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Aβ fiber detection using track-etched nanopore: effect of geometry and crowding

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Single nanopore technology is a versatile tool allowing the sensing, study and discrimination of (bio)macromolecules. The principle of the detection consists to measure transient changes in the ionic current inside the pore caused by the passage of an analyte[1]. This technology is an emerging way to study single protein as well large protein aggregates (such amyloids)[2]. The study and the detection of amyloids is challenging due to their shape (rod-shape) and their transient nature in solution.

To overcome this drawback, synthetic nanopore drilled in polymer membrane by the track etching method were developed[3]. Their tunable geometry allows the detection of amyloids fibers involved in numerous neurodegenerative diseases (e.g Alzheimer, parkinson)[4,5]. Moreover, track-etched nanopore could be easily functionnalized in order to reduce their fouling by amyloids adsorption. However, the main limitation is its low resolution preventing the detection and the discrimination of similar samples.

In a recent work, we studied the influence of pore geometry (conical or bullet-shape) on the translocation of amyloids inside track-etched nanopores. To do so, we produced AB-42 fibers of different lengths ; 247nm, 151nm, 114nm and 61nm. We evidence that the amplitude of blockades are larger and the dwell times are longer in a bullet shape nanopore (0.033 and 3s respectively) compared to a conical one (0.008 and 100ms respectively). Moreover, fibers could be discriminated by different parameters depending of the pore geometry. Indeed, the amplitudes of blockade are different with conical pore (0.008 and 0.004 for fibers of 247 and 151nm respectively). While with bullet shape nanopore, the dwell time as well the amplitude are different : 0.028, 0.015 for the amplitudes and 3s, 0.5s for the dwell times (for fibers of 247 and 151 nm respectively). In a second step we considered the effect of crowding. To do so, PEG-20K were grafted onto the pore walls to crowd the sensing zone. Interstingly, a large increase in the amplitude as well in the dwell time of blockade are observed (0.8 and 3.8s for a fiber with a length of 114nm). Under crowded condition, the dwell time is the parameter allowing the discrimination of different fibers (3.8s and 1s for fibers with a length of 114 and 67 nm respectively).

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