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News & Views

Wearable droplet microfluidics

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Point-of-care (POC) diagnostics, which aims at continuously measuring and screening dynamic chemical signals in human body, is attracting increasing attention among disease treatment, diagnosis, drug discovery and other biomedical fields [1,2]. Recent years have witnessed the booming development of miniaturized, minimal-invasive POC technologies, such as implanted electrochemical sensors [3,4], paper chips [5,6] and microfluidic devices [7–9]. Among them, microfluidics is one of the most promising strategy due to the accurate and user-friendly properties. However, most of the microfluidic POC devices are manually intensive and highly rely on bulky laboratory equipment such as syringe pumps, external valves and microscopes, which not only limit their applications in wearable devices, but also hinder their moving out of laboratory and into practical use [10,11]. These problems remain unsolved until now.

Recently, a novel wearable droplet microfluidic-based sensor has been developed for continuous, real-time, in situ sampling and analyzing tissue biochemical signals [12] (Fig. 1). This device integrates a miniature peristaltic pump, a microfluidic chip, an optical flow cell, electronics and a fluid reservoir cartridge into a single small, wearable package. By micro-dialysis and a screw-driven push-pull peristaltic micropump, molecules from the interstitial fluid can be collected and sent to the microfluidic sensor. Then by introduction of an immiscible oil and a colorimetric assay, solution containing target molecules will split into a stream of droplets and their concentration can be read out from the strength of the droplet color.

The key point of miniaturizing the droplet microfluidic sensors is the screw-based micropump. Compared to traditional peristaltic pump, this micropump has several distinctive innovations. The first is the synchronization of push and pull. By simultaneously pushing and pulling fluid through the probe, the flow rates are slowed down to ensure an adequate perfusate diffusion time at the probe membrane; pressure-driven fluid loss through the membrane is also prevented at the same time. The second is the screw thread-driven fluid transport. This not only induces much slower flow rates, but also avoids fluid interactions of perfusate and dialysate as well as the backflow of down-stream fluids. The third innovation is the utilization of the pulsatile flow, which enables reliable droplet generation of uniform volume and sample-to-reagent ratio. As a single oil pulse and a single aqueous pulse will lead to a single droplet production, the size of the droplet only depends on the aqueous pulse volume and can be tuned by changing tubing diameter and screw pitch.

The scientists have also investigated the practical application of their wearable droplet microfluidic-based sensor by employing them to monitor glucose in vivo. In this case, all reagents were premixed into a single solution before meeting the dialysate. The colorimetric assay was based on the Trinder reaction, where red/purple colored products were yielded after the mixture of the dialysate and the reagent. Results showed that the sensitivity of sensor was (0.026 ± 0.002) L/mmol, the limit of detection was about 68 μmol/L, and the linear response was up to at least 8 mmol/L. Moreover, the sensor featured high measurement frequency, which was a measurement every few seconds. More importantly, in the test of monitoring dermal interstitial glucose levels of human volunteers, the results from the sensor showed the expected trends, strongly demonstrating their capability in real-time, in vivo monitoring of dynamic physiological indexes.

To further evaluate the versatility of the sensor, lactate was chosen as the target molecule. Different from glucose assay, the lactate assay was performed in two steps. In the first step, lactate was broken down into hydrogen peroxide and pyruvate by lactate oxidase; while in the second step, the hydrogen peroxide was catalyzed by horseradish peroxidase to yield blue-green colored products. To meet this demand, a chip with double T-junctions was prepared. Transparent droplets containing lactate and lactate oxidase at 1:1 ratio was first generated at the T-junction in Step 1. Notably, the serpentine channel was designed to ensure a complete reaction. The completely reacted droplets then met with horseradish peroxidase at the second T-junction and developed blue/green colored droplets in Step 2. It was found that the quasi-linear detection scope of lactate was from 0.5 to 20 mmol/L, with a limit of detection of 17 μmol/L and a sensitivity of (0.1 ± 0.002) L/mmol. Also, the detection of lactate variation in human volunteers by the sensor showed promising results. These results indicated that the wearable droplet microfluidic-based sensor was highly versatile and could adjust to more complicated operation environments.

The wearable droplet microfluidic-based sensor is a remarkable milestone in microfluidic-based POC diagnostics. The most outstanding feature of the sensor is its small size and wearability. This feature makes the sensor applicable to subjects in continuous movement, such as walking, swinging and lifting, thus widely broadening its working scenarios. Another striking point is the autonomous operation. Once set-up, human interaction is no more

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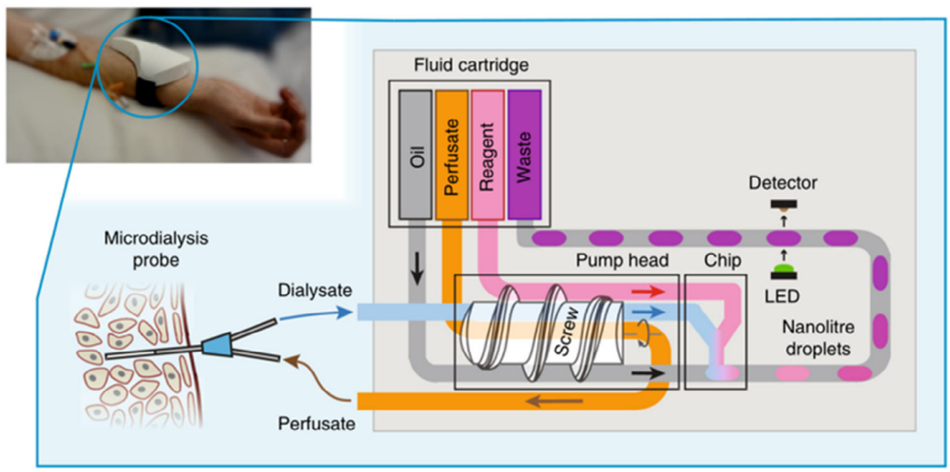

Fig. 1. Scheme of the operation of the wearable droplet microfluidic-based sensor. Perfusate is pumped into a micro-dialysis probe and dialysate is withdrawn into the sensor synchronously via a screw-driven peristaltic pump. The dialysate is then mixed with the analyte-specific reagent, through which colored products could be generated. The colored reaction products are divided into a stream of droplets by an immiscible oil flow. By reading the strength of the color, the concentration of the analytes could be obtained. Finally, the analyzed droplets are collected in a waste sachet for later disposal [12].

needed and the sensor will give a live feedback of the level of specific analytes spontaneously with a measurement every three seconds. Therefore, it is envisaged that this wearable sensor will find a large variety of applications in clinic where accurate and real-time monitoring is desirable and plenty of medical equipment is cluttered in the working space, or in the household where autonomous and easy operation is necessary. Future efforts can be focused on the combination of the wearable droplet microfluidic-based sensor with physical sensors, so that a wide range of physical properties and biochemical data will be measured in a simultaneous and cross-correlated way. This is bound to pave an inspiring road to the precision and personalized medicine and healthcare.

Conflict of interest

The authors declare that they have no conflict of interest.

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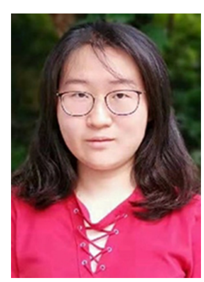

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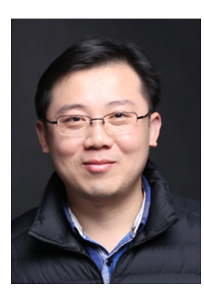

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