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Real Time Detection of Neuropeptide Y

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Abstract:
The issue of mental health has attracted a great deal of research interest to modern world, specilly after lock down. Different neurotransmitters, have been revealed to play key role in the deteroitation of mental health. Neurotransmitters are also involved in seveal physiological functions. Here in, we review and present a brief report on the detection of NPY, which plays a significant role behind mental health.
Keywords: NPY, Real time, detection, living cell.

Mental health is a severe clinical issue in modern globalized era especially in post covid pandemic era. People who were covid positive are experiencing several post recovery health issues. Due to prolonged lock down situation, whole human race is exposed to a new socio economic world, which affects their mental health. Patient suffering depression experiences several symptoms such as, physical-mental fatigue, indecisiveness, insomnia or hypersomnia, sudden loss or hike in interests, unexpected pleasure in all activity, restlessness or feeling slowed down, suicidal tendency, significant loss or gain in body weights. Hence, patient suffers due to severe effects on their ability to think, feel and behave in. Due to severe affects, depression has drawn enormous research interests of biomedical researcher and neuroscientists. Depression which lasts for at least two weeks is clinically termed as MDD.

Neuropeptide Y (NPY) is a structurally and biologically resembled member of polypeptide (PP) family, which contains 36 amino acid residues and a C-terminal amino acid residue.1-3 The hairpin-like three dimensional conformation of NPY, which is named as pancreatic polypeptide folding (PP-fold) confirms specific interaction between certain amino acid residues.4 The PP folding enables NPY to bind to specific Gi protein coupled receptors e.g., Y1, Y2, Y4 and Y5.1 Many diverse physio-pathological actions are associated with large distribution of NPY, which are mediated via the activation of the receptor. The wide spread distribution of NPY in central5,6 and peripheral7,8 nervous system is associated with several physiological phenomenon e.g., cardiovascular actions,

memory processing, epilepsy, sleep, pain, drug addiction and appetiten.9-14 Capillary electrophoresis-systematic evolution of ligands by exponential enrichment (CE-SELEX) was used for in vitro selection of aptamers for NPY.15 Other common quantitative detection tools used to detect NPY are radioimmunoassay,16 enzyme-linked immunosorbent assay17 and Liquid chromatography–mass spectrometry (LC-MS/MS). The performances of most of these techniques are based on the in vitro study18. However, all current techniques employed to study NPY lack the ability to perform in real time and hence could not be employed for in vivo cellular investigation.

In last decade proper probe molecule modified silicon nanowire based field emissive transistor (SiNW-FET) has evolved as a label-free, sensitive and selective biosensor for real-time measurements.19-21 The FET device includes a semiconducting SiNW channel connecting source and gate electrodes, which are assembled on the top of a Si wafer with an insulating dielectric surface layer.22 The insulating silicon oxide (Si-O) layer on SiNW prevents electrical leakage from the FET device to the electrolytic buffer media. The free silanol (Si-OH) groups on Si-O layer facile covalent conjugation to the linker like 3-aminopropyltrimethoxysilane (APTMS), which anchors suitable receptor molecules to recognize the analytic biomolecule. The bio recognition ability of the receptor linked to the NW surface affirms the selectivity of FET device. The modulation of conductance of SiNW channel due to applied external gate voltage manifests the sensing ability of SiNW-FET device. The gate voltage is tuned when target biomolecules bind on NW surface. The sensitivity of SiNW FET is significantly enhanced when a bio-interaction occurs in the subthreshold regime of NW, where the gating effect is most effective because of reduced screening of the charge carriers in SiNW. The high sensitivity of SiNW FET device is attributed to the utilization of large number of surface Si-OH groups to trap biological targets. The number of free Si-OH groups on the silica sheath on SiNW surface is high due to high surface to volume ratio of SiNW. There is a depletion or accumulation of charge carriers inside the SiNW-FET due to the interaction between receptor and targeted biomolecules. The change in the charge carrier density modulates the current flowing from source to gate electrode (I_{sd}), which can then be acquired as a signal detectable with a lock-in amplifier system. A small variation of local charge density inside NW-FET device is significantly enhanced due to large surface-to-volume ratio due to an electric-field effect. A metric calibration curve is constructed by converting the measured conductance change (ΔI_{sd}) due to the target–receptor binding to the change in calibrated gate voltage (ΔV_g^{cal}) for SiNW-FET. Quantitative analysis is performed using the calibrated response curve, where ΔV_g^{cal} is plotted against the concentration of bio-analytes.23, 24 SiNW-FET device functionalized with specific functional molecules are employed for selective detection of proteins,[19,25,26] metal ions,25 DNA,27,28 RNA,29 cancer biomarkers,[30] viruses[21,31] etc. SiNW-FET device shows very high sensitivity e.g., 10 pM detection limit for streptavidin, detection of single H5N2 AIV virus.21,31 SiNW-FT device is also employed for large scale

mapping of excitable cells e.g., neurons, cardiomyocytes and secretory cells with higher spatial resolution.[20,32,33]

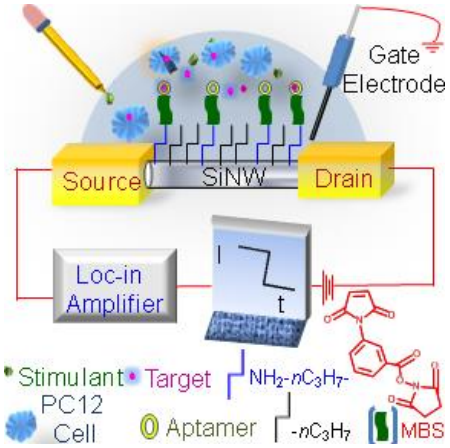

Figure1. Schematic representation of real-time detection of biological target released from PC12 cells after the addition of stimulant with specific aptamer modified MPC SiNW FET device.

Li et al has demonstrated the use of aptamer modified multiple-parallel-connected (MPC) SiNW-FET for the detection of dopamine, which has immense importance as neurotransmitter.34 The usage of SiNW-FET improved the detection limit to <10-11 M relative to other electrochemical techniques which exhibits nanomolar sensitivity. Moreover, aptamer modified MPC SiNW-FET has detection specificity distinguishing dopamine from other chemical homologues like ascorbic acid, catechol, phenethylamine, tyrosine, epinephrine, and norepinephrine. The same literature also reports the real time monitoring of DA release under hypoxic stimulation from PC12 and further reports that DA secretion is triggered by an extracellular Ca2+ influx, rather than that released from intracellular stores. Banerjee et al had developed a DNA-aptamer modified MPC SiNW-FET for real time and selecting sensing of NPY (referred to as NPY-specific aptamer/SiNW-FET). Aptamer dos not only recognize the target molecules, it also exerts strong electric field due to the interaction with NPY because of reduced screening effect in the depletion region or sub threshold region. Because of smaller size of aptamer, the gating effect due to aptamer-NPY interaction is stronger compare to other conventional receptors like enzyme or antibodies. An added advantage of usage of aptamer is its thermal stability and ability to regain its functionality by self-folding. While other recognizers e.g., proteins or antibodies have the probability of loss of thermal or chemical stability during electrochemical measurement. Current manuscript describes use of a NPY specific aptamer15 modified on MPC SiNW-FET to detect NPY with high sensitivity. The specific aptamer has the advantage of stronger electric field exerted due NPY and aptamer association near NW surface, which provide high sensitivity of SiNW-FET device for NPY detection. Further, aptamer modified SiNW-FET device was employed for the real time detection of NPY under hypoxic and histamine stimulation.

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