Detection of several cancer biomarkers by semiconductor Si nanowires

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Laboratory for Nanotechnology (LNT) - Research Institution of International Standard
I. Introduction about LNT

- The Laboratory for Nanotechnology (LNT) was officially established in September 2004.
- LNT has the following missions:
  - Developing the scientific research in Micro-Nanotechnology and transferring research results from universities to industry,
  - Supporting industrial sectors for doing research on materials and microelectronics,
  - Teaching the Micro-Nanotechnology for graduate and postgraduate programs,
  - Collaborating with joint-ventures and foreign companies for doing research, training and technology transfer in microelectronics and other sectors.
The LNT owns the Clean Room of with class 100-10000 for micro/nano device fabrication, characterization and applications.
Technological Facilities of LNT

- Manufacturing of Micro and Nano Devices:
  - Photolithography,
  - Wet etching and dry etching (RIE),
  - Thermal treatment (Oxidation / Annealing furnace),
  - Packaging (Dicing equipment, Bonding equipment),
  - Characterization (Surface Profiler, Optical thickness measurement equipment).

Core Research groups at LNT

- Nano Bio-Sensor Group,
- Light Emitting Diode (LED) Group,
- Radio Frequency Identification (RFID) Group,
- Solar Cell Group,
I. Internal collaboration:
02 biggest National Cancer hospitals,
Electronics Department of University of Natural Science (UNS) of VNU;
Biology Department of UNS,
Hanoi University of Technology,
National Institute for Epidemics diseases etc…

II. External collaboration:
Having direct and closed collaborations with ca. 10 international research groups

III. Research projects:
Currently running 05 research projects, including 02 key national research projects and 02 VNU key projects,
All projects relating to early diagnosing of diseases ...
II. Introduction about nanowire nanosensor

Definition:
Nanowires are wires having at least one dimension from 1 to 100 nm;
Your hair has diameter of 50,000-100,000 nm;
So, bundling at least ca. 1,000,000 nanowires = the size of your hair.
(very small, ultra high surface to volume ratios...)

bundle nanowires  single, selected wire
Nanowires with many new properties and applications

- Ultrahigh surface to volume ratios,
- New phenomena and properties: quantum confinement, strong influence of surface processes to resistance ...
- New devices with completely new capabilities and functions in: optics, electronics, magnetics, laser, ...
  and especially in sensor technology
A Si nanowire-based FET device configured as a sensor with antibody receptors (green), where binding of a protein with net positive charge (red) yields a decrease in the conductance.
Array of nanowires, coated with different bioreceptors for electrical and multiplexed detections
Configuration of nanowire nanosensor

SEM image of a Si nanowire FET sensor and Packaging with microfluidics and electronics;
Advantages of nanowire nanosensors

+ Biological recognition gives high selectivity,
+ Molecular size of the wire give high sensitivity (down to even single molecular level),
+ Label free, electrical read out (rapid, real-time -on-line),
+ Simultaneous and multiplexed detections

Bring New applications and possibilities in: Drug discovery, Food quality control (gene mutation...), Biological & chemical warfare, Environment quality control (gases, water...),

Especially, an detection of cancer biomarkers for early diagnosis
Biological detections by using nanowire nanosensors

Single virus detection in real-time

Protein detection

Real time detection of protein binding. SiNW surface was modified by biotin to detect streptavidin, detection limit of about 10 pM.
+ The ΔF508 mutation is responsible for 75% of the cases of the disease of Cystic fibrosis, one of the most common fatal genetic diseases.
+ SiNW was modified by peptide nucleic acid (PNA) that can distinguish wild-type from the ΔF508 mutation site in the cystic fibrosis transmembrane receptor (CFTR) gene.
The protein (tyrosine kinase Abl) is covalently linked to the surface of a SiNW, and then the conductance of the nanowire device is monitored to detect ATP binding and the competitive inhibition of ATP binding by Gleevec.
Multiplexed electrical detection of prostate cancer markers

+ Detection of prostate specific antigen (PSA) down to 0.9 pg/ml in undiluted serum;
+ 100-1000 times more sensitive than conventional methods;
+ Can be used for detecting other cancers and diseases

(More details: Zheng et al., Nature biotechnology, September, 2005.)
Other examples of cancer biomarker detections


Nanowire sensors for multiplexed detection of biomolecules, Bo He et al., *Current Opinion in Chemical Biology* 2008, 12:522–528

Label-free biomarker detection from whole blood, Eric Stern et al., *Nature Nanotechnology, Volume 5, Issue 2, pp. 138-142 (2010).*
III. Fabrication of complete nanowire nanosensors at LNT
Existing Problems of Nanowire technology

+ Problems:
  nanowire FET sensors fabricated by complicated & time consuming processes -> very high sensor cost (up to k$), low reproducibility...

Bundle nanowires  Select good one  Make contacts (E-beam lithography)

These limitations have rendered further studies and applications of nanowire devices. Therefore, although huge interest, investment, and study, but the devices are not commercially available yet.
Our newly developed technology for Inexpensive, wafer-scale nanowires

+ We have developed a new method that uses conventional IC techniques to pattern wafer-scale nanowires of many materials including metals, alloys, oxides, semiconductors etc…)

+ Generally, the newly developed technique uses the conventional IC technology, thin film depositions (both physical and chemical routes), and a normal etching to make the nanowires on the bearing wafers of silicon, glass, quartz, or even plastics.
Wafer-scale nanowire fabrication by Deposition and Etching Under Angle method (DEA)
Our fabricated nanowires

P. Offermans and Hien Duy Tong et al., *Apply Physic Letter*, 2009.
Ready for measurement silicon nanowires

Single nanowire with micro-contact paths to outer-world (control electronics), thus ready for measuring the biomarkers for cancer detection
Our fabricated nanowires

Array of Si nanowires for multiplexed detections
Our ready for measurement nanowire chips

Version 1  Version 2  Version 3
Measurement setup

LNT has complete setups, including:
+ **Chemical line** for surface modification
  (to bind the bioreceptors on the surface of nanowires), and

+ **Electrical line** for electrical detection of cancer biomarkers
On going work of cancer detection

+ After a couple of research and development years, We have mastered the fabrication technology to produce:
  **Inexpensive & ready measurement Si nanowire chips**

+ We now move to second phase of the project:

Utilization of the developed Si nanowire chips for Ultrasensitive and multiplexed detection of several Biomarkers for diagnosing of cancers.

+ The interest cancers are: prostate, breast, & liver cancers
Liver cancer: simultaneous detections at 10-100 fM of markers

Alpha-fetoprotein (AFP),
AFP-L3,
Des-gamma-carboxyprothrombin (DCP) & Protein (GP73)

This will really enhance an accuracy for diagnosing
Prostate cancer:

+ Detection of **prostate specific antigen** (PSA)

+ In particular, the expression of TMPRSS2:ERG fusion gene originating from circulating tumor cells (CTC) and its potential for monitoring prostate cancer with nanowire technology will be investigated. The direct detection of CTC's with nanowire technology will also be explored.
THANKS FOR YOUR ATTENTION