RESPONSIVE HYDROGEL SENSOR FOR MONITORING ANTIBODY PRODUCTION

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Precise control over the biomanufacturing process is crucial for maximizing yield and quality of monoclonal antibodies (mAbs); however, the industry does not have sensors capable of continuously monitoring either mAb yield or quality. Consequently, this production is plagued with poor quality control, reduced productivity, and increased costs. To develop such a sensor, we investigated the use of aptamers selective to human immunoglobulin G (IgG, sub-type of mAbs). First, we investigated the physiochemical properties of six different aptamers that bind to two distinct regions of the protein as well as tested their the binding affinity to human IgG, before and after standard sterilization procedures (autocalve and gamma irradation), using surface plasmon resonance (SPR, Figure 1). Chemical modification procedures were developed for immobilization of the aptamers onto a biotin capture sensor chip for use in SPR. Based on these results, two aptamers were selected which bind to separate regions of IgG, which have optimal physiochemical properties and have strong binding affinity to IgG. Similarly, the aptamers were modified to covalently bond and incorporate into a hydrogel network creating an IgG-sensitive hydrogel. In the presence of IgG in solution, both immobilized aptamers bind to the IgG molecule and form a new crosslink which subsequently causes shrinking (volume reduction) of the hydrogel [1]. This change in volume is monitored using our patent-pending magnetic transduction technique [2]. The degree of hydrogel shrinkage is measured using a magnetometer chip and fixing a permanent magnet to the hydrogel surface. An electronic reader with the magnetometer transduces the hydrogel response into an electrical signal. Response tests using this setup were performed in four different complex environments including industrial cell culture medium. The results show that this IgG-sensitive hydrogel is stable to autoclave and gamma irradition and responds to increasing and decreasing concentrations of IgG in various solutions (Figure 2). The magnitude of hydrogel response is used to correlate the change in IgG concentraion.

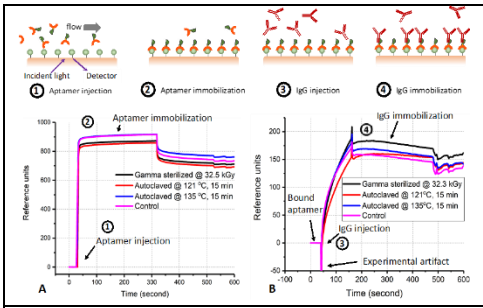

Figure 1 – Surface plasmon resonance (SPR) technique used to determine IgG-binding affinity of selected aptamers before and after sterilization.

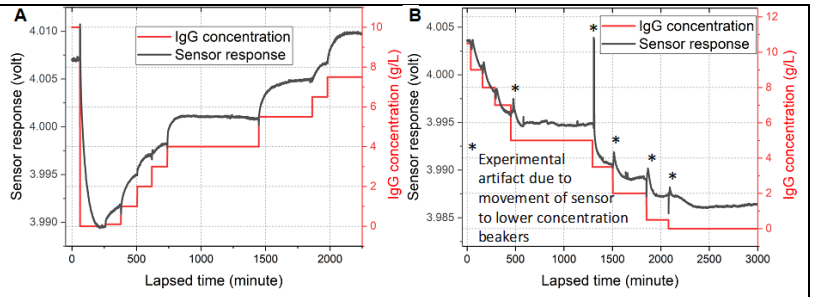

Figure 2 – Demonstration that the IgG-sensitive hydrogel can detect IgG over the entire commercially-relevant concentration range.

References:
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[2] T. Nguyen *et al.*, “Sensor-array for continuous monitoring of biochemicals for bioprocess control,” *2015 Transducers - 2015 18th Int. Conf. Solid-State Sensors, Actuators Microsystems, TRANSDUCERS 2015*, pp. 1684–1687, 2015.