Detecting and Characterizing Biological Reactions Using Nanopore Resistive Pulse Sensing

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Abstract

The prospect of using nanopores for bio-sensing purposes carries significant advantages. For instance, compared to other current types of biosensors, such as the commonly used immuno-sensors that rely on antibody and antigen interactions, nanopores require less material investment and do not require the use of possibly intrusive biochemical labels. This study attempted to demonstrate how nanopore-based biosensors could successfully detect biological reactions using nanopore resistive pulse sensing. Resistive pulse sensing is a technique used to detect and distinguish individual particles in fluid. It functions on the basis that a single particle moving through a pore while suspended in conductive fluid will cause a unique change in the electrical resistance of the pore. Various aspects of the translocating nanoparticle can be gathered by analyzing the attributes of this change in current. An effort was made to use nanopore resistive pulse sensing to detect and differentiate 100 nm polystyrene nanoparticles coated with streptavidin from the same particles with the addition of biotin bound to them. However, the streptavidin nanoparticles used had a tendency to aggregate due possibly to the fact that streptavidin possesses the ability to bond with multiple other particles. Not only did this result in a large distribution of particle sizes which made it very difficult to associate a unique sensory signal with a specific type of nanoparticle, the aggregated masses also frequently clogged the nanopores, impeding efforts to successfully collect usable data. Future progress will be greatly facilitated by the use of alternative nanoparticles or the creation of a method to keep the currently used nanoparticles from aggregating.

Methodology

Figure 2: Nanopore Device (Chip)

Figure 3: Experimental Setup

Figure 4a: Translocation signals of 100 nm PS-COOH

Figure 4b: Single translocation event of 100 nm PS-COOH

Figure 5: Single blockage event of 100 nm PS-COOH (notice permanent change in current rather than momentary dip observed in Figure 4b)

Figure 6: Results of successful translocation experiment of 100 nm PS-COOH

Results

Discussion

Results with 100 nm PS-COOH:

- Managed to successfully translocate 100 nm polystyrene particles modified with carboxyl (PS-COOH) through nanopores.
- Data recorded from the experiments (displayed in Figure 6) allows for the determination of size and concentration of the nanoparticles.
- However, the polystyrene modified with carboxyl was only a positive control since it did not serve as a reactant for a suitable to be studied reaction.

Results with 100 nm PS-SP:

- Streptavidin coated polystyrene (PS-SP) was supposed to be the main particle used in the actual experiments since it reacts with biotin particles.
- The reaction between streptavidin and biotin induces a change in the surface charge of the particle, which was what was supposed to be detected.
- Unfortunately, the streptavidin nanoparticles had a tendency to aggregate, leading to a wide variety of particle sizes and, more importantly, blockage of the nanopore (as seen in Figure 5), preventing further collection of usable data.

Conclusion

- Successfully detected translocation of 100 nm polystyrene particles modified with carboxyl.
- Failed to detect translocation of 100 nm streptavidin coated polystyrene particles due to aggregation of said particles.
- Therefore, will not be able to continue until aggregation issue is resolved.

References


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Background

Nanopores as Biosensors:

- Biosensors are any type of device that is used to detect the presence or concentration of a biological analyte.
- Immuno-sensors are an example of the capabilities and limitations of currently available biosensors.
- Nanopores offer advantages such as being label-free and high throughput while having low material requirement.

Resistive Pulse Sensing (RPS):