Millionfold Biomolecule Pre-Concentration Using Nano-fluidic Filters

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In all biomolecule-sensing technologies, detection becomes increasingly difficult or impossible when the analyte concentration is lower than a certain level (the detection limit). However, in complex blood-serum samples, most of the important biomolecule markers are available only in trace amounts (fM to nM). Therefore, the detection (or identification) of these markers after pre-fractionation and separation is extremely difficult. To solve this problem, numerous efforts have been made to develop a pre-concentration process before or after separation. So far, the single pre-concentration method with the highest concentration factor among all the strategies is micellar electrokinetic sweeping, which can achieve a concentration factor of 500-to 7000-fold [1,2].

Here, we present a novel way to achieve rapid pre-concentration for a charged biomolecule that can achieve an up to 10 millionfold sample pre-concentration within 30 minutes. Ionic charge separation will happen once the electrical field is applied across the nanofilter. It has been reported that a flow several times stronger than general electroosmotic flow, caused by induced-charge layer, will present with confined geometry [3,4]. As a consequence, a barrier that can trap both positively and negatively charged molecules is formed by extending the Debye layer (non-equilibrium charge polarization) into the microfluidic channel with a stronger carrier flow. This device can concentrate a sample without a complex buffer concentration variation (such as in electrokinetic focusing), any additional additive (such as SDS in micellar sweep techniques), and/or any other complex structure that will make the downstream analysis difficult. Because of the device’s simple structure, various integrations and applications are possible, including sample pre-concentration for advanced blood proteome analysis, sample injection for microchip electrophoresis/chromatography, and environmental trace analysis.

Figure 1: Pre-concentration phenomena for 100 minutes, starting from highly diluted 33 pM (10-12M) GFP solution. The detection condition barely detects the 33 µM GFP concentration, which means at 25 minutes or later, the concentration of the plug exceeds 1 µM. Voltage applied across top-down channel is 10 volts, while 4 volts along the top channel (pictures were taken by CCD camera with 1 second exposure).

Figure 2: Picture showing the electrokinetic capture/release profiles. After 250 seconds, the waste channel was floated to perform an EOF-driven CE in the top channel. Shown between 300 and 350 seconds is the releasing of captured proteins.

REFERENCES: