Complementary metal oxide semiconductor compatible silicon nanowires-on-a-chip: Fabrication and preclinical validation for the detection of a cancer prognostic protein marker in serum

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by,

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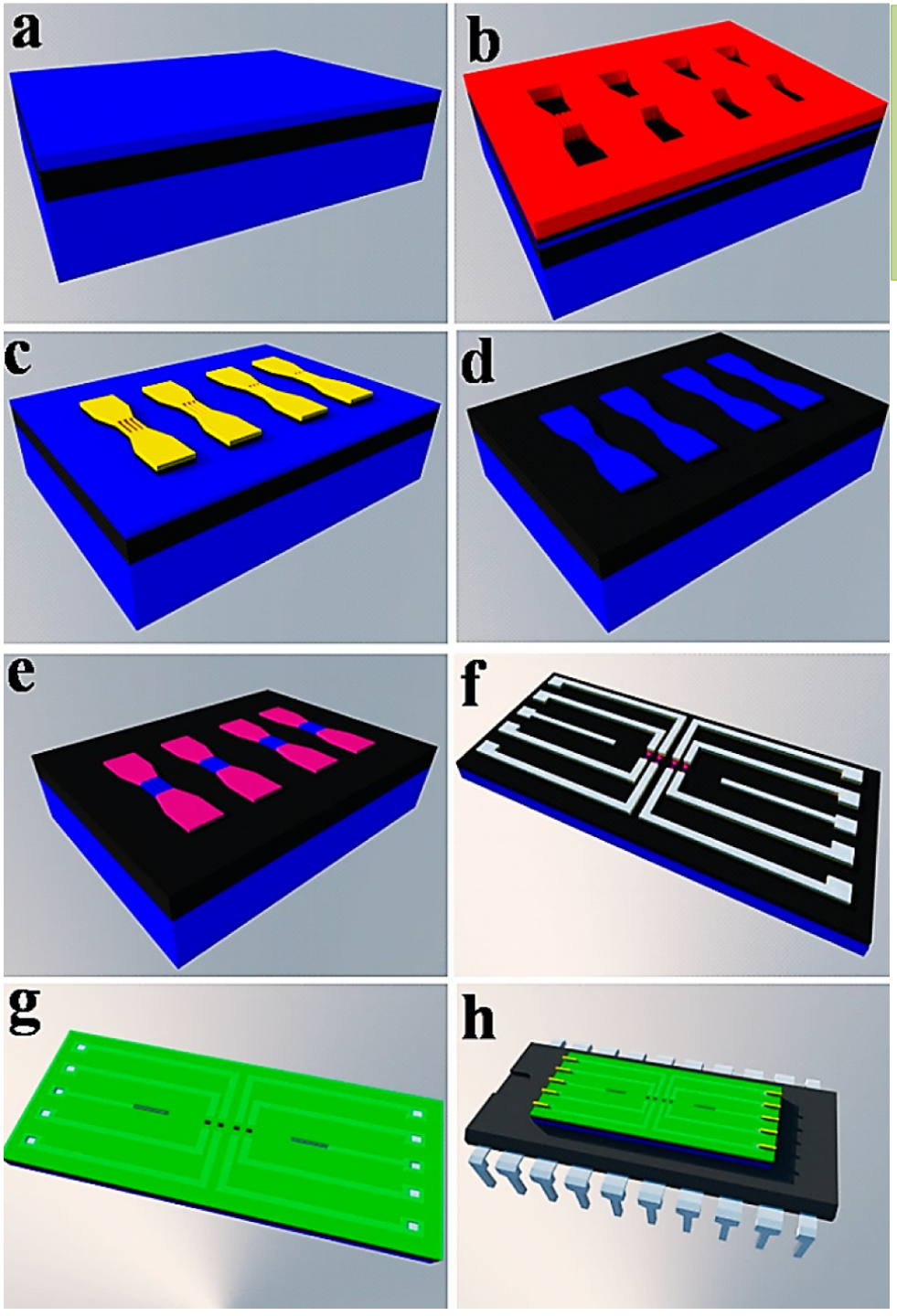
Introduction

- Silicon nanowire field-effect transistors (SiNW FETs) are one of the most promising label-free biosensing platforms owing to their inherent ultrahigh sensitivity.
- The basic sensing mechanism of SiNWs operated as a FET is the modulation of carrier conduction inside the nanowires.
- This modulation results from the binding of charged biomolecules on the surface of the SiNWs functionalized with molecular probes.
- Beside its excellent sensitivity and inherent label-free nature, the main advantage of SiNW FET biosensing is that the signal resulting from molecular binding is electronic.
- Despite continuous progress in silicon patterning

Introduction.....

- To foster the implementation of clinical SiNW biosensor for on-field diagnostic, it is necessary to develop on-chip devices with multiple-sensing arrays compacted in portable measurement systems.
- This work describes the development of a robust SiNW FET sensing platform.
- To validate the translational potential of the novel SiNW FET sensing platform, it demonstrates the possibility to detect activated leukocyte cell adhesion molecules (ALCAM: CD166) in serum at clinically relevant concentrations.
- ALCAM is a highly conserved 110 kDa multidomain transmembrane type 1 glycoprotein of the immunoglobulin superfamily.
- It is expressed in various malignant lesions such as melanoma and colorectal, gynecologic, and pancreatic cancers, and its expression is associated with adverse prognostic, for instance for esophageal, breast, and ovarian cancers.
- Beside this, ALCAM has been shown to be a suitable biomarker for early identification of patients at increased risk of mortality from acute ischemic stroke.



Schematic representation of the wafer-scale fabrication and packaging process of the Si NW chips.

(a−d) Silicon nanowire patterning by e-beam lithography, metal lift-off, and TMAH (tetramethylammonium hydroxide) wet etching, respectively.

(e and f) Selective ion implantation on source/ drain contacts and metal electrode patterning on SiNWs.

(g and h) Electrical contact passivation and packaging.

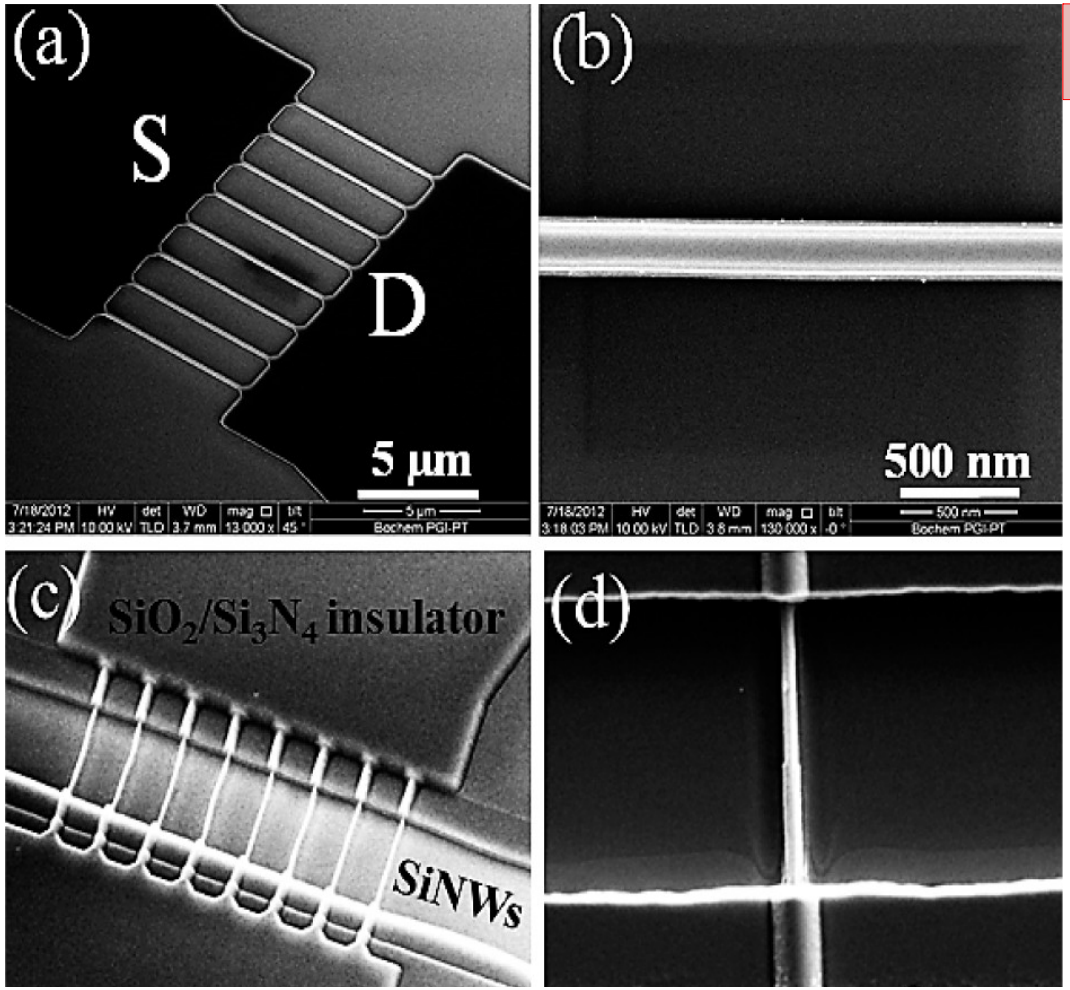
P-type SOI wafer, SiO_2 – ~44nm

Patterning Al nanostructures,

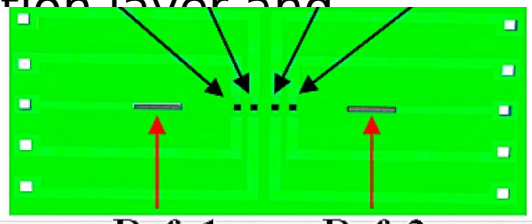
photoresist – PMMA

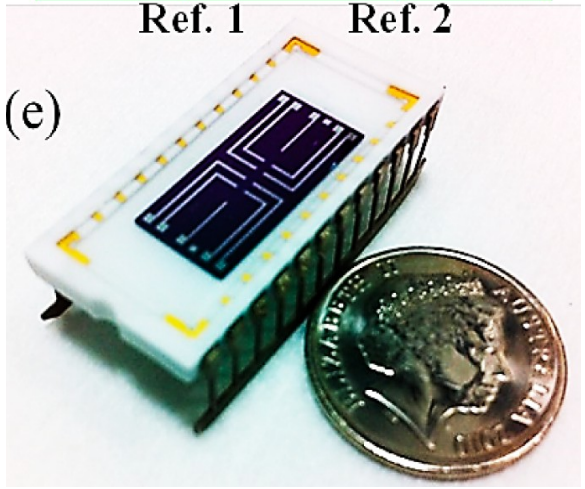
Al pattern – metal mask – pattern transfer on SiO_2 by RIE, TMAH wet etching to define width of SiNWs, SiO_2

SEM Images



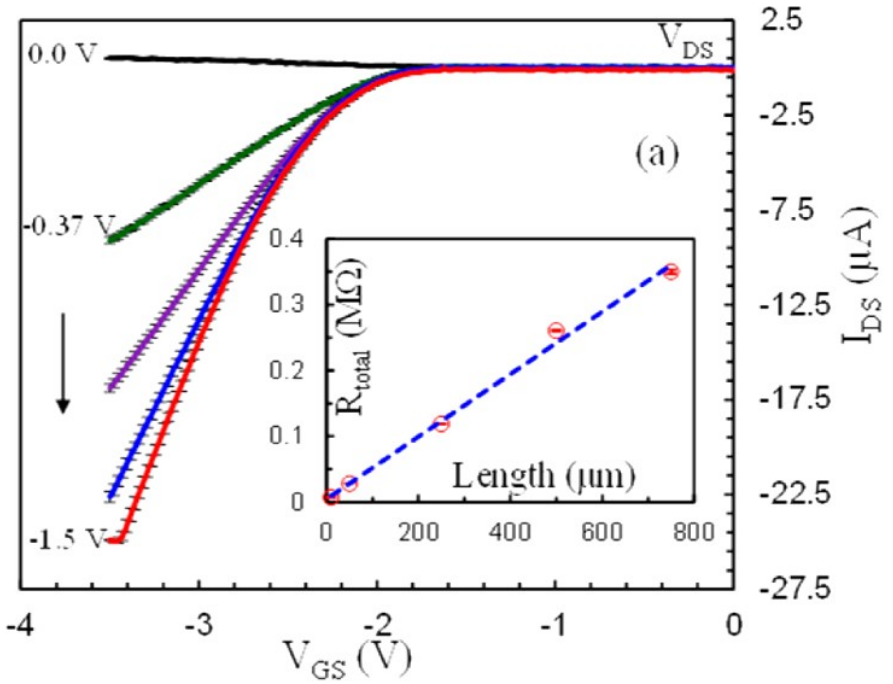
(a) Fabricated conformal SiNW arrays connected to microcontact regions;
(b) Magnification of a smooth,trapezoidal single SiNW after the TMAH wet-etching step;
(c and d) SiNW arrays after patterning the SiO2/Si3N4 protection layer and magn
nanov

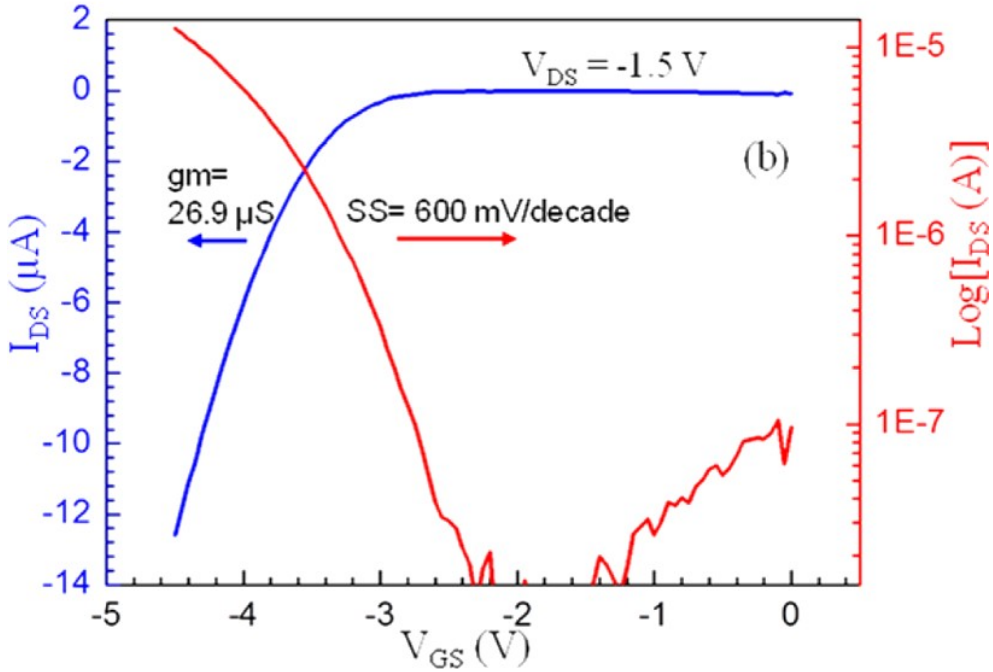




(e) Photographic picture of a SiNW-array device packaged in a white dual in-line package (DIP-24) ceramic housing.
Inset is the schematic layout of a single chip containing four arrays of SiNWs (C1−C4) and two built-in

Transfer characteristics of the SiNW FETs.



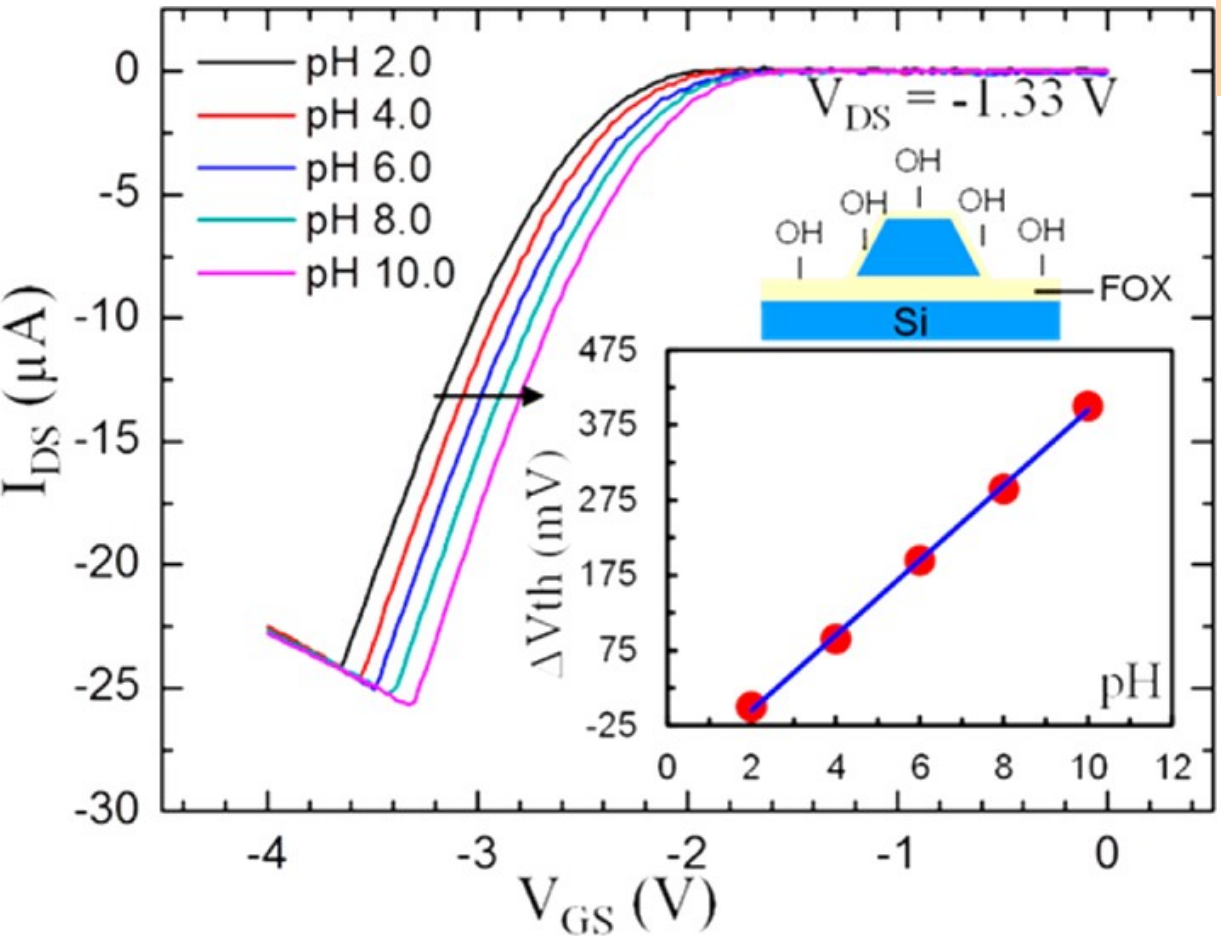


(a) Data obtained from four independent SiNW chips, VDS = 0.0− -1.5 V (−0.375 V steps). The inset shows the total contact resistance of the SiNWs.

(b) Transfer characteristic of the SiNW devices plot in linear and logarithmic scales.

- contact resistance = about 2.5 kΩ/contact point
- gate leakage current = <0.1 nA when measured in PBS
- buffer solution
- For VDS = −1.5 V, gm = 26.9 μS

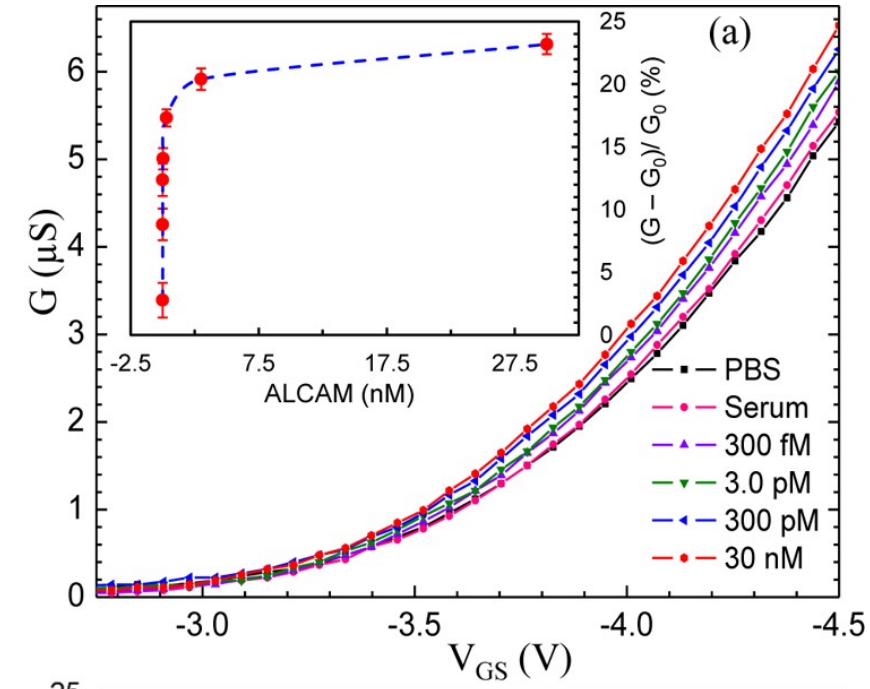
Transfer characteristics of SiNWs FET sensors at different pHs @ VDS = -1.33 V.

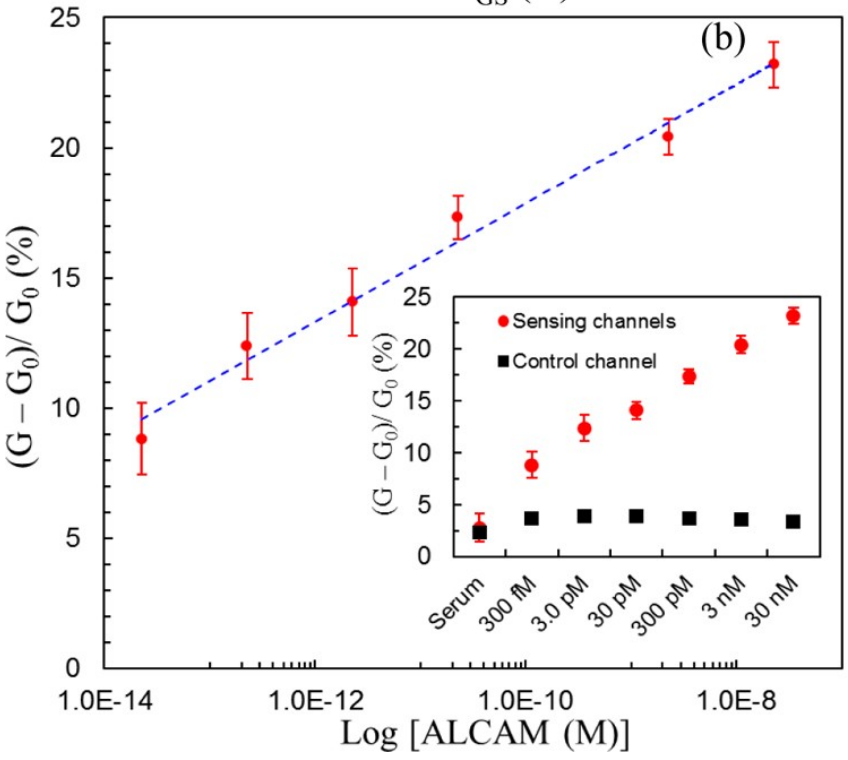


Front gate-source voltages (VGS) were applied to Ag/AgCl electrode immersed in the solutions. For increasing pH values, the VGS curve shift to more positive gate values. The device reaches the maximum current cutoff limit for VGS > −3.5 V. Inset shows the measured threshold voltages plotted against pH values.

ΔVth of the threshold voltage relative to the pH change (ΔpH) = 48 ± 1 mV/pH

Detection response of the fabricated SiNW FET biosensor in different ALCAM concentrations in 10% serum.





(a) Typical SiNW FET transfer function curves recorded from 0 to 300 fM, 3 pM, 300 pM, and 30 nM ALCAM; VDS = −2.5 V; measuring time <30 s. The graph shows a clear increase of nanowires' conductance when ALCAM molecules were selectively bound to the immobilized antibody. The inset plot demonstrates the sensitivity and linear response of the SiNW to ALCAM (300 fM to 30 nM, increasing the concentration 10-fold in each step).
(b) Plot of biosensor responses (in percent of nanowire conductance change; error bars represent standard deviations from three different sensing channels) vs logarithmic concentrations of ALCAM biomarkers from 300 to 30 nM. Limit of detection was calculated at ~183 fM. Inset compares the specific detection of

Conclusion

- A robust and compact CMOS-compatible SiNW FET sensing platform has been developed and validated for the highly sensitive and reliable detection of the cancer biomarker ALCAM.
- The quality of SiNW Chips has been demonstrated by a stable and reliable field-effect performance characterized in a portable multichannel low-noise readout device.
- In addition, the one-step direct detection capability without requiring complicated amplification step is a desirable feature for future point-of-care testing devices.
- Beside the sensor performance, the relative high manufacturing costs associated with state-of-the-art e-beam lithography remains a potential barrier to clinical implementation.
- This could be mitigated by using alternative nanowire patterning techniques (e.g., deep UV-lithography) or through the use of photolithographic process for structuring nanoribbons instead of SiNWs.


Thank
you...
Don't Fear Moving Slowly Forward,
Fear Standing Still.....