

DNA CAPACITIVE SENSOR

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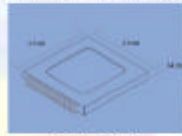
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The development of DNA-Sensors technologies is the most innovative branch of the molecular biology because these devices allows an easy, fast and reliable way to analyze many samples at the same time. At this purpose we're developing an innovative technology, patented by Technobiochip⁽¹⁾, based on nucleic acids dielectric capacitance measurement in order to reveal their presence or to evaluate their structural features. We use a commercial micro-fabricated array of capacitors developed for fingerprint recognition (Veridicom Inc., Santa Clara, CA). The device consists of a silicon chip containing 90.000 capacitor plates with sensing circuitry at 500-dpi pitch. The overall sensor size is 24 X 24 mm and its surface is covered by an inert glass layer.



Veridicom Fingerprint Sensor



Sensor size



TB TIP



Microscopy Image of sensors array

The presence of conductive material on the inert layer surface effectively created a two capacitors system, connected in series by a resistor formed by the conductive material itself. Under each capacitor is located an independent capacitance-measuring microcircuit (schematized in Figure 1) that return a value (grayscale) from 0 to 255. Technobiochip has developed a software that allows a differential measure between the reference and working samples in few seconds. Each image pixel depends from the capacitance value measured by a single sensor, to which is assigned a different color according to its magnitude (Fig. 2).

Technobiochip application exploits this array for the dielectric capacitance measurement of a solution containing DNA deposited on the sensor surface.

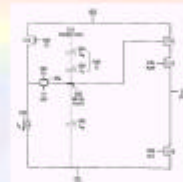
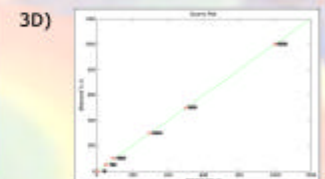
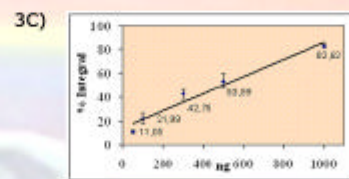
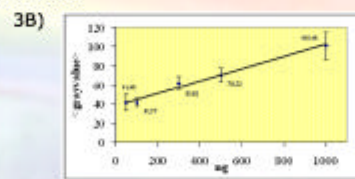
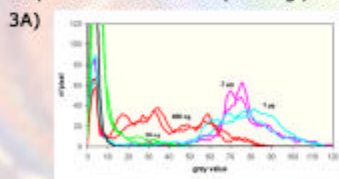


Fig. 1 Single-sensor equivalent circuit



Fig. 2 TB TIP Software

In this work we demonstrate the sensor ability to discriminate among different DNA concentrations. At this purpose a scale-down experiment was performed, in which DNA solution drops (from 2 µg to 20 ng, solubilized in 1 µl) were deposited directly on the sensor surface. Each time we included a drop of solubilization buffer as negative control. The Technobiochip software generates a peak-shaped curve in which the pixel number is graphicated vs each value (an example is shown in Fig. 3A). The data are further elaborated and the results are shown in Fig. 3B-3C: it is evident an response increase corresponding to the DNA concentration increase. The same data are elaborated by multivariate analysis PLS (Partial Least Square): in Fig. 3D are graphicated the sensor responses vs the corresponding predicted ones.

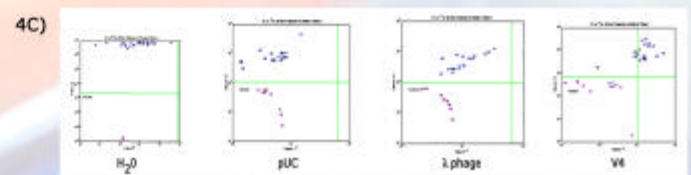
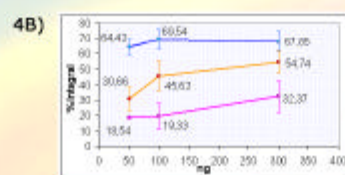
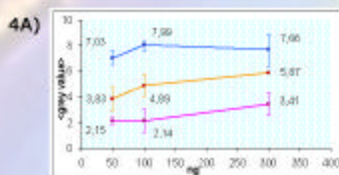


In 3A) an example of peak shaped curve obtained by the software is shown. The experiment is performed twice within the range 2 µg-20 ng utilizing 1 µl drops. The black line represents the negative control. In 3B) and 3C) are reported the mean sensors response (grayvalue) and the % Integral of the curve respectively, versus the DNA quantity (average of 10 repetitions).

$\text{grayvalue} = \sum n_i / \sum n_i$; where n_i is the number of pixel with a specific response i .
 $\% \text{ Integral} = \% \text{int} / (I_{\text{max}} - I_{\text{min}})$; where int is the curve integral and $(I_{\text{max}} - I_{\text{min}})$ represents the significant response range.
 In 3D) the PLS elaboration is graphicated, validated by "leave-one-out" method.

In another set of experiments we demonstrated the sensor ability to discriminate between different kinds of DNA. In particular we compared plasmidic DNA (small circular DNA molecules, characteristic of bacterial microorganisms), phagic DNA (virus characteristic DNA), and oligonucleotides (23-mer).

The results show a significant shift of the relative curves and indicate the possibility to recognize the corresponding DNA class. The SIMCA multiparametric method provides a prediction model for each kind of DNA (Fig. 4).



In Fig. 4 the sensor ability to discriminate among three different DNA kinds is shown: plasmidic DNA (blue lines), phagic DNA (orange lines), and oligonucleotides (pink lines). In 4A) e 4B) the mean sensors response (grayvalue) and the % Integral of the curve respectively are reported versus the DNA quantity. In 4C) the SIMCA elaboration is graphicated.