Electrical detection of amyloid-β aggregates using membrane integrated microfluidic transistors

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Abstract
Alzheimer's disease (AD) is a neurodegenerative disorder associated with a severe loss in thinking, learning and memory functions of the brain. There is currently no treatment that can effectively stop AD. Some drugs can however slow down the progress. Thus, early detection of AD is the key to manage the disease and develop better treatments. A common pathological change found in AD-affected brains is the accumulation of a peptide named amyloid-β (Aβ) that can form plaques. In this work, we design an organic electrochemical transistor (OECT) for *in vitro* detection of Aβ aggregates [1]. The OECT channel is integrated with a nanostructured isoporous membrane which has a strong affinity for Aβ aggregates. As Aβ aggregates are captured by the membrane, they block its pores that are smaller in size than the protein. As such they impede the vertical ion flow towards the channel and change the transistor characteristics (speed and output current). The sensor thus does not rely on fluorescent labels or redox molecules. Combining the high transconductance of the OECT with the precise porosity and selectivity of the membrane, the device detects the presence of Aβ aggregates in human serum samples with excellent sensitivity. Moreover, a microfluidic channel, where minute amounts of fluids can be precisely processed, stand as an ideal platform to provide a compact size of the device, a short detection time, and low analyte consumption. This is the first-time demonstration of a biofunctionalized, nanostructured, and isoporous membrane integrated with a high-performance microfluidic based transistor for biosensing. This robust, low-power, non-invasive, and miniaturized sensor aids in the development of point-of-care tools for early diagnosis of AD. We would now like to convert this OECT into a Coronavirus detection device by replacing the proof-of-concept recognition module with very recently published nanobody versions that recognize SARS-CoV-2 and MERS surface proteins [2]. The human ACE2 receptor protein, to which the virus binds with high affinity, will be evaluated as an alternative recognition module. Sensor performance will be tested with recombinant SARS-CoV-2 RBS (receptor binding domain of the spike protein) fusion proteins as described in the literature. We will also try to create more realistic dummy virus particles by decorating unrelated protein shells with the larger trimeric spike protein.

REFERENCES

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FIGURES

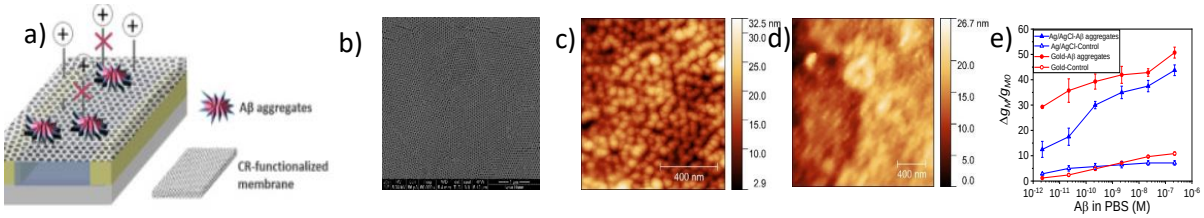

Figure 1: a) Schematic of target molecule binding on nanoporous membrane (NP) and b) its SEM image. c) and d) is the AFM images of NP before and after target molecules binding. e) is the sensitivity curve obtained by calculating the change of transconductance as a function of concentration.