PARYLENE ELECTROTHERMAL MEMS DRUG DELIVERY VALVE

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Introduction

In the past decade, the applications of Parylene in microelectromechanical systems (MEMS) devices have attracted significant attention especially for implantable drug delivery systems that integrate sensing, pumping, and valving[1,2]. These advanced drug delivery systems exploit the excellent mechanical and electrical properties of Parylene C by utilizing it as primary structural material in MEMS technology. An implantable microbolus infusion pump (MIP) (**Figure 1**) consisting of a drug reservoir, tuned inductive coil, catheter, and valve has been introduced for drug delivery in rats[3,4]. By inductively triggering the valve, a radioactive tracer is delivered into the circulation to enable rapid injection of a radiotracer for neuroimaging of brain blood flow in freely-moving untethered animals. A key requirement of the drug delivery system for mouse applications is the total weight and size of the implant; the weight must be less than 3 grams and the size must allow for subcutaneous implantation in a 40-gram mouse. In addition, the valve footprint should match the 330 μm inner diameter of the catheter. A MEMS Parylene C-based electrothermal valve is explored as a low-power, light-weight solution for the MIP drug delivery system.

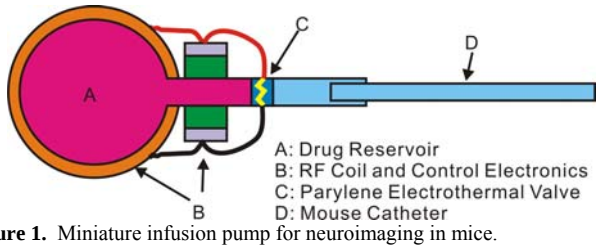


Figure 1. Miniature infusion pump for neuroimaging in mice.

Many groups have developed electrothermal valves for similar drug delivery applications[5,6]. These valves resemble electrical fuses and consist of a resistive heating element (platinum or gold) or metal/silicon nitride composite as a membrane. When electrical power is applied, the heater melts the thin film membrane and opens the valve. However, melting the membranes requires significant power to produce the necessary temperature. Here, we propose to use Parylene C as the heater-supporting membrane material in our electrothermal valve design. Parylene can be thermally oxidized and degraded at much lower temperatures (between 125°C and 200°C)[7] and is expected to enable low-power valves for use in wireless implants. In addition, this concept can adapted for the development of reconfigurable microfluidic devices.

Experimental

Design. The electrothermal drug delivery valve (**Figure 2a**) consists of an electron-beam evaporated platinum thin film heater embedded in the center of a 10 μm thick flexible Parylene C membrane. **Figure 2b** shows the serpentine pattern of the platinum heater (with a 20 μm wide wire confined in a 330 μm diameter circular area). Two contact pads (1.5 mm x 3 mm) connecting to the resistive element allow connection to external wires of the control circuitry. The meandering pattern of the heater was selected to maximize resistance of the heating element compared to the electrical contacts. When current is applied, most of the electrical power is consumed by this heater resistor and converted into thermal energy. This heat elevates the temperature of the Parylene C around the heater and thermally degrades the Parylene C membrane. The thermally-generated opening in the Parylene C membrane creates fluid flow path for the pressurized contents of the reservoir through the catheter and into the venous circulation (**Figure 2c**).

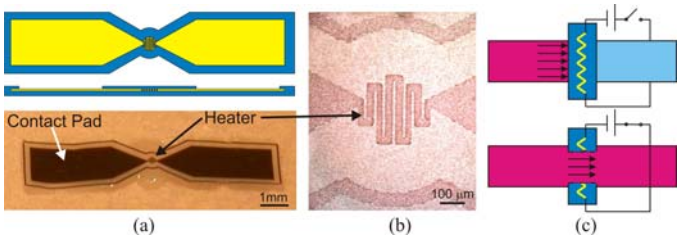


Figure 2. Parylene electrothermal drug delivery valve: (a) the device, (b) the heater, and (c) the operation principle of the valve.

Fabrication. The valves were constructed using standard microfabrication techniques. First, Parylene C (5 μm in thickness) was deposited on a 3 inch silicon wafer (**Figure 3A**). This is the first layer of the Parylene C/metal/Parylene C sandwich. Then liftoff lithography was performed and a 1000 Å thick platinum film was e-beam evaporated. Following liftoff, the heater and contact pad of the valve were defined (**Figure 3B**). The top Parylene layer (5 μm in thickness) was then deposited (**Figure 3C**). To completely open the contact pad, a thick photoresist layer (8 μm of AZ4400) was patterned as a mask for reactive ion etching (RIE) (**Figure 3D**). The Parylene C over the contacts was removed by oxygen plasma. Then the photoresist was stripped in acetone (**Figure 3E**). The entire wafer was immersed into DI water to release the Parylene C membrane and the individual devices were manually cut from the wafer (**Figure 3F**). Finally, the valves were thermally annealed in vacuum under nitrogen backfill conditions (2 days at 200 ºC).

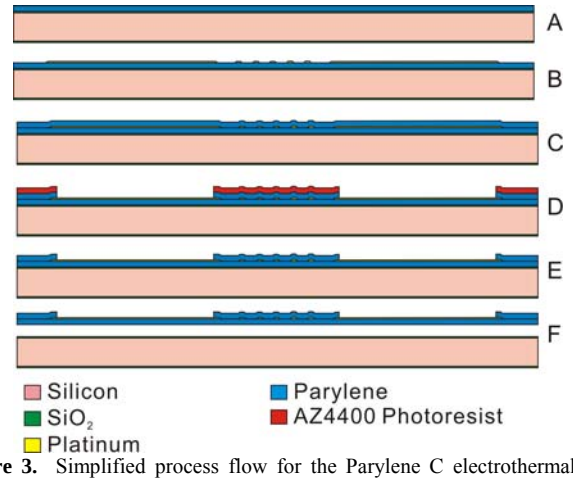


Figure 3. Simplified process flow for the Parylene C electrothermal drug delivery valve.

Benchtop Testing. The resistance, temperature coefficient of resistivity, overheat temperature, and valve opening power of the Parylene C electrothermal drug delivery valve were determined in benchtop experiments. To predict the theoretical resistance of the heater, sheet resistance of thin film platinum coated on a soda lime glass slide was first measured. The theoretical resistance of a resistor can be calculated by

$$R = R_s \frac{l}{w} \quad (1)$$

where R is the heater resistance, R_s is the sheet resistance, l is the length of the heater, and w is the width of the heater. The resistances of the fabricated valve devices were also measured and compared to the theoretical values.

Temperature coefficient of resistivity (TCR) is an important parameter to predict Pt heater resistance at different temperatures. The temperature dependence of Pt is approximately linear over the range of interest and can be express as

$$R(T) = R(T_o)[1 + \alpha(T - T_o)] \quad (2)$$

where $R(T)$ is the resistance at temperature T, T_o is an appropriate reference temperature, and α is the temperature coefficient of resistivity. The temperature calibration curve was experimentally determined by placing the

device in a temperature-controlled environmental chamber and recording the resistance at different temperature setpoints. The measurements were substituted into equation (2) to obtain TCR. In addition, the overheat temperature (OHT) allows the temperature of the heater to be calculated from its resistance. Heater resistances for different applied currents were obtained. Then the heater temperature can be estimated by using the following equation and the experimentally determined TCR:

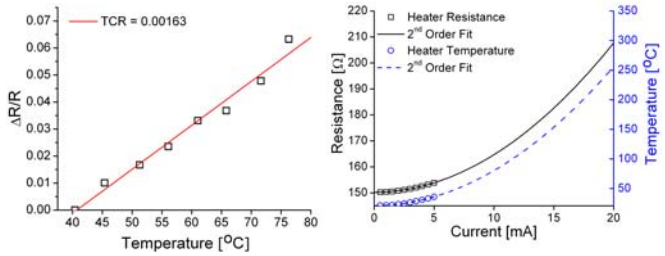
$$T = T_o + \frac{R(T) - R(T_o)}{\alpha R(T_o)} \quad (3)$$

The valve opening power and current were obtained by applying constant current starting from 1 mA and increasing in small increments; the current corresponding to Parylene C membrane valve opening was recorded. Corresponding opening power values were calculated. The devices were evaluated by using a laser-machined test fixture to allow rapid electrical connections and facilitate visual observation of the valve. The entire process was monitored by a compound microscope connected to a computer-controlled CCD camera capable of recording time lapse images.

Results and Discussion

Benchtop Testing. The sheet resistance measured from the e-beam evaporated Pt on the soda lime glass slide was 2.24±0.12 Ω/□ (mean±SE, n=5). The corresponding theoretical resistance of the heater based on equation (1) was 199.22 Ω. The measured value was 174.9±12.62 Ω (mean±SE, n=10) which is slightly lower than expected.

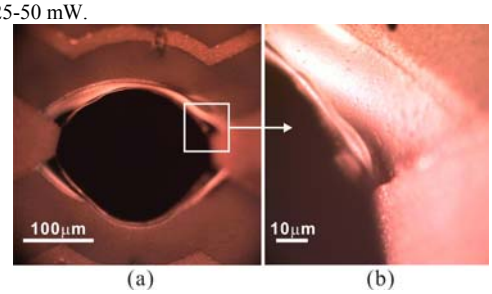
Figure 4a shows the results of TCR calibration experiment. A typical TCR for our e-beam deposited thin film Pt heater is 16.3 x 10^{-4}/°K which is lower than that expected for bulk Pt TCR (39.2 x 10^{-4}/°K). This TCR value was applied to the OHT measurements to predict the Pt heater temperature at different applied currents (**Figure 4b**). To protect destructive thermal degradation of the device under test, the OHT experiments were performed at lower currents and the results were extrapolated to higher current ranges by using a 2nd-order polynomial curve fit. As depicted in **Figure 4b**, the valve opening current is expected to be between 10 to 15 mA for Parylene C.



(a) (b)

Figure 4. Typical heater responses for (a) TCR and (b) OHT experiments.

Figure 5 shows an open Parylene C electrothermal valve after the application of 15mA in air. A further magnified view (**Figure 5b**) shows the edge of thermally generated valve orifice. Four devices were used for valve opening experiments (**Figure 6**). Both valve opening current and power decrease with increased heater resistance. This result indicates a longer and thinner heater will improve power consumption. Measured opening currents were 7-20 mA and the corresponding calculated power consumption was between 25-50 mW.



(a) (b)

Figure 5. Images showing (a) an open valve after 15 mA applied current and (b) magnified view of the edge of the valve orifice.

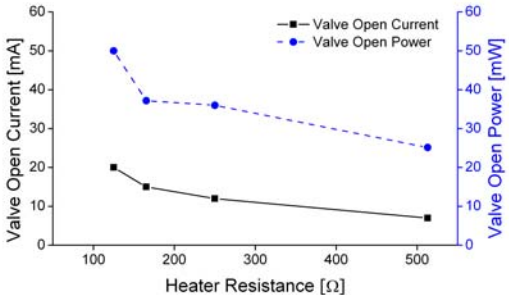


Figure 6. Valve opening current and power to heater resistance relationship.

Valve Assembly. The Parylene C drug delivery valve needs to be assembled in the path of the catheter to incorporate it into the microbolus infusion pump system. The electrical connections to control circuitry was established by using thin wires adhered with conductive epoxy (150°C for 15 hours). Then the valve was sandwiched between two lengths of catheter and secured with epoxy. The flexible Parylene C film allows the contact pad regions to be folded back over the catheter to minimize the overall valve footprint. The assembly process was performed under a stereo microscope (**Figure 7**).

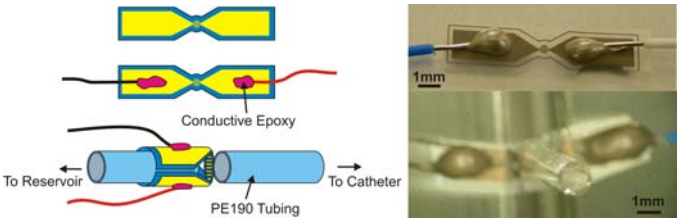


Figure 7. Device assembly for the Parylene MEMS drug delivery valve.

Conclusion

We successfully developed a disposable, low-power Parylene C MEMS valve for drug delivery application. The design, fabrication, and benchtop characterization were performed and investigated. TCR and OHT experiments allowed us to predict the temperature of the heater and determine the appropriate current to apply to open the valve. Opening powers of 25-50 mW were obtained. Further work will be done to reduce power consumption. Also, additional experiments will evaluate the performance of the valve in the presence of drug and *in vivo*. In addition, this Parylene C electrothermal valve will be integrated into a reconfigurable microfluidic device.

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