

## ■ Press Release

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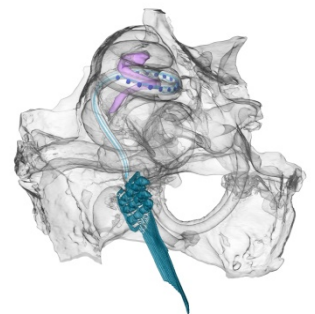
### Lighting array in the ear: First use of multi-channel cochlear implants with microscale light-emitting diodes

**A milestone in hearing research: Researchers at the University Medical Center Göttingen and the University of Freiburg combine for the first time gene therapy in the cochlea with optical cochlear implants to optogenetically activate the auditory pathway in gerbils. Published in EMBO Molecular Medicine.**

(umg/mbexc) Conventional hearing prostheses, so-called cochlear implants (CI), stimulate the auditory nerve of severely hearing impaired or deaf people by applying electric currents. However, the quality of this artificial hearing is far from the quality of natural hearing. This is particularly evident in a poor speech understanding in environments with background noise. Further, the perception of music is clearly restricted. In the future, a fundamental improvement in hearing could be achieved with a cochlear implant if it was possible to activate the auditory nerve spectrally selective. Since light – in comparison to electric currents – can be better spatially confined, this would enable a highly precise activation of the auditory nerve.

Hearing researchers from Göttingen led by Prof. Dr. Tobias Moser and a team of engineers from the Department of Microsystems Engineering (IMTEK) at the University of Freiburg led by Dr. Patrick Ruther have now taken a big step towards the development of an optical cochlear implant. Since the auditory nerve does not naturally react to light, it must first be made light-sensitive through gene therapy. An animal model for human hearing loss with a genetically modified, light-sensitive auditory nerve, developed at the Institute for Auditory Neurosciences and the Cluster of Excellence Multiscale Bioimaging: From Molecular Machines to Networks of Excitable Cells (MBExC) at the University Medical Center Göttingen (UMG), has now been used to test a new cochlear implant for hearing with light. The results show: Optical CIs based on microscale light-emitting diodes ( $\mu$ LED) enable the activation of the genetically modified auditory nerve with a high spectral precision. The research results were published in the renowned journal "EMBO Molecular Medicine" on June 29, 2020.

**Original publication:**  $\mu$ LED-based optical cochlear implants for spectrally selective activation of the auditory nerve. Alexander Dieter, Eric Klein, Daniel Keppeler, Lukasz Jablonski, Tamas Harczos, Gerhard Hoch, Vladan Rankovic, Oliver Paul, Marcus Jeschke, Patrick Ruther, Tobias Moser, *EMBO Molecular Medicine*, 29.06.2020, doi: 10.15252/emmm.202012387; \* equal distribution



**Optical cochlear implant in the cochlea of a gerbil:** The Reconstruction of the spiral-shaped cochlea of a gerbil (grey) was generated by X-ray tomography images at the Institute for X-ray Physics (Prof. Dr. Tim Salditt) at the University of Göttingen. The spiral ganglion with the auditory nerve cells is shown in purple. The optical cochlear implant is shown in blue, the  $\mu$ LEDs are visible as blue dots. Source: Prof. Salditt, University of Göttingen

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"This is an important milestone in the development of future clinical optical cochlear implants. We have taken a big step towards the clinical application of future optical cochlear implants," says the senior author of the publication Prof. Dr. Tobias Moser, Director of the Institute for Auditory Neurosciences, UMG, and spokesperson of the Cluster of Excellence Multiscale Bioimaging (MBExC).

### Detailed research results

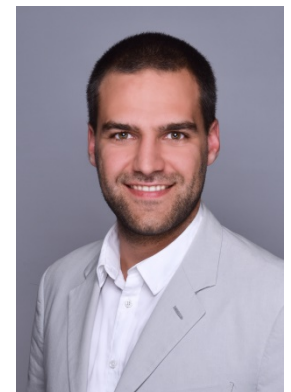
In previous studies, a maximum of three optical fibers were used to optically stimulate the auditory nerve and guide light from external lasers into the cochlea. In the recent study, optical cochlear implants with 16  $\mu$ LEDs (microscale light-emitting diodes) with an edge length of only 0.06 millimetres have been used for the first time to stimulate the auditory nerve in gerbils. These CIs, have been developed by a team of engineers led by Dr. Patrick Ruther, group leader at the Department of Microsystems Engineering at the University of Freiburg. They have been realized by integrating microscaled light-emitting diodes that are able to generate light at different sites within the cochlea independent of each other.

The results of the study prove that it is possible to stimulate the genetically modified auditory nerve using  $\mu$ LED cochlear implants developed specifically for this purpose. The strength of nerve cell activity scaled with the applied light intensity and number of simultaneously activated  $\mu$ LEDs. Of particular importance was the proof of high precision in the excitation of the auditory pathway, which allows a better pitch discrimination. "For the application of future optical CIs in patients, the collaboration of biomedical research with microsystems technology was an essential step, and I am glad that I was able to contribute to this work," says Dr. Alexander Dieter, one of the first authors of the publication. "These results give rise to the hope that artificial hearing will be possible in the future with improved hearing quality," says Dr. Dieter, who has earned his doctorate with the Neuroscience PhD program of the Göttingen Graduate Center for Neuroscience, Biophysics and Molecular Biosciences for work at the Institute for Auditory Neurosciences, UMG. He is now working at the Center for Molecular Neurobiology at the University Medical Center Hamburg-Eppendorf (UKE).

"The integration of miniaturised light sources with dimensions equivalent to the thickness of a human hair in a flexible cochlear implant consistent with the small cochlea of rodents is a technical masterpiece of the colleagues in Freiburg," says Prof. Dr. Moser. "Even though the development of optical cochlear implants for hu-



Dr. Alexander Dieter, first author, Center for Molecular Neurobiology at the University Medical Center Hamburg-Eppendorf (UKE), beforehand Institute for Auditory Neurosciences, UMG. photo: private



Eric Klein, first author, Department of Microsystems Engineering, University of Freiburg. photo: private



Prof. Dr. Tobias Moser, senior author, director of the Institute for Auditory Neurosciences, UMG, and spokesperson of the Cluster of Excellence Multiscale Bioimaging. photo: Moser/private

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mans will still take several years, current experiments already show that they have an improved pitch resolution compared to electric cochlear implants.”

Further refinement is needed to improve the energy efficiency and optical properties of optical CIs. "From a technical point of view, there is still a lot for us to do after this feasibility study," says Eric Klein, one of the first authors and doctoral student at the Department of Microsystems Engineering at the University of Freiburg. "However, we already know that lens systems can be combined with  $\mu$ LEDs and thus direct more light at higher precision onto the auditory nerve." The researchers in Göttingen now plan to perform long-term experiments with these optical CIs in animal models to investigate their usefulness for pitch discrimination at the behavioural level, and to test the long-term stability of the approach.

Prof. Dr. Moser expects the first clinical study in humans to be conducted in the mid-2020s. "We are very grateful for the extensive funding provided by the Federal Ministry of Education and Research, the European Research Council and the German Research Foundation. The further development towards clinical application requires endurance and visionary investors," says Prof. Dr. Moser. To this end, he and his colleagues have founded the Göttingen-based company OptoGenTech, a spin-off of the University Medical Center Göttingen.

### **Background: Hearing with cochlear implant**

*More than 460 million people worldwide suffer from hearing loss or deafness. They can perceive acoustic signals, such as human speech, very poorly or not at all. A reduced - or even non-existent - understanding of speech means that the affected patients cannot communicate with the people in their environment. This significantly impairs participation in social life, success at work, the enjoyment of music and the quality of life in general. In cases in which reduced hearing or even deafness is due to the loss of the auditory sensory cells in the cochlea of the inner ear, so-called cochlear implants (CIs) can provide relief. CIs stimulate the auditory nerve, which is normally stimulated by the auditory sensory cells, directly with electric current. The implants aim to mimic the natural stimulation patterns of the auditory nerve. In this way, an artificial auditory percept is created, which even enables the majority of the more than 700,000 implanted patients worldwide to understand speech after months of rehabilitation. However, hearing with a CI reaches its limits in environments with background noise. Moreover, patients who were hearing before, typically do not enjoy music. These limitations of hearing result from the relatively wide spread of the*

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*electrical excitation current in the cochlea: large sections of the auditory nerve are activated simultaneously, thus limiting the pitch precision of artificial hearing.*

**The Göttingen Cluster of Excellence Multiscale Bioimaging: From Molecular Machines to Networks of Excitable Cells (MBExC)** is funded since January 2019 in the framework of the Excellence Strategy of the German Federal and State Governments. Applying a unique and multiscale approach, MBExC investigates the disease-relevant functional units of electrically active cells of heart and brain, from the molecular to the organ level. The MBExC unites numerous partners from the university and extra-university institutions in Göttingen. The overall goal: to understand the relationship between heart and brain diseases, to link basic and clinical research, and thus to develop new therapeutic and diagnostic approaches with social implications.

### Further Information:

Institute for Auditory Neuroscience:

<http://www.auditory-neuroscience.uni-goettingen.de/>

Cluster of Excellence Multiscale Bioimaging (MBExC): <https://mbexc.de/>

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