Supplementary Information for

Cellular Bias on the Microscale: Probing the Effects of Digital Microfluidic Actuation on Mammalian Cell Health, Fitness and Phenotype

Sam H. Au,[1,2] Ryan Fobel,[1,2] Salil P. Desai,[3] Joel Voldman[3] and Aaron R. Wheeler[1, 2, 4 †]

[1] Institute for Biomaterials and Biomedical Engineering, University of Toronto, 164 College St., Toronto, ON, M5S 3G9

[2] Donnelly Centre for Cellular and Biomolecular Research, 160 College St., Toronto, ON, M5S 3E1

[3] Department of Electrical Engineering & Computer Science, Massachusetts Institute of Technology, 77 Massachusetts Ave., Cambridge, MA, 02139

[4] Department of Chemistry, University of Toronto, 80 St George St., Toronto, ON, M5S 3H6

† Corresponding Author
email: aaron.wheeler@utoronto.ca
tel: (416) 946 3864
fax: (416) 946 3865

Temperature Measurements

70 µL, 18 µL or 5 µL droplets of RPMI-1640 cell culture media supplemented with 10% fetal bovine serum and 0.06% (wt/v) Pluronic F88 (Brenntag Canada, Toronto, ON) were loaded onto DMF devices bearing 10 mm x 10 mm, 5 x 5 mm or 2.5 x 2.5 mm electrodes respectively. The electrodes were then charged for 15 minutes continuously using the methods and system described in the main text, with 400 V_{PP} driving potentials at 1, 10, or 18 kHz. A K-type KMQSS-010U-6 thermocouple (Omega Engineering, Inc., Laval, Canada) was inserted between the two plates to measure the temperature in each droplet as a function of time. Three replicate measurements were collected for each of the nine electrode size/frequency combinations.

The results of the temperature measurement experiments are shown in Figure S1. In some cases, droplet temperatures increased significantly– up to 25°C above ambient – during application of DMF driving potentials. While such effects are purposefully generated in specialized DMF devices modified to include resistive heaters (typically driven by DC potentials),[1] the data shown in Figure S1 were generated from droplets positioned on standard devices (with no heaters) driven by standard AC driving potentials. As far as we are aware, this phenomenon has never before been reported.

The data in Figure S1 suggest several trends. First, the conditions tested that are closest to those used regularly for digital microfluidics (i.e., 2.5 mm x 2.5 mm electrodes at 1 kHz or 10 kHz frequencies) have near-negligible effects on droplet temperature, with average temperature increases of 0°C and 2.3°C respectively. Second, elevated frequency or electrode size alone results in minor effects – e.g., 2.5 mm electrode/18 kHz and 10 mm electrode/1 kHz result in average temperature increases of 3.9°C and 2.8°C, respectively. Third, the large heating effects (i.e., temperature increases greater than 5°C) were only observed for conditions with both elevated electrode size and frequency.

It should be noted that the droplet temperatures in Figure S1 were measured in stationary droplets (not moving droplets, as in actual DMF experiments). We expect that the temperatures recorded in Figure S1 are on over-estimation of the temperatures of droplets in motion, as mobile droplets such as those described in the main text for manipulating cells, are repeatedly moved to device regions which have had time to cool, allowing heat to be dissipated more rapidly.

Potential Causes of Droplet Heating

A potential mechanism for the temperature increases represented in Figure S1 is resistive (Joule) heating, which is commonly observed in MEMS devices.[2] As frequency increases, the impedance of the digital microfluidic circuit decreases,[3] resulting in an increase in current which will increase the Joule heating. Another candidate is dielectric heating, which is caused by the frictional loss of energy of rotating dipoles in the presence of an applied electric field.[4] The power generated by dielectric heating scales with the square of electric field strength and linearly with applied frequency. Although DMF operation uses a much lower frequency range than those which are typically used for dielectric heating (MHz-GHz), the physical scale of DMF devices may render dielectric heating significant because large field strengths can be achieved over very short distances. Both mechanisms of heating are consistent with the frequency-dependent increases in temperature shown in Fig. S1, and in other experiments, much higher frequency waveforms led to even greater temperature changes (data not shown). In on-going work, we are evaluating these effects in more detail, but these observations are not the main focus of the work presented here.

References

1. J. H. Wei, W. S. Hsu, S. K. Fan, "Realizing temperature-controlled digital microfluidic chips with versatile microelectrodes." in *Digest of International Conference on Nano/Micro Engineered and Molecular Systems*, IEEE: New York, 2007; p 741-744; J. T. Cheng, C. L. Chen, Active thermal management of on-chip hot spots using EWOD-driven droplet microfluidics. *Exp. Fluids 49*. 1349-1357.
2. U. Seger, M. Panayiotou, S. Schnydrig, M. Jordan, P. Renaud, Temperature measurements in microfluidic systems: Heat dissipation of negative dielectrophoresis barriers. *Electrophoresis* 2005, *26*. 2239-2246.
3. D. Chatterjee, H. Shepherd, R. L. Garrell, Electromechanical model for actuating liquids in a two-plate droplet microfluidic device. *Lab on a Chip* 2009, *9*. 1219-1229.
4. C. Gabriel, S. Gabriel, E. H. Grant, B. S. J. Halstead, D. Michael P. Mingos, Dielectric parameters relevant to microwave dielectric heating. *Chem. Soc. Rev.* 1998, *27*. 213-224.

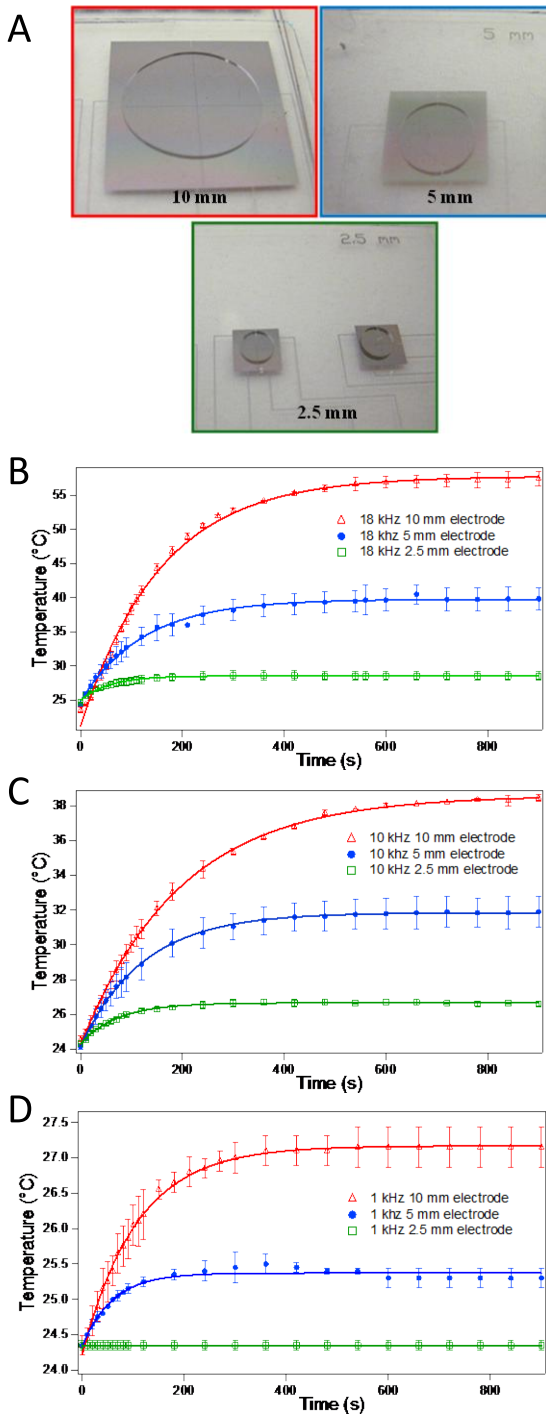

Figure S1: Droplet temperature in digital microfluidics. Images of 70 µL (top left), 18 µL (top right) and 5 µL (bottom) droplets on digital microfluidic devices (A). Graphs of the temperatures of droplets subjected to driving potentials on devices bearing 10.0 x 10.0 mm (red triangles), 5.0 x 5.0 mm (blue circles) and 2.5 x 2.5 mm (green squares) square electrodes at 400 Vpp at (B) 18 kHz, (C) 10 kHz and (D) 1 kHz frequencies. Error bars represent one standard deviation (n=3), and curves were added to guide the eye.