423f Multi-Analyte, Fiber-Optic Immuno-Biosensor with Automatic Control System for Rapid Anticoagulant Deficiency Diagnosis

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Protein C (PC), protein S (PS), antithrombin III (ATIII), and plasminogen (PLG) are four major anticoagulants in blood plasma. Deficiency of any of these anticoagulants may lead to venous thromboembolism (VTE), including heart attack, stroke, and lung embolism. Early diagnosis is critical to prevent the fatal VTE complications. To simultaneously quantify multi-anticoagulants in one assay for rapid and accurate disease diagnosis by the multi-biomarker information, a fiber-optic, multi-analyte immuno-biosensing system has been developed. Individual sensors were developed separately and the sensing protocol was optimized with the application of convective flow during the sample and reagent incubations. Convection facilitates the mass transport of analyte and reagent molecules to the sensor surface by reducing boundary layer thickness and the sensitivity of the sensors was significantly improved for samples with high viscosity (i.e. plasma). The optimal flow velocity for anticoagulant sensing was determined to be 0.7 cm/s, where the reaction kinetics changes from the mass-transport-limited to the reaction-limited. At the optimal flow velocities, the sensor size was reduced to 3 cm and the assay time was optimized to be 5 minutes. For the simultaneous four-factor quantification, four sensors were connected in series in a four-analyte sensing unit. The sensors demonstrated high specificity with minimal cross-reactivity to other analytes in the sample. The multi-anticoagulant sensing system was capable of quantifying PC, PS, ATIII, and PLG in their sensing ranges within 5 minutes, at an average signal-to-noise (S/N) ratio of 25. To make the sensing procedures more user-friendly, a prototype of an automatic flow control system consisting of electrical micro-pump and micro-valves was developed. A LabviewTM program was written to automatically perform the predetermined sensing procedures for simultaneous four-analyte quantification. This system is beneficial for clinicians to diagnose diseases rapidly, easily, and cost-effectively and to design an accurate patient care strategy from the multiple biomarker information. The principle of the multi-analyte detection in this system can also be applied for simultaneous monitoring of other disease-representing biomarkers, such as, tumor markers for cancer detection. This project is funded by the National Science Foundation (BES-0330075).