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Desktop Injection Molded Centrifugal Microfluidics for Infectious Disease Diagnostics Using Integrated Optical pH Sensors

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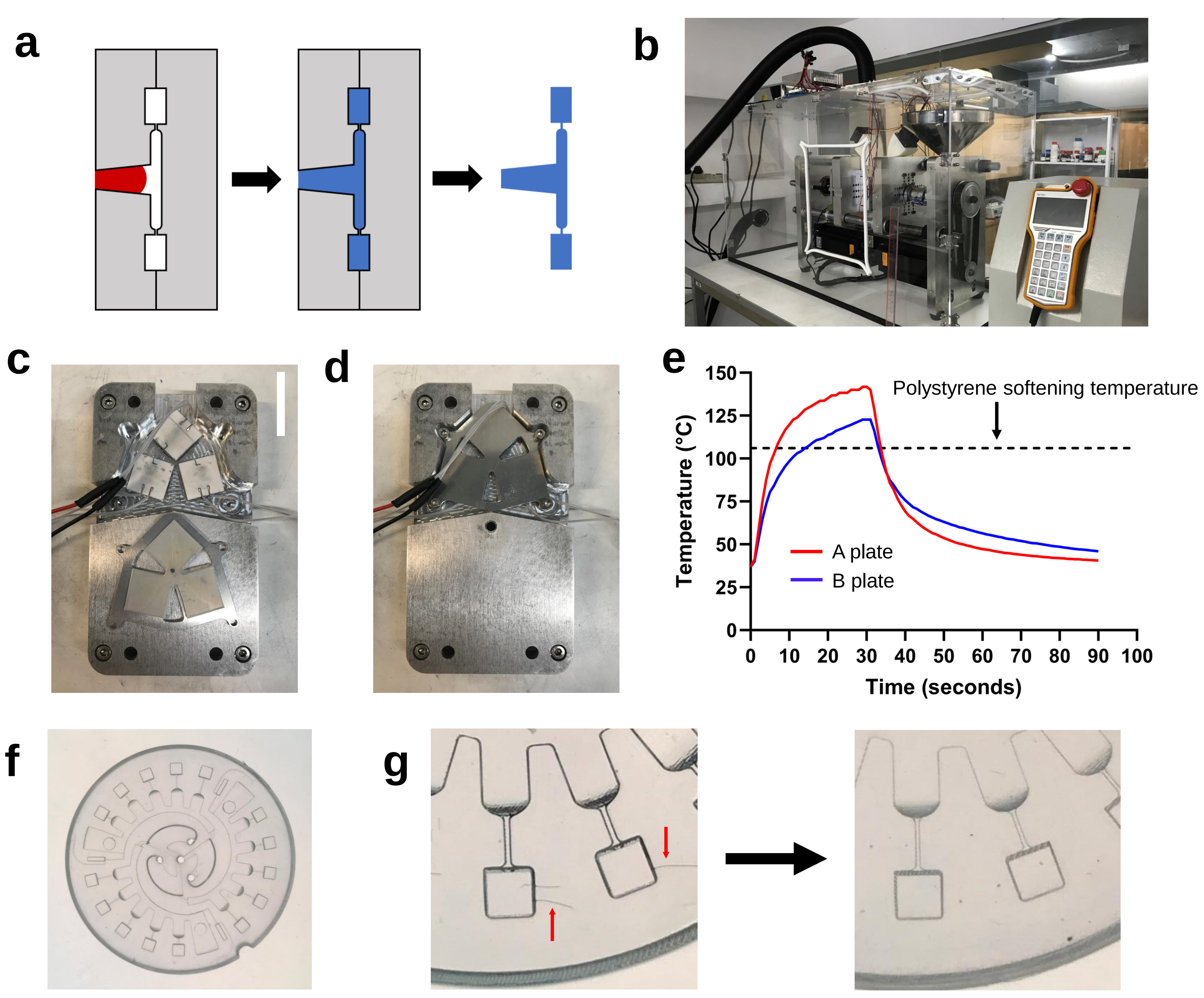
Introduction

A centrifugal microfluidic chip and detection methods were developed that permit rapid point-of-care multiplexed diagnostics of infectious diseases. The chips were fabricated out of polystyrene using a novel variothermal desktop injection molding (VDIM) process with cycle times under one minute. The chip design incorporates a novel central fluidic mechanism for sample loading and 15 fluidically separated reaction chambers which can multiplex diagnostic RT-LAMP assays. FITC-pHEMA optical pH sensors were used to generate readouts in minimally buffered RT-LAMP reactions, yielding results in 30 minutes, and these sensors can be integrated into the microfluidic chips. This technology should allow public health officials, medical practitioners, and even home users to monitor various infectious agents, including viruses.

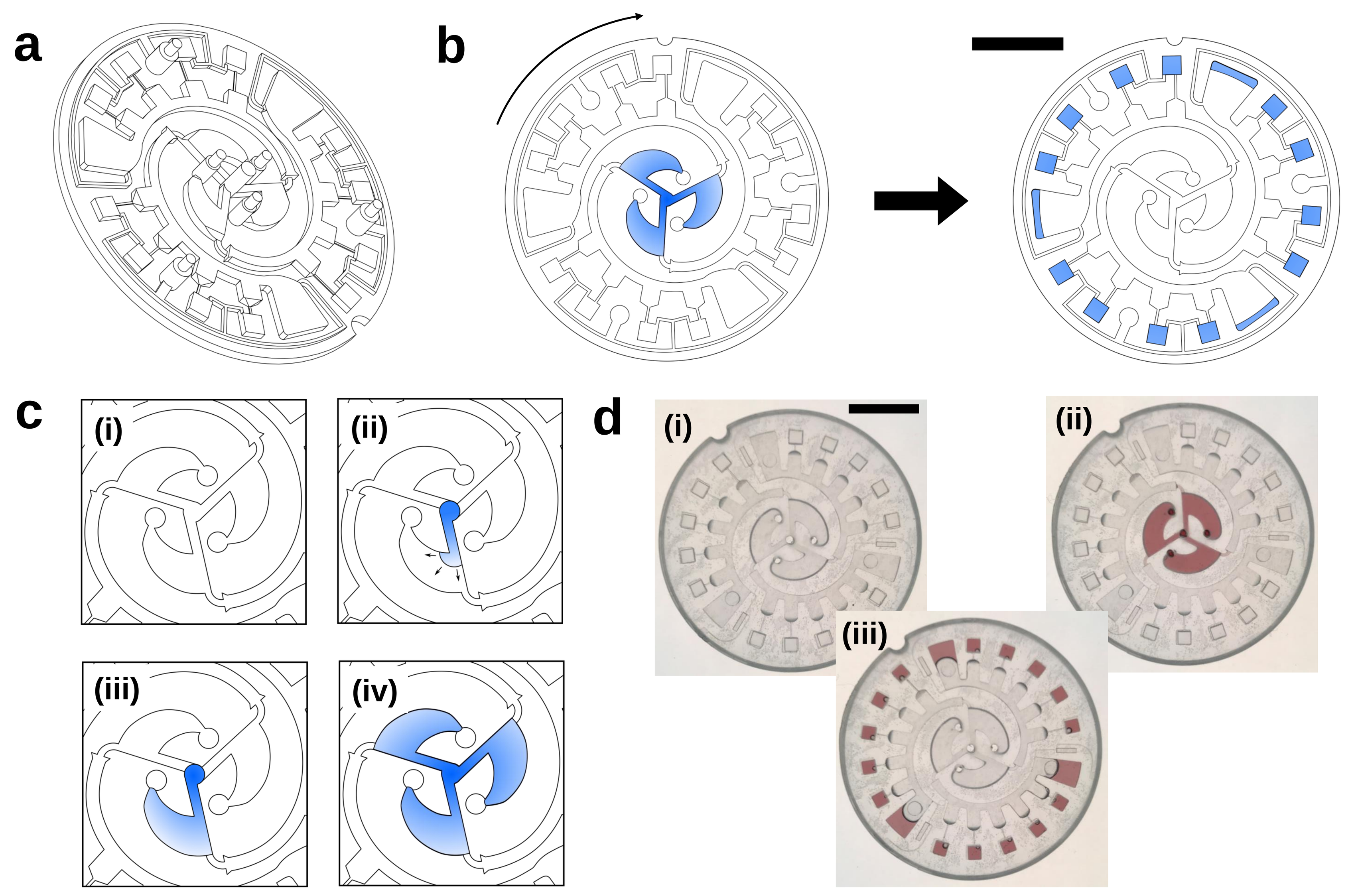
Experimental Results

Variothermal Desktop Injection Molding of Microfluidics



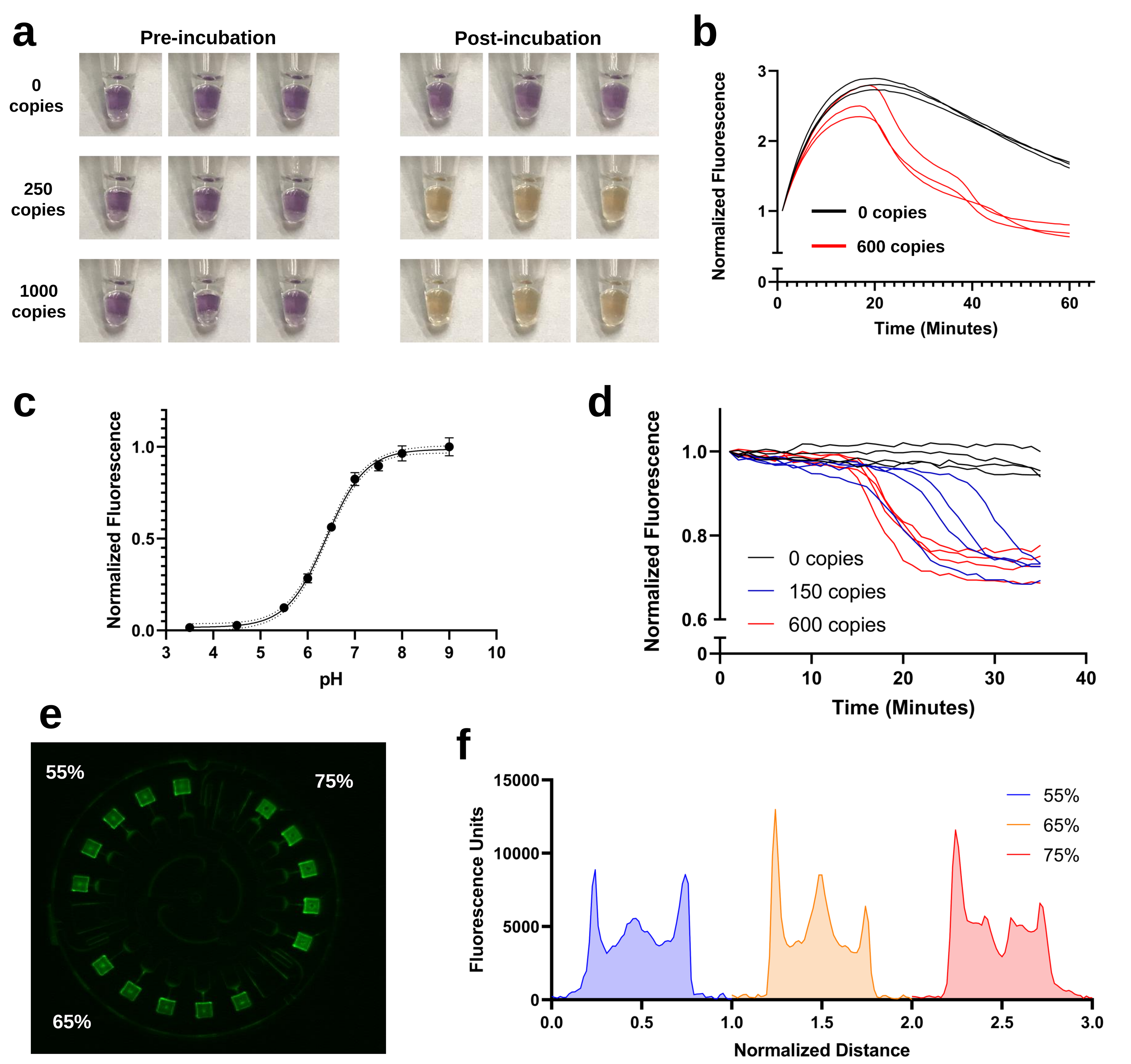
(a) Illustration of injection molding cycle. Molten plastic (red) is forced into a cavity, solidifies (blue), and is ejected. (b) Variothermal desktop injection molding equipment. (c) Backside of injection molding plate showing heating elements. Scale bar is 3 cm. (d) The assembled heating mechanism in the mold pate. (e) Heating and cooling profile of A and B molding plates. (f) Injection molded chip half. (g) Elimination of weld lines (indicated by red arrows) through variothermal molding.

Centrifugal Microfluidic with Novel Filling Mechanism



(a) Perspective view of centrifugal microfluidic chip. (b) Actuation of microfluidic via rotation. Scale bar is equivalent to 1 cm. (c) Sequential loading of central chambers. (d) Assembled centrifugal microfluidic chips (i) with central chambers filled (ii) and after actuation (iii). Scale bar is 1 cm.

Evaluation of Optical pH Sensors for RT-LAMP Reaction Readouts



(a) Images of RT-LAMP reaction tubes incubated with SARS-CoV-2 RNA and m-Cresol Purple pH indicator. (b) Fluorescence measurements of RT-LAMP reactions containing SARS-CoV-2 RNA copies and SNARF-1 pH indicator. (c) Titration of FITC-HEMA optical pH sensors drop-casted into polystyrene microwell plate. (d) Fluorescence measurements of RT-LAMP reactions containing SARS-CoV-2 RNA and incubated in microwells with drop casted optical pH sensors. (e) FITC-pHEMA in solution with indicated percentage of EtOH drop-casted into reaction chambers. (f) Representative line profiles of optical pH sensors in microfluidic chip chambers.

Summary

- Variothermal heating enables economical microfluidics prototyping via injection molding
- Centrifugal microfluidic chips effectively aliquot fluids and FITC-pHEMA sensors provide sensitive reaction readouts
- Optical pH sensors will be integrated into microfluidic chips and used for multiplexed diagnostics

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