# Electronic Detection of Biomolecules


## Summary

*The Vitrel group is dedicated to the research and development of in vitro biosensing technology using highly sensitive, disposable, low-cost electronic devices. The group is pursuing the detection of biomolecules (proteins, DNA, infectious agents, etc.) which will have utility for disease diagnosis.*


## State of the art

Currently, assays based on optical measurements are typically used for the detection of biologically relevant molecules. These techniques can vary from the ultra-sensitive and selective biomolecule recognition techniques, to sandwich immunoassay approaches. In general, these assays are relatively sensitive and inexpensive. However, these assays require a significant volume of biological fluid (e.g., serum), sometimes lack desired sensitivity and specificity, and typically detect only one type of molecule at a time. In addition, given the current budgetary constraints US health care system, a novel platform for direct molecule detection in real-time which combines increased sensitivity, an ability to multiplex, decreased requirement for reagents and biological fluids (e.g., antibody and serum), all for a fraction of the current price, would be highly beneficial.

## Vitrel technology

The technology platform the group is advancing for applications is *in vitro* direct detection (i.e. label-free) of biologically relevant molecules using nano-scale, disposable electronics. Currently, this group is fabricating such nano-scale, highly sensitive transistor devices for such applications. The group is optimizing the simple, low-cost fabrication of these devices which are functionalized with specific immune reagents.

***Device fabrication.*** The materials used to fabricate these devices include semiconducting nanowires, polymeric nanofibers and carbon nanotubes. These material are highly conductive and mechanically strong. A variety of room temperature fabrication techniques have been explored, These fabrication schemes enable large area transistor array manufacturing using relatively simple, inexpensive printing or spraying processes. The technology platform can readily be combined with a microfluidic platform into a “lab-on-a-chip” environment where electronic sensing replaces optical detection. Chips integrated with printed RFID technology is also being pursued.

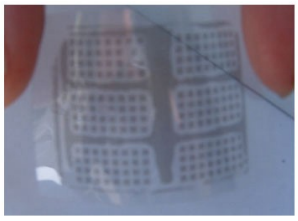

*Fig.1. Disposable electronic transducers*

***The detection scheme*** is illustrated in Fig.2. The devices are coated with a molecular layer that minimizes nonspecific binding. Antibodies of specific specificity are immobilized to the layer. The binding of the antibody to its cognate antigen results in a measurable alteration of the electrical conductivity of the device. In contrast, most conventional diagnostic devices utilize 2 antibodies ("capture" or "sandwich" technology) which are often measured indirectly using optical detection. Direct electronic detection (label-free) using nanotube-based transducers, offer several advantages. Such sensors are small, rapid and sensitive since all the current passes through the detection point. These devices are also capable of linking to any antibody. Moreover, due to decreased reagent cost and minimized production expenses, such devices can be manufactured at a fraction of the cost of conventional assays.

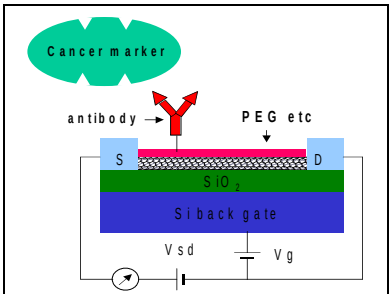


*Fig.2. Electronic Detection Scheme*

***Device operation.*** The devices are being constructed to operate in a serum environment with software algorithms evaluating the binding events and separate device response form electrochemical reactions.

## Current R & D areas

Current R&D areas include the detection of antibody-antigen binding and virus detection. Such a strategy can be employed as tools for disease diagnosis / prognosis as well as for the discovery of novel disease marker profiles. For all scenarios, the detection scheme involves coating the device with a polymer that negates non-specific binding. Extensive specificity and sensitivity experiments will be conducted to compare these nano-scale devices with the conventional assays.

***Early detection of cancer.*** We have embarked on a proof-of-principal project to detect the Prostate Specific Antigen (PSA); a protein whose levels increase in the blood when an individual has prostate cancer. Men over the age of 40 years are routinely tested for PSA levels using a sandwich enzyme-linked immunosorbant assay (ELISA). Our group has fabricated nanowires and nanotube devices which are coupled to anti-human PSA antibodies. The response of these devices to PSA in buffer is illustrated in Fig. 3. The device is specific as it does not respond to random proteins (e.g., serum albumin). Significantly, PSA binding results in a specific change in resistance. The current detection sensitivity is 1 ng/mL; with moderate improvement, sensitivity can be below 0.1 ng/mL, surpassing the sensitivity of current detection technologies.

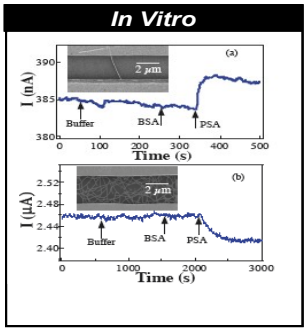


*Fig.3. BSA detection in vitro*

## Future opportunities

There are extensive opportunities for applications of this technology. For example, multiplexed arrays could be used for diagnostic / prognostic disease proteins as well as for disease marker discover (Figure 4). In addition, a variation of this system could be utilized for *in vivo* diagnostics within a living organ or cell.