Title: Small footprint optoelectrodes for passive light localization by the use of ring resonators

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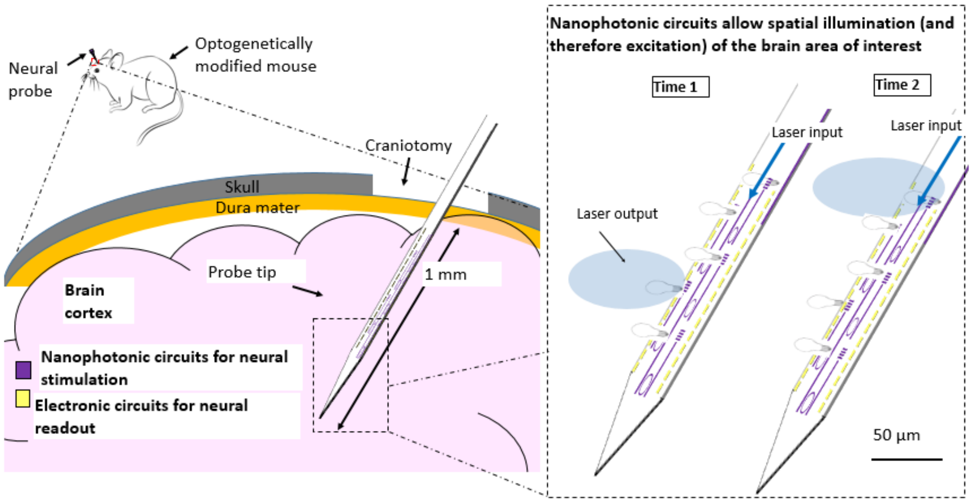
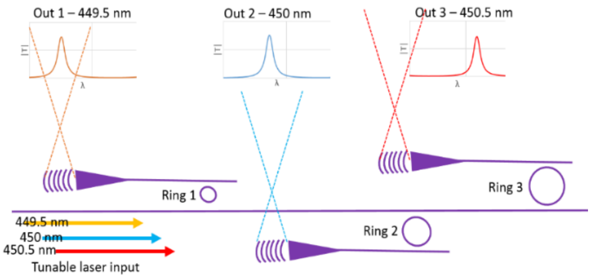
Abstract – *In vivo* neuroscience experiments aim at understanding how the brain works and how the neural activity at the network and single-cell level drives our behavior. These experiments rely on electrophysiology or optogenetic techniques *[1]*, which allow, respectively, to read and manipulate neural activity with high resolution (single neuron and single neural event, respectively). Importantly, combining these two approaches gives the ability to read neural activity while simultaneously silencing or exciting it *[2]*. These experiments' implementation is achieved by inserting in living mice's brain Michigan neural probes *[3], [4]*, which are microfabricated needles embedding sensors or stimulation sites.

One of the most significant challenges in the neural probes' field is to fabricate devices with both readout and stimulation sites providing, at the same time, the following features: (i) the capability of addressing individual sensors for accurate spatial control; (ii) the integration of a high number of sensors to simultaneously interface multiple neural cells; (iii) the minimization of tissue damage by both reducing implant size and keeping low sensor and actuator impact by employing a passive device, i. e., one that does not require any electrical current for circuit activation, which results in heat generation. Such a device allows for both accessing and controlling a high number of neurons with limited tissue impact for high-resolution neuroscience studies. Several state of the art devices address one or more of these features, but not all of them combined in the same device. In this work *[5], [6]*, we realize a neural probe that allows for simultaneous electrical readout and spatially addressable illumination. Our device integrates electronic and nanophotonic circuits onto two different layers, which allows for preserving a high density of sensors for both, while keeping small tip dimensions. Importantly, we report for the first time the use of nanophotonic circuits for passive on demand optical stimulation by the use of ring resonators. We will describe the stages of concept, design, fabrication and characterization of such devices, followed by preliminary *in vivo* experiments after the insertion of our tip in an optogenetically modified mouse. By doing this, we show the probe's capability of locally stimulating neural cells while electrically reading them. Remarkably, our probe allows for such simultaneous readout and activation in a minimally invasive way, thus potentially opening the path to improved neuroscience studies with low footprint, highly scalable and passive devices.

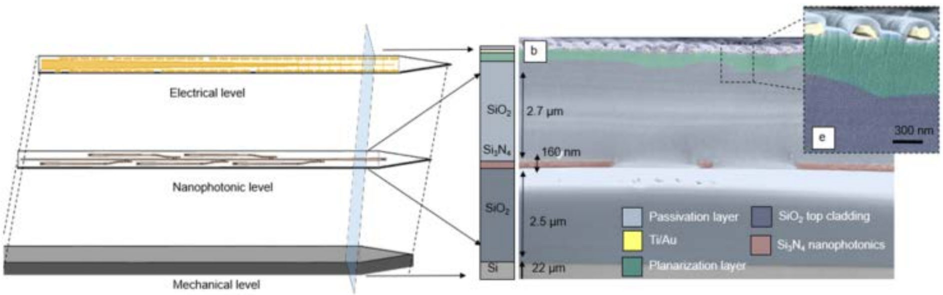
Sketch of our device inserted in a mouse brain (left) and experiment performed (readout with simultaneous excitation of selected areas of the neural network under study)



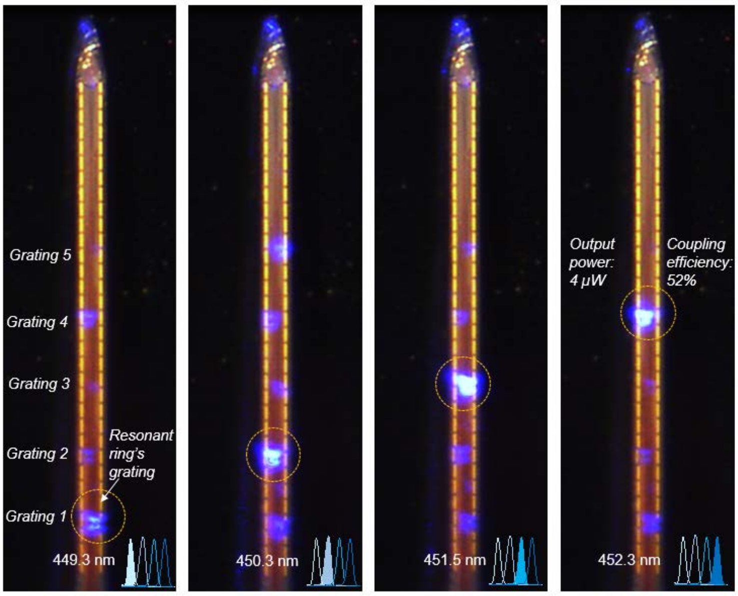
Nanophotonic circuit sketch showing the light output area selection by laser input wavelength tuning and the circuit elements: bus/input waveguide, ring resonators (optical switches) and output waveguides and gratings



Schematic representation of the probe, which is fabricated on different levels: mechanical, electrical and nanophotonic (left). False-color SEM micrograph showing the probe's cross section (right).



In vitro characterization of the probe's capability to deliver light to different areas of interest by the external laser's wavelength tuning.



References*:*

[1] E. S. Boyden, F. Zhang, E. Bamberg, G. Nagel, and K. Deisseroth, "Millisecond-timescale, genetically targeted optical control of neural activity," Nat. Neurosci., vol. 8, no. 9, pp. 1263–1268, 2005.

[2] C. K. Kim, A. Adhikari, and K. Deisseroth, "Integration of optogenetics with complementary methodologies in systems neuroscience," Nat. Rev. Neurosci., vol. 18, no. 4, pp. 222–235, 2017.

[3] Z. Fekete, "Recent advances in silicon-based neural microelectrodes and microsystems: A review," Sensors Actuators, B Chem., vol. 215, pp. 300–315, 2015.

[4] V. Lanzio et al., "High-density electrical and optical probes for neural readout and light focusing in deep brain tissue," vol. 17, no. 2, 2018.

[5] V. Lanzio et al., "Small footprint optoelectrodes for simultaneous readout and passive light localization by the use of ring resonators," Nature Microsystems and Nanoengineering, Under Review

arXiv:2009.01387 [physics.bio-ph], Sep. 2020.

[6] V. Lanzio et al., Scalable nanophotonic neural probes for multicolor and on-demand light delivery in brain tissue, *IOP Nanotechnologies, Under Review*