NAME: SID:

BioE 110

Biomedical Physiology for Engineers

Midterm Exam II Solutions

Spring 2013

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SID	

WRITE YOUR NAME AND SID ON THE TOP OF EACH PAGE!

If you need extra space, use the back of the sheet.
No computers or electronic communications devices allowed.

SCORE (for instructors only)

Question 1:		/25
Question 2:		/30
Question 3:		/20
Question 4:		/35
Question 5:		/35
Question 6:		/10
Question 7:		/30
TOTAL		/185

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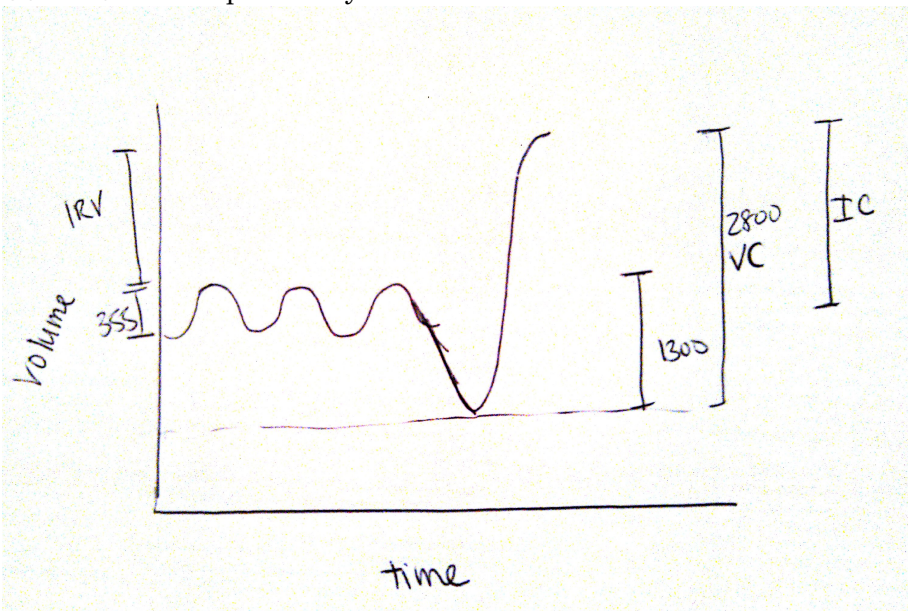
1. Consider the case of a 12-year old girl who comes to your pediatric clinic because she has been experiencing sudden episodes of shortness of breath and wheezing, which she describes as feeling like she needs to gasp for air. These episodes are sometimes triggered by exercise or exposure to cigarette smoke. On the physical exam she seems healthy, though you hear some high-pitched noises through your stethoscope when you ask her to exhale.

A. Noticing the dramatic rise in childhood asthma among your patient base, several months ago you decided to purchase a spirometer and get some of your office staff trained on how to use it. You therefore decide to order a spirometry study. However, the staff member who performs the test is not yet comfortable with either the terminology or the standard protocol and gives you the following narrative description of how the test went:

> "I started by asking her to breathe normally, as she would at rest. When she did this, she regularly inhaled and then exhaled 355 ml of air. After *inhaling* the last of these 'resting' breaths, I asked her to breathe *out* as much air as she could, which resulted in 1300 ml of air passing through the spirometer. After that complete exhalation, I asked her to inhale as much air as she could, which resulted in 2800 ml of air passing through the spirometer. I then asked her to forcibly exhale that breath and return to normal breathing. By the way: I don't know if this is important, but I noticed that when I asked her to forcibly exhale that last breath, it seemed a lot more steady than forced – almost like she was being careful not to blow too hard – and she didn't blow out quite as much air as I would have expected. In fact, I noticed that she was only able to *forcibly* exhale about 750 mL of air in one second and a total of 2000 ml."

Based on this information calculate the vital capacity, the inspiratory reserve volume, and the inspiratory capacity (in ml). (15)

Solution: The spirometry curve would look like this:



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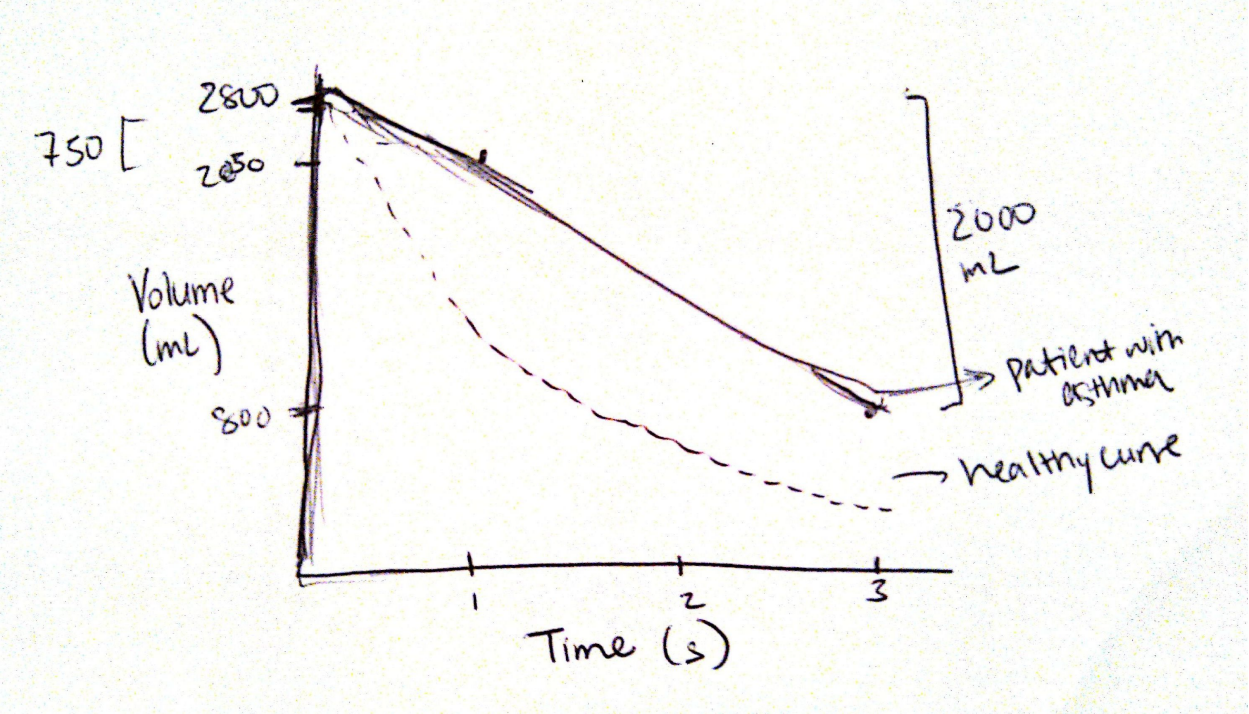
We can see from the graph that VC = 2800 mL, IRV = 2800-1300 = 1500 mL, and inspiratory capacity = 1500 + 355 = 1855 mL.
(Note- volume axis should also be labeled with mL for units. Drawing the graph wasn't required for this part of the problem).

B. Consider the last two sentences in the staff member's description. Plot the spirometer trace for that forced exhalation (i.e. volume vs. time), being sure to point out where 750 and 2000 ml fall on the curve. On the same set of axes, plot what the trace would look like if the girl was completely healthy. Would you expect the girl's FEV_1/FVC ratio to be higher, lower or the same as the normal case, and why? (10)

Solution: The plot is as follows (note that the curve for the patient with asthma would probably slightly convex, like the healthy curve, although it looks linear in the plot).



The girl's FEV_1/FVC ratio would be lower than the normal case because asthma is considered an obstructive disease. FEV_1 is decreased dramatically because the airways have increased resistance due to extra mucus production and tightening of the smooth muscles around the airways, making them narrower. Because the decrease in FEV_1 is so dramatic, it usually decreases more than FVC, so the ratio decreases.

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2. Continuing to consider the asthmatic patient in problem #1:

A. Suppose that you send a sample of the girl's exhaled breath for chemical analysis and also order an arterial blood gas sample. These show that the partial pressure of CO2 in exhaled breath and arterial blood are 27 mmHg and 41 mmHg, respectively. If her baseline respiratory rate is 13 breaths per minute, what is her alveolar ventilation rate (ml/min)? (10)

Solution:

Start by calculating the dead volume (V_D):

$$V_D = V_T * \frac{P_{a\,CO_2} - P_{E\,CO_2}}{P_{a\,CO_2}} = 355\ mL * \frac{41\ mmHg - 27\ mmHg}{41\ mmHg} = 121.22\ mL$$

(the 355 mL tidal volume was determined in Problem 1).

Then, we can calculate alveolar ventilation rate ($\dot{V_A}$)

$$\dot{V_A} = (V_T - V_D) * \frac{breaths}{minute} = \frac{355\ mL - 121.22\ mL}{breath} * 13\ \frac{breaths}{minute} = 3039.14\ \frac{mL}{minute}$$

B. Based on your answer in (A), estimate the rate at which she is producing CO2. Assume that CO2 rapidly and completely equilibrates across the alveolar membrane and that the alvelolar ventilation constant (K) is 863 mmHg. (10)

Solution:

We can find $\dot{V_{CO_2}}$ from the equation $\dot{V_A} = \frac{\dot{V_{CO_2}} * K}{P_{A\,CO_2}}$.

$$\dot{V_{CO_2}} = \frac{3039.14\ \frac{mL}{minute} * 41\ mmHg}{863\ mmHg} = 144.4\ \frac{mL}{minute}$$

C. If she is inspiring dry air at 25C, estimate the partial pressure of oxygen in her alveolus. Note that the partial pressure of water vapor at 37C is 47 mmHg, and air is ~20% oxygen by mole fraction. Assume that the air is fully humidified in the trachea and that she produces 7 moles of CO_2 for every 10 moles of O_2 she consumes.(10)

Answer:

First, estimate the partial pressure of oxygen in inspired air after it is humidified in the trachea. Assume that the barometric pressure of air is 760 mmHg, and use the water vapor and % oxygen values given in the problem.

$$P_{I\,O_2} = (P_B - P_{H_2O}) * fraction\ of\ O_2 = (760\ mmHg - 47\ mmHg) * 0.2 = 142.6\ mmHg$$

Then, we can use the alveolar gas equation. The respiratory quotient R is 7/10 (CO_2 eliminated/O_2 consumed), or 0.7.

$$P_{A\,O_2} = P_{I\,O_2} - \frac{P_{A\,CO_2}}{R} = 142.6\ mmHg - \frac{41\ mmHg}{0.7} = 84.0\ mmHg$$

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3. Answer the following questions about respiratory physiology in 3 sentences or less (5 each):

A. Alpha 1 antitrypsin deficiency is a congenital disease characterized by destruction and loss of elasticity of lung tissue. Patients with this disease often trap air in their lungs when asked to forcibly exhale. Why?

Solution: Loss of elasticity of lung tissue is characteristic of an obstructive disease, and we would expect to see increased compliance in the patients' lungs. The increased compliance leads to lower lung/airway pressures for a given volume. These lower pressures become important during forced expiration because intrapleural, airway, and alveolar pressures all become unusually positive, and if the intrapleural pressure becomes higher than the airway pressure, the transmural pressure may become negative, leading to airway collapse and air being trapped in the lungs.

B. Is it normal for oxygen transport at rest to be perfusion limited? Your answer should explain the concept of perfusion-limited flow and invoke the concept of an A-a gradient.

Solution: Perfusion-limited flow occurs when the partial pressure gradient between the alveolar and arterial regions quickly goes to 0 as blood is flowing across the capillary (this is the counterpart to diffusion-limited flow, in which the gradient would remain high throughout the capillary). Since the partial pressure gradient becomes 0 and therefore doesn't drive diffusion of gas across the capillary, the only way to increase the amount of gas transported would be to increase the blood flow (or perfusion), so the perfusion limits the transport. For a normal person, the A-a gradient (aka the partial pressure gradient between alveolar and arterial oxygen levels) is close to 0, so it makes sense that oxygen transport at rest is perfusion limited.

C. A patient who suffers from chronic anemia due to gastrointestinal bleeding might be expected to be hypoxic but still have a normal pulse oximetry value. Why? Your answer should include a brief description of what pulse oximetry measures and how.

Solution: Pulse oximetry measures oxygen saturation by using absorbance to determine what % of hemoglobin (Hb) is bound to oxygen. In a patient with anemia, it might be the case that most of the patient's Hb is bound to oxygen, but the patient has less total hemoglobin. Pulse oximetry only detects the % saturation, so it might still measure normal values for the patient.

D. Consider the following patients and rank their lungs in order of decreasing V/Q ratio [no explanations needed]: (1) A normal person taking a medication that causes modest pulmonary vasoconstriction ; (2) A patient with an obstruction in his right main bronchus; (3) A patient with a pulmonary embolism; (4) A normal person.

Solution: (3), (1), (4), (2)
The highest V/Q ratio results from Q approaching 0, which would be the pulmonary embolism case (when blood flow to alveoli is completely blocked). Vasoconstriction would also result in less blood flow, so V/Q would be high. Finally, the lowest V/Q ratio results from V approaching 0, which would happen if airflow were blocked by an obstruction in the bronchus.

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4. Suppose you are at a pharmaceutical company that is developing a new cholesterol-lowering drug called calstatin. You receive results from an internal preclinical study in which both calstatin and para-aminohippuric acid (PAH) were given to a 20 g mouse as single injections of 10 mg of drug. After equilibration the plasma concentration of calstatin is 1 mg/ml, the urinary concentration of calstatin is 0.02 mg/ml, the plasma concentration of PAH is 0.01 mg/ml and the urinary concentration of PAH is 6 mg/ml. The total urinary output is 0.9 ml in a 24h period and contains creatinine at a concentration of 0.5 mg/ml. Additional blood work reveals a serum creatinine concentration of 0.02 mg/ml white blood cell count of 15,000/µl, a platelet count of 200,000/µl, and a hematocrit of 0.45.

A. Calculate the renal clearance of calstatin. (10)

Solution: To determine the renal clearance of calstatin, we use the following equation:

$$C_{calstatin} = \frac{[U]_{calstatin} \times \dot{V}}{[P]_{calstatin}}$$

$$C_{calstatin} = \frac{(0.02\ \text{mg/mL}) \times \left(\frac{0.9\ \text{mL}}{1440\ \text{min}}\right)}{(1\ \text{mg/mL})}$$

$$C_{calstatin} = 1.25 \times 10^{-5}\ \frac{mL}{\text{min}}$$

If you calculated the clearance in mL/hour, then the answer would be 0.00075 mL/hr.

B. Estimate the glomerular filtration rate, stating any assumptions you make in doing so. (10)

Solution: Here, we assume that creatinine is a good glomerular marker and that serum [creatinine] is approximately equal to the plasma [creatinine]. To calculate GFR:

$$GFR \approx C_{creatinine} = \frac{[U]_{creatinine} \times \dot{V}}{[P]_{creatinine}}$$

$$GFR \approx \frac{(0.5\ \text{mg/mL}) \times \left(\frac{0.9\ \text{mL}}{1440\ \text{min}}\right)}{(0.02\ \text{mg/mL})}$$

$$GFR \approx 0.0156\ \frac{mL}{\text{min}}$$

If you calculated GFR in mL/hour, then the answer would be 0.938 mL/hr.

C. Calculate the effective renal plasma flow and renal blood flow. (15)

Solution: As we know from class, the effective renal plasma flow is equivalent to the clearance of PAH, an organic acid, from the body. Hence:

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$$RPF \approx C_{PAH} = \frac{[U]_{PAH} \times \dot{V}}{[P]_{PAH}}$$

$$RPF \approx \frac{(6 \text{ mg/mL}) \times \left(\frac{0.9 \text{ mL}}{1440 \text{ min}}\right)}{(0.01 \text{ mg/mL})}$$

$$RPF \approx 0.375 \frac{mL}{\text{min}}$$

If you calculated RPF in mL/hour, then your effective RPF would be 22.5 mL/hour.

To find RBF, we use the following relationship:

$$RBF = \frac{RPF}{1 - Hct}$$

$$RBF = \frac{0.375 \frac{ml}{\text{min}}}{1 - 0.45}$$

$$RBF = 0.68 \frac{mL}{\text{min}}$$

If you calculated RBF in mL/hour, then your RBF would be 40.9 mL/hour.

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5. Suppose you are an emergency room physician seeing a college student who played a three-hour tennis match on a very hot day, did not drink any water, and is now showing symptoms and signs of dehydration. Suppose the patient's "baseline" weight is 70 kg and he now weighs 64 kg, with all weight loss due to sweat, which comes entirely from the extracellular fluid and has an osmolarity of 150 mOsm/L.

A. Estimate the volume of this patient's total body water, extracellular fluid, and intracellular fluid before the tennis match. (15)

Solution: Before the tennis match, the total body weight of the college student was 70 kg. We know that total body water accounts for approximately 60% of body weight. (Note: The density of water is 1 kg/L or 1 g/mL):

$$TBW = (0.6)(70kg) = 42kg \times \frac{1L}{1kg} = 42L$$

Likewise, the ECF and ICF constitute about 20% and 40% of total body weight respectively. Hence:

$$ECF = (0.2)(70kg) = 14kg \times \frac{1L}{1kg} = 14L$$

$$ICF = (0.4)(70kg) = 28kg \times \frac{1L}{1kg} = 28L$$

B. Estimate the patient's extracellular fluid volume and osmolarity after the tennis match. Assume that before the match, he had a normal plasma osmolarity of 300 mOsm/L. (10)

Solution: To find the ECF volume after the tennis match, we first need to find the amount of volume lost through sweat (which, as stated, comes entirely from the ECF). The weight of water lost through sweat is 6 kg (i.e. 70 kg - 64 kg) and since the density of water is 1 kg/L, the volume of water lost through sweat is about 6L. Hence, the end ECF volume is:

$$ECF_{end} = 14L - 6L = 8L$$

The osmolarity, likewise is given by:

Amount of salt in sweat: $6L \times 150\frac{mOsm}{L} = 900mOsm$ of salt lost

Original amount of salt in ECF: $14L \times 300\frac{mOsm}{L} = 4200mOsm$ of salt in ECF before match

New amount of salt in: 3300 mOsm of salt (i.e., 4200 mOsm – 900 mOsm)

New Osmolarity: $\frac{3300mOsm}{8L} = 412\frac{mOsm}{L}$

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C. Suppose you manage to obtain a urine sample prior to treating this patient for dehydration. Would you expect his clearance of free water to be positive, negative, or zero, and why? (10)

Solution: You would expect the free-water clearance to be negative since a negative free-water clearance indicates net reabsorption of water in the nephrons. Since the patient is dehydrated, the body will likely try to maintain total body water and ECF volumes through water reabsorption in the nephrons of the kidney.

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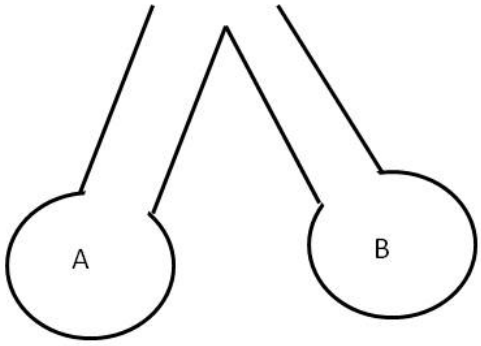
6. Consider a simplified alveoli system as shown below in which two alveoli (A & B) are the exact same volume, and no pressure gradient exists between them.

(A) Using Laplace's Law, explain how the **pressure** and **volume** of A and B would change if A suddenly became smaller (assuming there is no surfactant present). (5)

Solution: Laplace's Law states that P = 2T/R, where P is the internal pressure, T is the surface tension of the alveoli, and R is the radius of the alveoli. If R_A suddenly decreased, P_A would increase, so P_A would be > P_B, leading to a pressure gradient. Air would travel down the pressure gradient, so the volume of A and R_A would decrease even further, while the volume of B would increase, and R_B would increase. This would lead to P_A increasing more and P_B decreasing, which would make the pressure gradient even larger. This would be dangerous physiologically because small decreases in alveoli volume could lead to collapse, which would decrease the surface area available for gas transfer in the lungs.

(B) Explain how pressure and volume would change if surfactant were present. Identify a mechanism for this change. (5)

Solution: Surfactant decreases surface tension because surfactant molecules insert themselves between the water molecules lining the alveolar membrane, reducing the tendency of the water to collapse the alveoli. Therefore, the T term in the Laplace equation is much lower, causing P to also be much lower. Therefore, even if R_A decreases, P_A will still be relatively low, so the pressure gradient between A and B will not be as dramatic, so less air will leave A, reducing the tendency of A to collapse (so the volume of A will remain closer to normal).



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7. Answer the following short questions about renal handling of solutes in 3 sentences or less: (5 each)

A. Consider a glomerular capillary. Is the filtration rate higher at its start, near the afferent arteriole, or at its end, near the efferent arteriole? Justify your answer.

Solution: The filtration rate will be higher at the beginning of the capillary, near the afferent arteriole. This is because GFR is directly proportional to the hydrostatic pressure in the capillaries and inversely proportional to the hydrostatic pressure in the bowman's space and the oncotic pressure in the capillaries (see Starling's Equation for Nephron). As fluid gets filtered out of the capillaries, proteins are left behind (due to charge exclusion-based mechanisms in the capillarity basement membrane), increasing the protein concentration and the oncotic pressure as we move towards the efferent arteriole. Consequently, GFR decreases at the efferent end of the glomerular capillaries.

B. Reabsorption in the proximal tubule is usually described as isoosmotic whereas reabsorption in the ascending limb of the loop of Henle is usually described as hyperosmotic. What accounts for this difference?

Solution: Reabsorption in the proximal tubule is isosmotic because water and solutes are reabsorbed proportionally so the concentrate of the filtrate remains the same over the length of this tubule segment. By contrast, in the thick ascending limb, ions are reabsorbed but the segment is impermeable to water, resulting in the interstitial fluid being hyperosmotic in comparison to the filtrate. This difference is due to the presence of aquaporins in the proximal tubule (which allow water to follow solute) but not in the ascending, making the latter impermeable to water.

C. What is the single effect and how does it contribute to the corticopapillary osmolarity gradient?

Solution: The single effect describes the fact that the ascending limb of the Loop of Henle is not permeable to water but is permeable to sodium chloride, resulting in a net reduction of the osmolarity of the passing filtrate. By contrast, the descending limb is permeable to water resulting in an increase in osmolarity of the filtrate to match the adjacent interstitial fluid (which is concentrated with ions due to the movement of NaCl from the ascending limb). This results in a cortioccapillary osmolarity gradient where fluid in the descending limb is concentrated (i.e. higher osmolarity) while fluid in the downstream ascending limb is dilute (lower osmolarity).

D. Suppose you treat separate groups of animals with two different drugs: One that inhibits water channels in the proximal tubule and descending Loop of Henle, and the other that inhibits water channels in the distal tubule and collecting ducts. Which drug would interfere more with the action of antidiuretic hormone (ADH) and why?

Solution: The drug associated with the distal tubule and collecting ducts should interfere with the actions of ADH more. ADH makes principal cells in the distal tubule and collecting ducts water permeable by facilitating the insertion of water channels or aquaporins in these cells. Since the drug in question would close these same channels, it would directly interfere with the effect of ADH.

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E. In his guest lecture, Dr. Breslauer mentioned how his company, Refactored Materials, specializes in creating a scalable system for the commercial manufacture of spider silk fibers. However, as he outlined, several major technical challenges exist. List and briefly (1-2 sentences) elaborate on two separate technical challenges associated with the production of spider silk fibers that Dr. Breslauer mentioned in his presentation.

Solution: There were two main technical challenges that were mentioned in the lecture but we will accept other answers as long as they seem pertinent to the material presented in the guest lecture:

(1) Obtaining sufficient amounts of spider silk: Unlike silk from silk worms, spider silk is produced naturally in small quantities and can be difficult to harvest. One of the problems associated with commercializing spider silk products is obtain sufficient quantities of spider silk to spin fibers. (Note: This is why Refactored Materials is trying to create recombinant spider silk protein).

(2) Extruding the spider silk to create silk fibers: This problem was the central challenge of Dr. Breslauer's doctoral work here at Berkeley and the motivation for building the microfluidic devices outlined in the presentation. Spiders naturally extrude silk fibers but to do it artificially, one needs to control several parameters including the size of the orifice through which the silk is extruded, the coagulant used, the flow speed, etc.

F. Synthetic spider silk seeks to emulate the natural properties of silk fibers secreted by the *Araneus Diadematus* spider. Surprisingly, the physiology of spider silk production shares some striking similarities with solute handling in the nephron. Briefly (2 sentence maximum) describe how the *A. Diadematus* spider creates aligned silk fibers. **Your answer should mention the key ion(s) involved and their relative concentrations within the secretory organ of the spider.**

Solution: *A. diadematus* spiders produce silk through a specialized pyriform gland that is filled with silk protein. The gland has tapering end where a combination of a pH gradient, potassium secretion (i.e. high potassium concentrations within the gland) and sodium reabsorption (i.e. low sodium concentration within the gland) help align the silk proteins so that fibers are extruded from the tapered end of the gland.