$\qquad$ EXAM \#2 SOLUTIONS AND GRADING SCHEME

## Part I: Short Answer Questions

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) The metabolic pathway fragment shown below is regulated by repression.


Describe what happens in this pathway as the concentration of substrate Z increases.
As the concentration of Substrate $Z$ increases, it binds for a greater fraction of time to the operator site ahead of the gene for enzyme a, causing less mRNA coding for enzyme a to be made and, and hence less enzyme a is made, reducing the flow of material through the pathway. (+6 pts)
2. ( 6 pts ) A noncompetitively-inhibited enzyme is well-described by the parameters $\mathrm{K}_{\mathrm{I}}=4.37$ $\mu \mathrm{M}, \mathrm{K}_{\mathrm{M}}=0.736 \mu \mathrm{M}$ and $\nu_{\max }=0.224 \mu \mathrm{M}$ substrate/min. Which species binds to the enzyme more strongly, substrate or inhibitor? Give the logic behind your answer.

Since the substrate dissociation constant, $\mathrm{K}_{\mathrm{M}}$ is less the inhibitor dissociation, $\mathrm{K}_{\mathrm{l}}$, (+3 pts ) the substrate binds more strongly to the enzyme than the inhibitor (+3 pts).
3. (6 pts) Give two biologically relevant examples each where living systems make use of negative feedback control, positive feedback control and feedforward control.

Negative feedback control: body/cell T, blood pH, enzyme inhibition, repression ... Positive feedback control: allostery, parturition, arousal, urination, defecation, hunger Feedforward control: predator/hazard avoidance, migration ...
(+1 pt for each reasonable example)
4. (6 pts) What is "homeostasis"?

The tendency of an organism to maintain internal conditions and compositions within narrow, well-defined limits. (+6 pts)
5. (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 (mitochondiral) 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)
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6. (6 pts) The bacterium Escherichia coli is known as a facultative anaerobe, meaning that it can grow in the absence of oxygen or in the presence of oxygen. If E. coli could freely choose to live in an aerobic or an anaerobic environment, which would it choose and why?
E. coli would choose an aerobic environment as it could derive much more energy (ATP) from aerobic respiration ( 36 mole ATP/mole glucose) than from substratelevel phosphorylation (2 mole ATP/mole glucose). (+6 pts)
7. (6 pts) In some microbes, the reaction (pyruvate $+\mathrm{CO}_{2} \rightarrow$ oxaloacetate) occurs and is catalyzed by the enzyme pyruvate carboxylase which also includes the hydrolysis of one molecule of ATP. With this information, place upper and lower bounds on the value for $\Delta \mathrm{G}^{o^{\prime}}{ }_{\mathrm{rxn}}$, in $\mathrm{kcal} / \mathrm{mol}$, for the reaction (pyruvate $+\mathrm{CO}_{2} \rightarrow$ oxaloacetate) in the absence of pyruvate carboxylase. Justify your bounds.

Since the reaction is coupled to ATP hydrolysis with pyruvate carboxylase, that must mean it is energetically unfavorable on its own: so $\Delta \mathrm{G}^{\circ}{ }^{\prime}{ }_{r x n}>0$ (+3 pts). Now since the hydrolysis of only one mole of ATP is required to drive the carboxylation reaction, $\Delta \mathrm{G}^{\circ \prime}{ }_{\text {ATP }}$ hydrolysis is $-7.3 \mathrm{kcal} / \mathrm{mol}$, and $\left(\Delta \mathrm{G}^{\prime \prime}{ }_{\text {ATPhydrolysis }}+\Delta \mathrm{G}^{\circ}{ }^{\prime}{ }_{\text {rxn }}\right)<0$ for the coupled reaction to occur: $\Delta \mathrm{G}^{\circ}{ }^{\prime}{ }_{\text {rxn }}<+7.3 \mathrm{kcal}$ mole ( +3 pts ). So, we would expect 0 $<\Delta G^{\circ}{ }^{\prime}{ }_{\text {rxn }}<+7.3 \mathrm{kcal} / \mathrm{mol}$.
8. (6 pts) What is "flow work"?

Flow work is the work required to push material in to and out of (open) systems with flowing streams. (+3 pts) The rate at which flow work is performed is equal to the product of the pressure of a stream with its volumetric flow rate,
Wdot $_{\text {flowwork }}=\mathrm{P} \times$ Vdot. (+3 pts)

Part II: Detailed Questions

1. (26 pts) A branch point in a metabolic pathway is shown below. A carbon-containing substrate $S$ is acted on by two different enzymes, E1 and E2, to make two different products, P1 and P2. The flow of carbon through this branch point is directed by negative feedback control: E1 is uncompetitively inhibited by inhibitor I and E2 is noncompetitively inhibited by inhibitor I. Kinetic parameters and concentrations for the two enzymes are given in the table below. For this system, estimate the percentage of substrate carbon that flows from S to P1 when the substrate concentration is constant at 47.2 mM and the inhibitor concentration is constant at $14 \mu \mathrm{M}$. You may assume that the substrate and both products each contain the same number of carbon atoms and that no product is present initially. [Hint: If no P1 or P2 is present initially, the amounts of P1 and P2 formed will be proportional to their rates of formation]


| enzyme | $\left[\mathrm{E}_{\mathrm{o}}\right]$ <br> $(\mu \mathrm{M})$ | $\mathrm{k}_{\text {cat }}$ <br> $(\mathrm{mM} \mathrm{S} /(\min \bullet \mu \mathrm{M} \mathrm{E}))$ | $\mathrm{K}_{\mathrm{M}}$ <br> $(\mathrm{mM} \mathrm{S})$ | $\mathrm{K}_{\mathrm{I}}$ <br> $(\mu \mathrm{M} \mathrm{I})$ |
| :---: | :---: | :---: | :---: | :---: |
| 1 (uncompetitive) | 57.3 | 0.00142 | 40.0 | 12.0 |
| 2 (noncompetitive) | 32 | 0.003339 | 50.0 | 25.0 |

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(+8 pts for uncompetitive inhibition equation)

$$
\begin{aligned}
v_{1}(\text { uncompetitive })= & \frac{\frac{v_{\max }}{\left(1+[I] / K_{I}\right)}[S]}{\frac{K_{M}}{\left(1+[I] / K_{I}\right)}+[S]} \\
& =\frac{\frac{(57.3 \mu \mathrm{~m} \mathrm{E})(0.00142 \mathrm{mM} \mathrm{~S} /(\mathrm{min} \bullet \mu \mathrm{M} \mathrm{E}))}{((1+(14 \mu \mathrm{M} \mathrm{I}) /(12.0 \mu \mathrm{M} \mathrm{I}))}(47.2 \mathrm{mM} \mathrm{~S})}{\frac{(40.0 \mathrm{mMS})}{(1+(14 \mu \mathrm{M} \mathrm{I}) /(12.0 \mu \mathrm{M} \mathrm{I}))}+(47.2 \mathrm{mM} \mathrm{~S})} \\
= & 0.02700 \mathrm{mM} \mathrm{~S} / \mathrm{min}
\end{aligned}
$$

(+8 pts for noncompetitive inhibition equation)

$$
\begin{aligned}
v_{1}(\text { noncompetitive }) & =\frac{v_{\max }[S]}{\left(K_{M}+[S]\right)\left(1+[I] / K_{I}\right)} \\
& =\frac{(32 \mu \mathrm{~m} \mathrm{E})(0.003339 \mathrm{mM} \mathrm{~S} /(\mathrm{min} \bullet \mu \mathrm{M} \mathrm{E}))(47.2 \mathrm{mM} \mathrm{~S})}{((50.0 \mathrm{mMS})+(47.2 \mathrm{mMS}))(1+(14 \mu \mathrm{M} \mathrm{I}) /(12.0 \mu \mathrm{M} \mathrm{I}))} \\
& =0.03326 \mathrm{mMS} / \mathrm{min}
\end{aligned}
$$

$\left(+4\right.$ pts for $\left.v_{\text {max }}=\left[\mathrm{E}_{\mathrm{o}}\right] \mathrm{k}_{\mathrm{cat}}\right)$
( +4 pts for connection between noncompetitive inhibition equation)
$\% \mathrm{C}$ to $\mathrm{P} 1=v_{1} /\left(v_{1}+v_{2}\right)$
$=(0.02700 \mathrm{mM} \mathrm{S} / \mathrm{min}) /((0.02700 \mathrm{mM} \mathrm{S} / \mathrm{min})+(0.03326 \mathrm{mM} \mathrm{S} / \mathrm{min}))$
$=0.4481$
$\approx 45 \%$ C flows to P1
( +1 pt for correct \#; +1 pt for 2 sig figs on correct \#)
pulmonary vein

aorta

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2. (26 pts) A left ventricular assist device (LVAD) is an implantable pump that can be used to treat a patient whose heart muscle is too weak to provide adequate blood flow to the circulatory system on its own. An LVAD is connected as a shunt from the pulmonary vein to the aorta. A schematic diagram is given to the right. The total blood flow rate is $5.0 \mathrm{~L} / \mathrm{min}$; blood has a density of $1.056 \mathrm{~g} / \mathrm{mL}$. At rest, the mean velocity and pressure of the blood in the pulmonary vein are $30 \mathrm{~cm} / \mathrm{s}$ and 6 mmHg , respectively; the mean velocity and pressure of the blood in the aorta are $30 \mathrm{~cm} / \mathrm{s}$ and 90 mmHg , respectively. If the LVAD provides work at the rate of -0.00050 hp at rest, what is the rate of work, in hp , provided by the patient's left atrium and left ventricle at rest? [Note: $1 \mathrm{bar}=750.061 \mathrm{mmHg}, 1 \mathrm{~J}=10 \mathrm{~cm}^{3} \bullet$ bar, $1 \mathrm{~kW}=$ 1.34102 hp ]

System $=$ blood in L. atrium, L. ventricle, LVAD (+2 pts)
(+6 pts for energy balance equation)

$$
\frac{\mathrm{dE}_{\mathrm{sys}}}{\mathrm{dt}}=\dot{Q}-\dot{W}+\sum_{\text {in }} \dot{m}_{\text {in }}\left(u_{\text {in }}+\vec{V}_{\text {in }}^{2} / 2+g z_{\text {in }}\right)-\sum_{\text {out }} \dot{m}_{\text {out }}\left(u_{\text {out }}+\vec{V}_{\text {out }}^{2} / 2+g z_{\text {out }}\right)
$$

(+6 pts for eliminating unnecessary terms in energy balance equation)
$0=0-\dot{W}+\sum_{\text {in }} \dot{m}_{\text {in }}\left(\vec{V}_{\text {in }}^{2} / 2\right)-\sum_{\text {out }} \dot{m}_{\text {out }}\left(\vec{V}_{\text {out }}^{2} / 2\right)$
(+6 pts for expanding the work term into heart, LVAD and flow work components)
$\dot{W}=\dot{W}_{\text {heart }}+\dot{W}_{\text {LvaD }}-P_{\text {in }} \dot{V}_{\text {in }}+P_{\text {out }} \dot{V}_{\text {out }}=0$
$\dot{W}_{\text {heart }}=-\dot{W}_{\text {LVAD }}+\dot{V}\left(P_{\text {in }}-P_{\text {out }}\right)$
( +4 pts for handling the extensive units conversions required)

$$
\begin{aligned}
\dot{W}_{\text {heart }} & =-(-0.00050 \mathrm{hp})+(5.0 \mathrm{~L} / \mathrm{min})(6-90 \mathrm{mmHg}) \\
& =0.00050 \mathrm{hp}-420 \mathrm{~L} \bullet \mathrm{mmHg} / \mathrm{min} \\
& \times\left\langle\frac{1 \mathrm{bar}}{750.061 \mathrm{mmHg}}\right\rangle\left\langle\frac{1000 \mathrm{~cm}^{3}}{1 \mathrm{~L}}\right\rangle\left\langle\frac{1 \mathrm{~J}}{10 \mathrm{~cm}^{3} \bullet \mathrm{bar}}\right\rangle\left\langle\frac{1 \mathrm{~min}}{60 \mathrm{~s}}\right\rangle\left\langle\frac{1 \mathrm{~kW}}{1000 \mathrm{~J} / \mathrm{s}}\right\rangle\left\langle\frac{1.34102 \mathrm{hp}}{1 \mathrm{~kW}}\right\rangle \\
& =-0.0007515 \mathrm{hp} \\
& \approx-0.00075 \mathrm{hp}
\end{aligned}
$$

( +1 pt for correct \#; +1 pt for 2 sig figs on correct \#)
heart does work on the blood, and the magnitude of the heart's work is comparable to that of the LVAD.

