

Researchers supported by the Swiss National Science Foundation have succeeded in using X-rays to minutely observe a photosynthesis reaction and produce a movie of the event. The findings will aid understanding of similar processes in the human eye. Thanks to the new SwissFEL particle accelerator at the Paul Scherrer Institute, we can expect more discoveries of this kind.

Plants and algae are not alone in undergoing photosynthesis. Some bacteria also use energy from sunlight to grow and reproduce.

Researchers supported by the Swiss National Science Foundation (SNSF) have now demonstrated atomic-level processes at work in the light-driven protein "pump" of purple halobacteria. In so doing, the researchers have clarified how the pump works, which has long been a matter of debate. The findings will also help to better understand similar photoreceptors for this protein in the human eye.

Using a new technology, an international group of researchers from the Paul Scherrer Institute (PSI), Japan, Sweden and France captured physical and chemical events occurring in one thousandth of one millionth of a second (nanosecond). This enabled the researchers to produce a movie showing atomic-level processes at work within the pump – called bacteriorhodopsin – after it is activated by incoming light.

Obtaining the recordings required examining around 2 million small protein crystal samples with the free electron laser SACLA in Japan. The FEL hits the samples with very short, powerful X-rays, capturing precise moments. "It's like a strobe light," says Jörg Standfuss, a biophysicist and head of the serial crystallography research group. "Unlike a flashlight, it reveals flickers of motion in the dark." The ultrashort light pulses make it possible to record data before the samples are destroyed by the powerful X-rays. Thanks to the new SwissFEL facility at PSI in Würenlingen, which opened on 5 December 2016, researchers at Swiss higher education institutions no longer have to go halfway around the world to conduct their experiments.

Molecular crutch for defective photoreceptors

The bacterial pump results have application potential in different areas. For example, neurobiologists use similar pumps to specifically turn certain nerve cells in the brains of experimental animals on and off (optogenetics).

SNSF-supported research groups at PSI have been studying photoreceptors in the human eye for some time. "Vision is our most important sense. Even our inner clock is governed by these receptors in the eye," says Gebhart Schertler, biochemist and head of the Biology and Chemistry section. Mutations in these light receptors have effects comparable to what happens in the bacterial pumps. Mild cases can cause night blindness, whereas others can lead to degeneration of the retina (retinitis pigmentosa), culminating in total blindness. "Various therapeutic approaches have already been suggested, but up to now none has made it to market," says Schertler.

The results of research work at PSI from earlier analyses of these photoreceptors led to a collaboration with Roche. The goal is to find and develop compounds that could serve as a crutch to compensate the defective retinal proteins. Preliminary results of this investigation will be published soon. Although developing an actual drug could still take a long time, some very promising results have already been obtained.

More information: E. Nango et al. A three-dimensional movie of structural changes in bacteriorhodopsin, *Science* (2016). DOI: 10.1126/science.aah3497

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