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Creating aptamers and their use in Resistive Pulse Sensors

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Abstract

Resistive pulse sensors, RPS, are allowing the transport mechanism of molecules, proteins and even nanoparticles to be characterized as they traverse small channels. Here we present our recent advancement of the technique identifying key experimental designs for potential POC assays. The first assay utilized superparamagnetic beads, if the surfaces of the beads are modified with an aptamer, the frequency of beads (translocations/minute) through the pore can be related to the concentration of specific proteins in the solution. Herein, we have demonstrated the successful use of TRPS to observe the binding of two proteins, to their specific aptamers simultaneously. We then adapt the measurement strategy and demonstrate that the translocation times of particles can be used to infer the zeta potential to measure the change in zeta potential of DNA modified particles. By measuring the translocation times of DNA modified nanoparticles as a function of packing density, length, structure, and hybridisation time, we observe a clear difference in zeta potential using both mean values, and population distributions as a function of the DNA structure. Finally we present the first comparison between assays that use resistive pulses or rectification ratios on a tunable pore platform.

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1. Main text

One of the more recent technologies to implement aptamers is Tunable Resistive Pulse Sensing \(^1\)\(^-\)\(^7\) (RPS) which uses a polyurethane elastomeric membrane in which the pore is able to be mechanically manipulated in real time to alter pore geometry. In brief, the set up and theory for TRPS technologies is as follows: a stable ionic current is established by two electrodes, separated by a pore; as beads/analytes translocate the pore they temporarily occlude ions, leading to a transient decrease in potential known as a “blockade event”, by monitoring changes in full width

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half maximum (FWHM), peak magnitude ($\Delta i_p$) and peak frequency (events/min) it is possible to elucidate the zeta potential, size, and concentration of colloidal dispersions in situ, figure 1a, b.

1.1 Zeta potential measurements

The methodology for measuring zeta potential using RPS is based upon a similar concept that was published by Arjmandi et. al. using pyramidal pores. In brief, a calibration based zeta potential method is applied, based on the measurement of signal durations of translocation events as a function of voltage. The electrophoretic mobility is calculated from the derivative of medium particle velocity and applied electric field. The zeta potential of each particle can then be obtained from the measured electrophoretic mobility using the Smoluchowski approximation. We have demonstrated that TRPS can successfully detect and characterize both unmodified and DNA-modified particles in a single, real-time measurement, figure 1c. Charge distributions, rather than a single mean zeta potential value allow for more information to be extracted from a sample dataset using a particle-by-particle perspective.

![Figure 1a) Particle rate versus VEGF concentration with (white box) and without (blackbox) PDGF protein in solution. b) Particle rate versus PDGF concentration with (white box) and without (blackbox) VEGF protein in solution. c) Zeta potential versus particle size of streptavidin beads (green) and DNA modified particles, (blue). d) Schematic of the pore wall modification for current rectification studies and the typical signal.](image)

1.2 Current rectification

Finally we present the first comparison between assays that use resistive pulses or rectification ratios on a tunable pore platform. We compare their ability quantify the cancer biomarker Vascular Endothelial Growth Factor (VEGF). The first assay measures the electrophoretic mobility of aptamer modified nanoparticles as they traverse the pore. By controlling the aptamer loading on the particles surface, and measuring the speed of each translocation event we are able to observe a change in velocity as low as 18 pM. A second non-particle assay exploits the current rectification properties of conical pores.

References