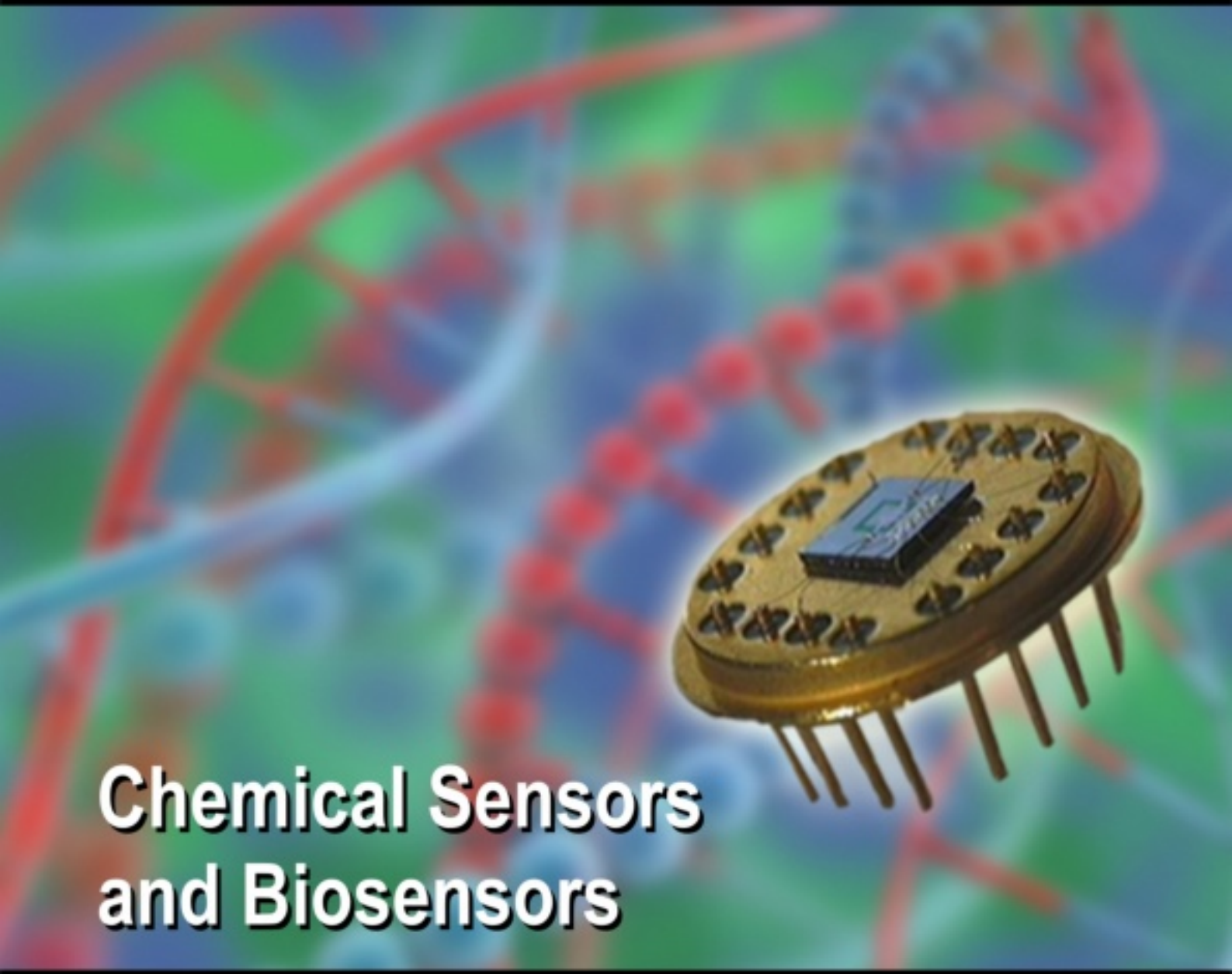
ISSN 1726-5749

SENSORS & TRANSDUCERS

vol. 88
2/08



Chemical Sensors and Biosensors

International Frequency Sensor Association Publishing

IFSA

Sensors & Transducers

Volume 88
Issue 2
February 2008

www.sensorsportal.com

ISSN 1726-5479

Sensors & Transducers Journal (ISSN 1726-5479) is a peer review international journal published monthly online by International Frequency Sensor Association (IFSA). Available in electronic and CD-ROM.

Sensors & Transducers Journal

Contents

Volume 88
Issue 2
February 2008

www.sensorsportal.com

ISSN 1726-5479

Research Articles

Authors are encouraged to submit article in MS Word (doc) and Acrobat (pdf) formats by e-mail: editor@sensorsportal.com
Please visit journal's webpage with preparation instructions: http://www.sensorsportal.com/HTML/DIGEST/Submition.htm

Sensors & Transducers Journal, Vol.88, Issue 2, February 2008, pp. 31-39

www.sensorsportal.com

Sensors & Transducers

ISSN 1726-5479

http://www.sensorsportal.com

Improving Probe Immobilization for Label-Free Capacitive Detection of DNA Hybridization on Microfabricated Gold Electrodes

[a*]Sandro Carrara, [a]Vijayender Kumar Bhalla, [a,b]Claudio Stagni, [b]Luca Benini, [b]Bruno Riccò, [a]Bruno Samorì

[a] Biochemistry Department, University of Bologna, Via Irnerio, 48 Bologna, Italy
[b] DEIS Department, University of Bologna, Viale Risorgimento 2, Bologna, Italy
[*]The corresponding author is now in Swiss Federal Institute of Technology – Lausanne (EPFL) - EPFL IC ISIM LSI1 - INF 333 (Bâtiment INF) Station 14 CH-1015 Lausanne
E-mail: sandro.carrara@epfl.ch

Received: 25 January 2008 /Accepted: 22 February 2008 /Published: 26 February 2008

Abstract: Alternative approaches to labeled optical detection for DNA arrays are actively investigated for low-cost point-of-care applications. In this domain, label-free capacitive detection is one of the most intensely studied techniques. It is based on the idea to detect the Helmholtz ion layer displacements when molecular recognition occurs at the electrodes/solution interface. The sensing layer is usually prepared by using thiols terminated DNA single-strength oligonucleotide probes on top of the sensor electrodes. However, published data shows evident time drift, which greatly complicates signal conditioning and processing and ultimately increases the uncertainty in DNA recognition sensing. The aim of this work is to show that newly developed ethylene-glycol functionalized alkanethiols greatly reduce time drift, thereby significantly improving capacitance based label-free detection of DNA. *Copyright © 2008 IFSA.*

Keywords: DNA biochip, Capacitance detection, Ion layering, Ethylene-glycol thiols

1. Introduction

DNA microarrays have changed genetics and medicine, introducing gene-based tests on a huge number of parallel analyses [1]. They have been used for population genotyping [2] and for disease predisposition testing [3]. The next step in micro-array technology is to provide point-of care devices for diagnostics at the patients' beds. For example, blood tests based on the simultaneous quantization

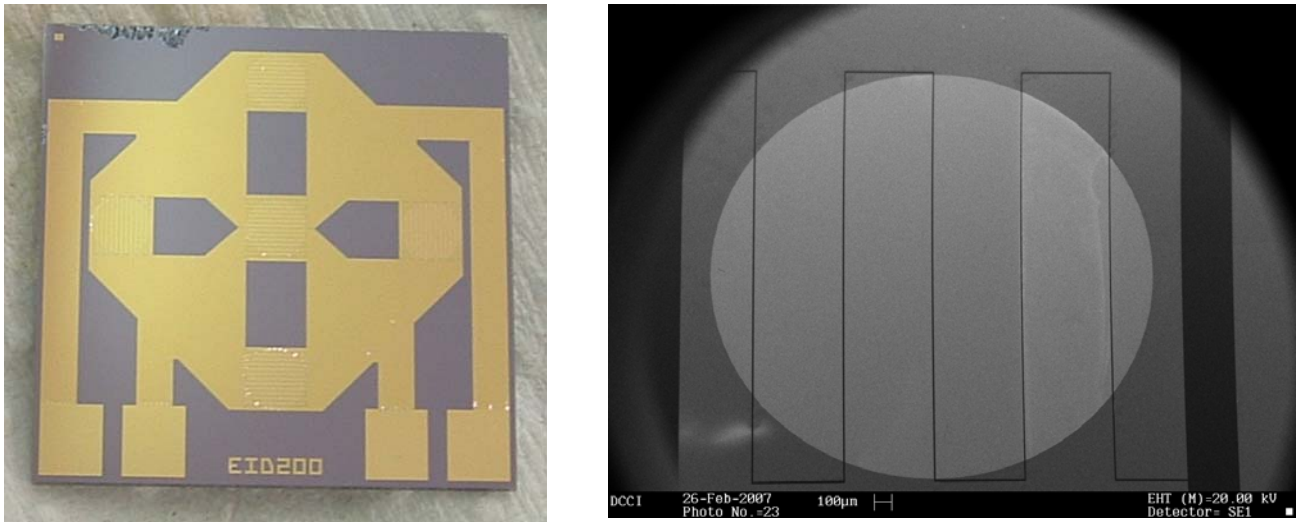
of different analytes can discriminate between healthy or diseased individuals [4] or proximity ligation–based multiplexed proteins can be detected via unique nucleic-acid identifiers followed by real-time PCR quantification [5]. Point-of-care solutions are also highly desired to address the new demand of personalized therapies, as related to the high variability of patient's response to the supplied pharmacological treatment. However, traditional high-throughput DNA arrays are based on fluorescent labels and optical readers, which remain costly and their usage is mostly limited to a laboratory environment. Direct electrical detection has been considered as a promising alternative as it is easily scalable and integrable into microelectronics chip. Label-free impedance biosensors were investigated for point-of-care developments, both for genomics, proteomics, metabolomics, and secretomics [6]. Starting from the very complete work of V.M. Mirsky in 1997 [7], chemical and biochemical detection by using capacitance measurements were widely investigated. Different antibody immobilizations were considered for detection optimization [8] and the technique was applied to DNA hybridization [9]. DNA hybridization was successfully demonstrated both on gold [10] and on silicon [11] electrodes, and verified also by using PNA (Peptide Nucleic Acid) probe molecule [12]. The detection limit was pushed down to femtomolar concentrations range [13], also working with macro-porous silicon [14], till the recent development of fully integrated DNA bio-chips [15, 16]. The ideal capacitance behavior of a sensing probe interface should provide a stable, sensitive and high-specificity response. Unfortunately, published data usually present large time drifts [8, 15]. The consequences of these large time drifts are: large standard deviation [15, 16], data points are largely scattered [7, 9], poor reproducibility from electrode to electrode, and an interface behavior that is very different from that of an ideal capacitor [17]. We have recently demonstrated that in these situations, more complicated models are required [17]. The goal of this paper is to report a new and improved functionalization protocol based on recently developed ethylene-glycol functionalized alkanethiols. This novel functionalization is shown to drastically improve the interface behavior of the sensing interface in capacitance detection of DNA. The special alkanethiols we use in our protocol were originally developed for Surface Plasmon Resonance-based protein and DNA sensors [18, 19], but they have never been used in impedance sensors. This paper demonstrates for the first time that they virtually eliminate the highly-undesirable time drift in interface impedance that characterized the previously described capacitance DNA-sensors, thereby significantly facilitating hybridization detection.

2. Materials and Methods

In this work, measurements were performed on a prototype biochip with gold electrodes on a silicon substrate. To obtain a proper DNA probe coverage, the gold electrodes were functionalized by using COOH terminated ethylene-glycol alkanethiols, and DNA single-stranded molecules terminated with NH_2 group. DNA hybridization was tested by using complementary and non-complementary single strand target DNA molecules. Details of the fabrication, functionalization, and hybridization experiments are reported in the following subsections.

2.1. Chip Fabrication

The biochip used in this work is depicted in Fig. 1 and it was fabricated by Olivetti I-Jet. A standard etching process is used to pattern the gold electrodes on the silicon substrate. To improve adhesion between the substrate and the electrodes, a 20 nm layer of Cromium was deposited, followed by a 560 nm layer of Gold using thermal evaporation. A standard chemical etching process was performed in order to pattern the interdigitated electrodes. Then, a passivation layer of Silicon Nitride was realized on top of the fabricated structures in order to define the proper areas of each sensing spots. The Nitride film was obtained by Plasma deposition (PECVD). The chip contains 5 spot areas with interdigitated electrodes. The spot diameter is equal to 2.5 mm.



(a) (b)

Fig. 1. Layout of the bio-chip: (a) optical image of the whole chip. (b) SEM image of a spot.

The electrodes are 500 µm wide and with a distance of 6 µm from each other. Fig. 1 shows the chip and the spot details. In Fig. 1(b), the dark zone on the interdigitated electrodes shows the Nitride passivation while the shiny zone shows the spot active electrodes area.

2.2. Thiols Monolayer Formation

Prior to the deposition of the first functionalization layer onto the gold electrodes, the bio-chip has been cleaned by exposing the chip to Piranha solution (H_2SO_4 : H_2O_2, in ratio 3:1) for 40 minutes. Following this step, a self-assembly monolayer was formed by using the new ethylene-glycol thiols (Prochimia, Sopot, Poland). The thiols form an insulating *Self Assembled Monolayer* (SAM) onto the electrode. The monolayers were prepared starting from a mixture of two modified alkanethiol molecules $HS(CH_2)_{11}(OCH_2CH_2)_3OH$ and $HS(CH_2)_{11}(OCH_2CH_2)_3OCH_2$-COOH. Both molecules presented an alkyl part of 11 Carbons, and a (ethylene-glycol) part $(OCH_2CH_2)_3$, terminated with an OH group or with a COOH group (31). The mixture is required to improve the hybridization rate which may decrease if the anchoring groups (COOH) are too close to each other. The mixture was prepared into a 2 mM ethanol solution with proportion 1.96 mM of -OH terminated thiols and 0.04 mM of –COOH terminated thiols. For SAM formation, the samples were incubated overnight, under dark conditions, in such a mixture. The samples were then rinsed and sonicated in ethanol for 10 min.

2.3. DNA Probe Immobilization

After the ethylene-glycol thiols monolayer formation, the bio-chip was incubated for 30 minutes in a water solution containing 0.05 M of NHS (*N*-hydroxysuccinimidyl esters) and 0.2 M of EDC (Ethyl-Dimethyl-aminopropyl Carbodiimide). After the incubation the bio-chip was washed in milliQ water and successively it was dried under Nitrogen flux. A TE buffer solution containing 30 nucleotides single stranded DNA molecules terminated with NH_2 groups at a concentration equal to 3 µM were heated for 5 minutes up to 75 °C in a water bath. Individual drops of 10 µl were then spread by means of a micropipette onto each single bio-chip spot and the chip was incubated with these drops for 2

hours at room temperature. After this second incubation, the bio-chip was washed with TE buffer and successively it was dried under Nitrogen flux.

2.4. DNA Target Hybridization

Target DNA solution (3 μM DNA 30-mer and TE 0, 3 M NaCl pH 7) was heated up to 75 °C, spread on the electrodes and cooled down to room temperature (for about 10 minutes). Finally the sample was washed in the TE buffer solution in order to remove the unbound DNA target. We have also checked the procedure, as in the past, with an independent standard optical detection test based on fluorescence molecules bound to DNA molecules [17]. We have tested the efficiency of the hybridization reaction in case of target molecules presenting complementary and non complementary oligonucleotides sequence with respect to the immobilized DNA probes.

3. DNA Target Detection by Capacitance Measurements

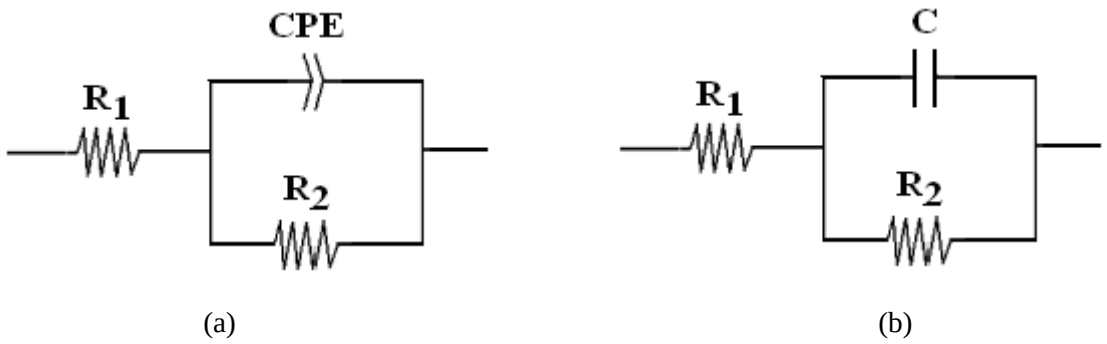
DNA detection is demonstrated by comparing measurements from bio-chip spots with the same DNA strands bound on the surface but exposed to different solutions with complementary or non complementary target molecules. All measurements were performed in the same TE buffer solution used during the hybridization step. 10 μl drops of PBS were spread with a micropipette on top of each single sensing spot. The individual bio-chip was measured by using a biosensor array measurement station developed in our lab. To improve the capacitance estimation, the charge-based capacitance measurement (CBCM) technique was implemented in this station [16]. A detailed description of the electronic system is out of scope of the present paper and it was already published [20]. After the SAM formation and before the first capacitance measurements on thiols monolayer, the spot electrode were left for conditioning in PBS buffer, in dark, for 24 hours. The conditioning was necessary to further stabilize the capacitance measurements on the so prepared electrode chips.

4. Results and Discussion

In our previous published paper on DNA capacitance detection, we had investigated the interface behavior of the sensing electrodes vs. frequency [17]. In that case, we immobilized directly the thiolated ss-DNA oligonucleotides onto the electrode gold surface without any preformed ethylene-glycol film. The published data presented large variations in frequency and, therefore, the interface behavior is highly different with respect to that of an ideal capacitor. The model shown in Fig. 2 (a) was then considered. The equivalent circuit element CPE present in the circuit is such that:

$$Z_{CPE} = \frac{1}{C_p (j\omega)^{\alpha}} \cong \frac{1}{\omega^{\alpha} C_p} \sqrt{1-\alpha^2} - j \frac{1}{\omega^{\alpha} C_p} \alpha \,. \tag{1}$$

It presents a reactance and a resistance component, both varying upon the frequency. This model approaches the ideal case, which is represented by the equivalent circuit reported in Fig. 2 (b), if the α parameter is close to the unity.



(a) (b)

Fig. 2. the electrochemical models describing two possible behaviors at the biochip/solution interface: (a) including a CPE element to account of the ions penetration through the sensing layers; (b) the ideal case without ions penetration through the sensing layer.

The ideal case presents a resistance R_2 in the GΩ range and a constant capacitor C. This capacitor should in principle be constant both in time and in frequency. However, our previous paper showed that the interface behavior is fitted by α parameter values equal to 0.775, 0.867, and 0.885 for the bare electrodes, the DNA probe, and the hybridized target DNA, respectively [17]. In the present work we investigate the interface behavior vs. frequency but in case of DNA probe immobilized on the electrode gold surface by means of thiols presenting additional functionality carried out by the ethylene-glycol molecular segment. Fig. 3 presents the capacitance measurements on such thiols monolayer as a function of frequency. It is evident that the frequency behavior of the interface is almost constant. The fitting with the CPE model returns us an α value equal to 1.015, very close to unity. A careful observation of Fig. 3 reveals that the measurement acquired at 10 Hz presents a capacitance value slightly smaller than those acquired at higher frequencies. If we fit the data without considering the first point, then the α value becomes equal to 0.998, improving by one order of magnitude the interface behavior ideality. Similar results were obtained in the bio-chip spots functionalized with the DNA probes and after the hybridization with target DNA molecules.

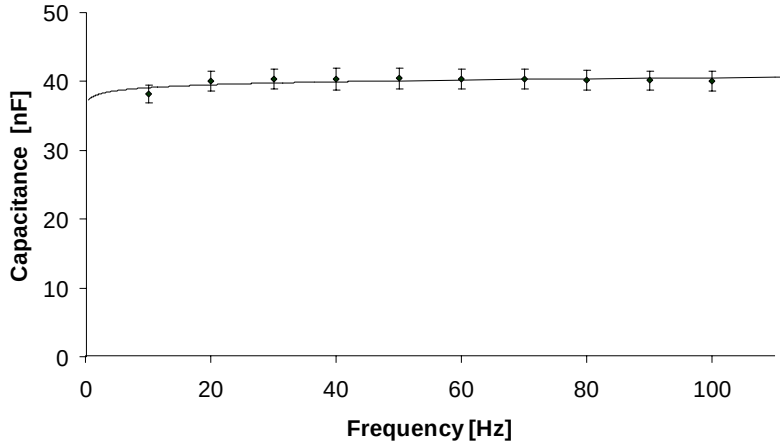


Fig. 3. Capacitance vs Frequency measured on different spots of a bio-chip functionalized with a self-assembled monolayer realized by using three(ethylene-glycol) thiols. The points are the experimental data while the continuous line is the fitting by following the model in Fig. 1(a).

Figs. 4 and 5 show these results. Both the presented cases are highly constant in frequency and the related α values are 1.009 and 1.022, for the probe and the hybridized target DNA, respectively. We observe α values slightly larger than unity even in the two cases including DNA molecules on top of

the ethylene-glycol thiols monolayer. An α value larger than one means an inductive behavior of the interface. Inductive behaviour was observed, for example, in polymer based materials [21, 22]. The slightly (two order of magnitude lower) inductive behavior of the ethylene-glycol monolayer surfaces at low frequencies may be due to a net ions adsorption into the monolayer, to a non-homogeneous current distribution, or to a potentiostat non-ideality of the sensing circuit (whose noise immunity reduces at low frequency). It is however important to stress that the interface is only very weakly inductive. Moreover, this behaviour can be completely avoided if we measure the interface at frequencies higher than 10 Hz. For fittings performed with frequencies larger than 10Hz, the α*value becomes* 0.998 for both the DNA probe and the target. This significant reduction of time drift is fully confirmed by the standard deviations of the data set. Standard deviations in Figs. 3-5 account for variations between different electrodes inside the same bio-chip: even though there is some residual variance, it is entirely due to differences between spots, not to the time drift of impedances. In fact, Fig. 6 presents a typical set acquired during 10 minutes on a single bio-chip spot where target DNA hybridization occurred. The data is almost constant over time, and there is no time drift, as observed with other DNA probe immobilizations [15], nor large data scattering [9]. In summary, Fig. 5 and 6 demonstrate that the ethylene-glycol thiols monolayer highly improve the ideality of the probe sensing surface for detecting the DNA hybridization on solid substrates. The behavior is improved both in frequency and in time. This results in an improved DNA detection capability as shown in Fig. 7. Three bio-chip spots were functionalized with the DNA probe molecules covalently immobilized on top of the ethylene-glycol thiols monolayer. However, spot #1 was used to detect the target DNA molecules, while spots #2, and #3 were used to measure the capacitance changes on non-specific DNA sequence and on a sample not presenting DNA molecules. The first spot shows an evident capacitance decrease coherently with previously observed capacitance variations in DNA detection [9, 15]. The second spot presents a slightly increased capacitance. This is probably due to a-specific physical adsorption, while the third spot does not present any significant capacitance variation. It is worth to point out that standard deviations presented in Fig. 7 are extremely small, as they are obtained on time data similar to that presented in Fig. 6. Such a very small standard deviation demonstrates that with the new functionalization it is easy to distinguish capacitance variations caused by DNA hybridization from those that are produced by the time drift of the interface capacitance itself.

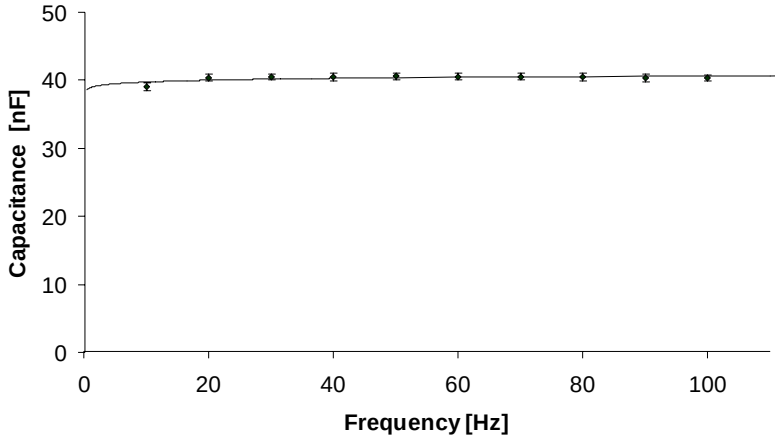


Fig. 4. Capacitance vs Frequency measured on different spots of a bio-chip functionalized with a ss-DNA probe molecules immobilized on top of a three(ethylene-glycol) thiols monolayer. The data points are fitted by using the model in Fig. 1(a).

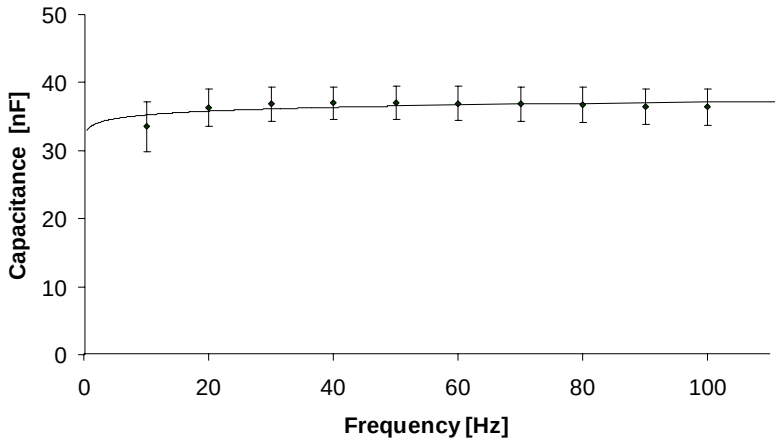


Fig. 5. Capacitance vs Frequency measured on the DNA hybridization on different spots of a bio-chip functionalized with a ss-DNA probe molecules immobilized on top of a three-(ethylene-glycol) thiols monolayer. The continuous line is the fitting by using the model in Fig. 1(a).

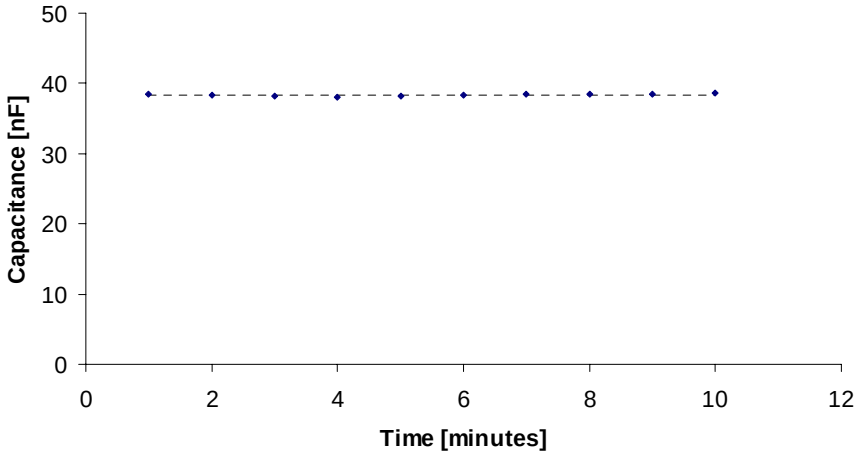


Fig. 6. Capacitance vs time measured on the hybridization with target DNA on a single bio-chip spot functionalized with a ss-DNA probe molecules immobilized on top of a three(ethylene-glycol) thiols monolayer. The points are the experimental data while the continuous line is just a constant.

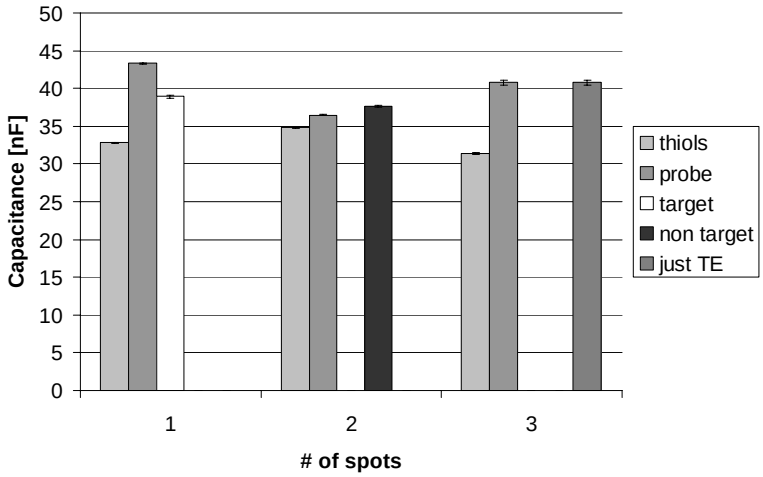


Fig. 7. DNA target detection on a bio-chip. Three different bio-chip spots are represented in the figure showing different capacitance variations corresponding to different sensing situations: target molecule (spot # 1), non-target molecule (# 2), and a different measuring buffer (#3).

Conclusions

The main contribution of this paper is in the identification and the characterization of a surface functionalization process which drastically reduces time drift of interface impedance and therefore enhances DNA hybridization detection via impedance measurement. We described in details the protocol to immobilize single strand DNA probe molecules onto bio-chip electrodes by means of ethylene-glycol thiols. COOH terminated thiols were used to construct a self-assembly monolayer onto electrodes. DNA probe molecules terminated with a NH_2 group were covalently immobilized on top of the formed thiols monolayer. It was shown that the so prepared sensing surfaces present interface electrochemical behavior close to that of an ideal capacitor. Capacitance was analyzed both in the frequency and time domain. The ideality is further improved in case of frequency measurements over 10 Hz. The optimized behavior of the new functionalization leads to very small standard deviations in data of spots, which correspond to different detection conditions. Such an interface behavior ensures a highly improved detection capability.

Acknowledgments

Olivetti I-jet is gratefully acknowledged for designing and fabricating the used bio-chips. The research has been financially supported by the European Project FP6 DINAMICS. Anil Leblebici is also acknowledged for her help in revising the manuscript.

References

[1]. G. C. Kennedy, H. Matsuzaki, S. Dong, W. -M. Liu, J. Huang, G. Liu, X. Su, M. Cao, et al., Large-scale genotyping of complex DNA, *Nature Biotechnology*, Vol. 21, No. 10, 2003, pp. 1233–1237.

[2]. S. Mouterau, R. Narwa, C. Matheron, N. Vongmany, E. Simon, and M. Goossens, An improved electronic microarray-based diagnostic assay for identification of MEF mutations, *Human Mutation*, Vol. 23, No. 6, 2004, pp. 621–628.

[3]. P. K. Riggs, J. M. Angel, E. L. Abel, and J. Digiovanni, Differential gene expression in epidermis of mice sensitive and resistant to phorbol ester skin promotion, *Molecular Carcinogenesis*, Vol. 44, No. 2, 2005, pp. 122–136.

[4]. G. Mor, I. Visintin, Y. Lai, H. Zhao, P. Schwartz, T. Rutherford, L. Yue, P. Bray-Ward, D. C. Ward, Serum protein markers for early detection of ovarian cancer, *Proc. Natl. Acad. Sci*., 102, 2005, pp. 7677-7682.

[5]. S. Fredriksson, W. Dixon H. Ji, A. C. Koong, M. Mindrinos, R. W. Davis, Multiplexed protein detection by proximity ligation for cancer biomarkers validation, *Nature Methods*, 4, 2007, pp. 327-329.

[6]. J. S. Daniels, N Pourmand, Label-Free Impedance Biosensors: Opportunities and Challenges, *Electroanalysis*, 19, 2007, pp. 1239 – 1257.

[7]. V. M. Mirsky, M. Riepl, O. S. Wolfbeis, Capacitive monitoring of protein immobilization and antigen-antibody reactions on monomolecular alkylthiol films on gold electrodes, *Biosensors and Bioelectronics*, 12, 1997, pp. 977-989.

[8]. M. Riepl, V. M. Mirsky, I. Novotny, V. Tvarozek, V. Rehacek, O. S. Wolfbeis, Optimization of capacitive affinity sensors: drift suppression and signal amplification, *Analytica Chimica Acta*, 392, 1999, pp. 77-84.

[9]. C. Berggren, P. Stalhandske, J. Brundell, G. Johnansson, A Feasibility Study of a Capacitive Biosensor for Direct Detection of DNA Hybridization, *Electroanalysis*, 11, 1999, pp. 156-160.

[10]. C. Guiducci, C. Stagni, G. Zuccheri, A. Bogliolo, L. Benini, B. Samorì, B. Riccò, DNA detection by integrable electronics, *Biosensors and Bioelectronics*, 19, 2004, pp. 781–787.

[11]. A. Balasubramanian, B. Bhuva, R. Mernaugh, F. R. Haselton, Si-Based Sensor for Virus Detection, *IEEE Sensor Journal*, 1530-437, 2005, pp. 1-5.

[12]. A. Macanovic, C. Marquette, C. Polychronakos1 and M. F. Lawrence, Impedance-based detection of DNA sequences using a silicon transducer with PNA as the probe layer, *Nucl. Acids Res*., 32, 2004, pp. 1-7.

[13].I. Bontidean, J. Ahlqvist, A. Mulchandani, W. Chen, W. Bae, R. K. Mehra, A. Mortari, E. Csoregi, Novel synthetic phytochelatin-based capacitive biosensor for heavy metal ion detection, *Biosensors and Bioelectronics*, 18, 2003, pp. 547-553.
[14].C. A. Betty, R. Lal, D. K. Sharma, J. V. Yakhmi, J. P. Mittal, Macroporous silicon based capacitive affinity sensor—fabrication and electrochemical studies, *Sensors and Actuators B*, 97, 2004, pp. 334–343.
[15].C. Stagni, C. Guiducci, L. Benini, B. Riccò, S. Carrara, B. Samorí, C. Paulus, M. Schienle, M. Augustyniak, R. Thewes CMOS DNA Sensor Array With Integrated A/D Conversion Based on Label-Free Capacitance Measurement, *IEEE Journal of Solid-State Circuits*, 41, 2006, pp. 2956- 2964.
[16].C. Stagni, C. Guiducci, L. Benini, B. Riccò, S. Carrara, C. Paulus, M. Schienle, and R. Thewes A Fully Electronic Label-Free DNA Sensor Chip, *IEEE Sensors Journal*, 7, 2007, pp. 577-585.
[17].S. Carrara, F. K. Gürkaynak, C. Guiducci, C. Stagni, L. Benini, Y. Leblebici, B. Samorì, G. De Micheli, Interface Layering Phenomena in Capacitance Detection of DNA with Biochips, *Sensors & Transducers Journal*, Vol. 76, 2007, pp. 969-977.
[18].J. Lahiri, L. Isaacs, J. Tien, G. M. Whitesides, A Strategy for the Generation of Surfaces Presenting Ligands for Studies of Binding Based on an Active Ester as a Common Reactive Intermediate: A surface Plasmon Resonance Study, *Anal. Chem.*, 71, 1999, pp. 777-790.
[19].W. Y. Chen, W. P. Hu, Y. D. Su, A. Taylor, S. Jiang, G. L. Chang, A multispot DNA chip fabricated with mixed ssDNA/oligo, ethylene glycol, pp. self-assembled monolayers for detecting the effect of secondary structures on hybridization by SPR imaging, *Sensors and Actuators B*, 125, 2007, pp. 607–614.
[20].C. Stagni, C. Guiducci, M. Lanzoni, L. Benini, B. Riccò, Hardware- Software Design of a Smart Sensor for Fully-Electronic DNA Hybridization Detection, Proceedings of the Design, Automation and Test Conference, DATE05 3, 2005, pp. 198-203.
[21].Wei-Chih Chen, Ten-Chin Wen, Chin-Chang Hu, A. Gopalan, Identification of inductive behavior for polyaniline via electrochemical impedance spectroscopy, *Electrochimica Acta*, 47, 2002, pp. 1305-1315.
[22].S. Carrara, V. Bavastrello, D. Ricci, E. Stura, C. Nicolini, Improved nanocomposite materials for biosensor applications investigated by Impedance Spectroscopy, *Sensors and Actuators B*, Chemicals, 109, 2005, pp. 221-226.

Guide for Contributors

Aims and Scope

Sensors & Transducers Journal (ISSN 1726-5479) provides an advanced forum for the science and technology of physical, chemical sensors and biosensors. It publishes state-of-the-art reviews, regular research and application specific papers, short notes, letters to Editor and sensors related books reviews as well as academic, practical and commercial information of interest to its readership. Because it is an open access, peer review international journal, papers rapidly published in *Sensors & Transducers Journal* will receive a very high publicity. The journal is published monthly as twelve issues per annual by International Frequency Association (IFSA). In additional, some special sponsored and conference issues published annually.

Topics Covered

Contributions are invited on all aspects of research, development and application of the science and technology of sensors, transducers and sensor instrumentations. Topics include, but are not restricted to:

- Physical, chemical and biosensors;
- Digital, frequency, period, duty-cycle, time interval, PWM, pulse number output sensors and transducers;
- Theory, principles, effects, design, standardization and modeling;
- Smart sensors and systems;
- Sensor instrumentation;
- Virtual instruments;
- Sensors interfaces, buses and networks;
- Signal processing;
- Frequency (period, duty-cycle)-to-digital converters, ADC;
- Technologies and materials;
- Nanosensors;
- Microsystems;
- Applications.

Submission of papers

Articles should be written in English. Authors are invited to submit by e-mail editor@sensorsportal.com 6-14 pages article (including abstract, illustrations (color or grayscale), photos and references) in both: MS Word (doc) and Acrobat (pdf) formats. Detailed preparation instructions, paper example and template of manuscript are available from the journal's webpage: http://www.sensorsportal.com/HTML/DIGEST/Submition.htm Authors must follow the instructions strictly when submitting their manuscripts.

Advertising Information

Advertising orders and enquires may be sent to sales@sensorsportal.com Please download also our media kit: http://www.sensorsportal.com/DOWNLOADS/Media_Kit_2008.pdf