Nanowire-Based Neural Probe for In-Vitro Drug Screening

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Technology description

Researchers and engineers from UC San Diego have developed a scalable hybrid integration scheme to fabricate vertically aligned individually electrically addressable Si nanowire probes in array configurations with sub-micrometer spatial resolution. This invention is a novel architecture of a neural probe, with high density nanowire electrodes and individual electrode addressability, forin vitrointracellular measurements. This advanced design permits a higher level of sensitivity in nanowire recordings from cortical neurons and promises to pave the way for scalable neurotechnologies suitable for large scale mapping of neuronal activity in 2D and 3D configurations, particularly for novel pharmaceutical platforms.

The developed technology has the potential to replace conventional planar microelectrode arrays. Its intracellular capability at high densities allows for precise measurement of neuronal activity and the minute potential fluctuations that precedes such activity. The applications can extend to longer MEAs for retinal studies and brain-slice measurements. The nanoscale 3D aspects will allow the studies and development of new frontiers in neuroscience and may impact our understanding of how neurons interact together in a neuronal network.Measurement of subthreshold activity using Si nanowire probes from human neurons opens up new prospects on mapping neuronal activity in large networks of neurons. Given the scalability of this new technology, the simultaneous recording of minute changes in cell potentials can uncover details on the synthesis, processing, and execution of neuronal network activity, spontaneously, or pharmacologically.In-vitro, highly parallel drug screening experiments can be performed without the need of the laborious non-scalable patch-clamp.

1-D electrophysiological probes of the needle and micropipette configuration were the first tools to measure action potentials in neurons. Since its development in the 1970s, this patch-clamp technique remains the standard in high fidelity detection of small potential subthreshold activity. However, the use of tapered submicron micropipette tips to patch into cell membranes and measure sub-threshold potentials and ionic currents are not scalable to large neuronal densities and to long recording times. Automated patch-clamp are scalable but cannot perform recordings from networks of neurons that resemble cell arrangements in organs from brain, to heart, to muscle, to liver, etc. Microelectrode arrays (MEAs) on the other hand are scalable but their planar geometry preclude intimate interaction and sufficient charge coupling between the neuron and the electrode site. The weakly coupled sub-

threshold activity in MEAs is usually below the noise level and is therefore lost and not observed in MEA measurements. None of prior technologies, can sense activity in 3D networks of neurons. Nanowire geometries are ideal for minimally invasive intracellular nanoscale probes but prior works have been limited to single nanowire device demonstrations or to devices encompassing ensembles of several nanowires and without sensitivity to subthreshold neuron activity or demonstration of interfacing with human neurons.

Related Materials

Ren Liu, Renjie Chen, Ahmed T. Elthakeb, Sang Heon Lee, Sandy Hinckley, Massoud L. Khraiche, John Scott, Deborah Pre, Yoontae Hwang, Atsunori Tanaka, Yun Goo Ro, Albert K. Matsushita, Xing Dai, Cesare Soci, Steven Biesmans, Anthony James, John Nogan, Katherine L. Jungjohann, Douglas V. Pete, Denise B. Webb, Yimin Zou, Anne G. Bang and Shadi A. Dayeh. High Density Individually Addressable Nanowire Arrays Record Intracellular Activity from Primary Rodent and Human Stem Cell Derived Neurons, Nano Lett, April , 2017

'Neuron-reading' nanowires could accelerate development of drugs to treat neurological diseases. UCSD News Release

Application area

Use as a potential platform to screen drugs for neurological diseases and study how single cells communicate with large cellular networks as well as examine neuronal health.

Advantages

The nanowire technology developed is nondestructive and can simultaneously measure potential changes in multiple neurons with the high sensitivity and resolution achieved by the current state of the art. Furthermore, this invention allows for the signal from each individual nanowire to be measured which offers the possibility of examining rapid and minute changes in neuronal cellular networks which may accelerate drug development for diseases of the central and peripheral nervous systems.

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