A FULLY AUTOMATED WIRELESSLY POWERED CENTRIFUGAL PLATFORM TOWARDS A SAMPLE-TO-ANSWER CHEMILUMINESCENT ELISA ASSAY FOR CVD DETECTION

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ABSTRACT

This paper describes the development of a platform where a silicon photo-multiplier (SiPM) sensor co-rotates with a "Lab-on-a-Disc" (LoaD). This platform includes a modular data-logger and, to avoid the need for electrical slip rings, it is wirelessly powered. This system is optimized for the detection of chemiluminescence. It is characterized on-disc using dilutions of HRP tagged antibodies and shows good agreement with a commercial luminometer. Additionally, preliminary work towards developing a fully integrated on-disc ELISA assay for CVD detection is presented.

KEYWORDS: Lab-on-a-Disc; CVD, Wireless Power Transfer, ELISA, Chemiluminescence.

INTRODUCTION

Over the recent decade, LoaD platforms have been increasingly leveraged for application in bio-medical point-of-care diagnostics [1]. These centrifugally pumped systems offer a platform independent of external pressure sources, and their pneumatic interfaces, and so ensure ease-of-use and minimum maintenance. However, making sensitive and time dependent measurements in a rotating reference frame can be challenging and reduces the sensitivity of the system. Simply stopping the disc to make measurements limits the number of assays which might otherwise be parallelized on a highly integrated platform. To this end, in this paper we report on the first application of a new, wirelessly powered readout method for the LoaD platform [2].

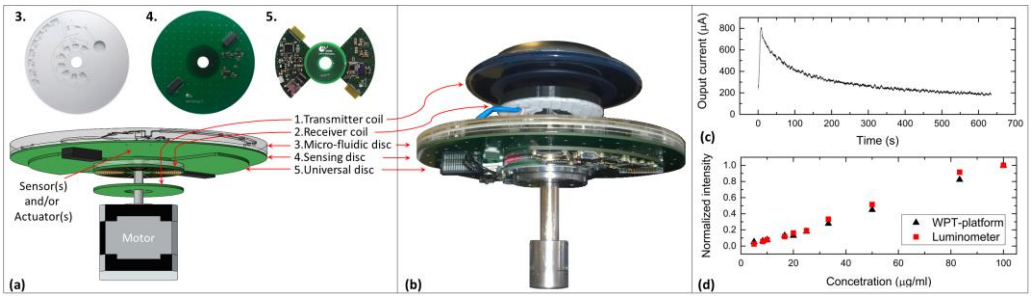

Figure 1: a) Schematic of the setup, with the transmitter and receiver coils underneath. b) Photo of the setup with the WPT-link on top, this configuration can be used for tightly packed spin stands that have no open space underneath. (c) Chemiluminescence response measured while spinning using the SiPM sensor on the disc when 50 µl of dilute detection antibody (at 10µg/ml) is added to 50 µl of ECL reagent. (d) Comparison of eLoaD performance, measured using diluted detection antibody, to a commercial luminometer (Promega GloMax, n=1).

EXPERIMENTAL AND RESULTS

The eLoaD platform is a printed circuit board designed to fit common spin stands, which contains a microcontroller, a Bluetooth module, an SD Card and the power management circuitry [3] to provide 5W of power drawn from commercially available wireless mobile phone chargers (Fig. 1 a & b). The capability of this extremely light platform is further expanded by a modular design whereby a suite of different sensors and actuators can be slotted into its core. In this work, we equip the eLoaD platform with a highly sensitive silicon photo-multiplier (SiPM) sensor in order to detect chemiluminescence. For characterization, we use a custom microfluidic disc where 50 µl of HRP tagged antibody (at varying concentrations) is mixed with ECL and the performance is compared to a commercial benchtop luminometer (Fig. 1 c & d).

The LoaD cartridge, which is built upon event-triggered dissolvable film technology [4], is based on adapting a standard, commercially available bead-based chemiluminescent ELISA protocol. The disc operates in two stages; in the first the standard benchtop protocol of diluting plasma 1:5,000 is replicated through using a series of mixing and metering structures (Fig 2). To save on disc real-estate, a centripetal pumping mechanism, based on combining a dense immiscible liquid with dissolvable films [5], is adapted so this entire stage can be located at the disc periphery. Next, the diluted

sample is pumped to the center of the disc where it is introduced into an incubation chamber, controlled by a centrifugo-pneumatic siphon valve, and incubated with magnetically immobilized microbeads; here 8 sequential processing steps are implemented and controlled by changes in disc spin rate.

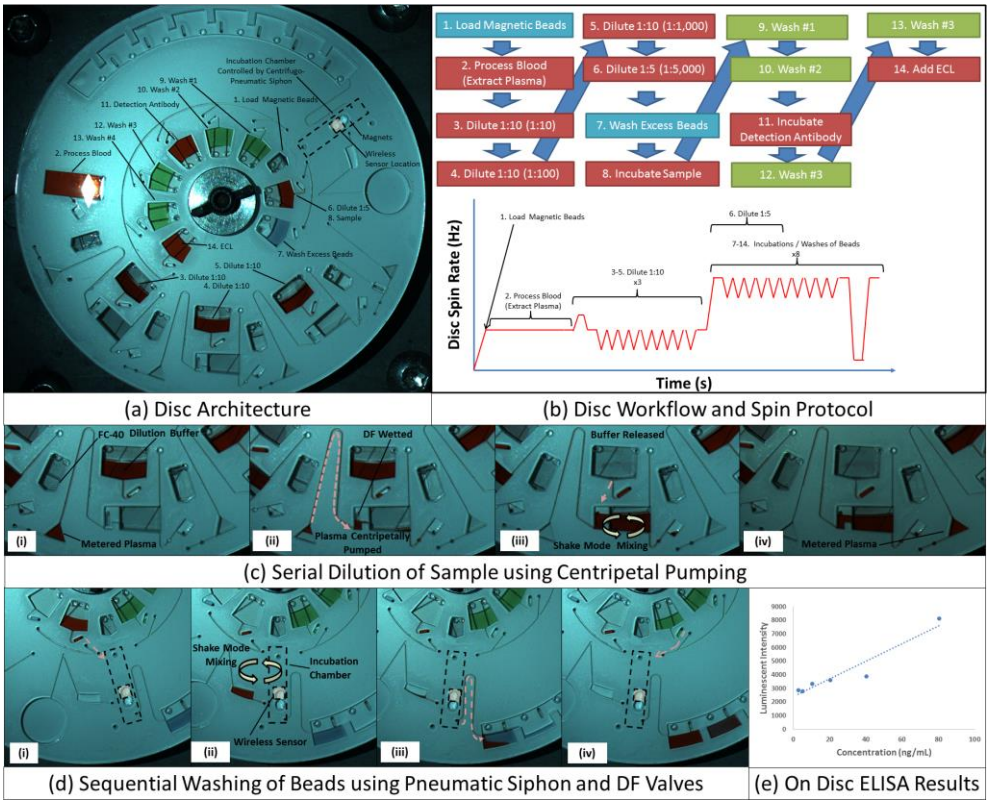

Figure 2: Disc for sample-to-answer, wireless chemiluminescent detection of CRP (a) Disc architecture showing blood processing chamber, serial plasma dilution chambers and the bead incubation chamber (b) Schematic of the on-disc work-flow and the spin profile used to automate the protocol (c) shows the serial structures used for plasma dilution. This sequence is performed 3 times in series (i) Plasma is metered in a triangular chamber, (ii) a DF dissolves and FC-40 is released, displacing the sample radially inwards to a dilution chamber, (iii) a second DF is wetted, releasing the dilution buffer. The sample is mixed and a pulse in disc spin-rate opens a valve. (iv) diluted plasma is metered for a subsequent pumping step. (d) bead incubation is controlled using a centrifugo-pneumatic siphon valve. This sequence is performed 8 times, (i) sample/wash/reagent is loaded into the chamber, (ii) the reagent is agitated, (iii) the disc is decelerated and the siphon primes. (iv) the liquid in the waste reservoir triggers an event-triggered DF, releasing the next sample/wash/reagent in the sequence. (e) preliminary results where steps 1, 7-13 are performed on-disc. ECL is added off disc and CRP measurements are made using a commercial luminometer.

CONCLUSION

As a next step, the automated centrifugal disc will be integrated with the wireless reader to demonstrate full, clinically relevant, sample-to-answer performance. The combination of the wirelessly electrified eLoaD with the LoaD platform offers great potential; the system is light, low cost and reuseable and can, in the future, offer enhanced capabilities such as active monitoring of liquid movement and closed-loop feedback to the spindle motor.

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