“Aptamer-Functionalized Field-Effect Transistors for Neurotransmitter Sensing”

The BRAIN Initiative aims to unite nanotechnology and neuroscience to investigate neural circuitry within the complex landscape of the brain at the spatiotemporal scales pertinent to information encoding. Investigating how malfunctioning neural networks, which underlie brain-related disorders, are associated with neurotransmitter flux necessitates chemically specific, in vivo neurotransmitter sensors. We propose coupling the molecular recognition properties of rationally designed, chemically synthesized DNA sequences, termed aptamers, with direct electronic detection via field-effect transistors. However, the discovery of neurotransmitter-specific aptamers has been impeded by conventional in vitro screening techniques. Thus, we developed “neurochips” having precise surface chemistries that enable high-affinity interactions between aptamers and target neurotransmitter molecules. Neurochips are able to capture and to sort aptamers targeting different neurotransmitters.

In parallel, we isolated high-affinity serotonin- and dopamine-specific aptamers via an alternative screening method. We then functionalized these aptamers onto the semiconducting channels of field-effect transistor arrays to monitor changes in neurotransmitter concentrations. We hypothesized that optimized binding-induced aptamer conformation changes will be transduced into electrical signals. Serotonin- and dopamine-specific devices showed high sensitivity with a detection limit of 10 fM. These devices retain their functionality in full ionic strength biological fluids including ex vivo brain tissue, suggesting a detection mechanism that corresponds to charge motion within Debye length limitations. We envision unprecedented capacity to measure neurochemical signaling directly, in vivo, and in real time, which will ultimately impact our understanding of brain function in relation to complex behaviors.

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