Glass nanopores for single molecule detection

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The resistive pulse technique was invented in the fifties by W. Coulter to count and analyze cells and is still an widespread device in hospitals and laboratories[1]. It is based on a current amplifier which measures the ionic current across a small orifice. Each time when a particle translocates through the orifice it blocks part of the volume available to the ionic current. This causes the ionic current to decrease. Measuring the number, length and amplitudes of these decreases allows counting and analysing the translocating particle.
In the last decades with advances in nanofabrication techniques the sensing limit was pushed to single molecules like DNA or proteins using nanopores in silicon membranes[2,3]. An alternative to these classical nanopores we pioneered glass nanopores made out of nanocapillaries[4]. They are cheaper, easier to fabricate and do not necessitate clean room facilities in contrast to nanopores in silicon membranes. Further the combinations with optical tweezers is very user-friendly while profiting from a higher force resolution[5]. We recently have shown that quartz nanocapillaries can be shrunken under a scanning electron microscope beam[6]. A decrease in the size of the glass nanopores increases the signal amplitude when a DNA translocates through it. Since glass nanopores possess a smaller noise than classical nanopores in silicon membranes, we can show that glass nanopores have a better signal-to-noise ratio[7].
The talk will give an introduction into the field of nanopores, explain the fabrication process of glass nanopores and show the effect of smaller nanopores diameter on the signal amplitude of translocating DNA. Further it will propose a model to explain the conductance through a conical nanopore and the decrease when DNA resides in it.

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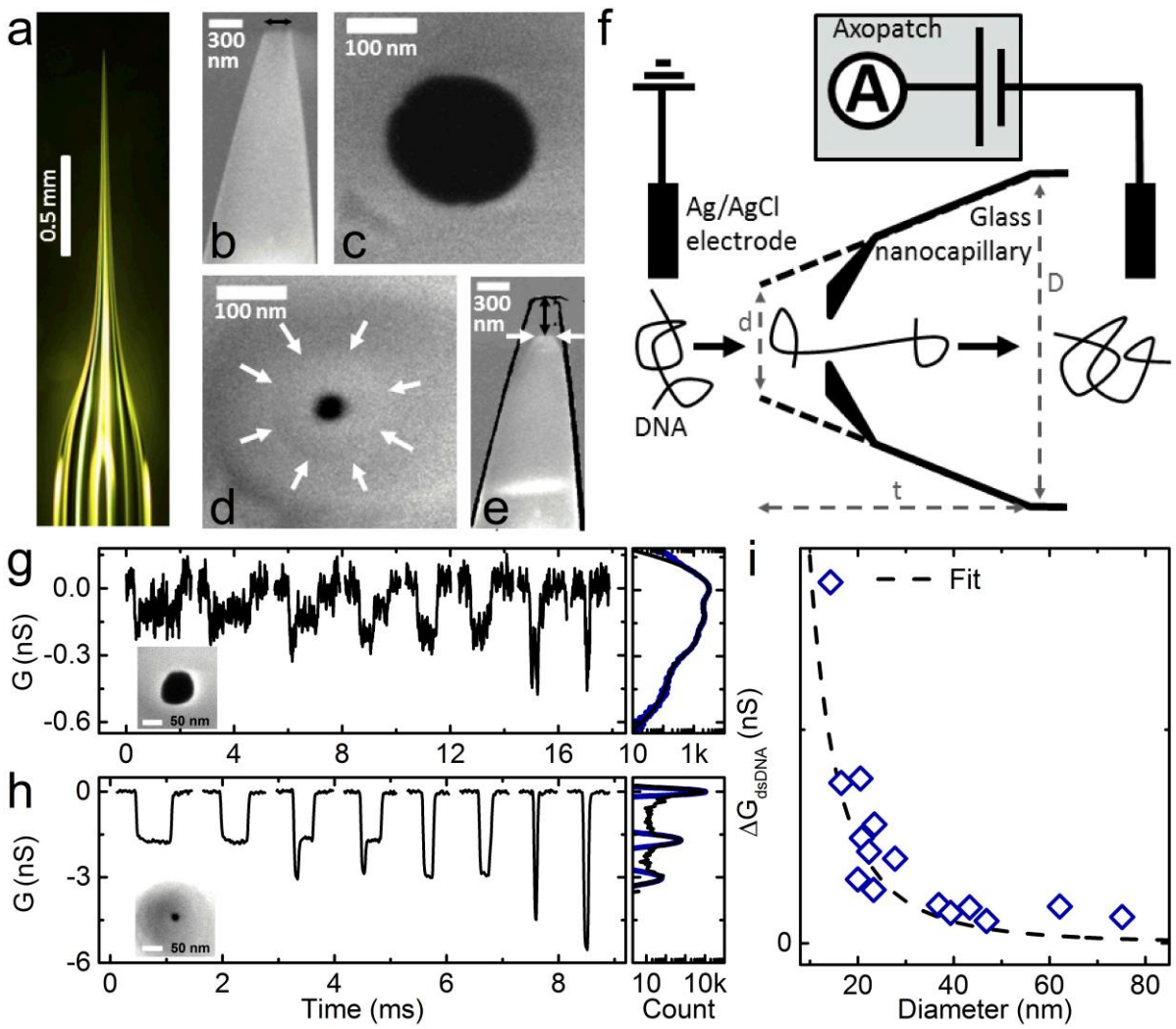

Glass nanocapillaries (Figure a) can be shrunken under an electron beam of an SEM. Figure b and c illustrate the tip of an unmodified nanocapillary from the side and the top. The tip is approximately 230 nm broad (black arrow) and the orifice measures 190 nm in diameter. After 4 minutes of irradiation the tip is now 180 nm broad (indicated by white arrows in d) and the orifice 25 nm big (black circle in d). The capillary has shrunken in horizontal (white arrow in e) and vertical direction (black arrow in e) due to the electron irradiation (see black line in e for original contour of nanocapillary). The capillary is then placed into a resistive pulse setup with a current amplifier. Scheme in f shows the setup and the effect of the shrinking process. DNA is added to the reservoir in front of the nanocapillary and is translocated through the glass nanopore by applying a potential. This translocation causes conductance decreases as demonstrated in Figure g and h. For smaller diameters bigger decreases in the conductance can be measured. Figure i shows the conductance decrease caused by one DNA molecule as a function of the diameter. A model was developed to simulate this dependence, which shows good agreement with the data (fit in i).