

Multiplex, Single Step, On Chip Detection of Mutations in Circulating Tumor DNA

Amanda Haack
Ori Hoxha
Shilpika Chowdhury
Taylor Lee

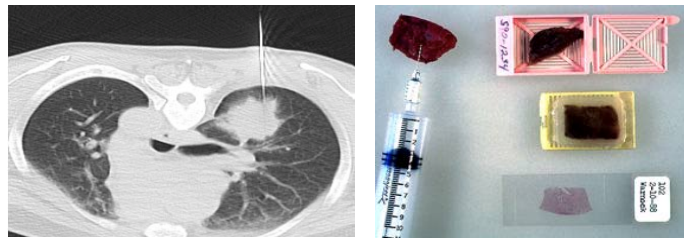
Gold Standard

Treatment Type



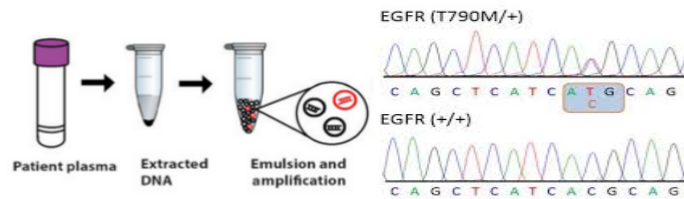
Radiation Therapy or Chemotherapy

Sample Collection



Tissue Biopsy

ctDNA Detection



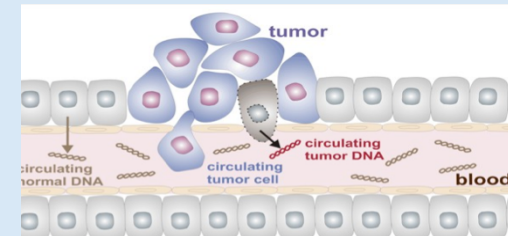
Off-Chip Detection

Improvement

Targeted Medication



“Liquid” Biopsy
(Blood Sample)



On-Chip Detection

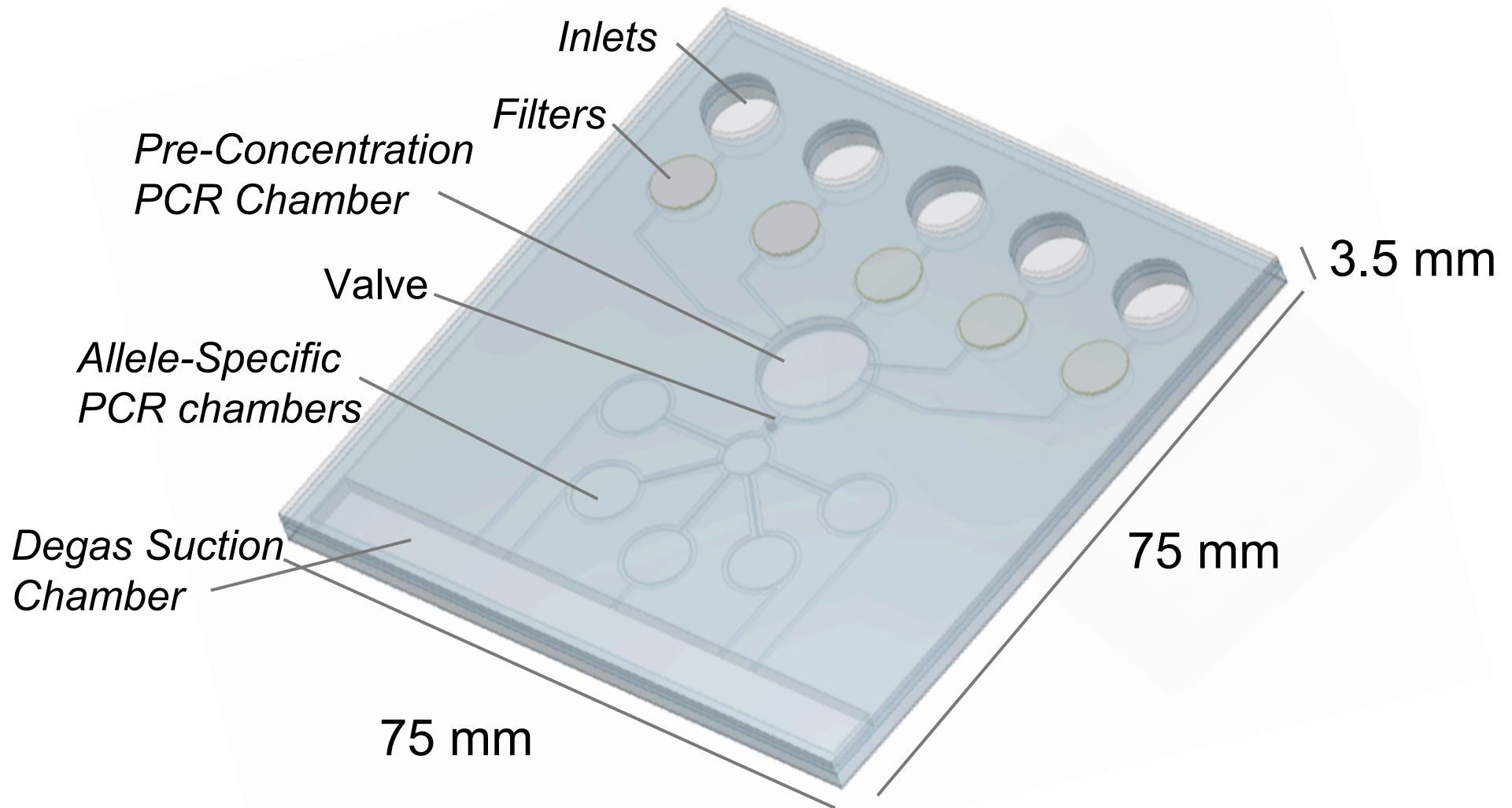


Oxnard et al. Noninvasive Detection of Response and Resistance in EGFR-Mutant Lung Cancer Using Quantitative Next-Generation Genotyping of Cell-Free Plasma DNA. *Clin Cancer Res.* **20**(6): 1698-705 (2014)
Situma et al. Fabrication of DNA microarrays onto PMMA with ultraviolet patterning and microfluidics for the detection of low-abundant point mutations. *Anal Biochem.* **340**(1):123-35. (2005)

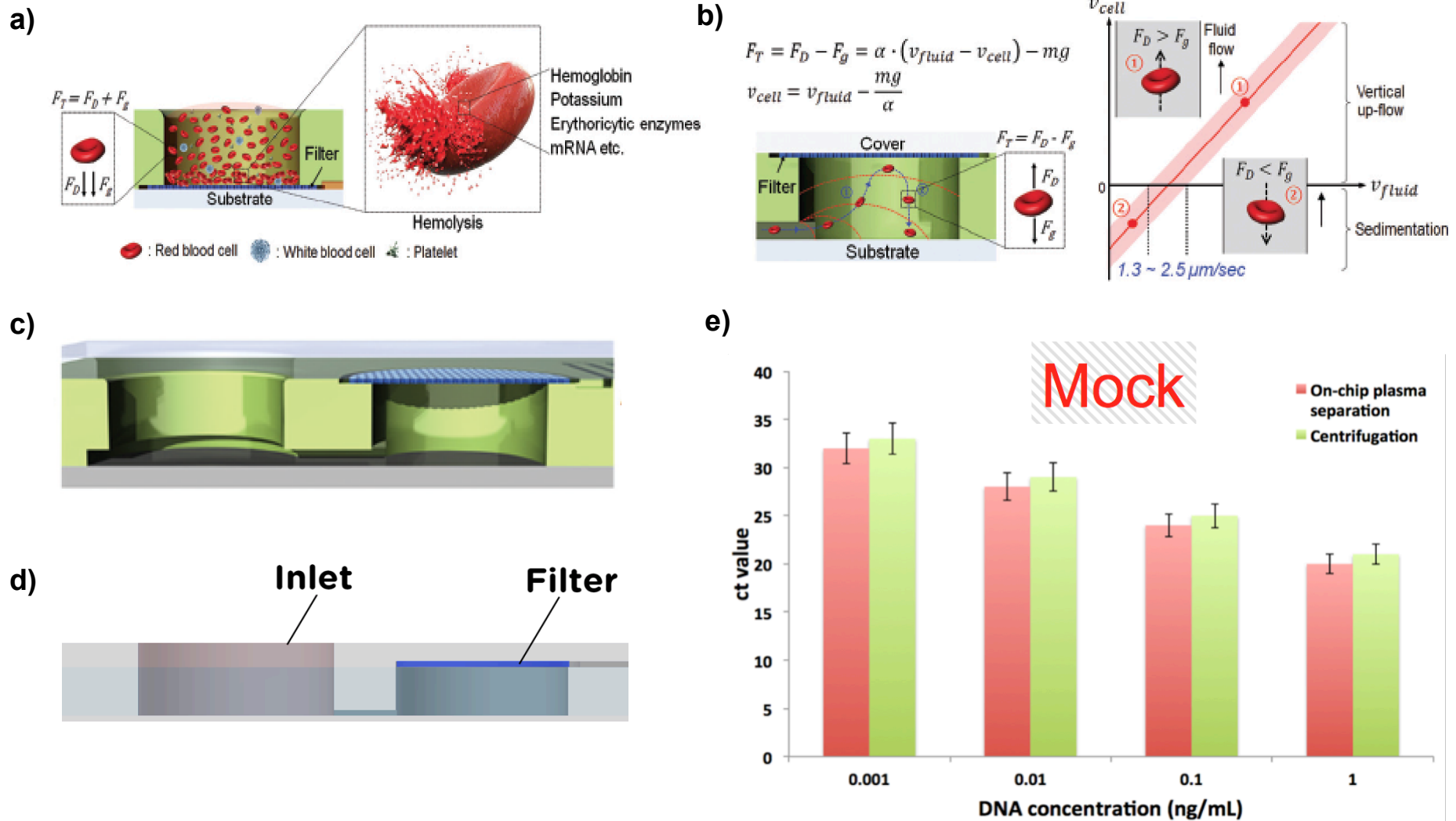
Take-Home Messages

1. We provide an **single-step, multiplex, on-chip, integrated detection platform** of the **5 most abundant cancer treatment response mutations** on the EGFR region (Exon 19 deletion, G719X, L858R, Exon 20 insertion and T790M) in about 10 minutes.
2. **On-chip sample preparation** module utilizing **filter on-top** configuration for separation of blood plasma with **recovery yield for circulating DNA as high as 99%**.
3. COMSOL simulation showed a **temperature gradient of less than 2°C** in the PCR chamber, allowing for **efficient and uniform amplification**.
4. The device shows a **limit of detection (LOD) as low as 0.0001 ng/mL** when tested with mutated DNA spiked human blood plasma.

We provide a **single-step, multiplex, on-chip, integrated detection platform** of the **5 most abundant mutations on the EGFR region**, Exon 19 deletion, G719X, L858R, Exon 20 insertion and T790M, in less than 10 minutes.

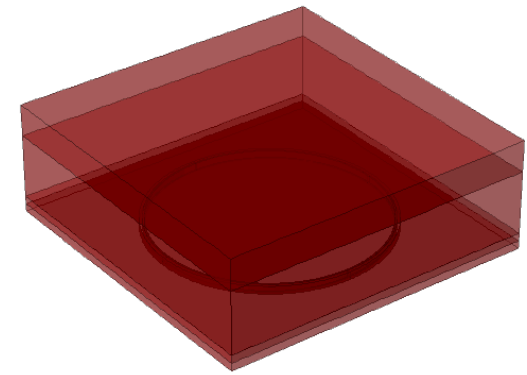
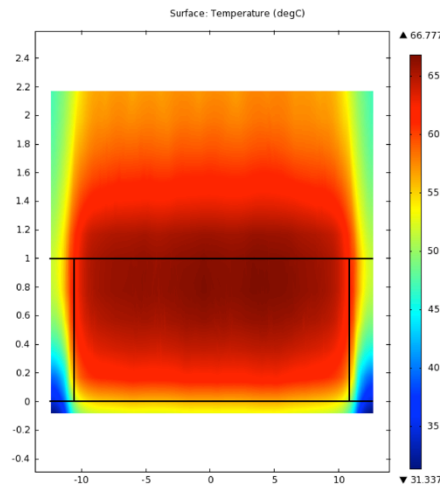
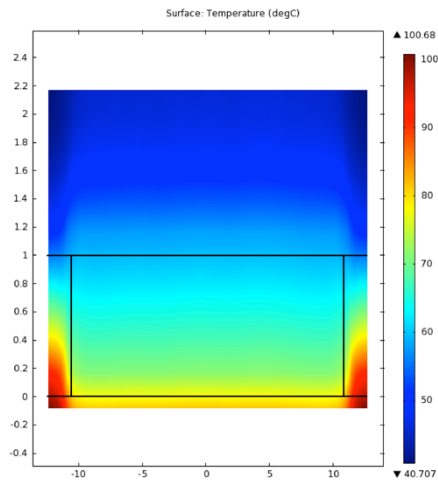


On-chip sample preparation module utilizing filter on-top configuration for separation of blood plasma shows **recovery yield for circulating DNA as high as 99%**.

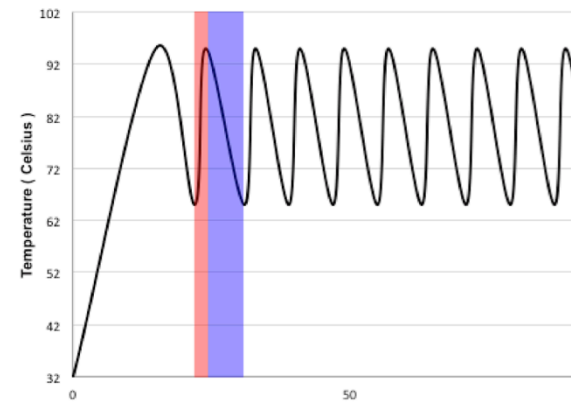
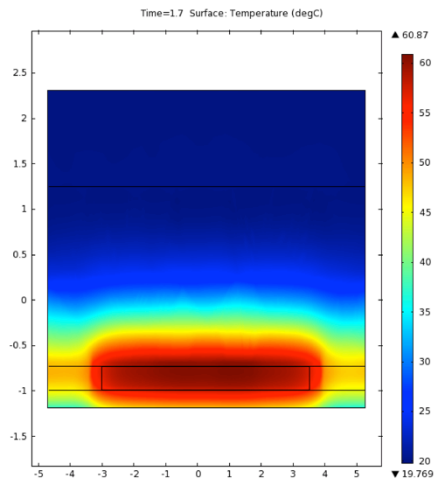
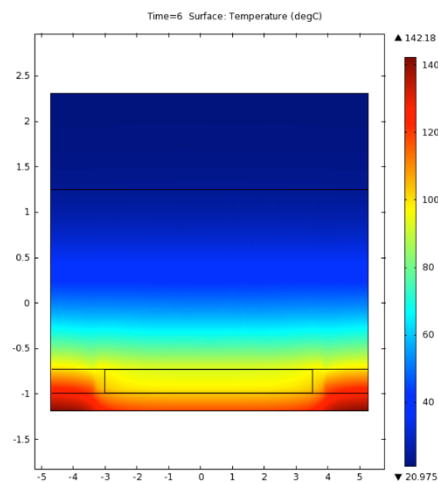


COMSOL simulation showed a **temperature gradient of less than 2°C** in the Allele-Specific PCR chamber along the perimeter of the chamber, allowing for efficient and uniform amplification.

Pre-Concentration:

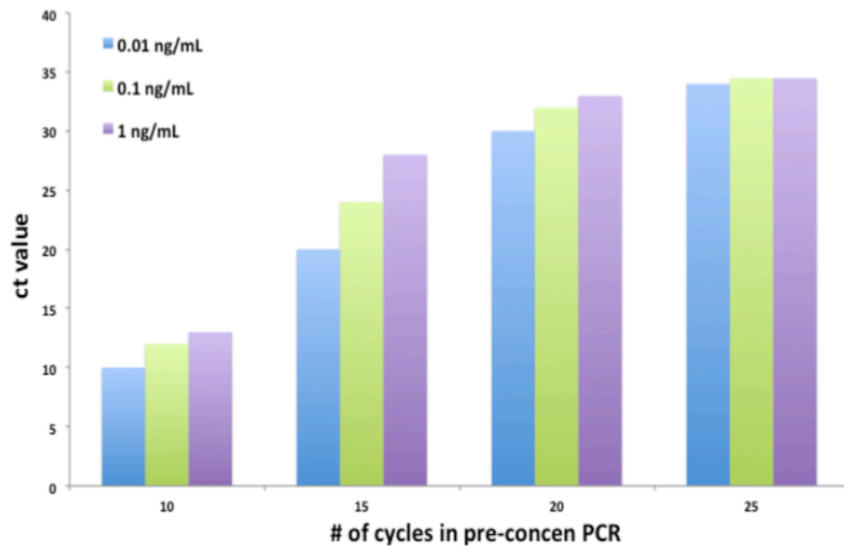


Allele-Specific PCR:

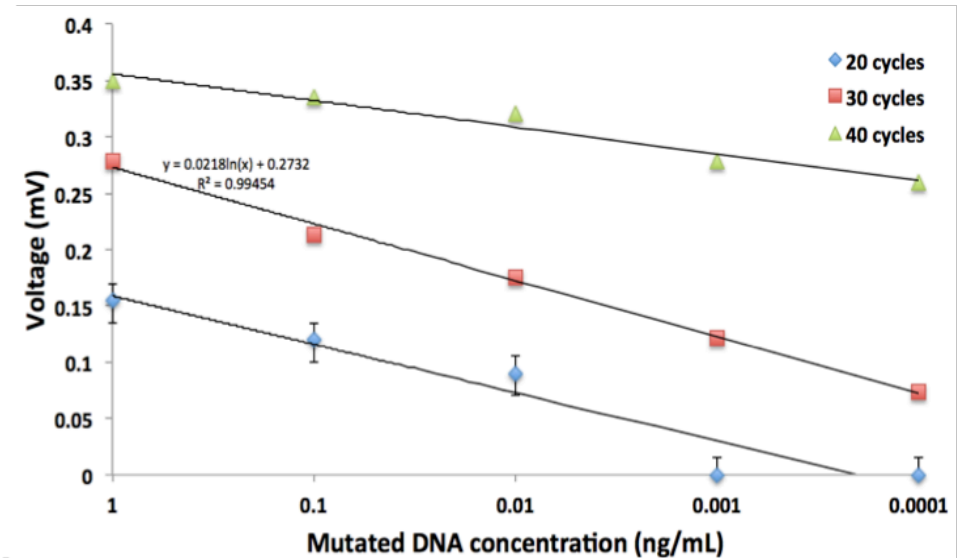


The device shows a **limit of detection (LOD)** as low as **0.0001 ng/mL** when tested with mutated DNA spiked human blood plasma.

a)



b)



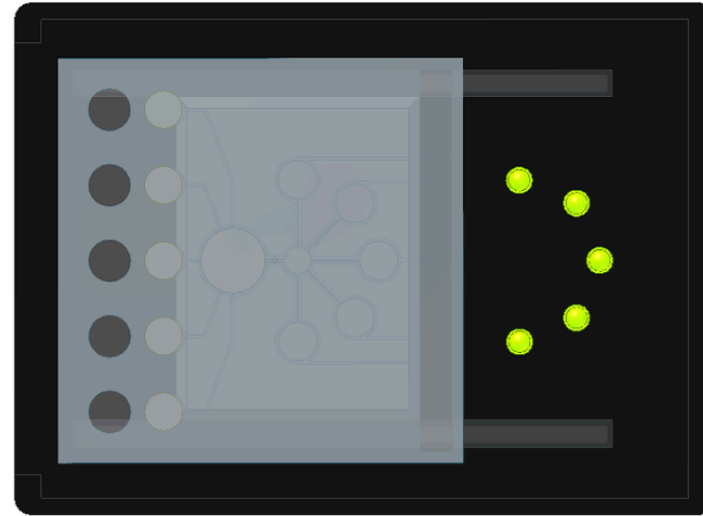
Mock

The Housing Unit:

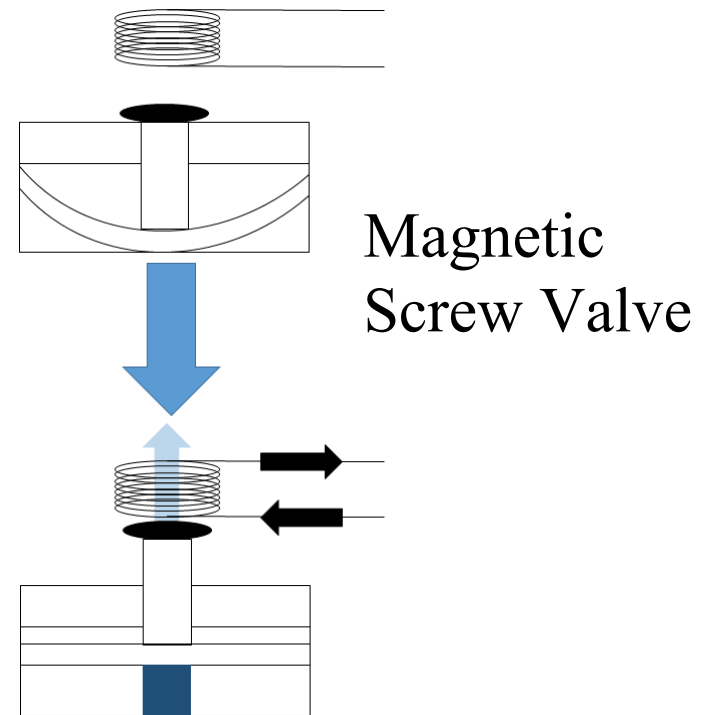
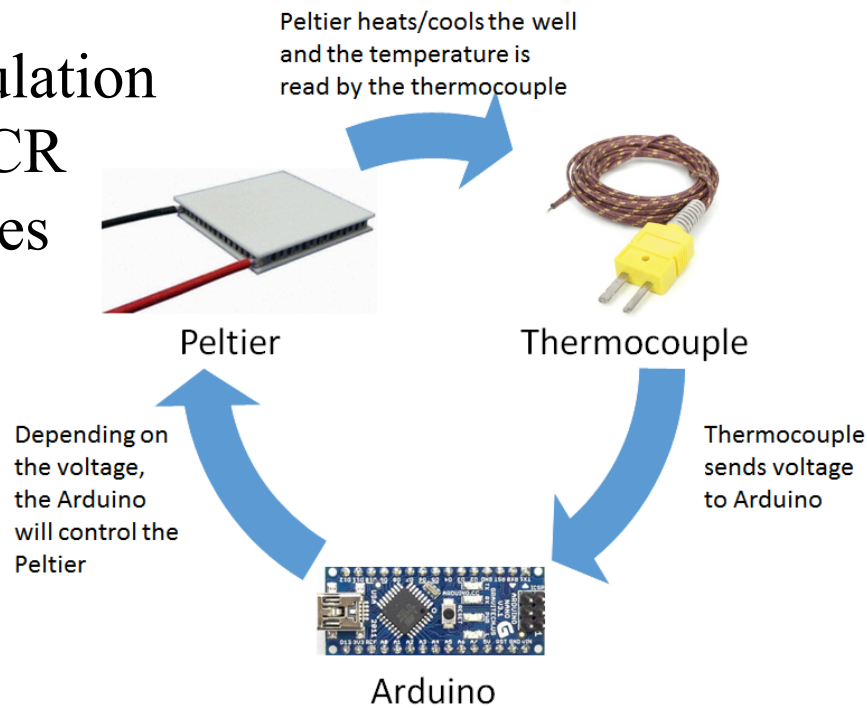
Regulation and automation of PCR and detection.

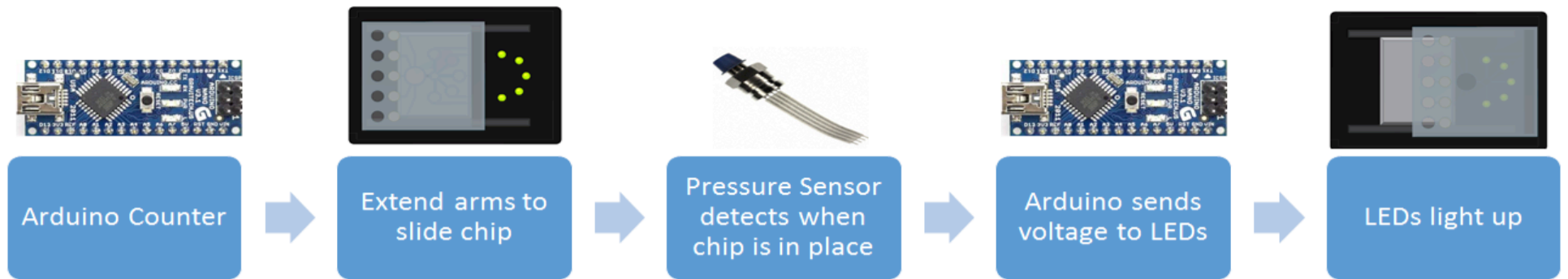


Overhead View of Inside of Housing Device



Regulation of PCR Cycles





How the LED array is activated.



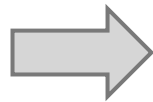
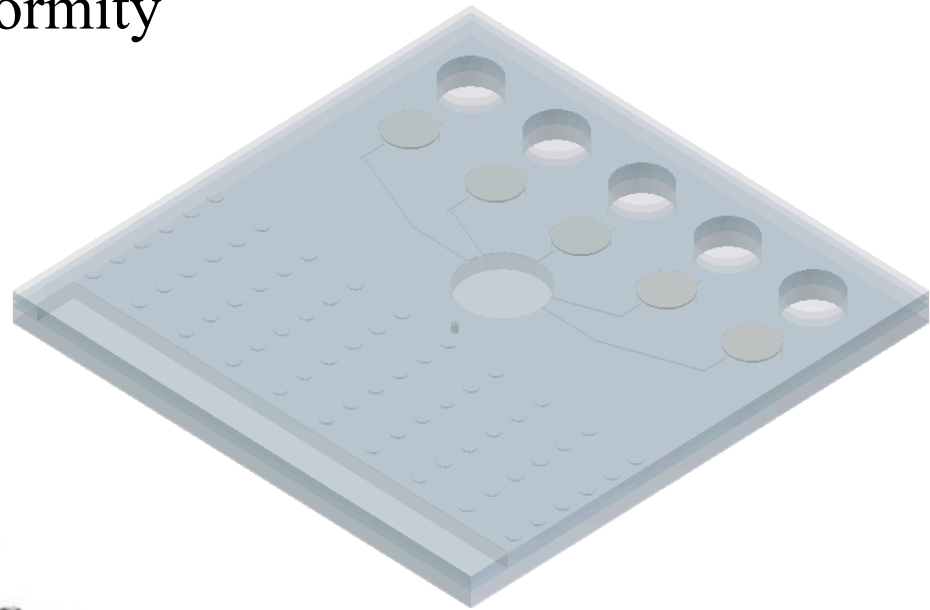
Detection and quantification of ctDNA

Future Device Developments

Increased Temperature Uniformity

High-Throughput System

Increased Portability

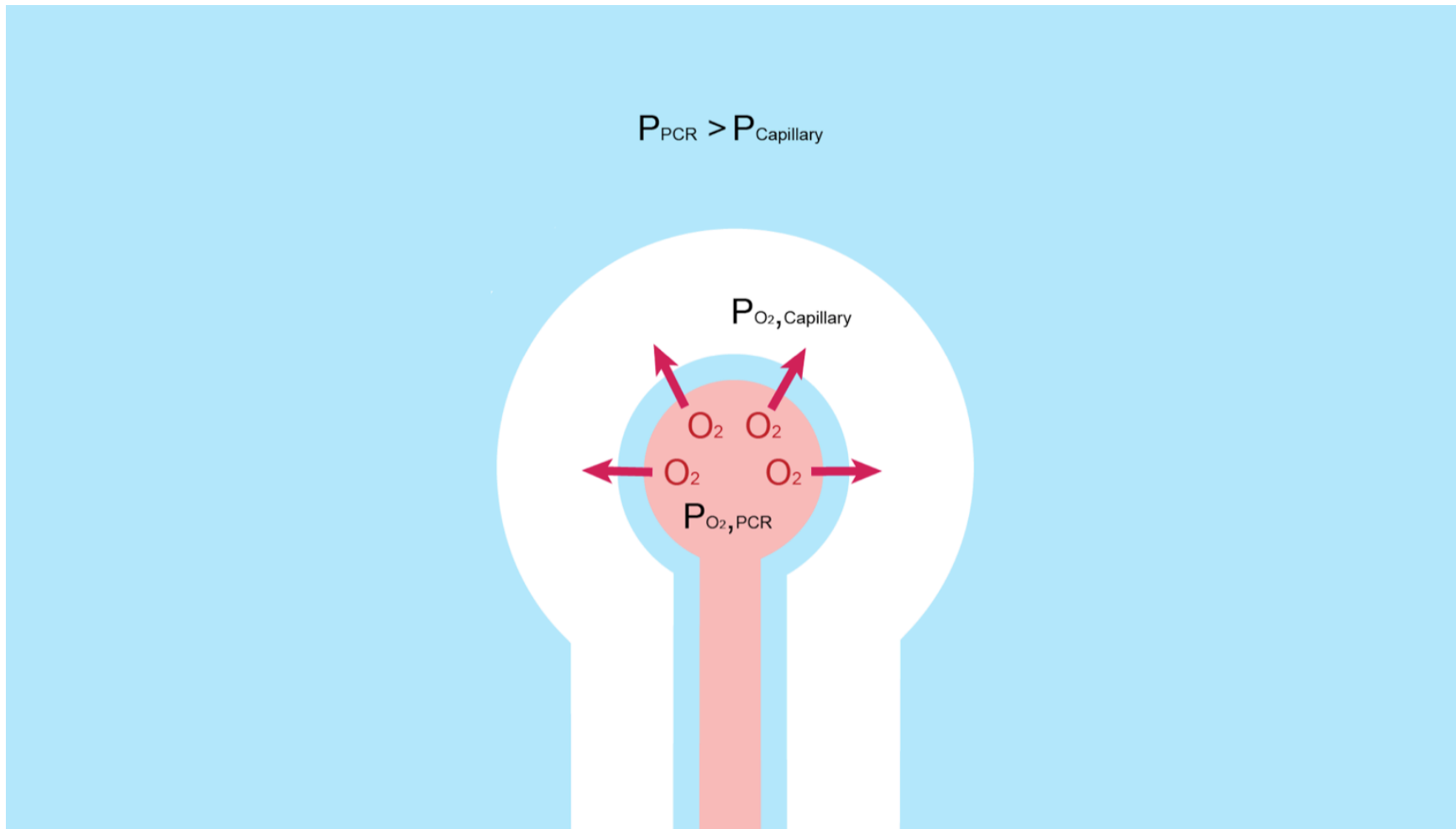


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Questions?

Bubble-Free Microfluidic PCR



Device Cross-Sections

