Spring 2005 (Przybycien) 42-101 Intro to BME NAME: _____

MAKEUP EXAM SOLUTIONS and GRADING SCHEME

Format: Open text, notes, homework and mind; closed neighbor.

Part I: Short Answer Questions (72 pts)

Short written-answer and short calculation questions - *No more than two or three sentences in answer to any question in this section please.*

1. (6 pts) Describe the two main differences between the rheological behavior of a Casson fluid, such as whole blood, and a Newtonian fluid, such as plasma.

   A Casson fluid exhibits a yield stress (fluid won't start to flow until a critical stress is applied – 3 pts) and shear-thinning behavior (fluid viscosity decreases with increasing shear stresses once applied stress exceeds yield stress – 3 pts). For Newtonian fluids, there is no yield stress and viscosity is constant.

2. (6 pts) Is the flow of air in the trachea during breathing laminar or turbulent? Justify your answer. The following data is available for this system: volumetric air flow rate during breathing is 6 L/min, length of the trachea is 20 cm, diameter of the trachea is 1.5 cm, density of air is 1.185 g/L, heat capacity of air is 0.238 cal, thermal conductivity of air is 0.0232 kcal/(hr•m^2•°C), viscosity of air is 1.75×10^{-5} Pa•s [=] kg/(m•s).

   Calculate the Reynolds number, $Re = \rho vd/\mu$. If $Re > 2100$ flow is turbulent. (3 pts)
   First find velocity from volumetric flow rate:
   $v = Vdot/(\pi r^2) = (6\ L/min)\langle 1000\ cm^3/1\ L\rangle/(\pi(1.5\ cm/2)^2)\langle 1\ m/100\ cm\rangle\langle 1\ min/60\ s\rangle$
   ≈ 0.566 m/s
   Next find Re:
   $Re = \rho vd/\mu$
   $= (1.185\ g/L)\langle 1\ kg/1000\ g\rangle\langle 1000\ L/1\ m^3\rangle(0.566\ m/s)(1.5\ cm)\langle 1\ m/100\ cm\rangle$
   $/(1.75\times10^{-5}\ kg/(m•s))$
   $\approx 575 \Rightarrow$ flow is laminar (likely transition flow) (3 pts)

3. (6 pts) The rate of substrate consumption, v in mmol/(L•min), for an enzymatically catalyzed reaction as a function of substrate concentration, s in mmol/L, is given by the equation $v = 5.3s^4/(1.67 + s^4)$. What does the form of this expression suggest about the nature of the enzyme-substrate interaction and the structure of the enzyme?

   The form of the equation, $v = v_{max}s^n/(K_M + s^n)$, suggests that the enzyme exhibits allostery (3 pts): multiple active sites for the same substrate wherein the binding of the first substrate makes the binding of the next substrate more favorable and so on. That n = 4 suggests that there are four active sites per enzyme molecule (3 pts).

4. (6 pts) The binding strength of a repressor to a unique operator site within an organism's genomic DNA is described by K_d = 24.3 nM. At what cytosolic repressor concentration, in nM, would expression of the genes within this operon, i.e. the genes under the control of this repressor-operator interaction, be attenuated by 90% relative to the unrepressed case?

   [repressor-operator complex]/[total operator] = [free repressor]/(K_d + [free repressor]) (2 pts)
   For 90% reduction in expression, expect that
   [repressor-operator complex]/[total operator] = 0.90. (2 pts)
   0.90 = [free repressor]/((24.3 nM) + [free repressor])
   [free repressor] ≈ 219 nM (2 pts)

5. (6 pts) Mylotarg™ (Wyeth Pharmaceuticals) is an anti-leukemia chemotherapy agent composed of an antibody covalently attached to a toxic antitumor antibiotic, calicheamicin. The antibody portion of Mylotarg binds specifically to the CD33 antigen; the CD33 antigen is a protein found on the surface of leukemic cells and some cells in blood that later give rise to red blood cells. If you were a protein engineer working on the next generation product for Wyeth, would you be interested in increasing or decreasing K_d for the antibody portion of the drug? Why? Why would this approach, covalently coupling a toxin to an antibody, be a promising approach to chemotherapy?

   It would be desirable to engineer the antibody to improve its binding strength, hence decrease K_d (2 pts), so that the same amount of CD33 binding could be accomplished at lower doses. Lower doses result in reduced side effects. (2 pts) The coupling of the toxin to the antibody ensures that only/mainly the targeted cells are affected/killed by the toxin. (2 pts) This also reduces side effects.

6. (6 pts) What is the "chemiosmotic hypothesis"?

   The chemiosmotic hypothesis describes how energy is derived from a gradient in proton concentration across a membrane: cells undergoing respiration pump protons outside the cell (mitochondrial) membrane when electrons from oxidized carbon sources are passed from carrier to carrier, building up a significant concentration difference; special membrane proteins called ATPases let protons flow back into the interior and harness some of the energy contained in this flow to make ATP. (6 pts)

7. (6 pts) Identify the four main phases of batch cell growth and describe what is happening during each phase.

   1. Lag phase: cells are adapting to their new environment, specific growth rate increases (from zero) (1.5 pts)
   2. Exponential growth phase: cells are growing as rapidly as they can as substrate is plentiful, specific growth rate equals μ_{max} (1.5 pts)
   3. Stationary phase: cell population no longer expands as substrate runs out and/or toxins accumulate, specific growth rate decreases to zero. (1.5 pts)
   4. Death phase/cryptic growth phase: cells are dying off, remaining cells survive on contents of ruptured cells, total number of cells decreases (1.5 pts)

8. (6 pts) The rate of insulin secretion from pancreatic islet cells, r in μinternational units/islet/min, as a function of glucose concentration, C in mg/mL, is given by the equation

$$r = 0.209/(1 + \exp\{-3.33C + 6.6\}).$$

What are the units associated with the constant "0.209"? Reformulate this equation so that the values for C in millimoles/L may be used to calculate r in μinternational units/islet/min.

Because the denominator must be dimensionless, the argument of a transcendental function such as exp must be dimensionless, the numerator must have the same dimensions as the LHS of the equation: "0.209" has dimensions of μinternational units/islet/min. (3 pts). If C is expected to have dimensions of mg/mL in the original equation, will need to multiply concentration in mM by the molecular weight of glucose and convert L to mL:

$$r = 0.209/(1+\exp\{-(3.33\ \text{mL/mg})(180\ \text{mg glucose/mmol})<1\ \text{L/1000 mL}>(\text{C mM}) + 6.6\}).$$

$$r = 0.209/(1 + \exp\{-(0.5994\ \text{L/mmol})(\text{C mM}) + 6.6\}).$$ (3 pts)

Spring 2005 (Przybycien) 42-101 Intro to BME NAME: _____

MAKEUP EXAM SOLUTIONS and GRADING SCHEME

Part II: Detailed Questions (52 points)

1. (26 pts) Iggy V. Leeg visits an amusement park and decides to take a ride on the BME Screamer, an infamous stand-up roller coaster. At one point during the ride, Iggy is subjected to an upward force of 225 N. Iggy has a mass of 69 kg; his head is located 57 cm above the center of his heart; his feet are located 126 cm below the center of his heart; his blood density is 1.056 g/mL; the acceleration due to gravity is 9.81 m/s^2. Estimate the pressure of the blood, in mmHg relative to atmospheric pressure, on the arterial and venous sides of the circulation in the regions of the feet and head during this particular point in the ride. Is the pressure drop from the arterial to the venous side of the circulation in the head affected by the upward force? Why or why not?

   At this point in the ride, Iggy experiences a larger effective gravitational acceleration: the acceleration due to gravity plus the additional acceleration due the upward force; he will feel heavier and his blood will exert more static pressure per unit height.

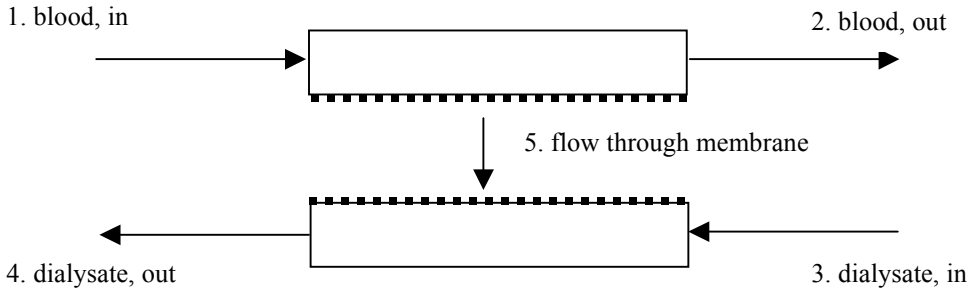
   First step is to calculate the effective gravitational field experienced by Iggy:
   $g_{eff} = g + a_{Screamer} = g + F_{up}/M_{Iggy} = 9.81\ m/s^2 + ((225\ N)/(69\ kg))\langle(m/s^2)/(N/kg)\rangle = 13.07\ m/s^2$
   $g_{eff} = ((13.07\ m/s^2)/(9.81\ m/s^2))\times g = 1.33\times g$ (4 pts)
   Iggy and his blood will weigh 33% more at this point in the ride than at 1×g

   At 1×g, 1 ft blood is equivalent to 23.8 mmHg at 1×g; so at 1.33×g, 1 ft blood will be equivalent to (1.33)×(23.8 mmHg) = 31.65 mmHg at 1×g. Since head and feet distances from heart are given in cm, convert ft blood to cm blood. In sum: (4 pts)
   (1 ft blood at 1.33×g)<30.48 cm/ft> = (30.48 cm blood at 1.33×g) = (31.65 mmHg at 1×g)
   OR get there from a force (pressure) balance: $\rho_{blood}(1.33\times g)h_{blood} = \rho_{Hg}gh_{Hg}$

   For the head, $P_{standing} = P_{lying\ down} - P_{57cm\ blood\ at\ 1.33\times g}$ (4 pts)
   Arterial side: $P_{standing}$ = (95 mmHg at 1×g)
   – (57 cm blood at 1.33×g)<31.65 mmHg/30.48 cm blood>
   = 35.812 mmHg at 1×g
   ≈ 36 mmHg at 1×g (1.5 pts)
   Venous side: $P_{standing}$ = (5 mmHg at 1×g)
   – (57 cm blood at 1.33×g)<31.65 mmHg/30.48 cm blood>
   = -54.18 mmHg at 1×g
   ≈ -54 mmHg at 1×g (1.5 pts)
   For the feet, $P_{standing} = P_{lying\ down} + P_{126cm\ blood\ at\ 1.33\times g}$ (4 pts)
   Arterial side: $P_{standing}$ = (95 mmHg at 1×g)
   + (126 cm blood at 1.33×g)<31.65 mmHg/30.48 cm blood>
   = 225.8366 mmHg at 1×g
   ≈ 226 mmHg at 1×g (1.5 pts)
   Venous side: $P_{standing}$ = (5 mmHg at 1×g)
   + (126 cm blood at 1.33×g)<31.65 mmHg/30.48 cm blood>
   = 135.8366 mmHg at 1×g
   ≈ 136 mmHg at 1×g (1.5 pts)

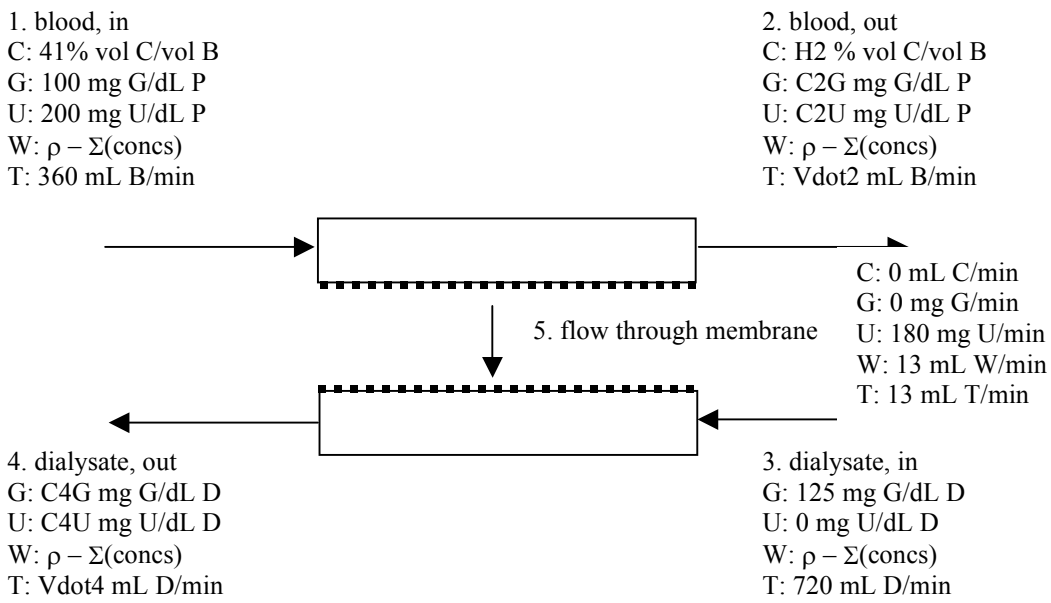
   Pressure drop from arterial to venous side is due to viscous drag on walls of vessels, not differences in elevation and will be unaffected by the applied force. (4 pts)

2. (26 pts) Consider the expanded view of a counter-current hemodialyzer below:



Assume whole blood = cells + (w)ater + (g)lucose + (u)rea. Whole blood flows in to the dialyzer at 360 mL/min with a hematocrit of 0.41; $C_{1,g}$ = 100 mg/dL plasma; $C_{1,u}$ = 200 mg/dL plasma. The water flow rate through the membrane is 13 mL/min; the urea flow rate through the membrane is 180 mg/min; there is no net glucose flow rate through the membrane. Dialysate flows into the dialyzer at 720 mL/min; $C_{3,g}$ = 125 mg/dL soln. Determine the composition (mg/dL plasma or soln for urea and glucose, hematocrit for cells) and the total volumetric flow rate (mL blood or soln/min) for streams 2 and 4 as appropriate. *Use our mass-balancing problem-solving format for this problem.*

Label diagram: (4 pts)



Notation: whole (B)lood, (P)lasma, (C)ells, (G)lucose, (U)rea, (W)ater, (D)ialysis solution, (T)otal stream

I haven't explicitly written out the concentration expressions for water in each stream, leaving these in terms of stream balances instead as "ρ-Σ(conc)". Can generate explicit expressions for water by subtracting the sum of the species mass concentrations in each stream from the overall stream mass concentration, i.e. the total stream density. Since for both units – the blood side of the dialyzer and the dialysate side – can write N-component + 1 mass balances, can opt out of using the water balances; these would be the most tedious balances to use anyways.

Basis: 360 mL/min blood in stream 1 (or 720 mL/min dialysate in stream 3) (4 pts)

Spring 2005 (Przybycien) **42-101 Intro to BME** **NAME:** _____

MAKEUP EXAM SOLUTIONS and GRADING SCHEME

Equations: Steady State Mass Balances: ΣIN = ΣOUT (8 pts)

Blood side of dialyzer: 4 components, 5 possible balances, 4 will be linearly independent

C: (0.41 dL C/dL B)(360 mL B/min) = H2*Vdot2 + 0 Eqn 1

G: (100 mg G/dL P)(1-0.41 dL P/dL B)(360 mL B/min)<1 dL/100 mL>
= C2G*(1-H2)*Vdot2*<1 dL/100 mL> + 0 Eqn 2

U: (200 mg U/dL P)(1-0.41 dL P/dL B)(360 mL B/min)<1 dL/100 mL>
= C2U*(1-H2)*Vdot2*<1 dL/100 mL> + 180 mg U/min Eqn 3

W: W IN1 = W OUT2 + 13 mL W/min Eqn 4

T: (360 mL B/min) = Vdot2 + (13 mL W/min) Eqn 5

Dialysate side of dialyzer: 3 components, 4 possible balances, 3 will be linearly independent

G: (125 mg G/dL D)(720 mL D/min)<1 dL/100 mL> + 0
= C4G*Vdot4*<1 dL/100 mL> Eqn 6

U: 0 + 180 mg U/min = C4U*Vdot4*<1 dL/100 mL> Eqn 7

W: W IN3 + 13 mL/min = W OUT4 Eqn 8

T: (720 mL D/min) + (13 mL D/min) = Vdot4 Eqn 9

DOF Analysis: (4 pts)

DOF = # unknowns (Vdot2, H2, C2G, C2U, Vdot4, C4G, C4U)
- #equations (7 independent mass balances)
= 0 ⇒ can solve

Method of Solution:

1. Eqn 5 ⇒ Vdot2
2. Eqn 1 ⇒ H2
3. Eqn 2 ⇒ C2G
4. Eqn 3 ⇒ C2U
5. Eqn 9 ⇒ Vdot4
6. Eqn 6 ⇒ C4G
7. Eqn 7 ⇒ C4U

Solution: (2 pts)

1. 360 – 13 = Vdot2 = 347 mL B/min
2. (0.41)(360) = H2(347)
   ⇒ H2 = 0.4254 vol C/vol B
3. (100)(1-0.41)(360)<1/100> = C2G(1-0.4254)(347)<1/100>
   ⇒ C2G = 106.527 mg G/dL P
4. (200)(1-0.41)(360)<1/100> = C2U(1-0.4254)(347)<1/100> + 180
   ⇒ C2U = 122.7768 mg U/dL P
5. 720 + 13 = Vdot4 = 733 mL D/min
6. (125)(720)<1/100> = C4G(733)<1/100>
   ⇒ C4G = 122.78 mg G/dL D
7. 180 = C4U(733)<1/100>
   ⇒ C4U = 24.5566 mg U/dL D

Spring 2005 (Przybycien) **42-101 Intro to BME** **NAME: _____**

MAKEUP EXAM SOLUTIONS and GRADING SCHEME

Stream 2

Vdot2	= 347 mL B/min
H2	≈ 0.43 v/v
C2G	≈ 107 mg G/dL B
C2U	≈ 123 mg U/dL B

Stream 4

Vdot4	= 733 mL D/min
C4G	≈ 123 mg G/dL D
C4U	≈ 25 mg U/dL D

Think: (4 pts)

1. $0 < Vdot2 < 360$ mL B/min, as expected since water exits blood through membrane
2. 720 mL D/min < Vdot4, as expected since water enters dialysate through membrane
3. 0.41 < H2, as expected since cells become more concentrated as water leaves
4. 100 mg G/dL P < C2G < C4G < 125 mg G/dL D; as expected since no net G transfer across membrane, G in stream 2 becomes more concentrated as water exits (but can't become more concentrated than in stream 3) and G in stream 4 becomes more diluted as water enters (but can't become more dilute than in stream 1).
5. $0 < C4U < C2U < 200$ mg/dL P; as expected since whole point is remove urea from blood and transfer it to urea; for urea transfer to occur into dialysate, C4U < C2U