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Characterization of liposomes and silica nanoparticles using resistive pulse method

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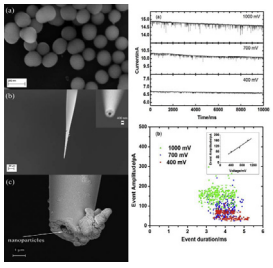
HIGHLIGHTS

- New technique for simultaneous nanoparticles size and velocity measurements is proposed.
- Show size distribution of 40 nm and 90 nm in radius SiO_2 nanoparticles and 40 nm liposomes.
- Measurements of electrophoretic velocity of 40 nm and 90 nm SiO_2 nanoparticles presented.
- Different particles concentrations were examined.

GRAPHICAL ABSTRACT

We demonstrated a novel approach to simultaneously measure electrophoretic velocity and size distribution of organic and inorganic colloids in a size range 40–200 nm. This precise and accessible, single particle resolution technique is a promising alternative to dynamic light scattering and laser doppler velocimetry.



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ABSTRACT

The ability to precisely count inorganic and organic nanoparticles and to measure their size distribution plays a major role in various applications such as drug delivery, nanoparticles counting, and many others. Here we employ a simple resistive pulse method that allows translocations, counting, and measuring size and velocity distribution of silica nanoparticles and liposomes with diameters from 50 nm to 250 nm. This technique is based on the Coulter counter technique but has nanometer size pores. It was found that ionic current drops when nanoparticles enter the nanopore of a pulled micropipette, producing a clear translocation signal. Pulled borosilicate micropipettes with opening 50–350 nm were used as the detecting instrument. This method provides a direct, fast and cost-effective way to characterize inorganic and organic nanoparticles in a solution.

1. Introduction

Size plays an important role in the properties of nanoparticles [1,2]. The ability to determine the size distribution and concentration of nanoparticles are extremely useful in numerous applications [3,4]. Traditionally, determination of the size and concentration of nanoparticles has been performed through chromatography [5], gel

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electrophoresis [6], or dynamic light scattering [7]. In addition to the above methods, the Coulter counter technique [8] also has been widely used for particle counting and sensing [9,10]. The counter uses a membrane with a single tiny pore to separate chambers, filled with particle-laden solution. The ionic current through the pore, created by electric potential applied between the two chambers, depends on the diameter of the pore and drops when it is blocked by the translocation of particles. By monitoring these signals it is possible to count the number of particles translocated through the pore from one chamber to another, and the particle size can be determined if the pore size is known. The size of particle which can be detected by this method is limited by diameter of the pore. Currently, commercially available Coulter counters have a sensing pore size about a few micrometers in diameter and can detect particles as low as several hundred nanometers. Recently, several research groups used solid-state nanopores [11,12] and biological membranes [13,14] which has a size of only few nanometers. Several groups used carbon nanotubes (CNT) as a nanopore, which has a diameter as low as ~1 nm, making it ideal for DNA sensing [15,16].

Glass pipettes have several advantages over other type of pores, since they are relatively inexpensive and can be prepared with a one step procedure. Depending on the different pulling conditions such as temperature, glass thickness, and pulling force, pipette diameters down to 37 nm can be achieved [17].

In this article, we demonstrate voltage controlled translocations of SiO_2 nanoparticles and liposomes, with diameters of 80 nm to 180 nm through different size glass pipettes. In addition to the resistive pulse method, we also used ImageJ software, which retrieves particle sizes from SEM images to verify our size measurements. We notice the dependence of particle concentration on signal frequency during translocations, which increases with the concentration of nanoparticles.

2. Materials and methods

In the translocation experiments, SiO_2 nanoparticles with average diameters of 80 and 180 nm (Fig. 1(a)) and liposomes with average diameter of 100 nm were used. The SiO_2 nanoparticles were purchased from Corpuscular Inc., Cold Springs, NY, while the liposomes were prepared using lipids from Avanti Polar Lipids Inc. with the composition of 52.5% POPC (1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine), 21% POPE (1-Palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanolamine), 13% POPI (1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-(1′-myo-inositol) (ammonium salt)), 3.5% POPG (1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-(1′-rac-glycerol)) and 10% cholesterol. These lipids are first dissolved in chloroform (CH_3Cl) for thorough mixing. Then the chloroform is dried by steady dry nitrogen gas flow, leaving the mixed lipids formed as a film at the bottom of the vial. This vial is again placed in a vacuum pump overnight for complete drying. Finally, the hydration of lipids are realized by adding 0.5 M KCl solution and shaking vigorously. The lipids will self close to form large vesicles once hydrated, due to the hydrophobic nature of the lipid tail and hydrophilic lipid head. The desirable size of liposomes is achieved by using an extruder with 100 nm filter, (Avanti Polar Lipids Inc extrusion module and polycarbonate membranes). Both SiO_2 nanoparticles and liposomes are typically negatively charged, and the amount of charge depends on the pH value of the solution in which they have been immersed.

Micropipettes with nanopores were fabricated from borosilicate capillaries with initial inner diameter 0.8 mm and outer diameter 1.5 mm. These capillaries were placed into a pipette puller (P-2000, "Sutter, Novato", CA) in order to achieve required orifice sizes. Prior to pulling, the glass pipettes were cleaned thoroughly with alcohol.

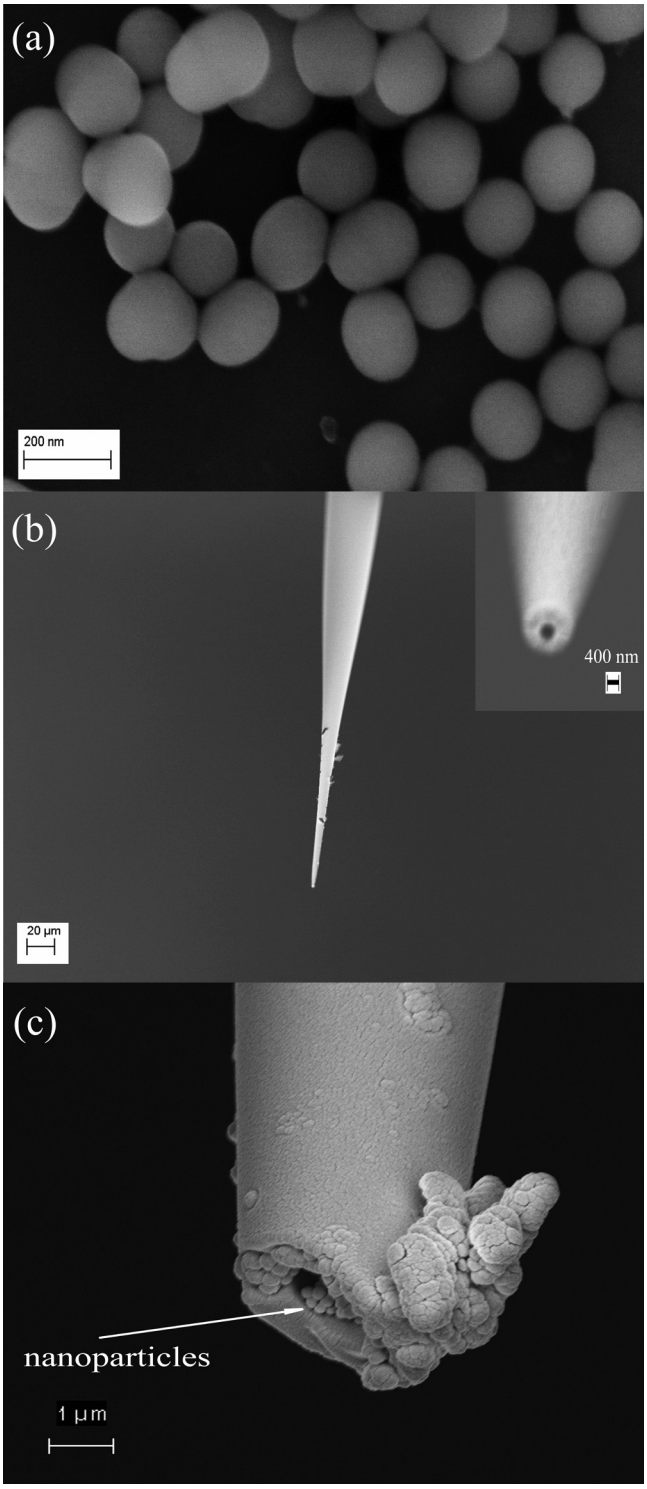

Fig. 1. (a) Silicon oxide nanospheres with average diameter 180 nm. The image was taken with Zeiss Ultra SEM. (b) Borosilicate glass capillary with a pore diameter at orifice around 320 nm (inset) (c) Image of the nanopipette with a broken tip, indicating presence of nanoparticles inside the capillary after the translocation experiment.

The inner diameters of the nanopores were determined by scanning electron microscopy (SEM) images (Fig. 1(b)) taken by *Zeiss Ultra* SEM. To prevent charging effect, these pipette tips were sputter-coated with thin platinum film before imaging.

The micropipettes with nanopores were filled with 0.1 M to 1.0 M potassium chloride (KCl) solution and immersed in the bath