

# A Graphene-PEDOT

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A graphene and poly (3,4-ethylenedioxythiophene):poly(styrenesulfonate) (PEDOT:PSS) modified conductive paper-based electrochemical impedance spectroscopy (EIS) aptasensor has been successfully fabricated by a simple and continuous coating process. A graphene/PEDOT:PSS modified paper electrode forms the nanocomposite providing a conductive and sensitive substrate for further aptamer functionalization of the biosensor. This low-cost paper-based aptasensor exhibits its sensitivity to carcinoembryonic antigens (CEA) in standard buffer solutions and human serum samples in a linear range of 0.77–14 ng·mL<sup>-1</sup>. The limit of detection (LOD) is found to be 0.45 ng·mL<sup>-1</sup> and 1.06 ng·mL<sup>-1</sup> for CEA in both samples, separately. This aptamer-based sensing device was also evaluated and received a good correlation with the immunoassay detection method. The proposed paper-based aptasensor has demonstrated its potential as a rapid simple point-of-care analytical platform for early cancer diagnosis in less developed areas where manufacturing facilities, analytical instruments, and trained specialists are limited.

electrochemical impedance spectroscopy

carcinoembryonic antigen

paper-based device

graphene

conductive polymer

aptamer

## 1. Introduction

Developing sensitive and reliable point-of-care (POC) devices for early cancer screening, diagnosis, and treatment monitoring is an important task in both the developing and developed world [[1](#)][[2](#)]. Promising interdisciplinary research grows on this context because POC analytical platforms can reduce cost, decrease the sample amount, achieve an on-site diagnosis and mitigate patient stress [[3](#)][[4](#)]. Additionally, with the discovery of tumor biomarkers, such as alpha-fetoprotein, prostate specific antigen (PSA) and carcinoembryonic antigen (CEA), the feasibility of analysis in oncology has been enhanced [[5](#)]. CEA is one of the most widely used tumor markers associated with colorectal cancer, pancreatic cancer, gastric cancer, and lung cancer [[6](#)]. Generally, the normal serum level of CEA in humans should be less than 5 ng/mL which is the cutoff value for the indication of cancer [[7](#)][[8](#)]. In addition, changes in serum CEA levels in patients with colorectal cancer can be used to detect early recurrence after surgery [[9](#)]. It also has been reported that elevated serum CEA levels might play an important role in predicting a poor prognosis for pancreatic cancer patients [[10](#)].

## 2. A Graphene-PEDOT:PSS Modified Paper-Based Aptasensor for Electrochemical Impedance Spectroscopy Detection of Tumor Marker

The clinical detection of CEA is mainly based on immunoassays. For example, chemical luminescence microparticle immunoassay (CMIA) and electrochemiluminescence immunoassay (ECLIA) are the two most commonly used immunoassays in hospitals [11]. The advantages of these methods are automatic batch inspection, simple operation, and wide detection intervals, but the disadvantage is that the equipment needed is expensive and cumbersome. In addition to conventional immunoassays, a Love Wave surface acoustic wave (SAW) sensor has been reported for the automatic and online detection of CEA in exhaled breath condensate [12]. Electrochemical immunosensors have recently been of interest to scientists due to their captivating properties, which include high sensitivity, fast response, short diagnostic time, and miniaturization [13]. For example, a new electrochemical immunosensor based on a AuNPs/PEDOT/GR composite was fabricated for enhancing the detection sensitivity of CEA in real human serum [14]. Furthermore, a conducting paper-based electrochemical immunosensor was developed for CEA sensing by progressively creating a poly (3,4-ethylenedioxythiophene):poly(styrenesulfonate) (PEDOT:PSS) film directly over the paper substrate [15]. This approach demonstrated the advantageous properties of a paper-based sensor including flexibility, lightweight, low cost, easy fabrication, biocompatibility, and biodegradability, which satisfied the demand for developing disposable POC devices for areas with a shortage of medical resources. Besides electrochemical immunosensors, a microfluidic paper-based electrochemical aptasensor was fabricated through wax printing and screen printing for simultaneous detection of CEA and neuron-specific enolase (NSE) in a clinical sample [16]. This method provided a great sensitivity of detection and a possible low-cost platform. However, the patterning processes for the devices and the synthesis of nanocomposites for sensing electrodes depend on customized equipment and well-trained personnel. These requirements might be difficult to satisfy in areas with limited resources, or remote or rural communities, where the demand for analytical devices is clearly evident [17].

In this work, a paper-based electrochemical aptasensor for CEA detection was developed using graphene ink and PEDOT:PSS progressively modified on paper substrate to form a conductive composite paper electrode. Graphene has excellent characteristics including ideal mechanical strength, good electrical conductivity and a high surface-to-volume ratio which makes surface transporting electrons highly sensitive to adsorbed molecules [18][19]. It also has been reported that the combination of graphene and PEDOT:PSS produces better sensing properties for working electrodes [20][21]. All fabrication steps were at room temperature and required no sophisticated printing techniques. Through the immobilization of aptamers, the newly conductive paper-based device demonstrated its sensitivity and selectivity of electrochemical measurements of CEA in serum samples. This inexpensive and disposable paper-based electrochemical sensor would provide a point-of-care biomarker analytical tool for cancer diagnostics in less industrialized or resource-limited areas where fabrication facilities and skilled personnel are limited.

We have developed an electrochemical paper-based aptasensor for CEA detection, based on a straightforward and continuous graphene/PEDOT:PSS modification process. The conductive paper electrode was further chemically functionalized in a specially designed reactor for the immobilization of CEA aptamer. The proposed aptasensor was applied for sensing CEA with EIS analysis. These results displayed a good linearity in the range of 0.76–14 ng·mL<sup>-1</sup> and a low limit of detection for CEA. In addition, this sensing system was successfully applied for the determination of CEA in human serum and compared with the immunoassay method. This method does not

require complicated fabrication techniques, costly substrates, or nanomaterials demanding specialized synthetic techniques. This new and sensitive paper-based aptasensor might be an alternative POC tool for cancer markers screening in less developed countries or resource limited areas.

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