Supplementary information

Memristive Effect as a Novelty in Drug Monitoring

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The "in-dry" measurement concept

When performing measurements in liquid conditions the Debye length may potentially mask the sensing outcomes in some cases, for instance for extremely low sample concentrations, a phenomenon known as Debye screening limitation.

For this reason, in the present work, this issue is taken into great consideration and all measurements are performed not-in liquid but in air, following a novel paradigm of detection via measurements in dry conditions, under controlled relative humidity, where the sample is thoroughly dried after the exposure to the target reagent, and only an ultra-thin layer of water formed by the ambient humidity is present and in high proximity to the nanowire surface.

Therefore, although the sensors are dried after bio-modification and cleaning steps, the nanosensor surface is never completely dry, allowing the sound condition of the proteins and the stable and proper interactions of the probe-target molecules system. Since the electrical characterization is performed in dry conditions there is a negligible Debye layer formation and the set-up is in the framework of Surface and Stern layers, namely at planes before the slipping plane. In addition, considering that, the Debye length is negligible consequently, the zeta-potential is negligible as well, and, therefore, in the suggested set-up the potential of interest is the surface potential and its variations.

The role of the ambient humidity

In order to ensure a proper control over the experimental conditions, the relative humidity (rH%) is continuously monitored. The higher the rH% in the treatment area the more hydroxyl groups are introduced on to the surface of the sensor, inducing perturbations to the conductivity of the device's channel, affecting in great deal the memristive signals and the obtained hysteresis. The charges of water molecules act on the virtual gate voltage similarly to those of charged chemical and biological species affecting the memristive behavior of the nanodevices.

The effect of varying rH% conditions on the electrical response of the nanodevice is intensively studied for bare nanostructures directly after the fabrication process. The rH% monitoring is performed using feedback from a Rotronic HC2-C04 Thermo-Hygrometer tool, while varying the environmental humidity in the measurement chamber. The Rotronic HW4 tool provides an accurate control of rH% of the measurement environment. A wet towel is introduced into the measurement chamber in order to raise the humidity, while Sodium Chloride ACS reagent, 99.0%, (Sigma- Aldrich - S9888) is used to achieve lower humidity values. Before the measurement procedure, a waiting time of 2 h is necessary in order to establish stable environmental conditions in the measuring chamber. In addition, before each individual measurement, a waiting time of 5 min to 20 min is necessary for regaining the equilibrium of the environmental conditions. Unstable rH% conditions during the measurements result to the introduction of significant noise to the electrical characteristics of the sensing devices, altering the electrical readout, and may ultimately inhibit the bio-detection mechanism. Indicative results for the average voltage gap value obtained by bare nanostructures in different rH% windows are shown in figure S1. Each voltage gap point represents the mean value of the voltage gap values obtained by the electrical characterization of a set of multiple single devices.

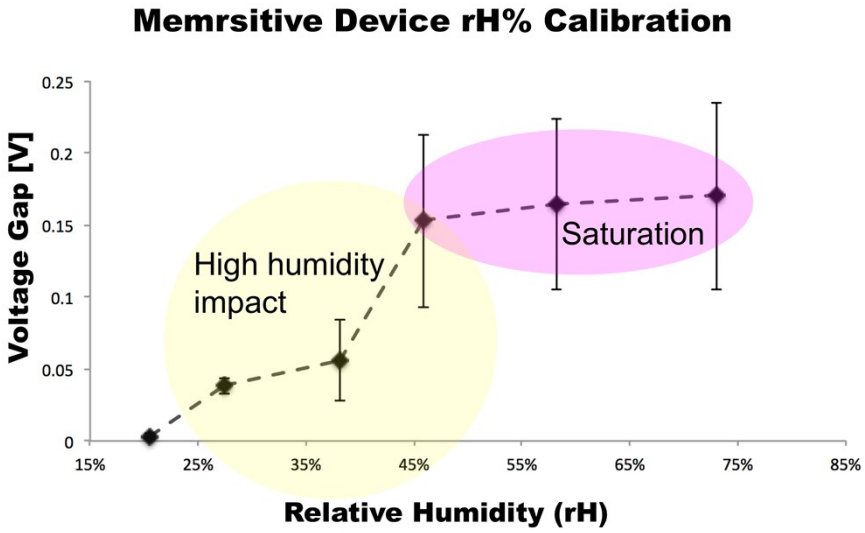

Figure S1. Memristive Device rH% Calibration: Average voltage gap value exhibited by non- bio modified nanostructures just after the fabrication process tested under different rH % windows.

Step-by-step preparation and measurements of TVF drug with memristive aptasensors.

The Electrical characteristics of memristive aptasensor for a systematic (step-by-step) preparation and measurements of TVF drug at different concentration is presented in the following figure.

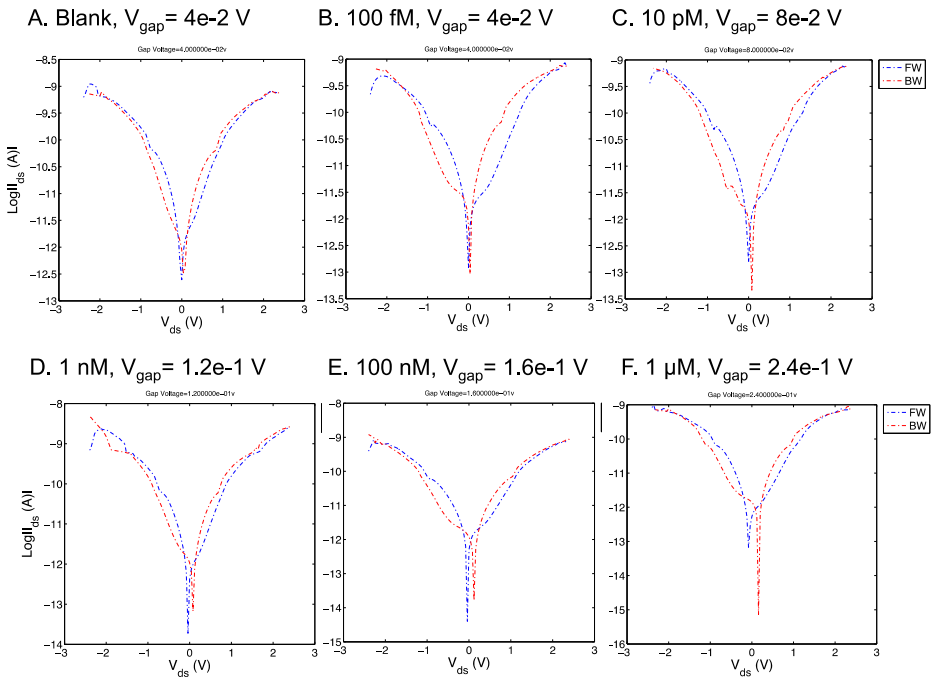

Figure S2. Electrical characteristics of memristive aptasensor: recorded signal in each step of in-serum TFV detection. The measured data for 9 individual Si-NWs were averaged and demonstrated as dose-response curve in figure 3b.

LOD calculation

The method of Armbruster et al.[1] has been employed to analyse the dose-response curves fitted to nonlinear functions, and to calculate the corresponding LOD:

First, the highest distinguishable blank measurement response (LOB) and, consequently, lowest measurable response ($LOD_{\Delta V}$) were calculated using Equations 1 and 2,[1] and then $LOD_{\Delta V}$ was converted to concentration, using the relevant fitting equations.

$$LOB = mean_{blank} \pm 1.645(SD_{blank}) \quad (1)$$

$$LOD_{\Delta V} = LOB \pm 1.645(SD_{lowest-concentration}) \quad (2)$$

Where, $mean_{blank}$ is the average of blank measurements SD_{blank} is the standard deviation of blank measurements, and the last parameter, $SD_{lowest-concentration}$, is the standard deviation of the lowest concentration after blank measurement.

For in-buffer monitoring, $mean_{blank} = 0.048\,V$, $SD_{blank} = 0.0179\,V$, $LOB = 0.077\,V$, and $LOD_{\Delta V} = 0.11$ for 9 different Si-NWs tested in this work. Inserting this in fitting equation of Figure 3-a gives a LOD=3.09 pM.

For in-serum monitoring, $mean_{blank} = 0.05\,V$, $SD_{blank} = 0.0355\,V$, $LOB = 0.108\,V$, and $LOD_{\Delta V} = 0.17$ for 9 different Si-NWs tested in this work. Inserting this in fitting equation of Figure 3-b gives a LOD=1.38 nM.

Positive and negative control

The regeneration and subsequent detection of 1 nM TFV (specific target) and Enzalutamide (non-specific target) after obtaining the dose-response curve in human serum confirmed the validity of data and reproducibility of regeneration.

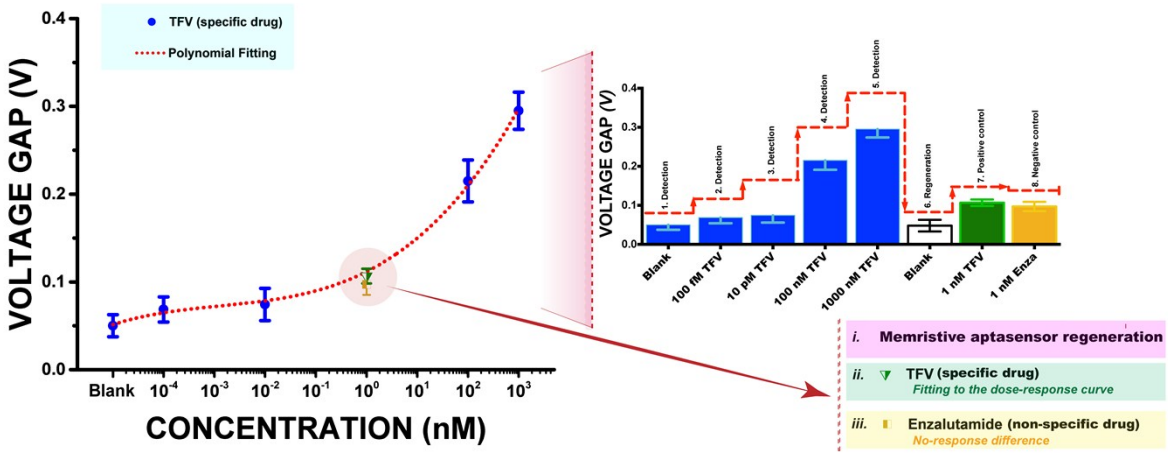

Figure S3. Positive and negative control for in-serum TFV monitoring: the regeneration of biosensor after detection of 1000 nM TFV in human serum (white bar). Detection of 1 nM TFV after regeneration that coincides with the observed dose-response curve as positive control (green bar). Detection of 1 nM Enzalutamide (Enza) without any regeneration as negative control (yellow bar).

References

1D. A. Armbruster and T. Pry, *Clin Biochem Rev*, 2008, **29**, S49–52.