Abstract

The use of biosensors for early stage disease detection and disease prognosis is becoming more and more popular every day. Among the different available biosensing platforms, Field Effect Transistor (FET) based sensors are the most popular nowadays for their various applications. The FET based biosensors offer the advantage of high sensitivity, low concentration of analyte detection, real-time sensing capability, quick response, and most importantly ease of integration with the integrated circuits (ICs). The wide usability of FET biosensors lies in the variable working characteristics such as working in chemical and physical medium and the variety of materials that are available for its fabrication. FET based biosensors have possibility of scalability and commercialization because they follow standard complementary metal-oxide semiconductor (CMOS) compatible fabrication process steps. This work majorly focusses on the development of highly sensitive biosensors based on the FET technology for saliva and plasma-based biomarker detection on a real time basis and the prospects of their batch fabrication.

In this work, a highly responsive FET biosensor based on tungsten trioxide (WO_3) thin film to detect physiological concentration of total ammonia (ammonium NH_4^+ and NH_3) in human body fluids is presented. The elevated level of ammonia in the body fluids indicates improper functioning of organs, mainly liver. Thus, real-time monitoring of ammonia concentration in human body fluid acts as a prognostic marker for liver disorders. It has been observed that the fabricated FET device shows reliable and accurate results towards ammonia sensing with the peak response of 498 at 100 μM and a limit of detection (LOD) of 6 μM. This is also capable of real-time detection of very low concentration of ammonia (2 μM) with a wide detection range from 2 to 100 μM. This study demonstrates a unique and stable sensing platform, that is capable of direct detection of ammonia concentration in human plasma, without any preprocessing of sample for point of care applications.

Apart from ammonia, the second most common analyte associated with the improper functioning of human organs is hydrogen sulphide (H_2S). Human plasma and saliva normally contain 10 μM to 100 μM of hydrogen sulphide, variation in this concentration range has been linked to various disorders. Owing to the advantages of layered transition metal dichalcogenides (TMDs) like high surface to volume ratio and good charge transport characteristics, an ultrasensitive field-effect transistor using layered TMDs is demonstrated to detect dissolved H_2S in plasma and saliva. The developed biosensor effectively utilizes a

few layers of $MoSe_2$ as a channel material for the FET device. The fabricated biosensor exhibits the highest response of 78 at the lowest H_2S concentration of 1 μM and a wide linear dynamic range (between 1 μM and 1 mM). With the lowest detection limit of 1 μM, the fabricated biosensor is appropriate for quick and real-time detection of H_2S in plasma and saliva for point-of-care applications.

Layered TMDs show promise for sensing due to their high surface to volume ratio but lack in selectivity. To address this issue, an innovative hybrid structure is proposed for precise bioanalytes detection. So, this work focusses on the organic/inorganic hybrid transistor structure for biosensing application. Organic polymers are crucial for the interfacial characteristics of the sensors as organic polymer film have redox sensitivity, bio-immobilization potential, and ion-to-electron charge transportation make it appealing for analyte sensing. With the excellent electron transport capability of inorganic 2D TMDs and high surface sensing capability of organic polymers via electron to ion transport, $MoSe_2$/P3HT hybrid transistor has been fabricated. This hybrid FET device is used for ammonia detection in saliva and plasma in the concentration range of 0.5 μM to 1 mM. This hybrid sensor shows improved response and more stable output towards the ammonia detection as compared to only inorganic or organic FET device.

Eventually, the device architecture of WO_3 FET device was further optimized and fabricated to demonstrate its applicability in another biosensing application. The channel surface of WO_3 FET device is modified with different bio linkers to make it specific for particular biomarker detection. In the first step of this work, WO_3 thin film channel layer is modified with (3-Aminopropyl) triethoxysilane (APTES) cross linker to bind the CYFRA 21-1 antibody with the channel layer, next the surface is modified with the bovine serum albumin (BSA) blocking agent to avoid any nonspecific interaction at FET channel surface. At last, CYFRA 21-1 antigen in artificial saliva interacted at the channel surface to detect oral cancer biomarker in saliva. The presented work demonstrated the detection capability of different CYFRA 21-1 concentrations in artificial saliva to detect oral cancer biomarker and showed a response in real-time. In this work, the FET sensors fabrication is demonstrated over entire 2-inch wafer and the uniformity among the device is tested from the prospective of batch fabrication and scalability.