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BioE 110
Biomedical Physiology for Engineers
Final Exam
Spring 2012

Name	
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:		/35
Question 2:		/20
Question 3:		/30
Question 4:		/15
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Question 6:		/20
Question 7:		/25
Question 8:		/20
Question 9:		/30
TOTAL		/230

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Potentially useful constants and conversions

$R = 8.31\ J\ K^{-1}\ mol^{-1}$

$R = 0.0821\ L\ atm\ K^{-1}\ mol^{-1}$

$F = 96\ 485\ C\ mol^{-1}$

$N_A = 6.022 \times 10^{23}\ mol^{-1}$

$k_B = 1.38 \times 10^{-23}\ J\ K^{-1}$

1 atm = 101.325 kPa

1 atm = 760 mmHg

1 cP = 1 mPa s

1000 L = 1 m^3

ln x = 2.303 log x

Elementary charge (*e*) = 1.6×10^{-19} C

K = 863 mmHg (alveolar ventilation equation).

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1. Suppose you are working at a startup company whose goal is to make nanoparticles for the controlled release of chemotherapeutic drugs for malignant brain tumors. You are currently working with a polymer-based nanoparticle rectangular prism-shaped capsule, which has a wall thickness of 1 nm and encloses a cavity with dimensions 100 nm x 75 nm x 500 nm. The walls of the nanoparticle are much like lipid bilayers in that they have a hydrophilic exterior and a hydrophobic interior. You are attempting to encapsulate and deliver a drug that has a molecular radius of 1 nm; you note from a previous employee's lab notebook that when this drug is dispersed into equal volumes of water and olive oil, the concentration of the drug is roughly three times higher in the olive oil phase than in the water phase. All characterization is to be carried out at 37C in water, which has a viscosity of ~0.7 mPa-s at that temperature.

A. Calculate the concentration of drug in the capsule needed to produce a steady-state flux into a drug-free bath of 2.6 x 10^{-14} mmol/sec. (15 pts)

J = P*A*c
c = J/(PA)

A = 2*(100*75 + 100*500 + 500*75) = 190,000 nm^2
P = KD/Δx = (K/Δx) **(kT/(6πRη)) = (3/10^-9 m)(1.38***10^-23 J/K)(310K)/(6π(10^-9 m)(0.0007 J/m^3)) = 0.972 m/s
So, c = 2.6*10^-14 mmol/s / (0.972 m/s * 190000 * 10^-18 m^2) = **0.14 mmol/m^3=0.14 μM**

B. If the nanoparticle encloses a 100 mM solution of NaCl and is placed in a bath containing 10 mM NaCl, and the reflection coefficients of Na+ and Cl- across the polymer membrane are both 0.5, what would be the steady-state osmotic pressure across the membrane (in Pa), and would water flow into or out of the nanoparticle? Neglect any nanoparticle volume changes associated with this water flow in your calculation. (10 pts)

Π = gCσRT = 2(0.090 mol/0.001m^3)(0.5)(8.31 J/K-mol)(310 K) = **231,849 Pa. Water will flow <u>into</u> the capsule.**

C. If the volume of the nanoparticle is increased by a factor of eight but the proportions (aspect ratio) are kept constant, by what factor would you expect the flux to increase? (10 pts)

This corresponds to stacking 8 such capsules in a 2x2x2 configuration, in which case the surface area for diffusion would increase by a factor of 4. Thus, the flux would also increase by a factor of 4.

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2. Consider a neuron that has the following intracellular and extracellular ion concentrations at 37 C:

Ion	Intracellular conc. (mEq/L)	Extracellular conc. (mEq/L)
Na+	15	140
K+	120	4
Cl-	10	36
Ca++	10^{-7}	2.5

A. Calculate the resting membrane potential of this neuron (in mV) assuming that the relative ion conductances for Na+: K+: Cl-: Ca++ are 1: 5: 3: 0. (10 pts)

Use Nernst equation to get equilibrium potentials for each ion: Eeq = -60 mV/z * log(ci/co)

Na+: z =1, ci/co =(15/140) = 0.107; thus ENa+ = -60*log(0.107) = 58.2 mV
K+: z = 1, ci/co (120/4) = 30; thus EK+ = -60*log(30) = -88.6 mV
Cl-: z=-1, ci/co = (10/36) = 0.278; thus ECl- = 60*log(0.278) = -33.4 mV
Ca++ : Ignore because g = 0

Use chord conductance equation to get Ememb:

Ememb = 1/9*(58.2 mV) + 5/9*(-88.6 mV) + 3/9*(-33.4 mV) = **-53.9 mV**

B. Consider a comparison between two neurons, one of which is normal and the other of which identical in all respects except that it harbors a mutation in a lipid synthase that doubles the membrane resistance without altering membrane capacitance or cytoplasmic resistance. Estimate by what factor the mutation would change the speed of membrane depolarization, and be clear on whether that speed would increase or decrease (10 pts).

Key parameter is the time constant (τ), which is proportional to Rm. Thus, if Rm doubles, τ will double also, and so one would expect membrane depolarization to occur ½ as quickly (or twice as slowly).

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3. Consider a 35-year old man who has a heart rate of 70 beats per minute, a stroke volume of 75 mL, and a blood pressure of 135 mmHg/75 mmHg.

A. If the diameter of this man's aorta is 25 mm and the total cross-sectional area of his systemic capillaries is 2200 cm^2, by what factor is blood flow faster in his aorta than in an average capillary? (10 pts)

Use continuity equation (v1A1 = v2A2):

Area of aorta = π*(0.5*2.5 cm)^2 = 4.91 cm^2
Area of capillaries = 2200 cm

So v(aorta)/v(cap) = A(cap)/A(aorta) = 2200/4.91 = 448 times faster.

B. Consider blood flowing through an arteriole. Imagine an experiment in which a drug is administered that constricts the arteriole, such that the relationship between the arteriolar radius (r, mm) and the plasma drug concentration (c, mM) is r(c) = 5 – 0.5c. For a fixed pressure drop per unit length ΔP*, Derive an equation that describes blood flow (Q) as a function of drug concentration (c) and blood viscosity η. At what plasma drug concentration would you expect flow to stop completely? (10 pts)

Q = ΔP/R = (ΔP)/(8ηL/πr^4) = ΔP*/(8η/πr^4) = ΔP*/(8η/π(5-0.5c)^4) = **ΔP*π(5-0.5c)^4/8η)**

Flow stops when Q = 0, which occurs when r(c) = 0, and this occurs at **c = 10 mM.**

C. Suppose the man has normal heart function at baseline and is given digitalis (digoxin), which as you may remember inhibits the Na+/K+ ATPase. Sketch the relationship between left ventricular pressure and volume during a single heartbeat ("P-V loop") before and after drug administration, being clear on what the differences are between the two loops and why.(10 pts)

See Fig 4-24C in text.

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4. Consider these general questions about ECF volume homeostasis (5 pts each).

A. You know from experience that eating a salty meal and drinking water causes you to retain fluid and temporarily gain weight, yet (thankfully) you do not go into congestive heart failure every time you eat a few slices of pizza and drink a bottle of water. Explain in 1-2 sentences the cardiac mechanism ensures that this extra fluid does not accumulate in your heart. Your answer should not involve secretion of any hormones.

The relevant mechanism is the Frank-Starling relationship. As venous return increases as a consequence of the excess ECF volume, the LV increases its output because of increased passive and active contraction of the myocardial muscle.

B. Now describe a renal mechanism involving the renin-angiotensin-aldosterone axis and a specific molecule and region of the nephron that ensures that you eventually lose the excess fluid volume described in A.

As ECF volume increases, the renin secretion falls, eventually reducing angiotensin II levels. This has the effect of relaxing the efferent and afferent arterioles and increasing GFR and urine output. (there are multiple possible answers – e.g. aldosterone effect on Na/K ATPase and sodium reabsorption in proximal tubule).

C. Suppose you administer 2 L of IV normal saline to a patient who has congestive heart failure. Several hours later, you notice the patient is coughing and having shortness of breath. Thinking in terms of Starling forces, describe two distinct mechanisms through which the saline infusion could increase capillary filtration and cause pulmonary edema.

IV NS both increases capillary hydrostatic pressure and reduces oncotic pressure (because of dilution of plasma protein). Together, these forces increase filtration and push fluid from alveolar capillaries into alveoli/alveolar basement membranes.

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5. Consider a patient with the following physiologic values. Assume all measurements are taken at atmospheric pressure (760 mmHg) and at so-called "body temperature pressure saturated" (BTPS) conditions. Note that the vapor pressure of water at BTPS is 47 mmHg and that the mole fraction of oxygen in inhaled air is ~0.21.

Pulmonary function tests:
Tidal volume (V_T) = 0.5 L
Vital Capacity (VC) = 7 L
Expiratory Reserve Volume (ERV) = 1.5 L
Forced expiratory volume after 1 sec (FEV_1) = 2.0 L
Breathing rate: 12 breaths/min
Fraction of CO2 in expired air (F_{ECO2})= 0.05

Arterial Blood Gas:
pO2 = 85 mmHg
PCO2 = 44 mmHg
pH = 7.37
[HCO3-] = 27 mEq/L

A. Calculate this patient's inspiratory capacity (IC) and inspiratory reserve volume (IRV) in L. (10 pts)

IC = VC – ERV = 7L – 1.5 L = **5.5 L**
IRV = IC – VT = 5 L – 0.5 L = **4.5 L**

B. At what rate (mL/min) are this patient's alveoli being ventilated with air? (10 pts)

VA = (VT – VD)*RR
VD = VT*(PaCO2-PECO2)/PaCO2 = 500 mL*(44 mmHg – 0.05*760 mmHg)/44 mmHg = 68.2 mL
VA = (500 mL – 68.2 mL)*12/min = **5181 mL/min**

C. If the patient takes a medication that increases his breathing rate to 18 breaths/min, to what value would you expect his arterial pCO2 to evolve (in mmHg)? (5 pts)

PaCO2 = PACO2 ~ 1/RR, so if RR increases by 1.5x, PaCO2 should fall by 1.5x, giving a value of 44 mmHg/1.5 = **29.3 mmHg**

D. Describe a renal mechanism that would eventually compensate for the altered pCO2 value described in C involving handling of HCO_3^-. Be clear on what direction the mechanism would act and where within the nephron it would do so (e.g., "increased absorption of HCO_3^- at the distal convoluted tubule") (10 pts)

As pCO2 falls, less CO2 will be available to epithelial cells in the proximal tubule for CA-mediated intracellular synthesis of H2CO3, which is needed for HCO_3^- reabsorption. Thus, plasma HCO_3^- eventually falls to offset respiratory alkalosis.

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6. Suppose you are a resident caring for a 55-year old female patient with a history of inflammatory bowel disease (IBD). (5 pts each)

A. Imagine that you have access to an imaging modality that enables you to measure the blood flow and ventilation in different regions of the lung. When this woman is walking around prior to her hospitalization, would you expect the ratio of ventilation to perfusion to be greatest in the lung apices or bases and why?

V/Q is greatest at apices, because gravity preferentially pools blood (Q) at lung bases. Air is much less dense than blood and is less sensitive to this effect.

B. Suppose this woman experiences an IBD flare and must be admitted to the inpatient ward of a hospital, where she is confined to lying in a hospital bed for several days while recovering and receiving IV medications. Under these circumstances, how would your answer in (A) to change?

The recumbent position places the apices and bases a more similar height, thus reducing the effect in (A) and brining V/Q ratios in these two parts of the lung closer together.

C. Suppose after spending several days inactive in her hospital bed, the woman suddenly experiences severe shortness of breath (dyspnea). In thinking through potential causes, you remember a medical student mentioning that the patient had complained the day before of a swollen, tender mass in her right calf, which you had dismissed as a bedsore. Both the mass and the breathing problems respond well to administration of heparin, an anticoagulant. Propose the most likely explanation for the mass and the dyspnea, explaining how the two are connected. During the dyspneic episode, how would the ventilation-to-perfusion ratio in the affected areas of the lung have changed and why?

This woman has likely suffered a pulmonary embolism created when prolonged bed rest has caused a thrombus to form in her calf (deep venous thrombosis). A portion of the clot broke off and has lodged in the pulmonary arterial circulation, creating a pulmonary embolism and cutting off blood flow to that portion of the lung. By definition, then V/Q to that portion of the lung goes to infinity (or significantly increases).

D. Suppose that you had not treated the symptoms in (C) in time and the woman needed to be placed on a mechanical ventilator. If the ventilator rate is set too high what would you expect to happen to urinary ammonium (NH_4^+) concentration over time and why?

Hyperventilation can cause a primary pulmonary alkalosis, which will eventually trigger a compensatory metabolic acidosis. In the kidney, this will manifest itself as reduced H^+ titration by NH_3, which will lead to a reduction in urinary NH_4^+.

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7. Suppose you are characterizing the clearance properties of three new drugs (1, 2, 3, and 4) as part of a preclinical trial. For each drug, you do an experiment in which you intravenously infuse a rat with a 1 μmol dose of the drug and measure steady state blood and urine concentrations of the drug over the next 48 hours. In the course of your studies, you learn that hematocrit of each rat is 0.45. The descriptions below summarize your findings:

Compound 1: Freely filtered at the glomerulus and neither reabsorbed nor secreted. Renal clearance = 1.50 mL/min.

Compound 2: Freely filtered at the glomerulus and heavily secreted into the renal tubule, such that all 1 μmol of the drug rapidly appears in the urine within 6 hours. Renal clearance = 6.00 mL/min

Compound 3: Cleared by liver, such that the entire 1 μmol is removed via the GI tract with chemical modifications. Renal clearance = 0 mL/min

Compound 4: Partially cleared by both the liver and kidney, such that 0.3 μmol is removed via the GI tract and 0.7 μmol is removed via the urine. Renal clearance = 2.50 μL/min.

Based on the above information:

A. Calculate the renal blood flow (mL/min) (10 pts).

Compound 2 has PAH-like properties, which means the clearance of this material is a surrogate for RPF. Thus, RPF = 6 mL/min and RBF = RPF/(1-Hct) = 6/(1-0.45) = **10.9 mL/min.**

B. If the clearance of Na+ is 1.0 mL/min, calculate the clearance ratio of Na+ (10 pts).

Compound 1 has inulin like properties, which means the clearance of this material is a surrogate for GFR. So CR(Na+) = Cl(Na+)/Cl(cpd 1) = 1.0 mL/min / 1.5 mL/min = **0.67**

C. If the steady-state plasma and urine osmolarity are both 300 mOsm/L, calculate the clearance of free water (5 pts).

CH2O = Vdot*(1 – Uosm/Posm) = **0** (since Uosm = Posm). i.e. no need to know Vdot.

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8. Answer the following true/false questions about renal solute handling and justify your answer in 1-2 sentences (5 pts each).

A. True or false: Countercurrent multiplication is made possible by the fact that the ascending and descending limbs of the Loop of Henle have nearly identical permeability to water.

False – This process is made possible by the fact that the ascending limb is significantly *less* permeable to water than the descending limb.

B. True or false: An insulin-secreting tumor of the pancreas would be expected to produce hypokalemia.

True – Insulin strongly promotes intracellular sequestration of K+, which reduces plasma K+ and causes hypokalemia.

C. True or false: Analogous to glucose, the majority of bicarbonate is reabsorbed in the proximal tubule via an Na+/HCO3- co-transporter on the luminal side of the tubular epithelial cells.

False – The majority of HCO3- reabsorption occurs by "reclamation" of HCO3- by secreted H+ coupled with generation and reabsorption of a new HCO3- produced by the intracellular carbonic anhydrase.

D. True or false: Urea recycling is based on the notion that antidiuretic hormone (ADH) has different effects on water and urea permeability in the cortical and outer medullary collecting ducts vs. the inner medullary collecting ducts.

True – ADH renders the cortical and outer medullary CDs permeable to water only whereas it renders the inner medullary CDs permeable to both water and urea. This enables preferential deposition of urea in the renal medulla, thus contributing to the corticopapillary osmolarity gradient.

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9. For patients with each of the following lab values, identify (10 pts each):

(1) His/her ongoing primary acid/base disorder, if any (your choices are acidosis, alkalosis, or no acid/base disorder).

If a primary acid/base disorder is present, also determine:

(2) The anion gap (and state whether this is elevated)

(3) Whether the primary acid/base disorder is likely respiratory or metabolic in origin.

Normal ranges are as follows:

P_aCO_2: 35-45 mmHg
P_aO_2: 80-100 mmHg
pH: 7.35-7.45
$[HCO_3^-]$ = 21-28 mEq/L
$[Na^+]$: 135-145 mEq/L
$[Cl^-]$: 98-108 mEq/L
Anion gap: 8-12 mEq/L

A. P_aCO_2= 41 mmHg; P_aO_2= 100 mmHg; pH = 7.44; $[HCO_3^-]$ = 27 mEq/L; $[Na^+]$= 138 mEq/L; $[Cl^-]$ = 101 mEq/L

No acid-base disorder.

B. P_aCO_2= 32 mmHg; P_aO_2= 99 mmHg; pH = 7.26; $[HCO_3^-]$ = 14 mEq/L; $[Na^+]$= 142 mEq/L; $[Cl^-]$ = 106 mEq/L

Primary acidosis; AG = 142 – 106 – 14 = 22 mEq/L (elevated); metabolic.

C. P_aCO_2 = 57 mmHg; P_aO_2= 97 mmHg; pH = 7.34; $[HCO_3^-]$ = 30 mEq/L; $[Na^+]$= 145 mEq/L; $[Cl^-]$ = 104 mEq/L

Primary acidosis; AG = 145 – 104 – 30 = 11 (normal); respiratory.

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