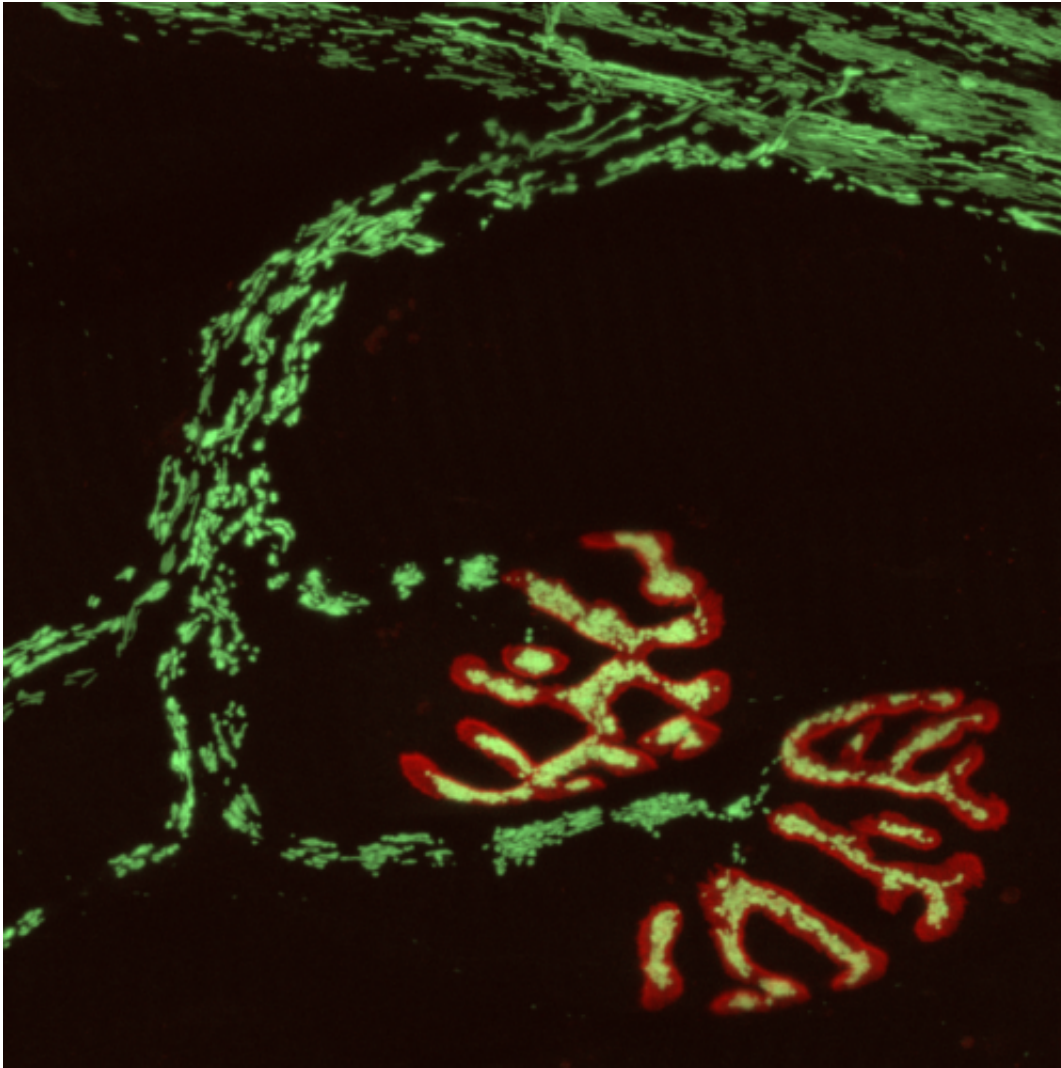


# Neuroimaging: Live from inside the cell

April 22 2014

---



The micrograph shows a peripheral nerve, with the neuromuscular endplates stained in red. The nerve-cell mitochondria were imaged with a fluorescent redox sensor (green in the cytoplasm, yellow at the endplates). Credit: M. Kerschensteiner and T. Misgeld

A novel imaging technique provides insights into the role of redox signaling and reactive oxygen species in living neurons, in real time. Scientists of the Technische Universität München and the Ludwig-Maximilians-Universität München have developed a new optical microscopy technique to unravel the role of 'oxidative stress' in healthy as well as injured nervous systems. The work is reported in the latest issue of *Nature Medicine*.

Reactive oxygen species are important intracellular signaling molecules, but their mode of action is complex: In low concentrations they regulate key aspects of cellular function and behavior, while at high concentrations they can cause "oxidative stress", which damages organelles, membranes and DNA. To analyze how redox signaling unfolds in single cells and organelles in real-time, an innovative optical microscopy technique has been developed jointly by the teams of LMU Professor Martin Kerschensteiner and TUM Professor Thomas Misgeld, both investigators of the Munich Cluster for Systems Neurology (SyNergy).

"Our new optical approach allows us to visualize the redox state of important cellular organelles, [mitochondria](#), in [real time](#) in living tissue" Kerschensteiner says. Mitochondria are the cell's power plants, which convert nutrients into usable energy. In earlier studies, Kerschensteiner and Misgeld had obtained evidence that oxidative damage of mitochondria might contribute to the destruction of axons in inflammatory diseases such as multiple sclerosis.

The new method allows them to record the oxidation states of individual mitochondria with high spatial and temporal resolution. Kerschensteiner explains the motivation behind the development of the technique: "Redox signals have important physiological functions, but can also cause damage, for example when present in high concentrations around immune cells."

## First surprises

Kerschensteiner and Misgeld used redox-sensitive variants of the Green Fluorescent Protein (GFP) as visualization tools. "By combining these with other biosensors and vital dyes, we were able to establish an approach that permits us to simultaneously monitor redox signals together with mitochondrial calcium currents, as well as changes in the electrical potential and the proton (pH) gradient across the mitochondrial membrane," says Thomas Misgeld.

The researchers have applied the technique to two experimental models, and have arrived at some unexpected insights. On the one hand, they have been able, for the first time, to study redox signal induction in response to neural damage – in this case, spinal cord injury – in the mammalian nervous system. The observations revealed that severance of an axon results in a wave of oxidation of the mitochondria, which begins at the site of damage and is propagated along the fiber. Furthermore, an influx of calcium at the site of axonal resection was shown to be essential for the ensuing functional damage to mitochondria.

Perhaps the most surprising outcome of the new study was that the study's first author, graduate student Michael Breckwoldt, was able to image, also for the first time, spontaneous contractions of mitochondria that are accompanied by a rapid shift in the redox state of the organelle. As Misgeld explains, "This appears to be a fail-safe system that is activated in response to stress and temporarily attenuates mitochondrial activity. Under pathological conditions, the contractions are more prolonged and may become irreversible, and this can ultimately result in irreparable damage to the nerve process."

**More information:** Michael O. Breckwoldt, Franz Pfister, Peter M. Bradley, Petar Marinković, Philip R. Williams, Monika S. Brill, Barbara Plomer, Anja Schmalz, Daret K. St. Clair, Ronald Naumann, Oliver

Griesbeck, Markus Schwarzländer, Leanne Godinho, Florence M. Bareyre, Tobias P. Dick, Martin Kerschensteiner and Thomas Misgeld, Multi-parametric optical analysis of mitochondrial redox signals during neuronal physiology and pathology, *Nature Medicine* (2014). [DOI: 10.1038/nm.3520](https://doi.org/10.1038/nm.3520)

Provided by Technical University Munich

Citation: Neuroimaging: Live from inside the cell (2014, April 22) retrieved 19 April 2024 from <https://medicalxpress.com/news/2014-04-neuroimaging-cell.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.