UNIVERSITY OF CALIFORNIA, BERKELEY

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO
SANTA BARBARA • SANTA CRUZ

DEPARTMENT OF BIOENGINEERING
94720-1762

BERKELEY, CALIFORNIA

BioE 121 **Midterm Solution** **L. P. Lee**

Problem #1.

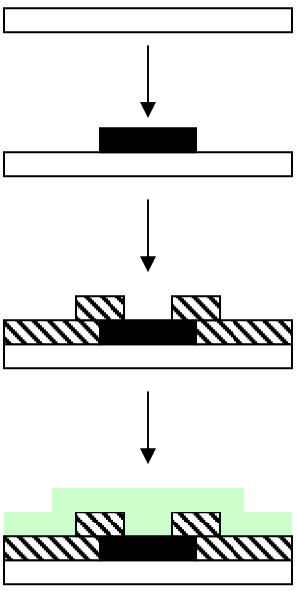
(a)

Table 1 Comparison of platforms for DNA electrochemical sensing

Type of sensor	Advantages	Disadvantages
Direct DNA electrochemistry	Highly sensitive (femtomoles of target); requires no labeling step; amenable to a range of electrodes	High background signals; cannot be multiplexed; destroys the sample
Indirect DNA electrochemistry	Highly sensitive (attomoles of target); usually requires no labeling step; multiple-target detection at same electrode	Probe substrate can be difficult to prepare; destroys the sample
DNA-specific redox indicator detection	Moderate to high sensitivity (femtomoles of target); well suited to multiple-target detection; samples remain unaltered	Chemical labeling step required unless 'sandwich' method used; sequence variations can be problematic
Nanoparticle-based electrochemistry amplification	Extremely sensitive (femtomole to zeptomole range, 10^{-15} to 10^{-21} moles); well suited to multiple-target detection with different nanoparticles	Many development steps in assay; reliability and robustness of surface structures problematic; sample usually destroyed
DNA-mediated charge transport	Highly sensitive (femtomole range) and simple assay; requires no labeling; uniquely well suited for mismatch detection; sequence independent; amenable to multiplexing; applicable to DNA-protein sensing step	Biochemical preparation of target sample required

Grading (5 pts):
+1 point for each sensor type. -0.5 points for missing/incorrect answer in any field

(b) (5 pts):



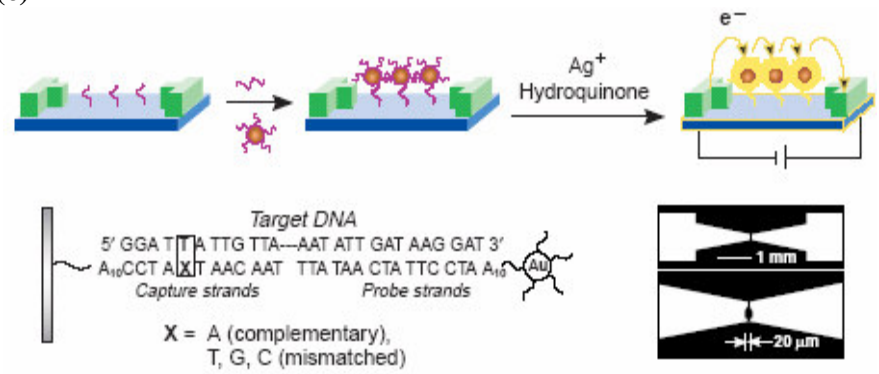
Substrate (+1 pt)

GMR deposition and pattern (no field generating strap required (+1 pt)

Electrode interconnect deposition and patterning (+2 pts)

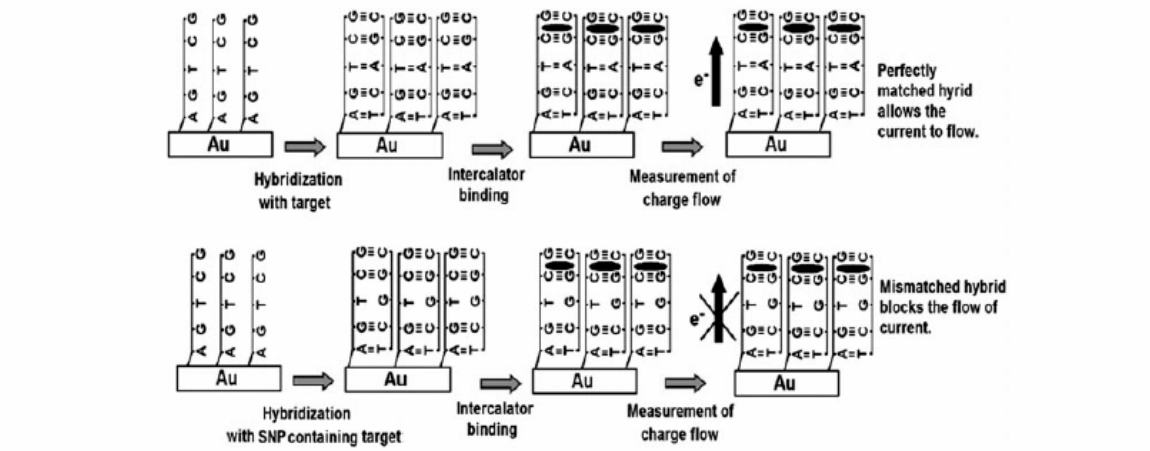
Insulation of device electronics (+1 pt)

(c)



(5 pts)
+2 pts for reasonable fabrication
+2 pts for describing electrochemical method
+1 pt for use of nanoparticles

(d)



Scheme 6. Electrochemical detection protocol of electrical DNA chips, produced by GeneOhm Sciences Inc. After hybridization of the probe with the target DNA, the hybrid-modified Au electrode is exposed to an intercalator solution. Then a current is applied to the hybrid from the electrode. If the hybrid is perfectly matched, the current flow reaches the intercalator and a high charge signal can be obtained. A mismatch in the hybrid blocks the flow of current, so no charge signal can be monitored from the hybrid.

(5 pts)
+1 point Describe SNP detection
+2 pts Electrical conduction through DNA base pair pi-bonds
+1 pt Clear indication of sensing method
+1 pt Describe how electrode/DNA is configured for sensing

Problem #2 (20 pts)

(a) (10 pts):

$$\lambda_D = \sqrt{\frac{\varepsilon k_B T}{2(Ze)^2 I}}$$ (2.5 pts for correct governing equations)

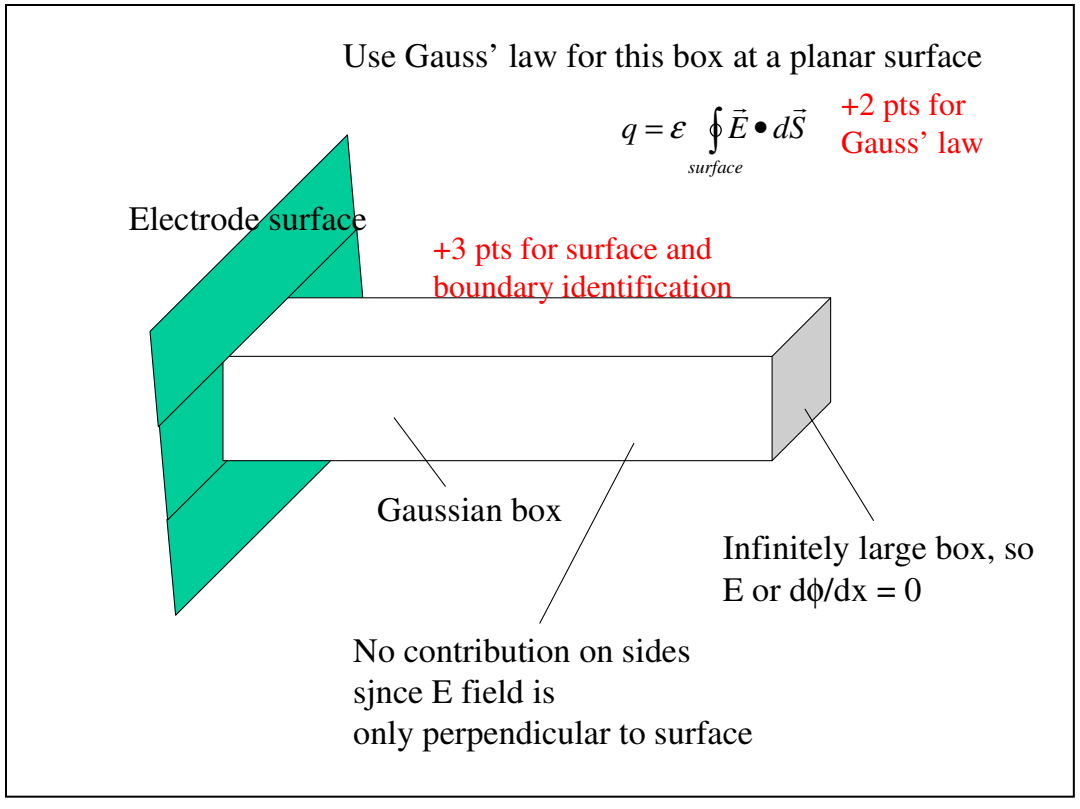
$$I = \frac{1}{2}\sum z_i^2 C_i$$

I_{NaCl} = 0.15 M (2.5 pts for correct ionic strength calculation)
I_{CaCl2} = 0.45 M

λ = 0.78 nm for NaCl (in water at 298K)
λ = 0.45 nm for $CaCl_2$ (in water at 298K)
(2.5 pts for correct math and reasonable values)

Screening length is small at *in vivo* ionic concentrations, therefore electrostatic interaction between charged proteins is insignificant unless the proteins are within a few atomic radii. (2.5 pts)

(b) (10 pts)



So, now, only the surface at the electrode contributes:

$$q = \varepsilon\varepsilon_0 \left(d\phi / dx\right)_{x=0} \int_{endsurface} dS$$

$$q = \varepsilon\varepsilon_0 A \left(d\phi / dx\right)_{x=0}$$

q/A is the solution phase charge density (σ_s)

Plugging in the equation given we have:

$$\sigma_s = -\left(8kT\varepsilon\varepsilon_0 n^0\right)^{1/2} \sinh\left(\frac{ze\phi_0}{2kT}\right)$$

+2.5 pts for obtaining correct solution

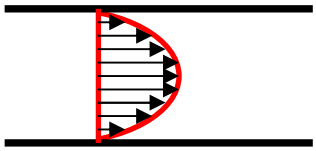
If you take another gaussian box that ends inside the conductor instead of at the surface (enclosing the surface charge) you find that the E field is zero there as well so that the total charge must equal zero. σ_m is the surface charge density.

Thus $\sigma_m = -\sigma_s = \left(8kT\varepsilon\varepsilon_0 n^0\right)^{1/2} \sinh\left(\frac{ze\phi_0}{2kT}\right)$

+2.5 pts for this relation

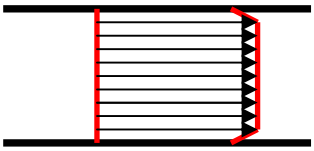
Problem #3 (20 pts total)

(a)



Pressure Driven Flow

(2 pts)



Electro-osmotic Flow

(2 pts)

Electro-osmotic flow is better because of the plug-like flat profile which enables higher resolution of separation. (1 pts)

(b) Assume uniform electric field:

$$u_i = \mu_i E = \mu_i \frac{V}{L}$$ (5 pts)

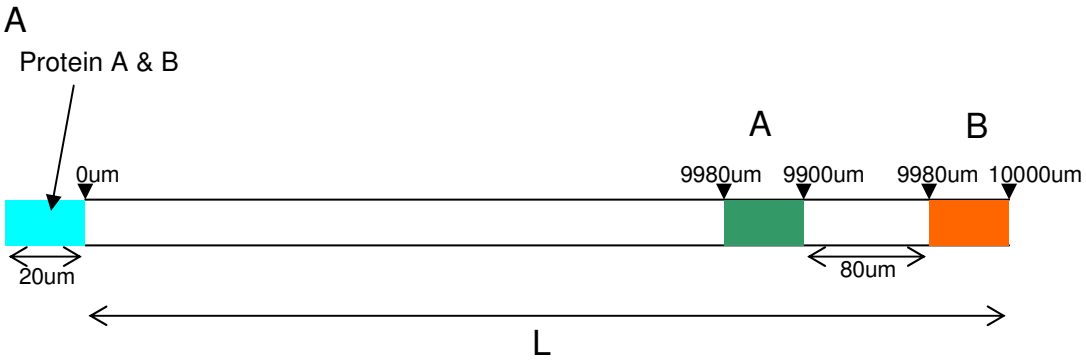
$$u_A = \frac{(1.0x10^{-8} m^2/v \cdot s)(200kV)}{1cm} = 0.2m/s$$ (2.5 pts)

$$u_B = \frac{(1.010x10^{-8} m^2/v \cdot s)(200kV)}{1cm} = 0.202m/s$$ (2.5 pts)

(c)

The time when protein B travel to the end of channel = $L/u_B = 0.01/0.202 = 0.0495s$

At that time, Protein A travels through distance $D_A = u_A$ x time = (0.2m/s) x (0.0495s) = 0.0099m = 9900micron



From diagram, the separation between the two bends when B reaches the detector is 80micron, which is greater than 20micron, hence the channel is long enough the detect the separation.

(5 pts)

Problem #4

(a) 10 pts total
A total of 7 lithography steps are needed. (3 pts, -1pts if the total number of steps is given instead of "lithography" steps)

Each of the lithography steps are used to pattern the following structures:

- Silicon – backside bulk etch
- PolySi Patterning
- Si3N4 Patterning
- Top fluidic chamber patterning (can be any non-conducting material that can be patterned)
- Top bath electrode
- Bottom front electrode
- Bottom fluidic chamber

(1 pt each, total of 7 pts)

(Valid fabrication steps are acceptable up to a maximum of 10 pts, however:
(-2 pts): if the pore is not created by SiO2 deposition or growing, because the pore diameter is around 1 micron, pore with such size cannot be created with regular patterning technique.)

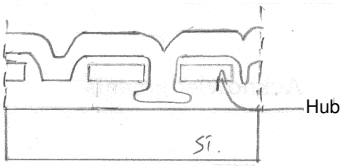
(b) 10 pts total
Any valid design for "Patch-clamp" based drug discovery system:

- Creativity – max 3 pts
- Validity – max 3 pts
- Fabrication – max 4 pts

If given design is not a patch-clamp based system, a maximum of 4 pts is given.

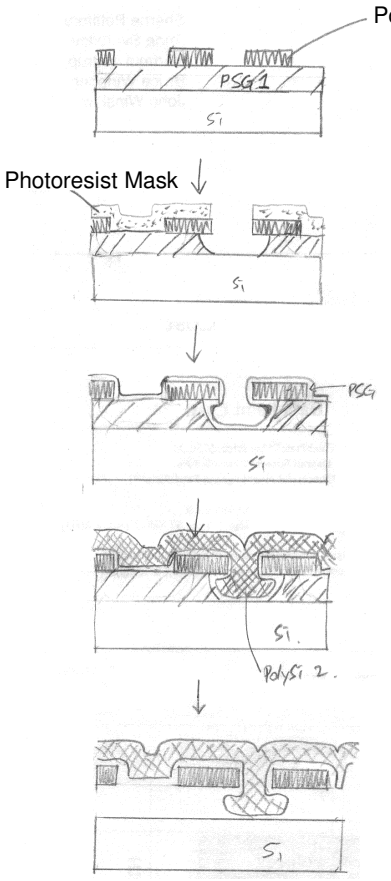
Problem #5 (Total pts 20)

Correct Structure



Acceptable Structures

(a)



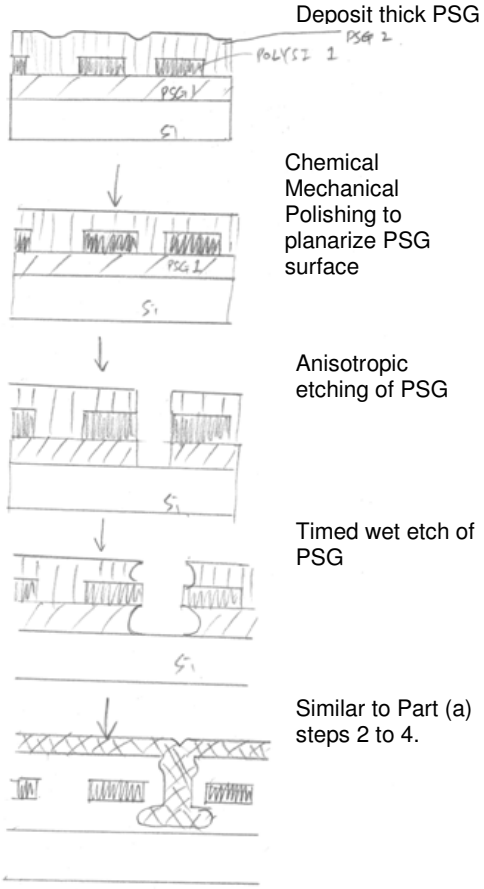
Apply PR Mask, then do timed wet etch of PSG1 to create undercut

Deposit thin PSG2

Deposit PolySi2

Release Structure

(b)



Chemical Mechanical Polishing to planarize PSG surface

Anisotropic etching of PSG

Timed wet etch of PSG

Similar to Part (a) steps 2 to 4.

(a) (10 pts total)
Show target structure and correct fabrication steps (max 10 pts), however:
(-2 pts) if fails to show how dimples are created.
(-2 pts) if shows dimples are created intentionally with a mask.

(b) (10 pts total)
Correct steps to fabricate the structure, (max 10 pts), however:
(max -4 pts) if fails to show CMP is used to planarized the surface.
(max -4 pts) if CMP is used at the wrong step.

Extra Points (20 pts)

For each part:
+1 pt for concept
+1 pt for clear presentation
+1 pt for detailed drawing
+2 pts for innovation and extra effort