Effects of Design Parameters on the Sensitivity of a Micro-Cantilever Based Biosensor

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Piezo-resistive actuation of a microcantilever induced by biomolecular binding such as DNA hybridization and antibody-antigen binding is an important principle useful in biosensing applications. As the magnitude of the forces exerted is small, increasing the sensitivity of the microcantilever becomes critical. In this paper, we are considering to achieve this by geometric variation of the cantilever. The sensitivity of the cantilever was improved so that the device can sense the presence of antigen even if the magnitude of surface-stresses over the microcantilever was very small. We consider a 'T-shaped' cantilver that eliminates the disadvantages while improving the sensitivity simultaneously. Simulations for validation have been performed using Intellisuite software (a MEMS design and simulation package). The simulations reveal that the T-shaped microcantilver is almost as sensitive as a thin cantilever and has relatively very low buckling effect. Simulations also reveal that with an increase in thickness of the cantilever, there is a proportional decrease in the sensitivity. This paper presents an analytical modeling and simulation studies of a piezoresistive cantilever used as MEMS based biosensor for the detection of cardiac markers. Diagnosis of Myocardial Infarction was achieved by the nanomechanical deflection of the microcantilever due to adsorption of the Troponin I complex. The deflection of the microcantilever was measured in terms of the piezoresistive changes by implanting boron at the anchor point where there is maximum strain due to the adsorption of the analyte molecules. The biochemical interactions between the Cardiac Troponin I (cTnl) complex and the immobilized antibodies would cause change in resistance of the piezoresistor integrated at the anchor point. A 'T' shaped microcantilever design was proposed for the study. The distal end of the device was coated with gold. The sensitivity of the cantilever was improved so that the device can sense the presence of antigen even if the magnitude of surface-stresses over the microcantilever was very small. To obtain an application specific optimum design parameter and predict the cantilever performance. The miniaturization of the cantilever-based biosensor leads to significant advantages in the absolute device sensitivity.

Effect of Laminin on the Interaction Between Islets and an Implantable Immunoisolation Polyurethane Membrane

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The development of bio-artificial organs (sequestered cell cultures, implanted within an isolating membrane) is complicated by dynamic and interrelated variables. The primary objective of an implanted membrane for sequestration of insulin producing cells is to provide a barrier to the host's immune system. Implicit in this structural relationship in systems designed for the treatment of diabetes is the ability to create an environment that is favorable to the sequestered cells' viability and at the same time facilitate the availability of the released insulin in a kinetic relationship consistent with the normal physiology. This investigation conducted under a Phase I SBIR grant explored methods to promote a favorable interaction between islets harvested from neonate rats with a polyurethane membrane during in-vitro culture experiments. Laminin (LAM) extracellular matrix was used to stabilize islets within polyurethane membranes or within cell culture well inserts. Results indicated that insulin produced by islets enclosed within the polyurethane membranes with and without LAM was present for up to six weeks. However, when evaluating the Glucose Stimulated Insulin Secretion (GSIS) there was no evidence of Insulin Response in any of the treatment groups. Further study using LAM and islets in the presence of a cell culture insert (8.0 micron polycarbonate membrane) demonstarted that LAM impeded flow of media through the membrane. When media sampled from the well was compared to inside the insert at the 11.2 mM glucose phase of the GSIS, the average insulin concentration from the well was $<45.8\%$ of that found inside the cup. In addition, there was evidence of a positive effect on β-cell rate of cell division in the presence of LAM. The average number of brdU labeled cells per islet was significantly greater following prolactin (PRL; positive control @ 500 ng/ml), laminin–1 (50 μg/ml) or the combination of PRL and LAM. The increases relative to the control islets averaged across the replications were: Laminin +1.5 times, Prolactin +5.9 times, PRL and LAM +6.8 times. In summary, there was no evidence of GSIS in experiments where laminin–1 was used to stabilize neonate rat islets within a polyurethane membrane. These results suggest that the presence of ECM on the inside of the polyurethane membrane impeded the insulin of the polyurethane membrane impeded the insulin diffusion kinetics through the membrane. The only potentially positive results from this study are that there is evidence of insulin diffusion over time indicating that the islets are functional, but a an unknown level of physiologic utility. Support for this study was provided by NIH SBIR Grant #1 R43 DK75220-01. Dr. Robert Sorenson, University of MN, and his lab graciously provided the neonate rat islets and advice.