Soft Lithography for Biological Applications

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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

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Device Design

- Laminar flow – Re ~ 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