

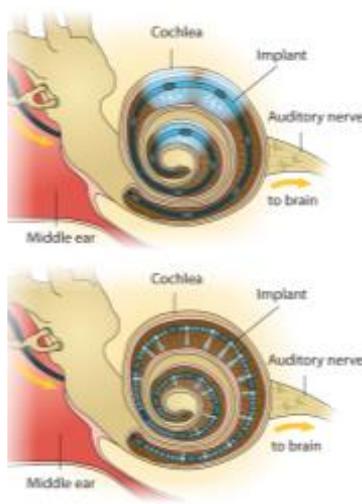
Hearing the light: Optogenetic Stimulation of the Auditory Nerve

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When hearing fails, speech comprehension can be restored by auditory prostheses. However, sound coding with current prostheses, based on electrical stimulation of auditory neurons, has limited frequency resolution due to broad current spread. We aim to improve frequency and intensity resolution of cochlear implant coding by establishing spatially confined optical stimulation of spiral ganglion neurons (SGNs). We have established optogenetic stimulation of the auditory pathway in rodents using virus-mediated expression of channelrhodopsins to render SGNs light-sensitive. Optogenetic stimulation of spiral ganglion neurons activated the auditory pathway, as demonstrated by recordings of single neuron and neuronal population responses at various stages of the auditory system. Fast opsins enabled SGN firing at physiological rates (hundreds per second). We approximated the spatial spread of cochlear excitation by recording local field potentials in the inferior colliculus in response to suprathreshold optical and electrical stimuli, which suggested a better frequency resolution for optogenetic than for electrical stimulation.

Towards characterizing the percept induced by cochlear optogenetics we studied activation of neurons in primary auditory cortex and performed a behavioral response in virus-injected gerbils. Various types of optogenetic responses were observed in auditory cortex. For the behavioral analysis we implanted an optical fiber into the round window of the injected cochlea. Subsequently, animals were trained in a detection task using the shuttle box paradigm. In parallel, optically driven auditory brainstem responses (oABRs) were measured during the period of behavioral testing to monitor the physiological response to optical stimulation of SGNs. We found that amplitudes, latencies and thresholds of oABRs stayed stable for a period of at least 3 weeks. During this period gerbils learned to avoid electric aversive stimuli cued by optical SGN stimulation within a few days and obtained

response rates of up to 95%. Behavioral thresholds of light amplitude were found to be below physiological thresholds ($< 3\text{mW}$, close to the threshold of the neurons in auditory cortex) and thresholds of light pulse duration were as short as 0.1ms . This study demonstrates that stimulation of channelrhodopsin-expressing spiral ganglion neurons with blue light creates both a stable physiological response and a robust auditory percept over several weeks. In summary, optogenetic stimulation of the auditory nerve is feasible and bears substantial potential for future application in research and hearing restoration.



Electrical versus optical stimulation of the cochlea

Top: in electrical CIs usually 12-24 electrodes are used to stimulate SGNs. Current spread leads to activation of a large population of neurons along the tonotopic axis, thereby limiting the frequency resolution and dynamic range of electrical coding.

Bottom: optical stimulation promises spatially confined activation of SGNs allowing for a higher number of independent stimulation channels and, thereby, improving frequency and intensity resolution.