Neurotransmitter multiplexed detection with graphene multitransistor arrays and novel aptasensors

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Neurotransmitters have a central role in neural communication, and dysfunction of their levels or transmission underlies brain diseases such as depression or schizophrenia. Thus, closely monitoring different neurotransmitters in the brain is of great relevance, but due to the brain's intricacies, measuring chemical neurotransmission remains a significant challenge [1]. Herein, we present a neural interface for multiplexed neurotransmitter detection based on graphene multitransistor arrays (gMTAs) functionalized with selective DNA aptamers. The gMTA chip was designed to allow six different functionalization areas, each with at least four micron-sized transistors. Previously, we achieved the lowest limit-of-detection ever reported for dopamine (1 aM) [2] with gMTAs, and we could discriminate dopamine with great sensitivity in artificial cerebral spinal fluid and brain homogenates, including in a mouse model of Parkinson's Disease. Now, we designed and synthesized a new aptamer for glutamate, which we combined with the dopamine aptamer and a previously published serotonin aptamer to perform multiplexed detection of these three important neurotransmitters in a single gMTA. Our new aptamer proved highly selective to glutamate against other neurotransmitters (Fig.1B). Selective functionalization of each set of transistors was achieved with a custom 3D-printed piece with micron-sized wells and a specially designed fixation method. The gMTA neural interfaces were tested and validated in physiological buffers and transgenic mice's *ex vivo* brain slices driven by optical stimulation. In DC and AC transistor operation modes, real-time biosensing was performed with custom-designed electronics and online signal processing. The platforms presented in this work can pave the way to novel neurotransmitter sensors suitable for real-world academic and preclinical pharmaceutical research and clinical diagnosis.

References

[1] Y. Zhang, *et al.*, Biosensors and Bioelectronics, 189 (2021): 113351.
[2] M. Abrantes *et al.*, Journal of Nanobiotechnology, 20.1 (2022): 495.

Figure

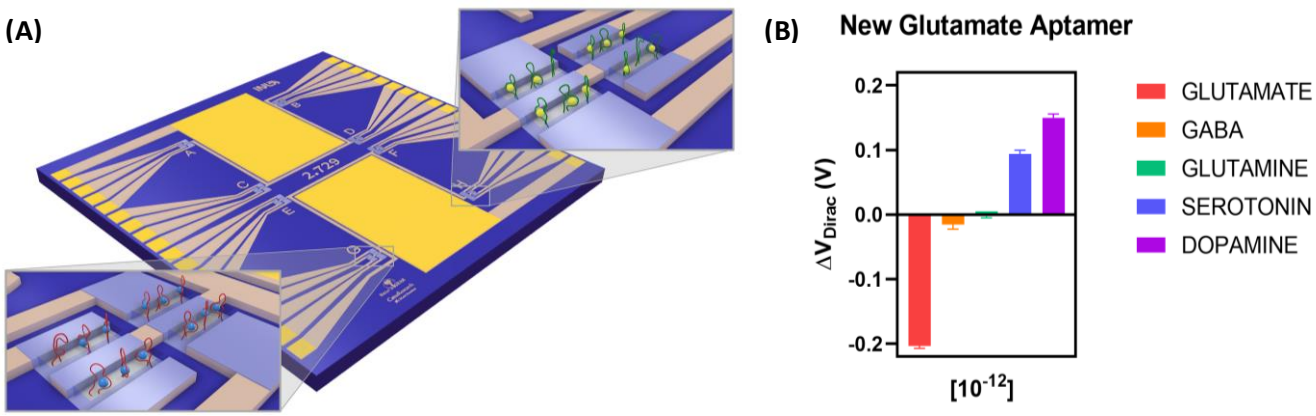

Figure 1: (A) gMTA for multiplexed detection of neurotransmitters, and (B) new glutamate aptamer's selectivity against different neurotransmitters for 1pM concentration in artificial cerebrospinal fluid.