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BioE 110
Biomedical Physiology for Engineers
Final Exam
Spring 2012

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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:		/35
Question 2:		/20
Question 3:		/30
Question 4:		/15
Question 5:		/30
Question 6:		/20
Question 7:		/25
Question 8:		/20
Question 9:		/30
TOTAL		/225

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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 (in μM) needed to produce a steady-state flux into a drug-free bath of 2.6×10^{-14} mmol/sec. (15 pts)

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)

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)

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

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

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).

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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)

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 drug plasma drug concentration would you expect flow to stop completely? (10 pts)

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)

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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.

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.

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.

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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)

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

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)

D. Describe a renal mechanism that would eventually compensate for the altered pCO2 value described in C involving handling of $HCO3^-$. Be clear on what direction the mechanism would act and where within the nephron it would do so (e.g., “increased absorption of $HCO3^-$ at the distal convoluted tubule”) (5 pts)

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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?

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?

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?

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 (NH4+) concentration over time and why?

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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).

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

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

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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.

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

C. True or false: Analogous to glucose, the majority of bicarbonate is reabsorbed in the proximal tubule via an Na^+/HCO_3^- co-transporter on the luminal side of the tubular epithelial cells.

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.

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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

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

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

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