



### **NEUREKA - A smart, hybrid neural-computo device for drug discovery**

NEUREKA will bring a paradigm shift in drug discovery for neurological diseases, a sector that suffers multiple, repeated failures exacerbating the economical and societal burden of these incurable diseases. It will do so by addressing a crucial shortcoming: the lack of in vitro systems faithfully reproducing brain pathology that enable the functional assessment of candidate compounds at multiple levels: from synapses to neuronal circuits. NEUREKA introduces an innovative, hybrid technology, whereby detailed, computational neuronal networks simulate dysfunction and drive cultured neurons to replicate in-brain disease conditions. Nanoelectrodes mediate the transmission between simulated and biological neurons. Akin to real synapses, nanoelectrodes contact cultured neurons at subcellular locations across the dendritic tree, soma and axonal branches, allowing to control and monitor neural activity with unprecedented accuracy. Biological neuronal responses registered by nanoelectrodes are fed back to simulated neurons, closing the loop and enabling control of activity states across the hybrid population. Complementing molecular deficits already present in culture models of a disease, computational models enable replication of both molecular and physiological deficits of neurodegeneration in vitro. Cultured neurons are driven towards pathological excitability states where deficits emerge, so as to optimize quantification of the impact of drugs, going well beyond standard cellular assays. A proof-of-concept will be provided for Alzheimer's disease, using human induced pluripotent stem cell (iPSC)-derived neurons exhibiting the pathology. NEUREKA will be used to demonstrate the effect of drug candidates across synaptic, neuronal and network functions.

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