AI-POWERED DIAGNOSTICS

Machine Learning Discrimination And Ultrasensitive Detection Of Fentanyl Using Gold Nanoparticle-decorated Carbon Nanotube-based Field-effect Transistor Sensors

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The opioid overdose crisis is a global health challenge. Fentanyl, an exceedingly potent synthetic opioid, has emerged as a leading contributor to the surge in opioid-related overdose deaths. The surge in overdose fatalities, particularly due to illicitly manufactured fentanyl and its contamination of street drugs, emphasizes the urgency for drug-testing technologies that can quickly and accurately identify fentanyl from other drugs and quantify trace amount of fentanyl.

For a long time, gas chromatography mass spectrometry (GC-MS) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) have been the standard practice for quantitative detection of fentanyl in many laboratories. However, certain limitations persist with this technique, including limited quantification capabilities which are less suitable for high-throughput screening. On the other hand, electrochemical methods are generally considered to be rapid, easy-to-use, and low-cost alternatives, making them particularly attractive for on-site quantitative analysis.

In this work, we aim to further enhance the specificity of fentanyl detection using an electrochemical sensor and achieve ultrasensitivity down to femtomolar level. To achieve this goal, carbon nanotube (CNT)-based field-effect transistors (FETs) were chosen for the development of fentanyl sensors. CNT-based FETs not only show high sensitivity and low limit of detection toward a wide spectrum of analyte, but also provide valuable insights into the mechanisms governing the sensor responses. The rich information garnered through the FET sensors has enabled us to identify multiple characteristics of sensor responses, ultimately enabling the utilization of machine learning methodologies for the discrimination and differentiation of distinct analytes.

Firstly, AuNP-decorated SWCNT-based FET sensors were employed for machine leaning-assisted identification of fentanyl from codeine, hydrocodone, and morphine. Distinctive sensing performance was observed for fentanyl, which led us to use machine learning approaches for accurate identification of fentanyl. A total of 15 features were extracted from the FET transfer characteristics for model training, and by applying a linear discriminant analysis (LDA) with leave-one-out cross-validation, a validation accuracy of 91.2% was achieved.

Meanwhile, to uncover the factors that contribute to the selectivity and enhanced sensitivity of the Au-SWCNT FET sensors toward fentanyl, a theoretical study based on density functional theory (DFT) calculations was carried out to explore the molecular-level interactions between this opioid and the Au-SWCNT hybrid structure. The results of DFT calculations revealed that the sensing capabilities of Au-SWCNT FET sensors toward fentanyl could be attributed to substantially larger interactions and induced electronic changes of this molecule with AuNP-SWCNT relative to the other tested opioid molecules.

Finally, fentanyl antibodies were introduced to the Au-SWCNT FET sensor as specific receptors, expanding the linear range of the sensor in the lower concentration range, and enabling ultrasensitive detection of fentanyl with a limit of detection (LOD) at 10.8 fg mL -1. The LOD of our sensor outperformed other electrochemical fentanyl sensors reported in the last 5 years.

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