Spherical Virus Detection Using Nanoscale Capillaries

Oliver G. Isik & Derek Stein | Stein Nanobiophysics Lab, Brown University Dept. of Physics

Project Objective

Nanopores are sensors used to detect DNA and, more recently, filamentous viruses by measuring electrical current across the nanopore. They have not been used to detect small, spherical viruses, such as those in Figure 1, despite how useful that could be. The difficulty with spherical viruses is that they move quickly and are difficult to detect. This project explores an improved approach to detecting spherical viruses.

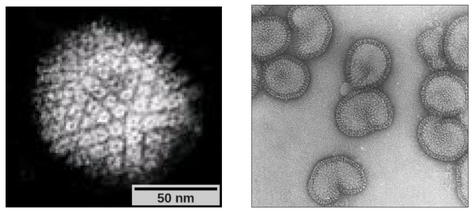

Figure 1: Herpes Virus (left) and Rauscher Leukemia virus (right).

Theory

Spherical viruses prove difficult to detect, mainly for two reasons:

- They are small (100 nm or less).
- They move quickly through a thin pore.

Particles spend less than 10 μs in the nanopores, and their signals are hard to distinguish from noise. Our strategy involves lengthening the nanopore to extend time particles spend inside it; see Figure 2.

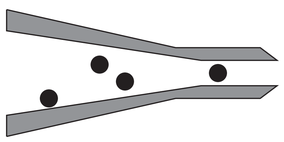

Figure 2: Schematic of capillary with spherical particles inside.

To detect viruses using nanopores, a voltage is applied across the nanopore, creating a current according to Ohm's Law: $V = IR$.

The presence of a resistive spherical particle decreases the current by an amount dictated by capillary and particle size.

For a 150 nm wide nanopore, a particle diameter of 110 nm, and capillary length 3 μm, $\Delta I/I \approx 1.9\%$.

The particle's motion is controlled through the following physical phenomena:

1. Electro-osmosis. $v \propto -\Delta V$.
2. Electrophoresis. $v \propto \Delta V$.
3. Poiseuille Flow. $v \propto \Delta P$.

Preliminary Results

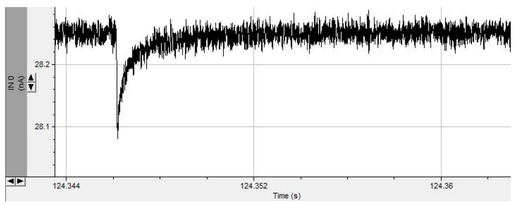

Figure 6: Change in current indicating passage of a nanosphere. Solution: 1 M KCl / 10 mM Tris; pH 10, $\sigma = 10.7$ S/m. Nanospheres at 1.6×10^{11} particles/mL. $\Delta I = 0.16$ nA for $\Delta I/I = 0.56\%$; expected $\Delta I/I = 0.7\%$ for this capillary.

Figure 6 shows the change in current caused by a 100 nm silica nanosphere inside the capillary. The immediate drop and gradual rise of current indicates passage first through the narrowed tip of the capillary, then through the widened end.

Other detections have been made, but signals are very difficult to distinguish from noise, either due to low ΔI, high signal frequencies, or too short passage time.

Apparatus and Experimental Design

This experiment uses hollow glass capillaries. We heat and pull them apart to create 1–5 μm long pores; see Figure 3.

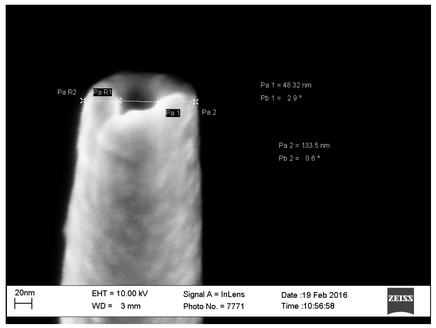

Figure 3: Image of 150 nm capillary tip under electron microscope.

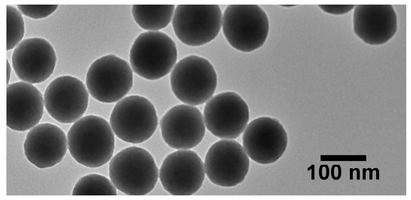

Figure 4: Electron microscope image of 110 nm silica nanospheres used for testing the nanocapillary sensors.

In preparing an experiment, the capillaries are first plasma cleaned. The salt solutions, ranging from 0–2 M KCl at various pH levels, are bath sonicated and filtered.

To test the apparatus, we use 110 nm silica nanospheres, shown in Figure 4.

We designed and fabricated a fluidic cell for this project, shown in Figure 5. The capillary is secured between two salt solution baths with inserts for electrodes on either end. On one end, a membrane separates the solution from a pressure insert. The cell is placed in a Faraday Cage to prevent any electrical interference.

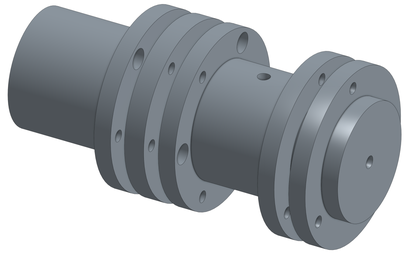

Figure 5: Fluidic cell used for holding capillary, salt solution, electrodes, and pressure inserts.

Concluding Remarks

- Spherical virus detection proves more difficult due to the decreased time particles spend inside the nanopore; by making pores longer, we hope to counter this problem.
- We have designed a new apparatus to better control pressure and voltage across an extended nanopore.
- Preliminary tests show some detection while highlighting bizarre behavior remaining to be explained.

Next Steps: We are about to move on to biological molecules, and will re-optimize pressure, voltage, salt concentration, and pH accordingly.

References

[1] L. Bocquet and E. Charlaix, "Nanofluidics, from bulk to interfaces", Chemical Society Reviews **39**, 1073–1095 (2010).

[2] C. Dekker, "Solid state nanopores", Nature Nanotechnology **2**, 209–213 (2007).