

Soft Lithography for Biological Applications

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Team 3

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Overview

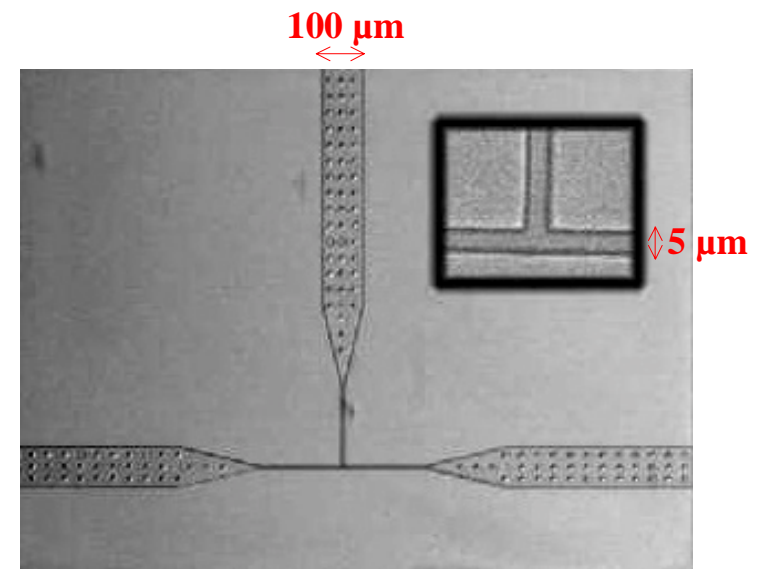
- DNA sizing and sorting
 - Macro vs. Micro
 - Advantages of soft lithography
- Valve fabrication using soft lithography
- Improved design

DNA Sizing & Sorting

- Sizing
 - Gel Electrophoresis
 - Pulsed Field Electrophoresis
 - Limited by size of molecule
- Sorting
 - Flow Cytometry

Microfluidic Device for DNA Sorting & Sizing

- Sorts DNA using electric fields
- Short Operating Time
- Sizes large DNA (up to 200 kbp)
- Fabricated from a silicone elastomer
 - Biocompatible
 - Durable
 - Cheaper (~5¢/mL vs. ~\$2.50/ mL)

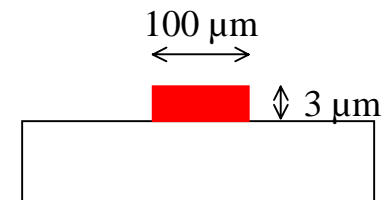
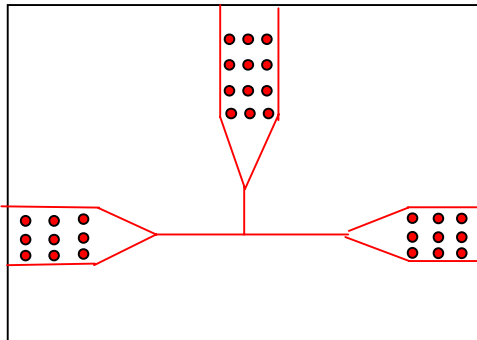


Device Fabrication

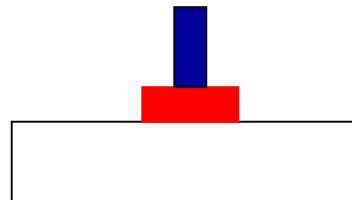
- Make negative master in silicon wafer
 - Pattern oxide surface using photolithography
 - Etch by reactive ion etch (RIE)
 - Use oxide as mask for Si underneath and etch with KOH
 - Glue Al cylinders to entry points on mold
- Pour liquid elastomer on mold
 - Cure at 90 °C
- Remove elastomer from master and bind to coverslip
- Soak surface in dilute HCl to make device hydrophilic

Fabrication

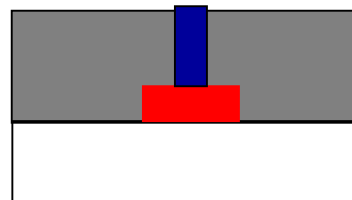
Negative Photoresist on Silicon



Glue aluminum cylinders to Si mold



Pour liquid elastomer

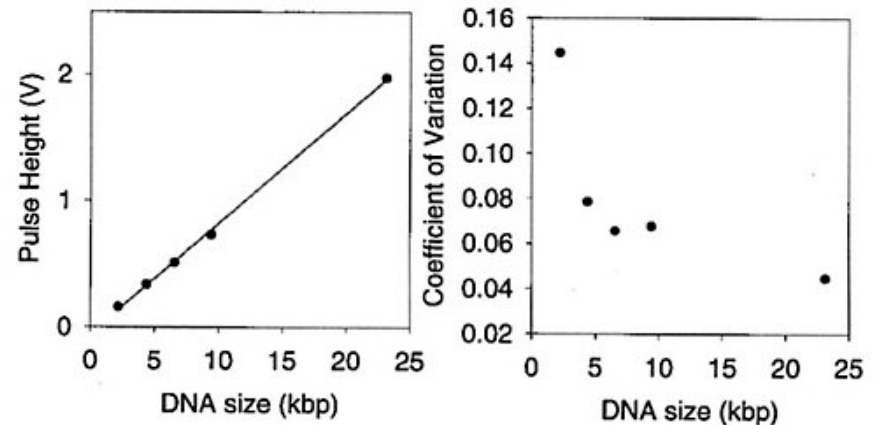
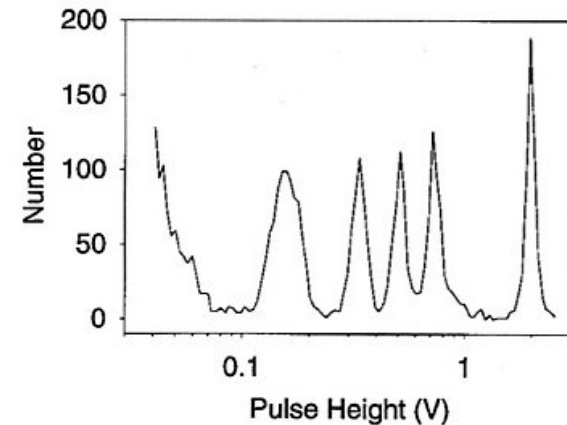


Device Design

- Laminar flow – $Re \sim 0.06$
- Design specifications
 - 100 μm large channels
 - 5 μm channels at T junction
 - 3 μm channel depth
 - Support pillars to prop up large channels and prevent bowing

Experimental Results

- System was able to size DNA molecules from 2 kbp to 200 kbp
- Advantages
 - Detection volume of 375 femtoliters
 - Analyzes 3000 molecules in 10 minutes
 - Resolution improves with increasing DNA length
 - Can actively sort molecules

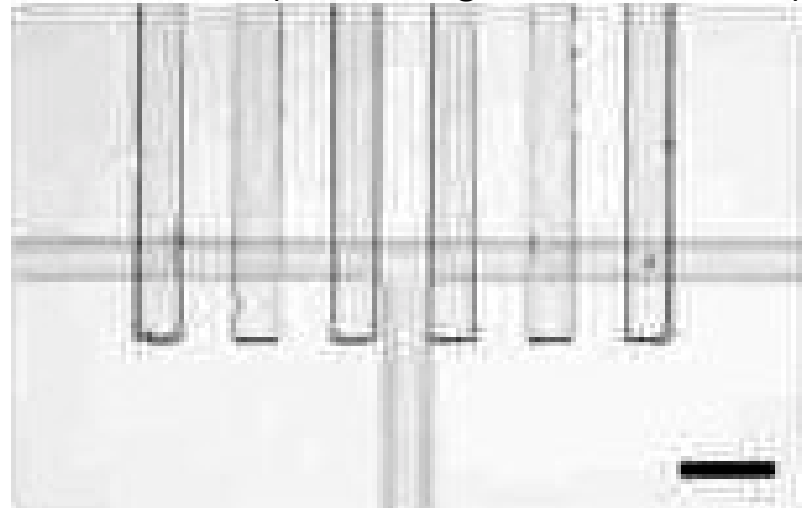


An Improvement – Microvalves

- Use valves instead of electric fields
 - Gentler to molecules
 - Better control
- Example design

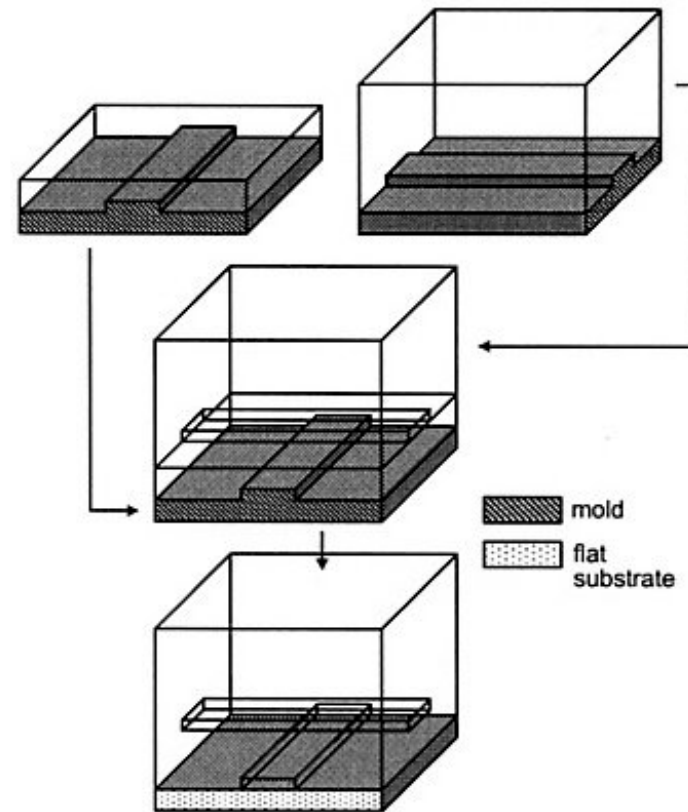
Includes multiple valves that could be used to induce peristaltic flow

(M.A. Unger *et. Al.*, 2000)



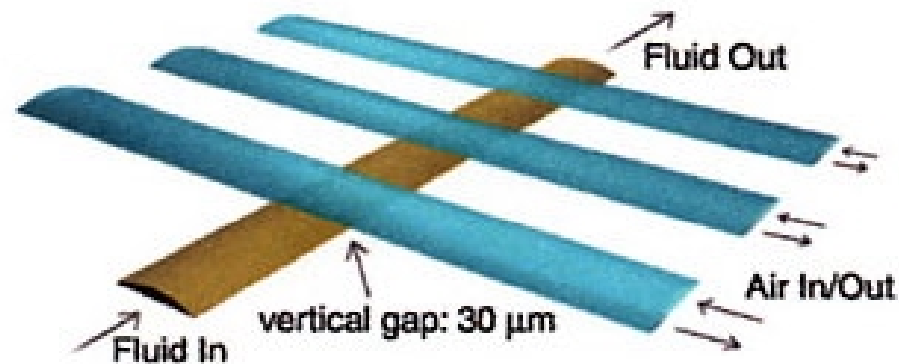
Multi-layer Soft Lithography: Fabrication

- Bond layers of elastomer; each layer separately cast from a silicon mold.
- Bottom layer: excess component A
Top layer: excess component B
- Top added to bottom
– Reaction seals layers



Multilayer Soft Lithography: How it works

- Flow air through upper channel
- Channel membrane deflects downwards, closing lower channel

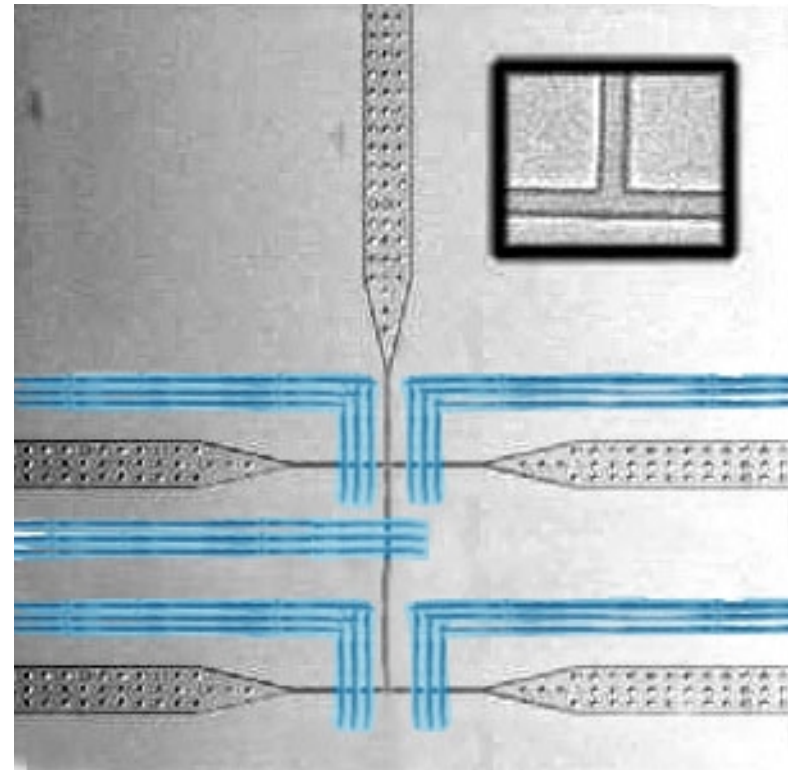


Advantages over Si-based Valves

- Valves close linearly with applied pressure
- Soft membrane allows complete valve sealing
- Small size allows dense integration of pumps and valves on single chip
- Transparent to visible light

A Suggested Design

- Improvements
 - Valves for controlling direction of fluid
 - Cascaded exit channels for sorting multiple items
 - Multiple valves allows for peristaltic flow control
 - Building on a Si chip could allow integration of electronic control system



Advantages of New Design

- Advantages
 - Exit channels can be directed to reactors on the same chip for subsequent processes
 - Allows for more flexibility as a tool in biological research

References

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