

**Position Paper: Design, Materials and Measurement Issues for Biological Microreactors
(BioMEMS)**

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Abstract: Although fundamental obstacles and challenges exist, to the successful commercialization of BioMEMS products, Motorola is developing a new methodology for fast and cost-effective product development. We combine concurrent predictive modeling from conceptual design and system performance analysis, materials processing properties qualification, and through to end-product monolithic integration. Within the scope of this workshop, Ceramic MicroSystems Technology and its applications in genomic analysis will be explained and rapid prototyping of microfluidic and array-based BioMEMS devices will be described. Progress made towards testing and measurement at the microscale will be described to illustrate the motivation behind modeling efforts.

Introduction: In recent years, application of MicroElectroMechanical Systems (MEMS) technology in the biology field has continued to advance at the fastest growth rates in the overall MEMS multi-billion dollar market. Miniaturization of analytical instrumentation represents a new “paradigm shift” in biological and pharmaceutical research that is expected to possibly replace conventional approaches to sample handling and analysis. However, successful commercialization of BioMEMS requires substantial efforts in adapting some of the current industrial platforms for clinical diagnostic devices and developing high throughput, screening assay methods.

The biomedical community faces increasingly difficult challenges to moving into manufacturing of bioMEMS containing feature sizes approaching a few microns or below. Some of the basic challenges are materials-related, such as bioactive materials for creating a microenvironment for low, unspecific adsorption to preserve biomolecular functions (e.g. Polymerase in pcr reactions), or microfabrication-related, such as hybrid and/or monolithic integration technologies and on-chip fluid interconnects for the microfluidic components. In an effort to meet these challenges, motorola is developing new concepts, closely coupled with the global microfluidic community, which aim to provide adequate methods and standards addressing these important issues.

Motorola labs' research groups have been engaged in a variety of activities including simulation of fundamental working principles of complex microfluidic channels and multi-physics interactions (e.g. Capillarity, electro-thermal response), plus 3-d CAD design and solids modeling, materials biocompatibility assessment and qualification. Characterization of bioMEMS materials with dependencies on processing and microstructure verifies designs. Accurate characterization and metrology are key enablers for developing affordable bioMEMS process technology and improving manufacturing yields. Several applications of these techniques will be discussed to provide some highlights of today's manufacturing methodology challenges.

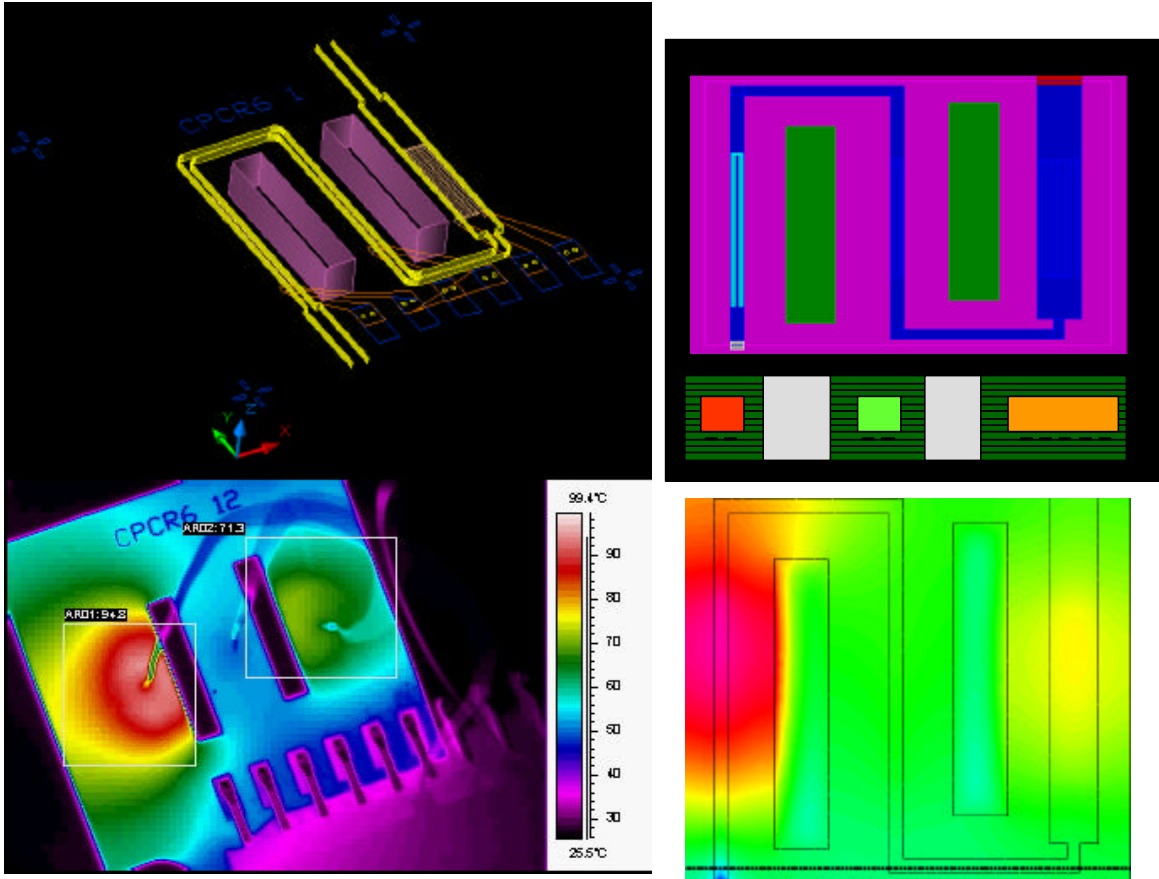


Figure 1 (top) CAD Design of 3 biological reactors with integrated heaters fabricated by Multilayer Ceramic; (bottom) IR microscopy image showing similar thermal profile than CFD Model (right)

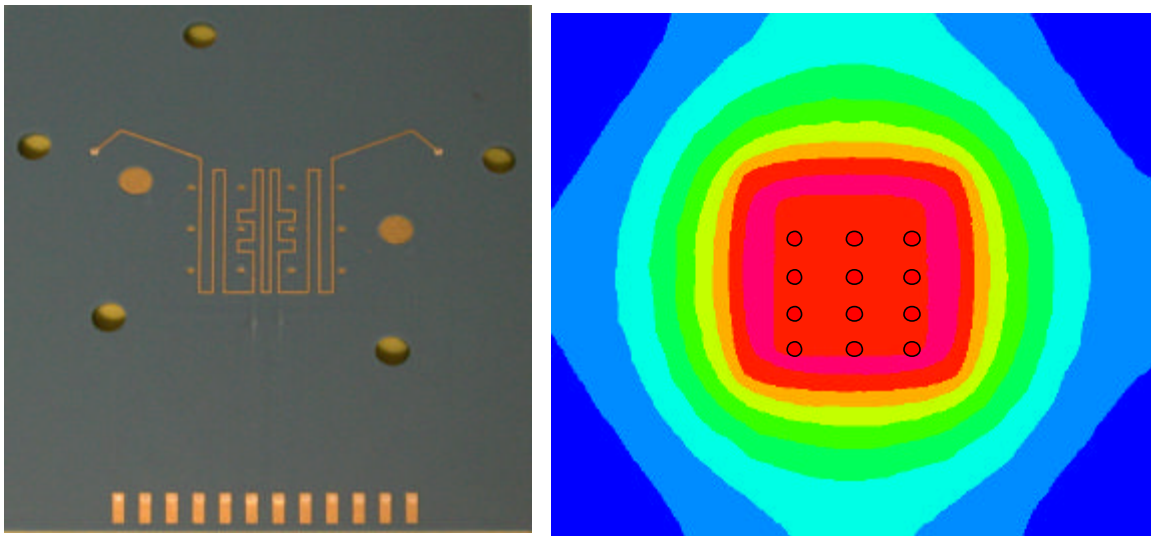


Figure 2 Electrode array with integrated heater in ceramic and thermal modeling of a 50 ul liquid over the array. The thermal distribution reveals a gradient of only 1°C over the entire array.

Ceramic MicroSystems Technology: Multi-layer Ceramic MicroSystems Technology is a unique platform technology enabling new breakaway opportunities in microfluidic manipulation and micro-scale chemical reactions. In particular, Multilayer Ceramics has been successfully established for manufacturing narrow-channel microreactors for the reaction of liquid-liquid flow for direct methanol fuel cells (DMFC) and also continuous flow PCR reactions for DNA amplification. Several new methods of manufacturing ceramic materials at the microscale, to enable the definition of fluid carrying microchannels with “high-resolution” control over the feature geometry and textures, promises to revolutionize BioMEMS fabrication. This materials and processing platform allows the development of vertical integration of microfluidic and microreactor components with sophisticated functionality. For example, the design and fabrication of genomic electrochemical bioassay devices (Figure 1) and fluidic modules based on continuous-flow streams with integrated thermal control functionalities have been demonstrated.

A miniaturized biological reactor with integrated heater /RTD temperature sensor was built in our ceramics and used for continuous DNA amplification reactions by PCR protocols. The thermal response of the resistive-silver heater stripe was simulated using the “thermal transfer” algorithm of Chemical Fluid Dynamics Simulation tools (CFDRC, Huntersville, Al). Heat generation was attributable to Joule heating of the heater lines and the heat loss mechanisms modeled include conduction through the ceramic substrate layers, conductive stripes and natural convection/radiation from the top surfaces to ambient. Insulation in air cavities, designed to space the three different PCR reactors (@ 94/57/72 C), were also modeled. “Brick” elements were used to represent the geometry of the microchannels (250 and 500 μm^2 cross-section) and solutions for the steady-state temperature and transient response were then compared with IR microscope data for model validation. Figure 2 shows the modeled temperature distribution over the PCR microdevice, which matches the IR measurements.

Conclusion: To make detailed simulation of microfluidic device performance, generally applicable and reliable, practical testing and analytical measurement techniques at the microscale are still needed to validate all our models. Based on the knowledge gained about the fundamental behavior of fluids and biomolecules combined with the microdevice behavior, enhanced process manufacturing will have a huge impact on near term feasibility of a large range of BioMEMS applications such as for mass scale, affordable genomic analysis.