Lab on a Chip

COMMUNICATION

Doping of a dielectric layer as a new alternative for increasing sensitivity of the contactless conductivity detection in microchips†

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This communication describes a new procedure to increase the sensitivity of C⁴D in PDMS/glass microchips. The method consists in doping the insulating layer (PDMS) over the electrodes with nanoparticles of TiO₂, increasing thus its dielectric constant. The experimental protocol is simple, inexpensive, and fast.

Hybrid PDMS/glass microchips represent a potential alternative for producing miniaturized analytical systems.[1,2] This kind of a microfluidic platform is advantageous because polymeric microchannels can be easily fabricated by soft lithography and reversibly or irreversibly sealed against a flat plate of glass containing other integrated analytical elements like electrodes.[3] Furthermore, PDMS/glass microchips exhibit good inter-assay precision (chip-to-chip reproducibility).[4] In microfluidic devices, capacitively coupled contactless conductivity detection (C⁴D) has proven to be an useful tool for determination of a wide range of compounds, including biomolecules,[5–9] organic,[10–12] and inorganic ions.[13–17] Recently, C⁴D was also used in the characterization of stationary phases.[18,19] This detection method has appreciable advantages such as instrumental simplicity, low cost, and high compatibility with miniaturization techniques.[15]

In C⁴D measurements, the electrodes are physically separated from the electrolyte solution by a dielectric layer (see Fig. S1†).[20] The noncontact mode between the electrode and the solution avoids a number of problems often found with conventional conductometry (contact-mode) and faradaic electrochemical methods, including contamination and passivation of the electrodes, effects of non-reproducibility of the surface, and electrical interference between the detector circuit and the separation field applied in capillary electrophoresis.[21,22] Probably, the main limiting factor reported for the C⁴D system is its poor limit of detection (LOD). Some alternatives to improve the

LOD for this technique have been previously published, as: (i) the application of high voltage excitation signals (hundreds of volts),[23] (ii) the use of a ground plane to reduce the stray capacitance,[23] (iii) the design of semicircular electrodes[14] and (iv) dual top-bottom electrodes,[17] (v) new materials used as dielectric,[24] (vi) hybrid conductivity detection in which the excitation electrode is kept in contact with the solution,[25] as well as (vii) new detection cell geometries.[26]

Considering the advantages of C⁴D and its wide use in analytical applications, this communication describes a simple approach to increase the normally deficient sensitivity (expressed in term of LOD) of this detection system on hybrid PDMS/glass microchips (but not limited to this combination). Our approach consists in doping the insulating membrane (PDMS) over the electrodes with nanoparticles of TiO₂ (NP–TiO₂) to increase its dielectric constant. The theoretical basis of the method relies on raising the magnitude of dielectric constant of the PDMS membrane by adding NP–TiO₂; in consequence, the C⁴D signals are increased as discussed in the ESI†. The use of semiconductors for increasing the conductivity of dielectrics is already adopted in the fabrication of flexible materials for high-density energy storage in capacitor applications.[27–29] Finally, since our intent was just to study the effect of the doping on C⁴D sensitivity, the LOD values were estimated for microchips presenting the same configuration and incorporating different levels of NP–TiO₂. Additionally, the same experimental conditions were employed in all cases.

The fabrication of the proposed devices involved five main steps: (i) sputtering deposition of the electrodes (Ti/Au) on glass; (ii) addition of NP–TiO₂ in different percentages (0, 10, 25, and 50% m/m to PDMS) during the PDMS preparation using its monomer and curing agent (PDMS$_d$); (iii) electrical isolation of the electrodes using a PDMS$_d$ dielectric membrane deposited by spinning, followed by the polymer curing; (iv) fabrication of PDMS microchannels by soft lithography; and (v) irreversible sealing of the glass/PDMS$_d$/PDMS device. More details about the steps (i), (iv), and (v) can be found in ref. 2. PDMS was adopted as a dielectric because it facilitates the sealing step, achieved by simple contact among the layers after oxidation of the PDMS$_d$ and PDMS surfaces in O₂ plasma.[30] Regarding the deposition of PDMS$_d$ membranes, these were coated on glass by spinning at 1000 rpm during 10 s. Afterwards, the curing step was performed at 90 °C for 5 min resulting in 50 μm thick PDMS membranes. Fig. 1 shows the device scheme constructed in three-layers (Fig. 1a) and a photograph of the resulting device (Fig. 1b), which presented two receiver electrodes, e$_{r1}$ and e$_{r2}$. The use

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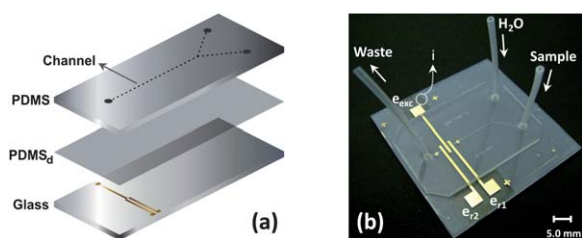
Fig. 1 Expanded view of the layers composing the microfluidic device (a) and a photo of the microchip (b) containing PDMS doped ($PDMS_d$) with NP–TiO_2 1% m/m (this percentage was selected because it allows for the visualization of the electrodes; levels of NP–TiO_2 above 5% m/m make the $PDMS_d$ membrane opaque). e_{exc}, excitation electrode; e_{r1} and e_{r2}, receiving electrodes; and i, glass/$PDMS_d$ interface.

of either e_{r1} or e_{r2} did not alter the analytical responses; e_{r2} was employed during the sensitivity measurement.

A field-emission gun scanning electron microscopy (SEM-FEG) micrograph of the NP–TiO_2 is depicted in Fig. 2, the diameter of the nanoparticles ranged between 30 and 45 nm. The evaluation of the roughness parameters of the surfaces of the dielectric layer, in turn, involved the (i) root mean square (RMS, statistical measure of the magnitude of a varying quantity) and the (ii) surface area ratio (S_{ar}, increment of the interfacial surface area relative to the area of the projected x, y plane). Fig. 3 shows atomic force microscopy (AFM) images obtained for $PDMS_d$ membranes doped with 0, 10, 25, and 50% of NP–TiO_2. As verified in this figure, the addition of increasing levels of NP–TiO_2 generated surfaces with roughness and an area greater than the native PDMS, as expected. On the other hand, the doping of the PDMS membranes did not lead to an appreciable lowering of its ohmic resistance; all the electrodes remained electrically insulated from solution with increasing levels of NP–TiO_2 (Fig. S2†), ensuring conductivity measurements under contactless-mode.

Flow analyses were carried out in order to assess the effect of the doping process on the C^4D sensitivity. The device has two inlets and one outlet (for waste) vias. Conductivity measurements were carried out in real time while either water or analyte solution was flowing through the microfluidic channels, driven by two external syringe pumps. First, water was circulated for approximately 10 min for the signal stabilization. Once a stable signal was obtained, samples were introduced generating a potential change on the receiving electrode. Next, water was added resulting in a decrease of the signal nearly to its initial value. The analytical responses recorded in this study were associated to the signal difference after stabilization of the signal from the sample and its baseline (water) values. The experimental conditions for all microchips in the sensitivity tests were: 20 s salt-injection
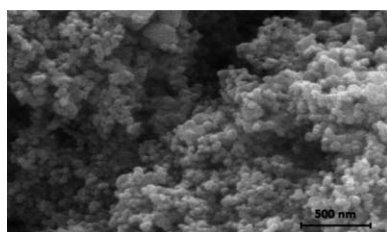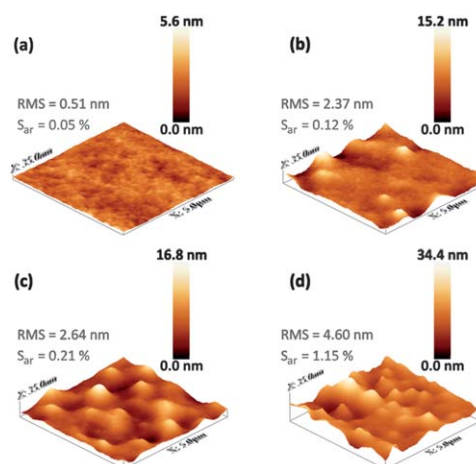

Fig. 3 Images of atomic force microscopy recorded for the $PDMS_d$ membranes containing 0 (a), 10 (b), 25 (c), and 50% m/m of NP–TiO_2 (d). In each case, the RMS and S_{ar} values are specified.

time; 1.0 mm for electrode width and spacing; Y-shaped microfluidic channels (see Fig. 1) presenting 250 μm width and 50 μm depth; 100 μL min^{-1} flow rate; 400 kHz frequency; and peak-to-peak potential equal to 2.5 V_{p-p}. The LOD values were determined using standard solutions of NH_4Cl (diluted in water) and calculated based on the parameters of the analytical curve at 95.0, 99.0, and 99.9% confidence levels. This method presents higher statistical reliability compared to the other techniques (either visual or the signal/noise ratio) because it does not relate to qualitative factors, but to the confidence interval of the regression.[31] We performed five measurements for each concentration level.

Fig. 4 shows the analytical responses obtained for each $PDMS_d$ membrane using NH_4Cl standards used for the calculation of LOD; the calibration curves are shown in Fig. S3a†. The analysis of residues and F test for linearity validated the linear fit for all calibration curves.[31] LOD values calculated for each doping level were: 385.5 (0%), 269.9 (10%), 144.8 (25%), and 14.7 μmol L^{-1} (50% of NP–TiO_2). There was a noticeable reduction in the LOD values with increasing levels of NP–TiO_2, as well as an increase in analytical

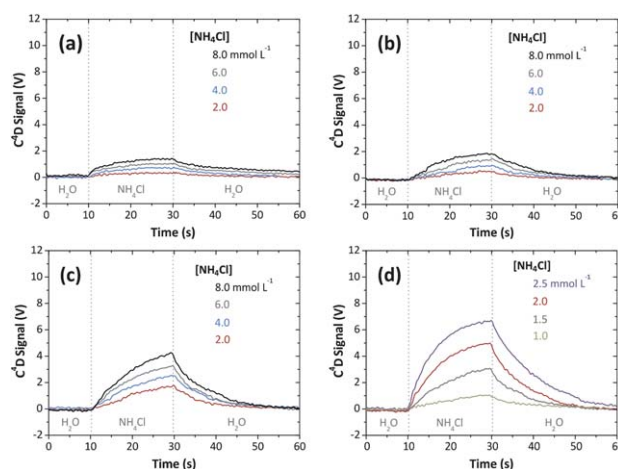**Fig. 2** Image of field-emission gun scanning electron microscopy of the NP–TiO_2.

Fig. 4 Transient signals of C^4D obtained for NH_4Cl standards for the following doping percentages: 0 (a), 10 (b), 25 (c), and 50% m/m (d) of NP–TiO_2 in $PDMS_d$ membranes.

sensitivity (slope of the calibration curves) as shown in Fig. S3b†. Such results ensure our initial goal of developing a method to improve the sensitivity in C⁴D microchips, given that all parameters were kept the same. The improvement was over 25 fold when comparing 0 to 50% doping level. Regarding the 0 and 10% of NP–TiO₂, in turn, this improvement was nearly 2 fold. On the other hand, it is important to highlight that the absolute values of LOD can be further improved combining other alternatives already reported in the literature, including: (i) improved electronic circuitry for reduction of the baseline noise;[32] (ii) Faraday shield between the electrodes to reduce the stray capacitance;[23] and (iii) application of higher amplitudes to the excitation electrodes.[23]

The PDMS used in this study has a ε value of 2.65 (25 °C, 1 kHz),[33] while the TiO₂ possesses the following properties: the rutile crystalline state[34] and ε equal to 86.00 (25 °C, 1 kHz).[35] Mixture laws reported in the literature permit the dielectric constant of composites (PDMS$_d$/NP–TiO₂ in this study) with those of its pure constituents to link.[36] Among these laws, the Looyenga law is derived from a model consisting of spherical particles,[37] being applicable to the PDMS$_d$/NP–TiO₂ given the spherical shape of these nanoparticles (see Fig. 2). This model is widely applied in the literature.[36,38,39] Applying the Looyenga law, ε values for PDMS$_d$ doped with 10, 25, and 50% in NP–TiO₂ were calculated. Fig. 5 presents LOD values and C⁴D signals as a function of ε. The considered responses were obtained for the same NH₄Cl concentration (2 mmol L⁻¹), used to ensure a constant conductance in all cases and, thus, a direct dependence of the signal regarding the capacitance.

Concerning the variation of the C⁴D response as a function of ε, the linear behaviour verified is in concordance with the theoretical considerations described in the ESI†. Once the electrodes used in this study had the same dimensions and geometry, the microchips differed only in terms of the surface area of the dielectric (Fig. 3) and ε as the intervenient factors in the capacitance. The increase in the surface area of the PDMS membranes for higher doping levels tends to increase the number of charge carriers generating higher conductance values.[40] Nevertheless, as confirmed by the analysis of residues and F test, the analytical signals and dielectric constants exhibited a linear relationship so that, presumably, the variations in the area were not sufficient to affect the C⁴D responses. The effect of the area of the

surface, if significant, would result in a positive deviation in the C⁴D signal vs. ε curve.

As seen in Fig. 4, the noise was uniform for all systems, thus contributing equally to the calculation of LOD. Therefore, we can assume that the variation of the LOD values as a function of ε, which decreased asymptotically, is attributed to the non-linear increase of the analytical sensitivity (see Fig. S3b†).

A new strategy for increasing the C⁴D sensitivity in glass/PDMS hybrid microchips is reported here. This strategy, which consists primarily in raising the dielectric constant of the insulating layer, involved an experimental protocol that is simple, inexpensive, and fast. Moreover, the addition of increasing levels of NP–TiO₂ did not affect the PDMS curing step, and proved to be effective regarding the increase in sensitivity for C⁴D. In further investigation, other doping percentages, dopant substances (conductors and semiconductors), dielectrics, and thickness of insulation of the electrodes may be investigated aiming for a more significant increase in sensitivity. This research field is very important concerning the instrumental chemical analyses; since presenting satisfactory LODs, C⁴D will become a competitive alternative to the faradaic electrochemical methods, in which the electrode/solution interactions generate a number of drawbacks. In this context, the contactless conductivity detection represents an attractive tool for various purposes and matrices employing, for example, titrations, capillary electrophoresis, or chemical sensors. Finally, by using different dielectrics, dopants, and doping methods, it is important to note that the described approach can be extended to other microfluidic platforms, like glass/PMMA, glass/glass, among other possibilities.

Fig. 5 Effect of the doping of the PDMS insulating layer on the detectability in C⁴D considering the LOD values and signals obtained for NH₄Cl 2 mmol L⁻¹. The dielectric constants are related to the doping levels of 0, 10, 25, and 50% m/m of NP–TiO₂ in PDMS$_d$ membranes, shown in the top axis.

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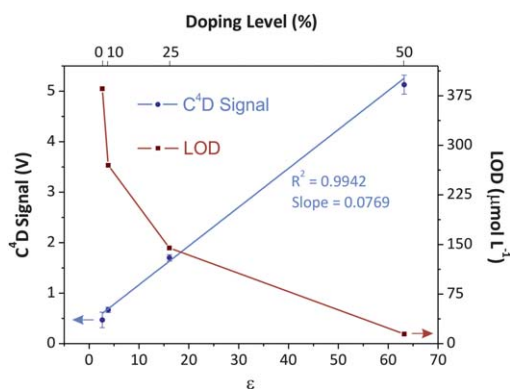
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