# Protein with contradictory properties: secret revealed

**A protein with contradictory properties sparked the interest of scientists at the Max Planck Institute for Medical Research: Despite its large negative surface charge, it has a strong tendency to take up electrons, which are also negatively charged. The researchers discovered positively charged calcium ions inside the protein very near the electrons, counteracting their charge. They see this as a natural way of handling opposing electrical charges and allowing the protein to optimally fulfill its biological function.**

## Fascinating discovery

Energy flows through living cells in a variety of ways: one is by electrons moving along a series of protein molecules, as in an electric cable, passed from one protein to the next. While studying such proteins, researchers from the Max Planck Institute for Medical Research found an unusual version of cytochrome *c*.

Cytochrome *c* is a very common protein that transfers electrons from one protein to another. However, the newly discovered protein differs from "standard" cytochrome *c* in two ways. First, it has a much higher affinity for electrons than normal cytochrome *c*. Second, it has a strongly negative electric charge, whereas cytochrome *c* typically has a strong positive charge. This combination of properties is unexpected, since a strong negative charge would normally make it more difficult for a protein to store electrons, as they are likewise negatively charged, and negative charges repel each other.

## Calcium ions play a key role

This apparent contradiction intrigued Thomas Barends, research group leader at the Max Planck Institute for Medical Research. He and his team set out to investigate it – with surprising results. These have now been published in the Journal of Biological Chemistry and highlighted as the "Editor's Pick".

"It was fascinating to discover calcium ions so close to where the electrons are stored. It means that the protein keeps the electrons in a very advantageous place, because the positive charge of the calcium ions compensates the electrons' negative charge. This was surprising for us at first, since we had not seen calcium used in this way inside a protein before," explains Thomas Barends, a structural biologist. According to the results, a calcium cation – a positively charged calcium ion – is located at a distance of less than 0.7 nanometers from the iron atoms the protein uses to store electrons. Even on the scale of molecules, that is very close.

The conclusion that the team drew from this discovery is the following: "This arrangement could enable the protein to have a high affinity for electrons despite its negative charge, which we think it needs in order to bind to another protein to which it can pass the electrons at a later stage. In this way, it can optimally fulfill its biological function."

## Experimental and computational proof

To prove that the calcium ions are actually the cause of the protein's high affinity for electrons, the Max Planck team studied the proteins with and without calcium and compared the data – no easy task, since calcium is a very common element and so contamination of the experiments was a constant problem. At the same time, a group of theoretical chemists from the University of Bayreuth led by Matthias Ullmann carried out computer simulations, also with and without calcium. Their results confirmed the interpretation of the Max Planck team's data.

## Advanced understanding of the principles behind protein functions

The new research findings provide a fine example of how nature resolves contradictions – in this case, by adjusting local electrical charges inside a protein so that its affinity for electrons is increased. This discovery is relevant both for understanding how energy flows through cells and also for developing new man-made proteins for nanotechnological applications.

**Publication:**
M. Akram, D. Hauser, A. Dietl, M. Steigleder, G.M. Ullmann, T.R.M. Barends. Redox potential tuning by calcium ions in a novel *c*-type cytochrome from an anammox organism. *Journal of Biological Chemistry, Volume 301, Issue 2, February 2025, 108082*

## Press release

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## Further information

Thomas R. M. Barends
Phone: +49 (0) 6221 486 508

Carola Ronellenfitsch
Phone: +49 (0) 6221 486652

- Max Planck Institute for Medical Research