Post-doctoral positions in "Hybrid strategies for vision restoration" at the Center for Synaptic Neuroscience and Technology The Italian Institute of Technology, Genova, Italy

The Center for Synaptic Neuroscience and Technology (https://www.iit.it/it/nsyn-unige/) of the Italian Institute of Technology (IIT; https://www.iit.it/) in Genova is opening three postdoctoral positions in the field of advanced neural interfaces for neuronal photostimulation and their application for restoration of vision in neurodegenerative diseases of the retina, such as Retinitis pigmentosa and macular degeneration. The position will be under the supervision of prof. Fabio Benfenati, Dr. Elisabetta Colombo and prof. Stefano Di Marco.

In the recent years, we have pioneered active light-sensitive interfaces for neuronal stimulation using organic electronics (*Nature Materials* 2017; *Nature Nanotechnology* 2020a; *Nature Reviews Materials*, 2020; *Nature Nanotechnology* 2021; *Nature Communications* 2022) and photochromic compounds (*Nature Nanotechnology* 2020b; *Adv. Sci.* 2020; *Nanomedicine* 2020; *Light: Science & Applications* 2024; *Nature Review Bioengineering* 2024). Moreover, an advanced version of the polymer-based prosthesis as an injectable "liquid prosthesis" made of nanoparticle (NP) suspensions has been developed. These technologies are quickly evolving from a proof-of-principle stage to real prostheses implanted in rodent and pig models of degenerative blindness.

The research project will include:

1. **Hybrid electrical synapses for cell-targeted photostimulation in retina and brain.** We demonstrated that polymeric NPs form "electrical synapses" with target neurons that are capacitively depolarized to rescue vision in animal models of Retinitis pigmentosa (RP). To make photostimulation cell-specific, we plan to functionalize NPs with recombinant antibodies targeting mGluR6, a unique marker of ON-bipolar cells. This would allow targeting the ON-pathway in a gene-free fashion and restoring the ON/OFF-signature of retinal processing responsible for spatial resolution and contrast sensitivity. We will also exploit the effects of polymeric NIR-sensitive NPs in the brain to stimulate denervated neurons on demand.
2. **Membrane-targeted photochromic compounds for neuronal photostimulation.** The project aims at investigating novel intramembrane, azobenzene-based actuators that elicit light- triggered neuronal stimulation. The actuators dwell into the membrane and behave as light-driven molecular machines that bidirectionally perturb the membrane, impacting on its passive and active properties and eventually on neuronal excitability. We will exploit these compounds for brain and retina with nanostructures capable of slow and prolonged release in the nervous tissue. In the retina, preliminary ex-vivo evidence shows that these bifunctional compounds successfully recreate the mosaic of ON and OFF cells that generates visual acuity and contrast sensitivity, representing a very interesting solution for transferring this strategy to RP patients.
3. **Boost plasticity of the retina and the visual cortex to improve processing and perception of bionic inputs.** We plan to enhance the plasticity of the retina by either downregulation of the transcription factor REST, a physiological repressor of neuronal genes or by environmental enrichment (EE) characterized by high-level multisensory stimulation, physical activity and social interaction. The same strategies will be employed at the level of the primary visual cortex.

The experimental work will involve ex vivo electrophysiology of retina and brain slices studies as well as *in vivo* studies in experimental models of retinal degeneration including in vivo transduction with viral vectors, electrophysiology, functional 2-photon imaging and study of light-driven behaviors.

The successful applicant should have completed a PhD in Biotechnology, Molecular Biology, Neuroscience, Bioengineering or similar. An in-depth expertise in molecular and cellular biology, *ex vivo* electrophysiology and *in vivo* functional studies will be greatly appreciated together with the possess of a certification for animal experimentation. The position will be for 2 years, renewable up to 4 years. Salary will be highly competitive and commensurate with qualification and experience.

Please submit your application, including a detailed curriculum and one-page research statement in PDF format to fabio.benfenati@iit.it and elisabetta.colombo@iit.it quoting "*Postdoc position in hybrid strategies for visual restoration*" in the subject line. Candidates should also request reference letters to be sent directly in PDF format by the Referees to the above mail addresses.

Deadline: 31/10/2024