Multicriteria Optimization in Sensor Design and Fabrication for DNA Thermosequencing Platform

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The future personalized medicine is not possible except with the aim of genomic information, which provide a deep understanding of all of the species and their biological mechanisms. Speciation and biological function are primarily determined by the organism's DNA sequence. For the past three decades, Sanger's method has been the primary DNA sequencing technology; however, inherent limitations in cost and complexity have limited its usage in personalized medicine and ecological studies.

It was shown that a new technology, Thermosequencing, could potentially reduce both the cost and complexity of DNA sequencing by using a pico-calorimetric assay nanofabricated in microfluidic platform [1-6]. To optimize the efficiency and fabrication of the technology, Finite Element Analysis was used to model the Thermosequencing system by simulating the DNA incorporation reaction series and the resulting product concentration and heat production. Different models of the Thermosequencing platform were created to simulate the effects of the materials surrounding the system, to optimize the geometry of the system, and to concentrate reaction heat into specific regions for detection in the real system (Fig.1). The resulting concentrations of reaction products were used to calibrate the reaction speed and to design the heat sensors in the Thermosequencing technology (Fig.2, 3). We recommend a modified gated structure for the microfluidic detection platform by using control valves and show how this new platform could dramatically improve the detection efficiency (Fig.1). We illustrate the design and experimental results of a primary template as well as different advantages and potential applications of the Gate-Controlled Magnetic Bead (GCMB) platform for DNA sequencing and genetics.

In addition, fabrication of the sensor made of array of nano-calorimeters, PDMS wells, and control channels have been studied and optimized which could pose significant effects in the system. To increase heat production for detection robustness, the amount of reaction, and consequently the amount of DNA on the bead, must be increased. To prevent thermal and chemical crosstalk between neighboring wells, insulation in the form of control channels must be installed to limit the volume of reaction. We investigated noise and common-mode rejection issues for sensor robustness and detection accuracy. Finally it will be discussed how the proposed micro-fabricated system is useful for a number of other bio-species detection and sorting templates.

1. Esfandyarpour, H, et al., EIPBN2007, 2007.
2. Esfandyarpour, H, Davis RW, NSTI-Nanotech 2007, Vol.3. pp 422-425.
3. Esfandyarpour, H, et al. Proceeding of Int'l COMSOL Conference, 2007, pp-141-147.
4. Esfandyarpour, H, Davis RW, ICNMM2007, Proceedings of, 2007, ref- 3119.
5. Esfandyarpour, H, et al., accepted to IEEE Sensor Applications Symposium, Feb. 2008.
6. Esfandyarpour, H, et al., Int'l Sensors & Related Networks Conf., Proc. of, 2007, pp 178-181.

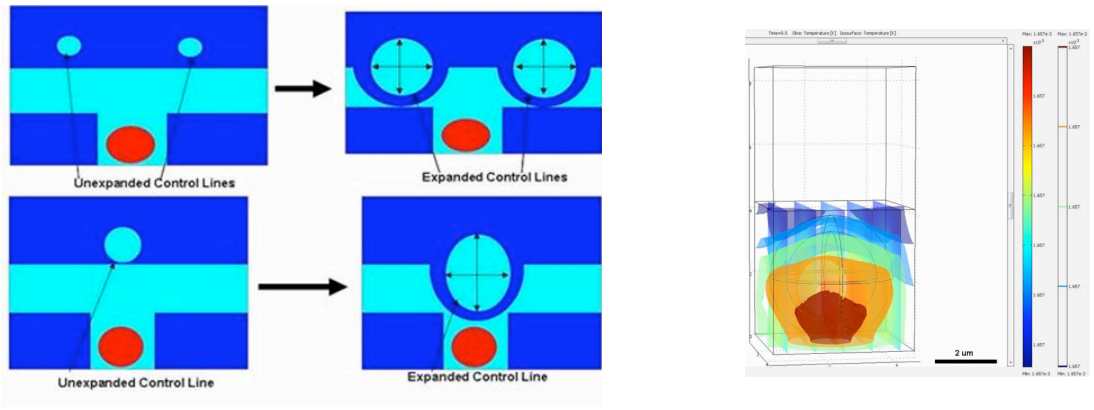

Figure 1. Gated Structure- Left: Control channel schematics for the double (top) and single (bottom) control line systems. In both cases, pressurization of the control channels induces expansion for mass and thermal insulation of the well; Right: The temperature change in the 1-Control Channel System with 2.8µm Invitrogen Dynabead™ at 0.5s. The density, heat capacity, and thermal conductivity characteristics are calculated and simulated. The difference in temperature change between this model and the standard 1-Control Channel System is around small (~90µK).

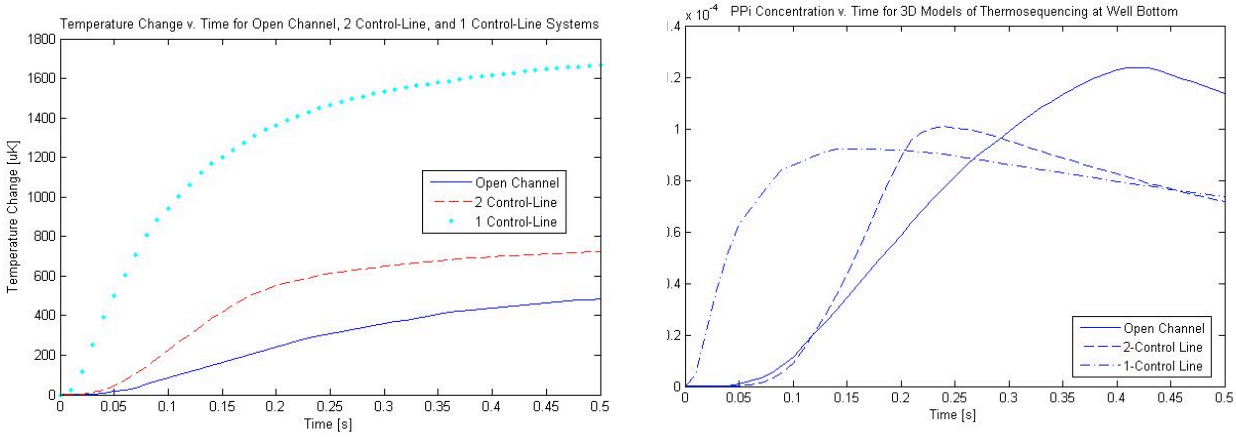

Figure 2. Comparison of the temperature change (left) and PPi Concentration (Right) for the Phase 1 Open-Channel, Phase 2 2 Control-Line, and Phase 2 1 Control-Line systems from 0 to 0.5 seconds. It is apparent that the insulated systems have higher temperature change due to the decrease in the thermal conductivity and the decreased heat absorption by the fluid surrounding the reaction.

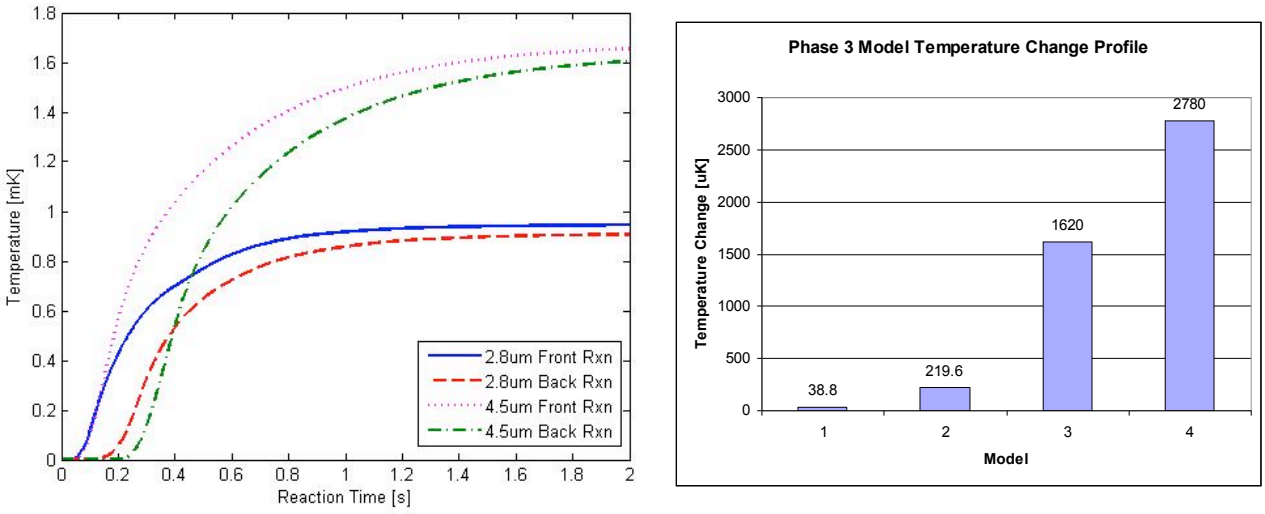

Figure 3. Temperature Change Differences for Reactive DNA Beads with Nonreactive Neighbors (left); Optimization of Temperature change in alternative models (Right). Temperature change in the system is at 2.779 mK. Temperature change increases with less water volume, greater amount of DNA, and faster convective flow.