2 Micromachining

1. Glass substrates commonly used for chip making are (a) soda-lime, (b) borosilicate and (c) fused silica or quartz.
The process of photolithography starts with the generation of a photomask which is produced by laser or e-beam ablation. Then, a glass substrate which is coated with Cr/Au metals and with photoresist is exposed to UV radiation through the photomask. The substrate is then developed to expose the Ar/Cr etch mask, which is in turn developed to expose the glass. This is etched to produce glass channels. Finally, all the remaining photoresist and metals are removed to leave only glass on surface.

2. An etch mask is formed on top of the glass substrate to protect the area that is not intended for etching; whereas a photomask is placed on top of the etch mask to transfer the pattern on it by UV exposure.

3. Both positive and negative photoresists are used to transfer the pattern for etching onto a substrate by photolithography. For positive resists, exposure to UV light weakens the chemical structure of the resist so that it becomes more soluble in, and is washed away by, the developer solution. The photomask, therefore, contains an exact copy of the pattern which is to be fabricated on the substrate.
Negative resists behave in just the opposite manner. Exposure to the UV light causes the negative resist to become polymerized, and thus more difficult to dissolve. Therefore, the negative resist remains on the surface wherever it is exposed, and the developer solution removes only the unexposed portions. Photomasks used for negative photoresists, therefore, contain the inverse or photographic "negative" of the pattern to be transferred.

4. The addition of NH_4F is used as an F^- buffering solution to maintain the etch rate of HF.
Without buffering, as HF is consumed, the etch rate would decrease. But with buffering of F^- from NH_4F, the etch rate will become more uniform.

5. Deep-glass etching increases the channel depth, and hence the optical pathlength in absorbance or fluorescence detection is enhanced. This is useful in enhancing the optical signals, and so the optical detection sensitivity is increased.

6. RIE (reactive ion etching) is a method used to perform anisotropic etching of Si. Reactive gas species, such CF_6 or SF_6, are used to produce a plasma in the etch chamber. In this dry etch process, charged gaseous species formed in the plasma react with the surface Si atoms. The product species then leave the surface thermally, if the vapour pressure is high enough, or as a result of ion bombardment.

7. Room temperature bonding is desirable because

(1) it allows bonding between different types of glass substrates having different thermal expansion coefficients (e.g. soda-lime glass and fused quartz);
2) it allows successful integration of organic layers (e.g. biochemical coating) as well as other temperature-sensitive layers (e.g. metal electrodes) into the glass chip, which might otherwise be ruined at an elevated temperature;
3) it will not deform channel geometry due to thermal stress introduced at high temperatures;
4) it allows the glass chips to be easily cleaned, re-assembled, and reused after they have become contaminated.

8. Hot wire imprinting and hot embossing are two simple methods for imprinting microstructures into polymeric substrates. Both methods typically use amorphous polymers because of their relatively low and well-defined glass transition temperature (T_g), which range from 120 to 180 °C.

In hot wire imprinting, microchannels are imprinted using small-diameter chrome wires pressed into the polymer substrate. This is achieved by heating the substrate above its glass transition temperature and applying force to the wires.
Hot embossing uses a micromachined silicon master with raised three-dimensional structure that can be fabricated by a variety of methods. Channels are formed by pressing the template into the polymeric substrate while heating it to a temperature above its T_g. The use of hot-embossing allows for more complex channel patterns, but requires more effort in making the embossing master.

9. In injection molding, a vacuum pump must be used to remove the air between the mold and the replica, so that it adheres and conforms fully to the microstructures defined by the mold.

10. A positive relief Si master is more easily created by etching than a negative relief master. Since the positive relief on the Si master is produced, the pattern must be transferred first to a Ni electroform mother (negative) and then to a Ni electroform daughter (positive). Finally, it is the use of this electroform daughter to produce the channel pattern in the correct relief (i.e. negative).

11. Problems associated with the use of polymeric chips are that:
i. polymeric materials usually show different UV transmittances. Both the polymeric substrates and bonding materials can also show auto-fluorescence;
ii. polymeric materials have low dielectric breakdown voltages which prevent the use of high electric fields in CE applications.
iii. deep PDMS channels are prone to collapse under high suction.
iv. PDMS surfaces are hydrophobic and cause problems in liquid-filling of aqueous solutions into the channels. Moreover, the EOF in polymeric channels is 10-fold less than that in glass or Si chips;
v. PDMS chips can easily be swollen by organic solvents;
vi. the thermal conductivities of polymeric chips are low, and this might have a problem in dissipating heat.

12. Ablation of PMMA chips can be achieved using radiation of different wavelengths (e.g. visible, UV or X-ray). For instance, molecular fluorine excimer laser (157 nm), diode-pumped Nd:YVO4 laser (532 nm) and X-ray synchrotron radiation (7-9Å) have been employed to ablate PMMA.

13. It is because PDMS cannot seal well to chip surfaces when the surface roughness is large, and this includes the thickness of any coated metal electrode. The maximum value of metal electrode thickness is 200 nm.

14. Soft bake is performed after the photoresist has been spin-coated on the surface so that the solvent evaporates away and the photoresist will adhere well to the surface. Hard bake or post-exposure bake is then performed after the photoresist has been exposed to UV in order to complete polymeric cross-linking. A final hard bake may also be performed after photoresist development to evaporate all the developer solvent.

15. Metal layers are deposited on a substrate by various methods, such as sputtering, electroless deposition, electrolytic plating or electroplating.

16. Chromium, titanium and tantalum (or Cr, Ti, Ta) have been used as metal adhesion layers to pattern metal on wafers.

17a. Electroless deposition of silver was carried out using a commercially available silver-plating package (HC- 300 kit and No. 93 sensitizer) from Peacock Laboratories (Philadelphia, PA). The HC-300 kit consists of three parts: a silver solution, an activator solution, and a reducer solution. The concentrates from each of these solutions were diluted in deionized water in a 3.5:100 ratio. Immediately prior to electroless deposition, the diluted silver solution, activator solution, and reducer solution were mixed in equal proportions to form the electroless silver-plating solution.

b. For electroless deposition of tin on chip substrate, surface sensitivation is first performed using an aqueous solution of tin(II) chloride ($SnCl_2$) (1.0 g/l) and concentrated hydrochloric acid (HCl) (0.1 ml/l). The surface was then activated using a solution of palladium(II) chloride ($PdCl_2$) (1.0 g/l) and concentrated HCl (0.1 ml/l).

For electroless deposition of nickel, we used a solution containing 20 g/l of sodium hypophosphite ($NaH_2PO_3 \cdot H_2O$), 40 g/l of nickel sulfate ($NiSO_4 \cdot 6H_2O$), 100 g/l of sodium citrate ($NaC_6H_5O_7 \cdot 2H_2O$), and 50 g/l of ammonium chloride (NH_4Cl). Each glass slide with the desired patterns of surface sensitizers/activators was dipped into this electroless solution, held at 75 ˚C, for 30 s. After the deposition process was completed, the glass slides were cooled and rinsed with DI water. The glass slides with the deposited nickel layer were often annealed at an elevated temperature (< 400 ◦C).

c. For electroless deposition of copper, surface treatment is required. First, the slide was immersed in a sensitizing solution (containing $SnCl_2$ 15 g/L, HCl 50 mL/L, and some tin

pellets) for 5 min. After a sonication rinse with DI water for 20 s, the sensitized surface was immersed in a solution of 18 mM ammoniacal $AgNO_3$ for another 3 min.
After another 20 s of sonication with DI water, copper plating was carried out in a 1:1 mixture of solutions A (containing 24 mM $CuSO_4$, 10 mM $NiCl_2$, and 0.3 M formaldehyde) and B (containing 0.25 M NaOH and 0.16 M sodium potassium tartrate) at room temperature. Deposition took place over the catalytic silver particles for 45 min to form the micropattern of the electrode.

d. The procedure used for electroless deposition of gold consisted of three principal steps. First, Sn^{2+} was adsorbed onto the substrate surface by immersion of the CE chip (5 mm of the channel outlet) into a solution of 26 mM $SnCl_2$ and 70 mM trifluoroacetic acid prepared in water for 3 min (with stirring). The chip was thoroughly rinsed with warm water (60 °C) since rinsing of the glass substrate in warm water at this temperature was reported to improve electroless gold deposition on glass. In the second step, the sensitized chip was immersed in an aqueous solution of ammoniacal $AgNO_3$ (29 mM) for 2 min (with stirring). In this step, a redox reaction led to the oxidation of Sn^{2+} to Sn^{4+} and the reduction of Ag+ to Ag; i.e., the surface became coated with nanoscopic silver particles. After Ag deposition, the chip was then rinsed thoroughly in warm water (60 °C) several times. Finally, the Ag-coated chip was immersed in a gold plating solution (22-23 °C) consisting of 7.9 mM $Na_3Au(SO_3)_2$ (commercial plating solution diluted to 40 times), 127 mM Na_2SO_3, and 625 mM formaldehyde (with stirring). The chip was kept in the gold plating solution for 5 h to result in a good deposition.

18. The SU-8 developer solution is propylene glycol methyl ether acetate.

19. The chemical compositions of metal etchants are given as follows:
a. for chromium, it is $CeSO_4/HNO_3$;
b. for gold, it is KI/I_2 or HCl/HNO_3 (3:1);
c. for silver, it is $NH_4OH:H_2O_2:H_2O$ (1:1:20)

20. Sonication during etching helps produce smoother channels since the etching chemicals are being distributed continuously onto the surface and the etched products are being removed immediately by the sonication process.
It has also been found that etching in an ultrasonic bath facilitates the detachment of hydrogen bubbles at the surface, which is suggested to be one of the causes for surface roughening.

21. Various mold-releasing agents are used in PDMS casting depending on the substrate of the molding master. In the case of silicon, 3%(v/v) dimethyloctadecylchlorosilane, trichloro(3,3,3-trifluoropropyl)silane and dichloromethylsilane have been used.

22. The weight of the PDMS slab is measured. Then a reported value of water content in PDMS of 0.38% (w/w) was used to calculate the amount of absorbed water.

23. To perform irreversible bonding of PDMS with another substrate, both surfaces are first treated by either an O_2 plasma, a Tesla coil, RIE, an ozone generator or a mercury

vapor lamp. Then the PDMS chip and the substrate are put intimately together for irreversible bonding.

24. In order to fill aqueous solutions into PDMS channels, they need to be primed with ethanol (up to 5%), Tween 20 (0.1% v/v), or BSA(1% solution in PBS). PDMS chip can also be filled by immersing the chip in the buffer solution in an ultrasonic bath for 5-10min. The channels can also be primed with CO_2 gas, and so after solution filling, CO_2 bubbles disappear since the gas is readily dissolved in aqueous solutions.

25. The unit of dpi indicates the resolution of an image in dots per inch.
Since 1 in. = 2.54 cm,
the spacing between 2 dots in a 3600-dpi image is given by
1 in. / 3600 dots = 2.54 cm / 3600 dots = 7.05 μm / dot.
This makes the smallest channel width to be 3 x 7 μm = 21 μm.

26. The final concentrations of the two chemicals are calculated as follows:

for HF, it is (49% x 0.200 L) / 1 L = 9.8%
for HNO_3, it is (70% x 0.140 L) / 1L = 9.8%

27. Glass chips which contain Au/Cr electrodes cannot be thermally bonded since the Cr adhesion layer cannot withstand high temperatures. After grain-boundary diffusion of Cr to the Au layer, Cr is oxidized, and the metal electrode will be degraded.

28. a. Titanium is used as an adhesion layer.
b. Undercutting will occur, thus enlarging the width of the microchannel
c. The exposed Ti is first passivated using electroplated Au before HF etching starts.

29. Isotropic etching occurs when the dissolution rate of silicon is equal in both the vertical and horizontal directions. In this case, a rectangular cross section with rounded semicircular corners is produced. Anisotropic etching occurs when the dissolution rate is much faster in one direction as compared to the other. In this case, a trapezoidal cross section with V-shaped corners is produced.

30. The photomasks are shown in Fig. S2.1.

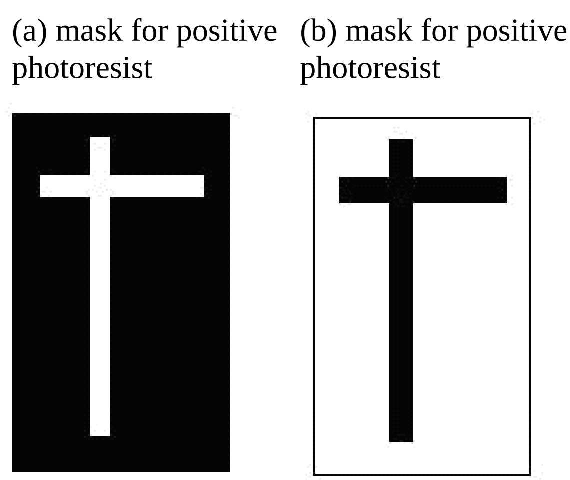

Fig. S2.1

31. Drilling is required so that holes can be made for reservoirs to hold reagents and buffers. Bonding is needed to seal the etched channel in order to produce a closed capillary for liquid delivery and separation.

32. Hole-drilling can be preformed via diamond bit drilling, ultrasonic drilling or electrochemical discharge drilling. In drilling by using a diamond drill bit, it is spun rapidly and scrapes out glass debris as the bit is pushed through the hole.
In ultrasonic drilling, the drill bit is forced to go up and down the hole, but it does not spin. The impact of the bit into the glass performs the drilling.
In electrochemical discharge drilling, a metal point that is served as the cathode is brought into contact to the glass substrate at the drilling location. The glass surface with the cathode and anode are immersed in an electrolyte solution (e.g. NaOH). An electric discharge at the metal point then produces localized heating or sputtering. The metal point is slowly pushed through the glass as drilling continues.

33. The chemical equation for HF etch is
$SiO_2(s) + 6HF(aq) \rightarrow H_2SiF_6(aq) + 2H_2O\ (l)$
HCl helps to remove the precipitated particles produced during the etch process, and results in a smooth channel surface.

34. The channel depth will be 4 µm/min x 6 min =24 µm
The channel width will be 10µm + 24µm + 24µm = 58 µm

35. Quartz cannot be bonded to glass since the two materials have different annealing temperatures and thermal expansion coefficients. Attempted thermal bonding will result in cracking.
To solve this problem, one can use low-temperature bonding with either HF or potassium silicate.

36. The advantages of using PDMS to fabricate microchips are:
i. Rapid prototyping and production - multiple chips can be cast from one Si mold.
ii. Good optical properties – the UV transmittance is good, down to ~230 nm.
iii. Low cost – polymeric chips are more cost-effective to produce, as compared to quartz, glass and Si chips.

37. Polymeric materials commonly used for microchip fabrication are PDMS, PMMA, PC, PET, PTFE, FEP, COC, and PS.

38. Five micromachining methods for making polymeric chips are described as follows:
1) Injection molding: Ni electroform is used to create acrylic chips via injection molding. The electroform is prepared from a Si master fabricated by wet etching.

2) Ablation: radiations of various wavelengths (IR, visible, UV, X-ray) have been employed to ablate channel structures to fabricate plastic chips.
3) Wire imprinting: A nichrome wire is clamped between the plastic substrate and a glass slide. Then the assembly is heated to imprint a channel on the plastic substrate.
4) Compression molding: A Si master with positive relief structures is first created, and the master is used to imprint the channel pattern on the plastic substrate.
5) Casting: liquid prepolymer is poured into a molding master fabricated from a Si master. After curing, the plastic chip is peeled off from the master.

3 Microfluidic flow

1. In laminar flow, the fluid moves in layers called laminas. The closer the fluid layers are to the surface, the slower they move. Moreover, the fluid layers slide over one another without the fluid being exchanged or mixed between the layers.
In turbulent flow, secondary random motions are superimposed on the principal flow and there is an exchange of fluid from one adjacent sector to another. More importantly, there is an exchange of momentum such that slow moving fluid particles speed up and fast moving particles slow down.

2. Active micromixers have moving parts, or external power sources for solution mixing. On the other hand, a passive mixer is based on the change of channel geometry or topology to increase the contact surface area between mixing streams. Examples of active mixer include oscillating EOF induced by sinusoidal voltages, ultrasonic mixer, and magnetic bar stirring. Examples of passive mixers include grooved channels, distributive mixing by splitting liquid streams and recombining them, and vertical pillars arranged perpendicularly to the flow.

3. In the use of PZT, it is a bulk piezoelectric transducer attached to a 0.15-mm thick Si membrane created by anisotropic etching of Si. The PZT transducer, which is powered by ac voltage, can generate a great force to produce the bulk acoustic wave energy for liquid mixing. The disadvantage is that a lot of heat is generated.
In the use of the piezoelectric ZnO film, it is deposited on the back side of the etched membrane on a Si wafer. Acoustic flexural plate waves are generated for liquid mixing, but this will only function efficiently at a certain harmonic frequencies. The Al electrodes patterned on the ZnO film consist of concentric circles, serving to focus the acoustic energy at a few hundred micrometer above the liquid air interface. This method results in a lot less heat than the PZT-actuated mixer, and can be more compatible with heat-sensitive or biological samples.

4. To increase the mixing rate, it is necessary to induce off-axis or lateral liquid transport within the channel. The presence of the slanted wells leads to lateral transport within the channel and rapid mixing of two liquid streams undergoing EOF. Since EOF is a wall-driven phenomenon, some liquids would enter and follow the contours of the wells, and