# Researchers discover turbo switch of calcium pump in biological cells

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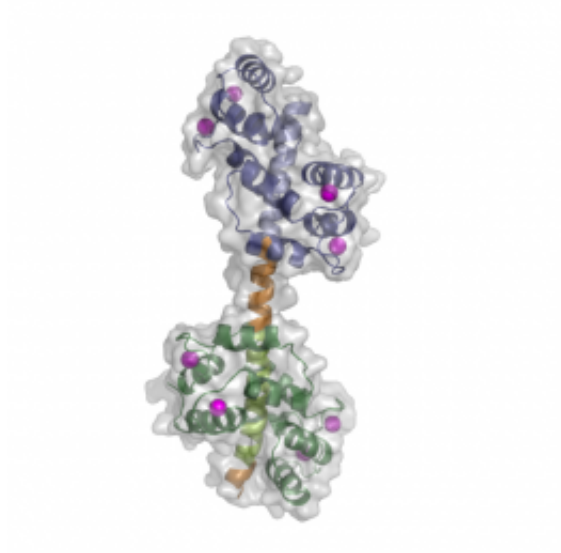


This shows the structure of the calcium pump switch in cells of the plant thale cress (Arabidopsis thaliana). Credit: Henning Tidow et al.; University of Aarhus

When animals and plants are exposed to influences such as bacterial attack, odour and cold, calcium ions flow into the cells. The calcium provides the cells with a signal about what is going on outside, but as high concentrations of calcium are toxic to the cells, it must be quickly pumped out again. Researchers from the Danish National Research Foundation's PUMPkin Centre at both the University of Copenhagen and Aarhus University have now shown that calcium pumps in the cell's outer membrane adjust the pump speed very accurately to the calcium

concentration. These findings have just been published in the journal *Nature*.

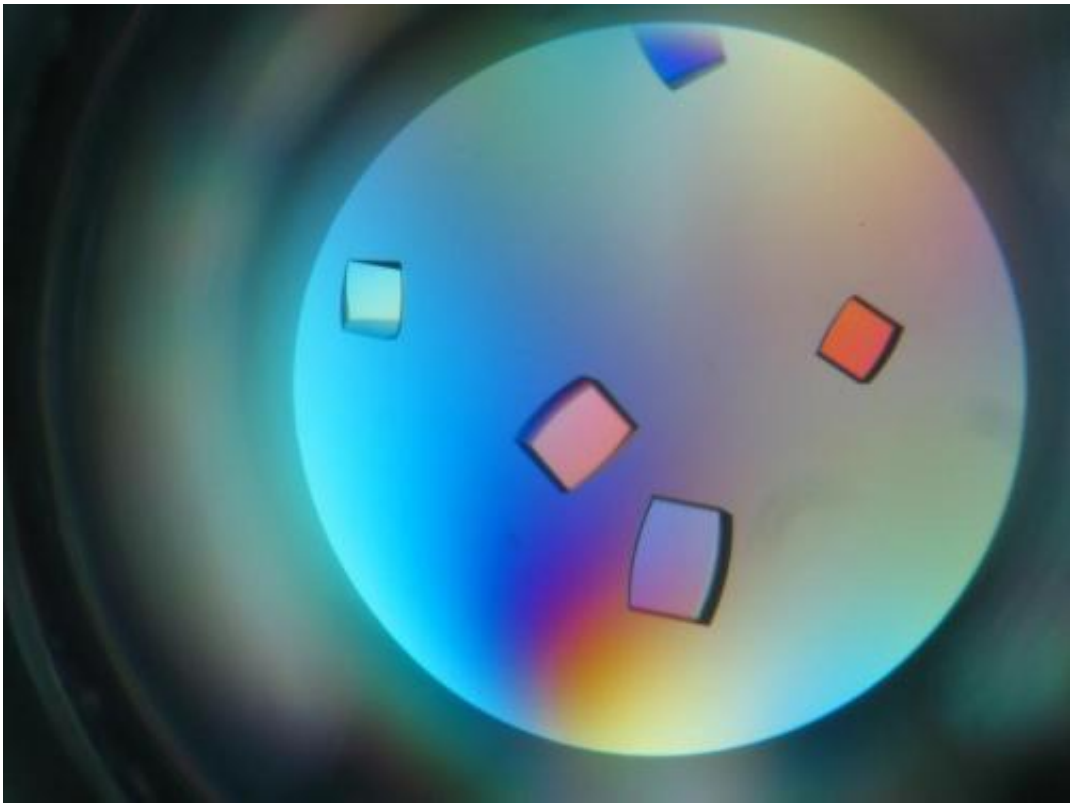
The calcium pump is located in the thin membrane that surrounds the cells of humans, animals and plants. Leading researchers from Aarhus University and the University of Copenhagen have now provided new information of how the calcium pump regulates the amount of calcium in the cells. This amount is critical to the health and survival of the cell.

"It turns out that the calcium pump can accurately measure the cell's calcium content and adjust its speed in accordance with this information. This prevents the concentration of calcium ions in the cytoplasm from reaching a critical concentration that damages the cells. The calcium pump is inactive when the concentration of calcium is low, but it is activated stepwise when the calcium concentration increases," say Postdoctoral Fellows Henning Tidow and Lisbeth Rosager Poulsen, who took part in the joint research project.

The researchers' starting point was the calcium pump located in the cell membrane of the model plant thale cress (Arabidopsis thaliana), but the regulatory mechanism also applies to the corresponding calcium pump in humans and animals.

Previous studies have shown that calcium pumps in both animals and plants work together with a protein called calmodulin. When there are many calcium ions in a cell, some of these bind to calmodulin, which is thereby able to activate the calcium pump.

"We purified the part of the calcium pump that interacts with calcium-activated calmodulin, and we managed to crystallise a protein complex. To our great surprise, we found that the calcium pump binds two calmodulin proteins, and not just one as always assumed," explains Dr Tidow.



This shows crystallized samples of the calcium pump complex of thale cress (Arabidopsis thaliana). Credit: Henning Tidow, University of Aarhus

The fact that two calmodulin proteins are involved in the regulation of the calcium pump activity means that the calcium pump has three steps. It is switched off when no calcium-activated calmodulin is bound, it pumps at medium speed when binding occurs at one calmodulin protein, and it pumps at full speed when both calmodulin proteins are bound.

"Calcium pumps need considerable energy to transport calcium out of the cell. It is therefore important that they are only activated when there is a need to remove calcium. With two calmodulin-binding domains in the calcium pump, the cell can adjust the transportation to be energy efficient, at the same time as being able to quickly reduce the number of

calcium ions if the concentration approaches a toxic level," Dr Poulsen concludes.

The researchers also used mathematical network modelling to further identify whether the calcium pump works differently depending on whether it is activated by zero, one or two calmodulin proteins. This revealed another characteristic of calcium pump regulation of calcium in the cell.

"We could show that the cell only responded to incoming calcium when concentrations above carefully defined threshold values were found. This may be important for the way cells define their status in the circadian rhythm or during cell division, for example," concludes Dr Tidow.

**More information:** DOI: 10.1038/nature11539

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