Three Dimensional Thermal Effects in MEMS Devices

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ABSTRACT

A three dimensional thermal imaging system is being developed for measuring temperature profiles in MEMS-biomedical devices. These devices rely on a thermal microablation of the dead-skin layer in order to sample transdermal fluids. This is accomplished using microheaters embedded into a PDMS microchannel device. In order to determine the proper functioning as well as long-term safety of the devices, a temperature profile of the device and the skin in contact with the heaters is needed. The results of simple analytical models are used to optimize a prototype device. Using a three-dimensional chemical imaging microscope and temperature-dependent fluorophores, the temperature profile in a sample can be determined quantitatively as well. We demonstrate the technique on a model sample, and discuss extension to other applications such as thermal imaging in biological systems.

INTRODUCTION

Thermal phenomena play an important role in both biological processes and device fabrication. In biological systems, temperature has the roles of an environmental parameter to which organisms must adapt, both macroscopically, as in an animal's regulation of body temperature, and microscopically, as in temperature dependence of gene expression. Thermal effects are also critical in bio-MEMS devices, in particular those employing resistive heating elements. The effect of heat generation by active devices on the biological system it interacts with must be considered. Thermal phenomena may also play a critical role in the device functionality.

One such device is the Bio-Fluidic Integrable Transdermal (B-FIT) Microsystem [1] currently being developed at the Georgetown Advanced Electronics Lab (GAEL), and funded by DARPA [2], to detect and assess glucose levels as a physiological indicator of health. The basic concept and operation of the B-FIT is illustrated in Figure 1. A micro-fluidic sampling system coupled with thermal micro-ablation elements enables body analyte sampling at the Stratum Corneum (SC)/Viable Epidermis (VE) interface without invasive extraction of interstitial fluid. The thermal micro-heaters create micro-pore openings in the dead skin layer (SC), then a physiological fluid, which has been encapsulated in individual B-FIT reservoirs, is released using electrolytic gas bubble formation that acts as the fluidic driving mechanism. The physiological fluid bathes the micro-pore region and the biomolecules contained within the bubble-driven fluid, in conjunction with capillary action, allows for fluidic mobility towards the glucose detection subsystem. Up to 2000 individually addressable analysis systems can be fabricated in a 1 cm^2 area. It also incorporates colorimetric detection allowing fast information transfer to a health care provider or an individual user. Figure 1 also depicts the three possible (controllable) states of the individual micro-capillary systems. The leftmost post-sampling micro-capillary shows an

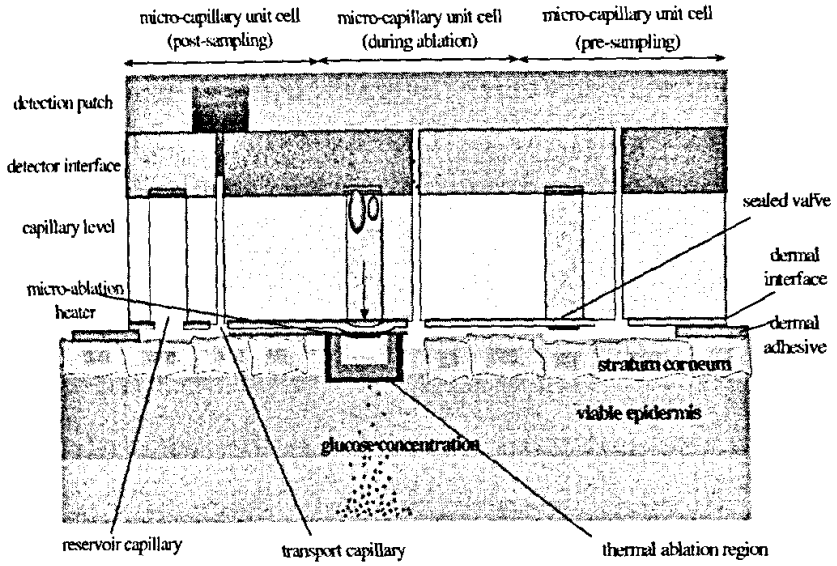

Figure 1: B-FIT cross section and operation sequence

exhausted capillary-reservoir pair that has already been used for an analysis procedure. It shows the completed thermal ablation and subsequent SC repair, an emptied reservoir, and capture of glucose from exposed interstitial fluid, indicated by the shaded area of the glucose detection patch at the upper surface of the chip. The middle micro-capillary system depicts a thermal ablation in progress, while the rightmost capillary system is ready for a future, on-demand analysis. All subsystems (microfluidic transfer, microheaters, detection patch) in the device have been fabricated, and current work involves integrating these into a working device.

Precise control of the temperature profile in the skin is vital to proper functioning of the patch. The temperature must be sufficiently high to ablate the dead skin layer, but the temperature must not cause permanent damage to the living cells nor cause pain through the nerve cells in the viable epidermis. This will require detailed knowledge of the effects of heating time and power on the different layers of the skin. We show modeling results indicating optimal parameters for the heat pulse, tests of a prototype device on cultured skin, and preliminary development of a novel method for imaging the temperature profiles.

EXPERIMENT

1-D Analytical Model: Constant Heat Flux

Heating the SC is a three-dimensional, transient problem. However, some insight can be gained from one-dimensional (depth) transient analyses. The transient analyses proceed up to the point of vapor formation (assumed to occur when water reaches 100°C). The dynamics of bubble formation and explosive expansion introduce too many unknowns to allow useful modeling. Simplifying assumptions may be possible after ablation experiments are begun.

One-dimensional analyses were developed to examine the time-dependency of temperature profiles through the SC and the epidermis, and through the device-dermal interface layer. The

former provides estimates of temperatures at nerve endings during and after heating pulses. The latter indicates the relative amounts of heat that enter the SC and the device, and whether the saline fluid in the reservoir may be heated to the boiling point.

With a constant heat flux applied to the SC surface at its interface with the resistive heater, an analytical expression is available for the temperature at various depths as a function of time. The heater controls would likely impose a given heat generation rate (current flow), but, for a thin heater with a small thermal capacitance, this can be approximated by imposing a constant heat flux. The difference between the temperature at the SC surface, T_W, and the temperature at some depth x, T_X, is given by:

$$T_W - T_X = 2 * (Q_W/k) * \sqrt{(\alpha * t)} * [(1/\sqrt{\pi}) - \int_{(\zeta x/2)}^{\infty} \mathrm{erfc}(\zeta/2)\, d(\zeta/2)] \qquad (1)$$

where Q_W is the heat flux rate, k the thermal conductivity, α the thermal diffusivity, x the depth into the sample, t is the time from pulse start, $\zeta_X/2 = x/(2*\sqrt{(\alpha*t)})$ is the normalized depth and erfc is the complement of the error function. For a given target surface temperature, this expression provides the temperature at some internal depth "x" at time "t."

Three dimensional thermal imaging

While two-dimensional imaging of temperature in biology has been extensively studied, there are few quantitative studies on three dimensional temperature profiles in humans or other organisms. Even using tomography, reconstruction of internal temperature profiles from measurement of surface temperatures is not be possible without a detailed knowledge of tissue thermal properties [3]. The only demonstrated method for measuring three dimensional temperature profiles is using magnetic resonance imaging (MRI) [4]. This method has been applied to cryotherapy [5], but is impracticable for our application.

In order to measure the temperature profiles in the B-FIT Microsystem and skin in contact with it, we have begun to develop a method based on three-dimensional fluorescence imaging of temperature dependent dyes. Laser scanning confocal imaging techniques have found wide use in both biological and other areas for imaging in depth as well as lateral directions, and for improving lateral resolution [6]. In this technique, which is usually based on a standard fluorescence microscope, laser light is focused onto the sample, and the fluorescence emission measured. The emitted light passes through a pinhole in the focal plane of the objective or a second lens inserted in the optical path. This effectively removes light emitted from regions of the sample that are out of the focal plane.

An alternate technique is to use numerical deconvolution of the emitted far field radiation, measured at a number of positions of the focal plane in the material, to calculate the three dimensional fluorescence profile [7]. We use this full field laser scanning mode because of fast the rate at which data can be collected, allowing us to follow the thermal ablations occurring on the time scale of 10's to 100's of milliseconds.

A temperature dependent fluorophore, Europium (III) thenoyltrifluoro-acetonate (EuTTA), is dispersed or dissolved in the sample. This dye has seen frequent use in microthermal imaging in two-dimensions, for example in imaging failure in integrated circuits [8] and biological imaging [9]. A sharp fluorescence emission band centered at 615 nm originates from the Eu ion. This is excited by an energy transfer from the TTA ligand, which is excited by green or UV light. The

transfer is highly temperature dependent, giving this material a strong temperature dependence in the range 0 to 100°C – the fluorescence emission drops by several orders of magnitude in this range. A mercury UV lamp is used as the excitation source. Images are taken at a series of discrete wavelengths using a FALCON™ Chemical Imaging Microscope (ChemIcon, Inc.). Images are taken at different focal planes in the sample and the results deconvoluted to give the three dimensional profile. An image is formed from the integrated peak intensity of the 615 nm emission. Pixel intensities from the images, along with the literature calibration [10], provide a quantitative measurement of the temperature.

RESULTS AND DISCUSSION

Modeling results

The curves in Figure 2 were produced using the 1-D model described above. A desired temperature at the interface (x = 0) can be achieved by an infinite variety of heat flux rates and application durations (t). For such a surface temperature (100°C and 123°C are shown in the Figure) and a given time, the curves show the temperature at any normalized depth.

We have used this analysis to estimate allowable heating durations to avoid pain or epidermal tissue damage. Nerve ending may come up to the underside of the epidermis, which is estimated here to be 100 microns from the SC surface. Although subjective, the pain threshold at a nerve ending is roughly 45°C. Thus, if the furthest depth of the epidermis is held below 45°C, we expect to maintain the pain-free aspects of the B-FIT design. For surface temperatures of 100°C and 123°C, the dotted lines in Figure 2 show the normalized depths at which 45°C is reached. Given the desired value of x and assumed value of α, the limiting value for t is determined, showing that pulses of 24 and 5 msec, respectively, are permitted.

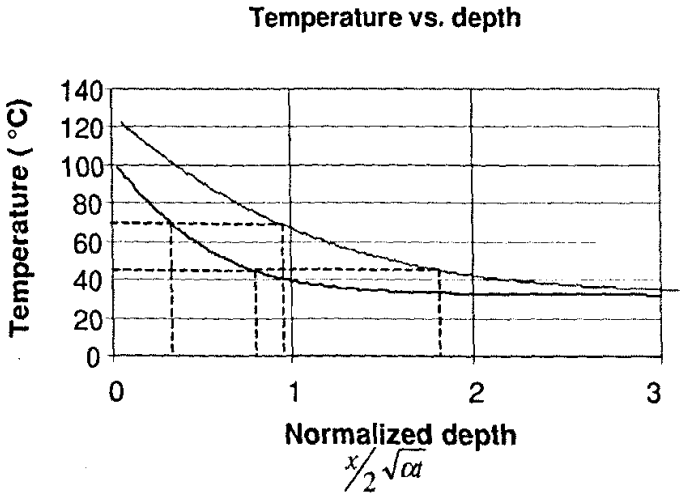

Figure 2. Temperature Profile in SC as Function of Surface Temperature, Thermal Properties, and Heating Duration. Upper curve corresponds to T=123°C of the SC, lower T=100°C.

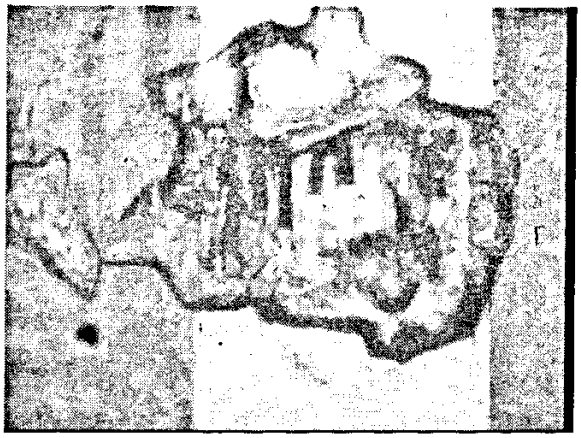

Figure 3: A micrograph showing the Apligraf during microablation. The image is taken through the skin side, with the microheater visible below the stratum corneum cells being ablated.

The results of this modeling allow us to optimize the heating necessary for SC ablation. Figure 3 shows the results on a prototype B-FIT device in contact with a sample of Apligraf® cultured skin, just after the ablation has begun. The image is taken through the cultured skin; by backing up the focus, the viable skin layer could be imaged. While the SC cells are destroyed, the cells in the viable epidermis are not.

Measurement of thermal profiles in a test sample

As a proof of concept for the method, we have prepared a test sample and performed preliminary characterization at various temperatures. Europium (III) thenoyltrifluoro-acetonate (EuTTA), was mixed into an epoxy resin, along with a 40 gauge Ni-chrome wire heating element and a thermistor probe. Both were embedded approximately 1 mm below the surface. For preliminary analysis images were collected at a single focal plane.

The preliminary fluorescence chemical imaging results are shown in figure 4. The image on the left shows the wire and dye-doped epoxy at room temperature with no current through the wire. In the right hand image, 7.5 volts (400 mA) were applied across the wire heater. A strong decrease in emission near the heater is clearly visible. Using literature values for the temperature

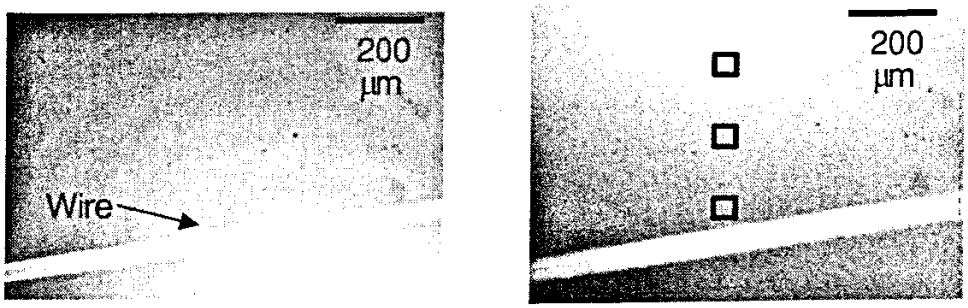

Figure 4: Thermal imaging near a wire heater. In the image on the left there is no applied current, in the one on the right the current is 400 mA. The brightness has been adjusted between the two images.

dependence of the fluorescence emission from EuTTA [10], we estimate temperatures of 55.3 °C, 54.5 °C and 51.6 °C in the lower, middle and upper regions of interest shown in the image on the right. We are currently performing a more thorough analysis of this data to determine the entire temperature profile and match it with the known heat transfer solution for a cylindrical source with given power input and thermal properties.

CONCLUSION & FUTURE WORK

The results of thermal modeling of the temperature profile in the SC under thermal ablation allowed optimization of the applied heating pulse profile. This optimization was confirmed by microscopic imaging of thermal ablation. In addition, we have demonstrated a general technique for measurement of three dimensional temperature profiles using temperature dependent dyes and fluorescent chemical imaging. Current work involves test sample measurement at various focal planes and deconvolution of the data to give the full three-dimensional temperature profile. Once we have demonstrated this on the test sample, we will measure fully functional B-FIT devices that are scheduled to be completed and used in animal testing within the next year.

ACKNOWLEDGEMENTS

This work is supported in part through a BioFlips DARPA-MTO (DAAD19-00-1-0390, Program Manager: Dr. Michael Krihak, and ARO Technical Monitor Dr. Robert Campbell).

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