

Overcoming the Debye screening limitation with hybrid graphene-carbon nanotube devices for multi-biomarker diagnostics of sepsis

Marcin Szymon Filipiak

Field-effect transistors are the basis of all nowadays electronics and have been around for more than 70 years now. It is comprised of three terminals – source and drain with a switchable semiconducting channel in between, and gate. The functioning of a field-effect transistor would be much easier to understand with the water tap analogy. The pipe that delivers the water is the *source* and the water outlet – *drain*. The valve can be considered the *gate* that we can turn and thus control (*electric field effect*) the water flow (in the FET - *electrons and electron holes*) from the tap.

As the mass production of electronic microchips is well established, researchers are trying to make use of FETs in (bio)chemistry for determining important body parameters – biomarkers specific for a certain disease. From 2004, after the experimental proof of existence of single-sheet graphene, new era in FETs began using graphene as the semiconducting channel. Graphene is simply a part of layered graphite found in all the pencils we use every day. It possesses remarkable properties – strength, conductivity and amazing thickness of one atom only. It is also incredibly sensitive to anything that sticks to its surface changing the in-plane flow of electrons and electron holes. Therefore, it has been extensively studied as a transducer (converter of (bio)chemical information to electronic signal that we can easily record) in the context of biosensors (biologically inspired device that is aimed on determining the amount of certain molecules (proteins) in *e.g.* bodily sample). The issue here is that FET devices have troubles when measurements are performed in the complex bodily fluid sample that is full of different ions and other proteins that disturb the aforementioned conversion process. The ions (electrolytes) in the sample limit the “sight” of the FET biosensor and therefore decrease the electric signal that the device generates (in scientific terms it is called the *Debye screening*). We will overcome this limitation by building up a three dimensional structure on which more interactions (binding events) of different classes of analytes can occur.

We will start with a single-sheet graphene as the base element. The two-dimensionality of graphene is also its drawback – the interactions between the graphene sheet and the analyte can only occur at the interface. In this project, we will be using single-walled carbon nanotubes (sheets of graphene rolled in a specific way) as building blocks for the three-dimensional network on top of graphene. Carbon nanotubes can differ from each other dramatically exhibiting both metallic (conducting) and semiconducting behaviour. In here, we will use high purity sorted semiconducting carbon nanotubes that would enhance the surface area of analyte-(bio)receptor interactions and not affect the outstanding electronic properties of the graphene. There has been no scientific literature examples of application of such hybrid nanomaterial in FET-based biosensing.

Why we are doing it? Some diseases unfortunately don't have just one specific biomarker that gives diagnostic information to a physician, but rather several *quasi*-specific ones that can occur also in different conditions. One example of such a condition is sepsis - life-threatening organ dysfunction caused by a dysregulated immune system as a result of a systemic infection. Annually, more than 49 million people experience this condition, of which as many as 1/5 die - 11 million people a year. Fast and precise diagnosis of sepsis is very difficult due to the heterogeneity and non-specificity of this condition in different patients. In general, sepsis can be divided into 3 major stages: pro-inflammatory, anti-inflammatory and organ failure. For each of those stages, certain biomarkers concentrations in patient's blood increase. The anti-inflammatory biomarkers in the first stage include C-reactive protein (CRP), which also happens to be a common biomarker of inflammation of clinical importance in distinguishing between bacterial and viral infection. Other, newly discovered biomarker is pancreatic stone protein (PSP). In the final, organ dysfunction stage, lactate levels in blood are increased.

The project is aimed at using the hybrid SWCNT/graphene devices to determine the concentrations of all aforementioned biomarkers in parallel and correlate the acquired signal that would help the medical staff to rapidly (within 20 minutes!) and correctly diagnose the patient with sepsis and apply the appropriate therapeutic approach. We expect that with our novel hybrid nanomaterial we will achieve this goal and help decrease the death toll of sepsis.