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

EXAM #2 SOLUTIONS and GRADING SCHEME

Part I: Short Answer Questions (48 pts)

Short written-answer and short calculation questions. I'll be looking for significant keywords, equations and/or diagrams. - *No more than two or three sentences in answer to any question in this section please.*

1. (6 pts) Some of our favorite bodily functions, including urination, defecation, parturition and arousal, are said to be regulated by a positive feedback control mechanism. Briefly, how does positive feedback control work and why would nature have developed this form of control for these functions?

   In positive feedback, the error signal increases with time (3 pts) as the output variable is added to the setpoint to compute the "error" signal. The growing error signal may be used to force a change of state (3 pts), which is desirable in the bodily functions mentioned.

2. (6 pts) The hydrolysis of ATP to ADP and inorganic phosphate is an energetically favorable reaction, with $\Delta G^{\circ\prime} = -7.3$ kcal/mol. Yet in the absence of a suitable hydrolytic enzyme, the rate of ATP hydrolysis in solution is negligibly slow. Why, in principle, is this the case?

   While the reaction is energetically favorable, the kinetic barrier for the reaction, the activation energy is very large (6 pts), resulting in a very slow reaction in the uncatalyzed case.

3. (6 pts) *E. coli* is a facultative anaerobe, a microorganism that can live under either aerobic or anaerobic conditions. If *E. coli* could choose its preferred environment, which would it be? Explain your answer.

   E. coli would prefer aerobic respiration as it can make 36 moles of ATP per mole glucose versus 2 moles of ATP per mole glucose for substrate level phosphorylation. (6 pts)

4. (6 pts) Describe what a "Nernst potential" is.

   The Nernst potential is the electrical potential difference across a membrane arising from different concentrations of charged molecules and ions on opposite sides of a semi-permeable membrane. (6 pts)

5. (6 pts) Calculate the free energy per mole of Na^+ for transport of Na^+ out of a cell. For this system, the membrane potential is 50 mV negative inside (positive outside), the Na^+ concentration is 12 mM inside and 150 mM outside, and the temperature is 310 K. [Gas Constant: R = 8.3145 J$(K^{-1})(mol^{-1})$; Faraday: F = 96,485 J$(V^{-1})(mol^{-1})$]

   $\Delta G(\text{inside} \rightarrow \text{outside}) = RT\ln(C_{out}/C_{in}) + zF\,(\psi_{out} - \psi_{in})$ (3 pts)
   $= (8.3145\ \text{J/K/mol})(310\ \text{K})\ln(150\ \text{mM}/12\ \text{mM})$
   $+ (+1)(96{,}485\ \text{J/V/mol})(+50\ \text{mV})$<1 V/1000 mV>
   $= +11{,}334.3$ J/mol (2 pts)
   $\approx +10{,}000$ J/mol (1 sig fig, 1 pt)

   This is an unfavorable transfer, requiring energy to occur (Na^+ going against both concentration gradient and potential gradient)

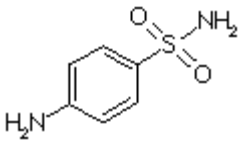
6. (6 pts) Two companies make competing biosensors for the early detection of mutated forms of the p53 tumor suppressor protein, a marker for breast cancer and other cancers. Company A uses an antibody that binds p53 with K_d = 2 nM as the basis for its sensor. Company B uses the MDM2 protein, a negative regulator of p53 that binds p53 with K_d = 580 nM, as the basis for its sensor. All other things being equal, which biosensor would be more sensitive? Explain your reasoning.

   The sensor having the binding group with the smaller K_d, the antibody-based sensor, will be more sensitive as binding of target species will be stronger (3 pts). This means that at any given analyte concentration, a greater fraction of the binding group would be complexed to the antibody than would be complexed to the MDM2 protein (3 pts).

7. (6 pts) What are the "proximity effect" and the "orientation effect"?

   These effects describe ways in which enzymes accelerate reaction rates. The proximity effect describes how enzymes bind reactants and bring them close together so that the reaction can occur (3 pts). The orientation effect describes how the bound reactants are oriented with reactive portions close to one another to facilitate reactions (3 pts).

8. (6 pts) Sulfanilamide (right) is an antibiotic that inhibits an enzyme in the synthetic pathway for folic acid in bacteria. If *p*-aminobenzoic acid (far right) is a substrate for this enzyme, what type of inhibition is likely occurring in the presence of sulfanilamide? Explain your reasoning.



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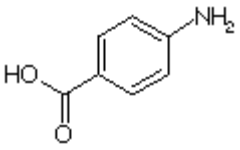

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   The chemical, shape and size similarity (3 pts) of sulfanilamide with *p*-aminobenzoic acid suggests that sulfanilamide binds to the same site on the enzyme as *p*-aminobenzoic acid; seem very likely that sulfanilamide is a competitive inhibitor (3 pts).

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Part II: Detailed Questions (52 pts)

1. (26 pts) The muscles surrounding the veins in your legs help to pump venous blood, via a squeezing action, from your legs back up to your trunk. Calculate the steady-state rate of work, in Watts, expended by the leg muscles surrounding a vein that extends from your ankle to your hip. For the purposes of this problem, we will assume that you are in a standing position, that your hip is 1.0 m above your ankle, that the volumetric flow rate in this vein is constant at 0.50 mL/s, that the diameter of the vein is 0.12 cm and is constant throughout the length of your leg, and that the blood pressure at your ankle is 88 mmHg and that at your hip is 60 mmHg. [Additional information: density of blood is 1.056 g/mL, acceleration due to gravity is 9.806 m/s^2, and (1 mmHg) = (133.3616 Pa)]

   Application of energy balance: system = blood in vein

   $dE_{sys}/dt = m_{dot}(u_{ankle} + v_{ankle}^2/2 + gh_{ankle}) - m_{dot}(u_{hip} + v_{hip}^2/2 + gh_{hip}) + Q_{dot} + W_{dot}$
   (general energy balance, 10 pts)

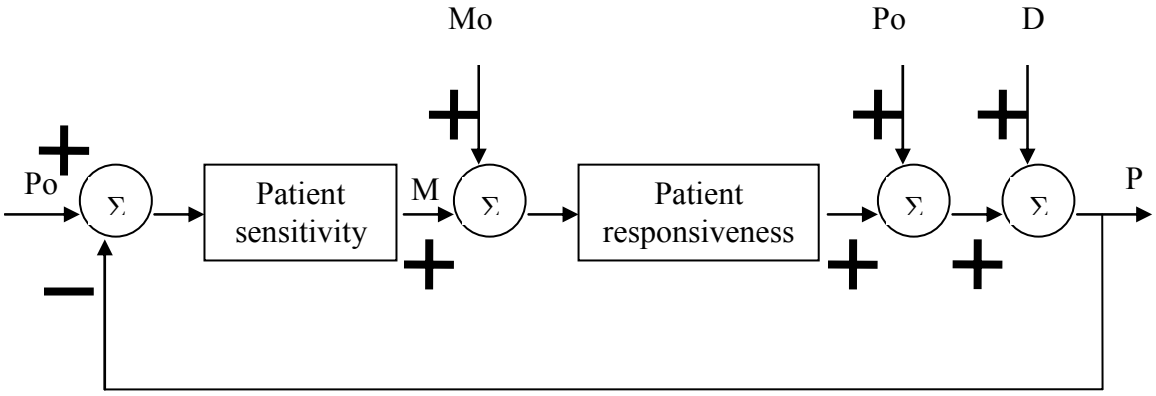
   Assumptions: steady state, no change in T, no heat transfer

   $0 = m_{dot}(gh_{ankle} - gh_{hip}) + P_{ankle}V_{dot} - P_{hip}V_{dot} + W_{dot,muscles}$
   $0 = V_{dot}\rho_{blood}g(h_{ankle} - h_{hip}) + V_{dot}(P_{ankle} - P_{hip}) + W_{dot,muscles}$
   (simplified energy balance, 10 pts)

   $-W_{dot,muscles} = (0.50\ mL/s)(1.056\ g/mL)\langle 1\ kg/1000\ g\rangle(9.806\ m/s^2)(0 - 1\ m)$
   $+ (0.50\ mL/s)(88 - 60\ mmHg)$
   $*\langle 133.3616\ Pa/1\ mmHg\rangle\langle 1\ kg/m\bullet s^2/1\ Pa\rangle\langle 1\ m^3/10^6\ mL\rangle$
   $= -0.00499\ kg\bullet m^2/s^3 \langle 1\ Watt/1\ kg\bullet m^2/s^3\rangle$
   (units conversions, 3 pts)
   (correct numerical answer, 2 pts)

   $W_{dot,muscles} \approx +0.0050$ Watts, energy supplied by muscles to blood in vein
   (sig figs, 1 pt)

2. (26 pts) A block diagram roughly approximating a patient's use of a morphine infusion pump (a pump that delivers fluids to the bloodstream) to manage post-operative pain is shown below. For this system, the pump delivers a constant, basal flow rate of morphine as specified by a doctor and set by a nurse; the patient can increase the flow rate of morphine above this basal level if pain makes them uncomfortable.



Specific points of information concerning the block diagram:
Po is a variable representing the patient's tolerance of serious pain
P is a variable representing the pain level experienced by the patient
Mo is a variable representing the constant (basal) flow rate of morphine set by the nurse
M is a variable representing the additional flow rate of morphine specified by the patient
The patient's sensitivity to pain is represented by a gain equal to (-Gs)
The patient's responsiveness to morphine is represented by a gain equal to (-Gm)

a. (2 pts) What does the variable D represent? Give an example that describes D that is relevant to the scenario associated with this problem.

Disturbance – sneezing, nurse moves patient, etc.; something that causes sudden increase in pain.

b. (2 pts) What is the error signal in terms of the variables associated with this problem?

Error = Po – P

c. (2 pts) What type of control does this diagram represent?

Negative feedback

d. (2 pts) What is the output variable?

P

e. (2 pts) What are the input variables?

Po, Mo, D

f. (4 pts) Explain why M and Mo come together in the diagram.

The total flow of morphine is that set by the nurse plus that added by the patient.

g. (6 pts) Explain why the gains for both patient sensitivity and patient responsiveness are negative.

Gs: When P>Po, the error is negative, but need more, not less morphine
Gm: As morphine flow increases, pain decreases

h. (6 pts) Develop an equation for the output variable in terms of the input variables; the output variable should only appear once in the equation.

Error = Po – P
M = –Gs*Error
Total morphine = M + Mo
Patient response to morphine (the change in pain) = –Gm*total morphine
Pain after morphine addition = Patient response to morphine + Po
P = Pain after morphine addition + D

P = –Gm(–Gs(Po – P) + Mo) + Po + D

$\therefore$ P = Po – GmMo/(1+GmGs) + D/(1+GmGs)