LS 30B-3 Midterm 1

Elizabeth Frances Elton

TOTAL POINTS

65.5 / 76

QUESTION 1

1 Orca/Sea Lion/Squid Model 11.5 / 14

- ✓ - 1 pts Orca birth rate - missed proportionality constant (.005) or per capita term (extra R(t-17) needed!)
- ✓ - 0.5 pts Orca birth rate - Time delay in both L and R required
- ✓ - 0.5 pts Sea Lion death rate due to crowding (0.4*L^2) - missed per capita term or proportionality constant
- ✓ - 0.5 pts Sea Lion predation rate (0.1*R^2*L) - missed per capita (orca) or sea lion proportionality

QUESTION 2

Modifying GI Model 10 pts

2.1 Time Delay 4 / 4

- ✓ - 0 pts Correct

2.2 Type I Diabetes and Insulin Production 2 / 2

- ✓ - 0 pts Correct

2.3 Type II Diabetes and Glucose Secretion 2 / 2

- ✓ - 0 pts Correct

2.4 Kidney Failure and Excretion of Glucose and Insulin 2 / 2

- ✓ - 0 pts Correct

QUESTION 3

Explaining HPG Model 10 pts

3.1 Comparison of Oscillations 4 / 5

- ✓ - 1 pts No mention of stable vs neutral oscillations (but might have mentioned negative feedback loop with implicit time delay, which is important for part b)

  ST is also oscillating after perturbation.

3.2 Properties Causing Oscillations 5 / 5

- ✓ - 0 pts Correct

QUESTION 4

HPG Model and Tumors 14 pts

4.1 Transition from Oscillations to No Oscillations 2 / 2

- ✓ - 0 pts Correct (We gave full credit for saying Hopf bifurcation, although reverse Hopf bifurcation is the best answer.)

4.2 Change Model to Stop Oscillations 4 / 4

- ✓ - 0 pts Correct

4.3 Type of Equilibria 4 / 4

- ✓ - 0 pts Correct

4.4 Limit Cycle Attractor Trajectories 4 / 4

- ✓ - 0 pts Correct

QUESTION 5

Basics of Neuron Model 11 pts

5.1 Action Potential 1 / 5

- ✓ - 1 pts Minor error in graph
- ✓ - 1 pts Stage 1 is incorrect
- ✓ - 1 pts Stage 2 is incorrect
- ✓ - 1 pts Stage 3 is incorrect

5.2 Match Trajectories 5 / 6

- ✓ - 0.5 pts Incorrect iv equilibrium - unstable spiral inside LCA ("unstable spiral" only - OK; "LCA" only - incorrect)
- ✓ - 0.5 pts Incorrect v equilibrium - unstable spiral inside LCA ("unstable spiral" only - OK; "LCA" only - incorrect)

QUESTION 6

Altering Gamma 11 pts

6.1 w'-nullcline **1 / 2**

✓ **- 1 pts** Incorrect/missing graph

6.2 Equilibrium Points **6 / 6**

✓ **- 0 pts** Correct

6.3 Explain Failure to Re-Polarize **2 / 3**

✓ **- 1 pts** No mention of how the new stable equilibrium point (the one furthest to the right) prevents the cell from repolarizing/returning to resting potential.

QUESTION 7

7 Euler's Method for Delay Differential Equation **6 / 6**

✓ **- 0 pts** Correct

Midterm 1 Exam (Version A)

First Name: Elizabeth

Last Name: Elton

Last 6 digits of UID: 986788

Section # (TA): Ming (3C)

Signature:

Instructions: Do not open this exam until instructed to do so. You will have 1 hour and 50 minutes to complete the exam. Please print your name and the last 6 digits of your student ID number above and on each page of the exam. You may not use books, notes, or any other material to help you. You may use a scientific or 4-function calculator for this exam. Please make sure your phone is silenced and stowed at the front of the room. We are providing plenty of space for each problem, so you should not need additional space to answer the problems. However, you can use scratch paper which you will not turn in and which will not be graded.

Please do not write below this line.

Problem	Max	Score
1	14	
2	10	
3	10	
4	14	
5	11	
6	11	
7	6	
Total	76	

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1. (14 points) Last week, TV news stations broadcast video of a pod of orcas catching and feeding on a California sea lion off the Palos Verdes Peninsula. These sea lions feed primarily on squid. Write a system of differential equations to model the interaction of orca (R), sea lion (L), and squid (Q) populations. All rates are per month. If you do not remember a particular function's formula, sketch a graph of the function for partial credit.

   - In the absence of sea lions, the squid population will exhibit logistic growth, with a per capita growth rate of 0.1 and a carrying capacity of 5,000. (Note: The logistic growth equation is $X' = rX(1 - X/k)$.)
   - Each sea lion preys on squid at a rate that increases steeply as the squid population increases, but reaches a maximum of 400 squid per month. (Use a steep increasing sigmoid function for this.)
   - The birth rate of sea lions is proportional to their predation rate on squid, with a proportionality constant of 0.001.
   - Sea lions are nearing their carrying capacity in Southern California, so their per capita death rate due to crowding is proportional to the sea lion population with proportionality constant 0.4.
   - Orcas work together to catch sea lions, so each orca preys on sea lions at a rate that is proportional to both the orca population and the sea lion population, with proportionality constant 0.1.
   - Orcas have an average gestation period of 17 months, so the birth rate of orcas is proportional to the predation rate on sea lions 17 months earlier, with a proportionality constant of 0.005.
   - 0.1% of orcas die each month.

$$Q' = \underbrace{0.1Q\left(1 - \frac{Q}{5000}\right)}_{\text{squid growth}} - \underbrace{L\frac{400Q^5}{1+Q^5}}_{\text{sea lion-squid predation}}$$

$$L' = \underbrace{0.001L\frac{400Q^5}{1+Q^5}}_{\text{sea lion birth}} - \underbrace{0.4L}_{\text{sea lion death}} - \underbrace{RL0.1}_{\text{orca-sea lion predation}}$$

$$R' = \underbrace{0.1RL_{(t-17)} \cdot 0.005}_{\text{orca birth}} - \underbrace{0.001R}_{\text{orca death}}$$

$$\boxed{\begin{aligned} Q' &= 0.1Q\left(1 - \frac{Q}{5000}\right) - L\frac{400 \cdot Q^5}{1+Q^5} \\ L' &= 0.001L\frac{400 \cdot Q^5}{1+Q^5} - 0.4L - 0.1RL \\ R' &= 0.005 \cdot 0.1RL(t-17) - 0.001R \end{aligned}}$$

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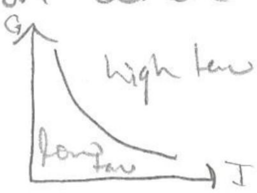
2. The differential equations for the glucose-insulin model are given below.

$$I' = \frac{k_1 G(t-15)^4}{1+G(t-15)^4} - k_2 I$$

$$G' = \frac{k_3}{1+I^2} + G_{ext} - k_4 G - GI$$

a. (4 pts) Until 1991, physiologists did not incorporate time delay into this model. How would that change the behavior of the model? Use the Hopf bifurcation diagram to explain your answer.

Not including time delay would mean that the system would have a stable spiral trajectory w/ a stable equilibrium point and dampening oscillations in a time series. Adding/increasing the time delay would lead to a Hopf bifurcation where the equilibrium would become unstable ?



, and you would have persistent oscillations (that return to their pattern no matter the perturbation) due to a limit cycle oscillator (which is unstable).

Modify the differential equation model (above) to answer each subquestion below (start from the original model for each subquestion). You do not need to write any differential equations that are not altered for each subquestion. You can make up parameters as necessary. If you forget the formula for a function, you can sketch it for partial credit.

b. (2 pts) In people with Type I diabetes, the immune system attacks the pancreas (which produces insulin), so the body produces very little insulin. Assume the patient does not yet take any external insulin.

$$I' = \frac{0.01 G(t-15)^{1}}{1+G(t-15)^{1}} - K_2 I$$

Setting k_1 to a low value (like 0.01) would lower the max amount of insulin that can be produced. Additionally, 'n' can be lowered from 4 to 1 to lower insulin production

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Modify the differential equation model (copied from above) to answer each subquestion below (start from the original model for each subquestion). You do not need to write any differential equations that are not altered for each subquestion. You can make up parameters as necessary. If you forget the formula for a function, you can sketch it for partial credit.

$$I' = \frac{k_1 G(t-15)^4}{1+G(t-15)^4} - k_2 I$$

$$G' = \frac{k_3}{1+I^2} + G_{ext} - k_4 G - GI$$

c. (2 pts) In people with Type II diabetes, glucose secretion by the liver is less sensitive to the insulin concentration in the bloodstream.

$$G' \quad \frac{k_3}{1+I^{1}} + G_{ext} - k_4 G - GI$$

I^{n} 'n' represents the sensitivity of the system, so lowering 'n' from 2 to 1 would decrease the sensitivity

d. (2 pts) Kidney failure impairs (reduces) the excretion of glucose and insulin from the body.

Making k_2 and k_4 small values would reduce the rate of excretion of both substances. Dividing k_2 and k_4 by some number would achieve the same effect.

$$I' = \frac{k_1 G(t-15)^4}{1+G(t-15)^4} - \frac{k_2}{4} I \quad \text{OR} \quad 0.001 I$$

$$G' = \frac{k_3}{1+I^2} + G_{ext} - \frac{k_4}{4} G \quad \text{OR} \quad 0.001 G \quad - GI$$

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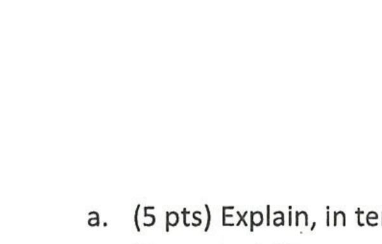
Last six digits of UID: 986788

3. Imagine you run into a student who is taking LS 30A right now, and they wonder why gonadal hormones like estrogen oscillate. They have learned about feedback loops, state space, vector fields and trajectories and have seen exponential and logistic growth and the shark-tuna and frictionless spring models, but have not yet studied any other topics. You can refer to the HPG model's differential equations as given below. You should not need all the space provided for each subquestion. You may use diagrams, but should also provide verbal explanation.

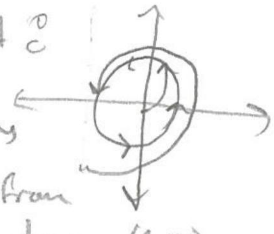
$$H' = \frac{1}{1+G^n} - k_1 H$$
$$P' = H - k_2 P$$
$$G' = P - k_3 G$$

a. (5 pts) Explain, in terms this person would understand, how the oscillations of the gonadal hormones in the HPG model are different from what the student has seen so far.

So far you've seen the exponential and logistic growth in predator-prey models like the shark-tuna model. In this model, population can increase until it reaches a carrying capacity (which acts as a stable equilibrium).



Trajectories that begin above or below this value move towards the stable equilibrium. The trajectories of oscillations show similar behavior, except they're attracted to a closed loop instead of a point.



Additionally, the oscillations of the HPG model differ from what you've seen in the shark-tuna (S-T) model in that no matter how you perturb the HPG system, the long-term behavior will be that of the closed loop. In the S-T model, if you disturb the system slightly, the long-term behavior can be completely different.

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b. (5 pts) Explain, in terms this student would understand, what properties of the HPG model cause oscillations. Be specific!

The HPG model has oscillations because it has:

1. a negative feedback loop
2. an (implicit) time delay
3. sensitivity

The HPG model illustrates a negative feedback loop because an increase in H (hormones in the hypothalamus) eventually lead to a decrease in H. The system is therefore also sensitive because the change in H depends on the value of G (illustrated in the term $\frac{1}{1+G^n}$). The system also has an implicit time delay because it takes time for the H (hypothalamus) P (pituitary) and G (gonads) to communicate. However, this isn't necessarily enough for the system to oscillate! The value of 'n' (which represents sensitivity) needs to be a high enough number for oscillations to occur.

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4. In a healthy adult before menopause, gonadal hormones oscillate. However, tumors in the hypothalamus and tumors in the pituitary gland can both cause gonadal hormones to stop oscillating. You can refer to the HPG model's differential equations as given below.

$$H' = \frac{1}{1+G^n} - k_1 H$$
$$P' = H - k_2 P$$
$$G' = P - k_3 G$$

a. (2 pts) In mathematical terms, what do we call this transition from oscillations to no oscillations?

(Hopf) bifurcation

b. (4 pts) Describe two ways a tumor might change the HPG model to cause oscillations to stop. Be specific!

1.) The tumor in the hypothalamus could decrease its sensitivity to gonadal hormones, causing the oscillations to stop.

2.) The tumors in the pituitary could remove it from the system entirely, leaving just the communication between the hypothalamus and gonads, thus removing the time delay and therefore the oscillations.

c. (4 pts) In this model, we have one equilibrium point. What type of equilibrium point does the model have for a healthy adult before menopause? How does this equilibrium point change if a tumor causes gonadal hormones to stop oscillating?

In a healthy adult, the model has a (unstable) limit cycle attractor.

If oscillations stop, the system would have a stable spiral.

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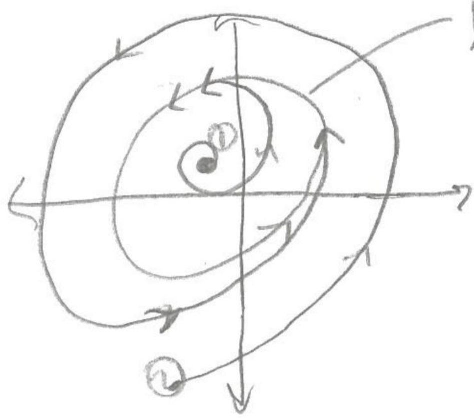
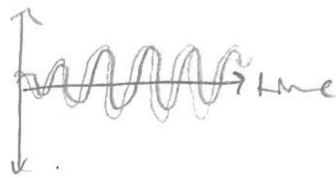
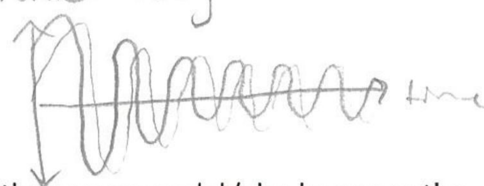
d. (4 pts) When your model is showing oscillatory behavior, it has a limit cycle attractor. Describe what happens to trajectories inside and outside the limit cycle. You may sketch, but you should also describe verbally.



Trajectories inside the attractor spiral out until they reach the behavior of the attractor:

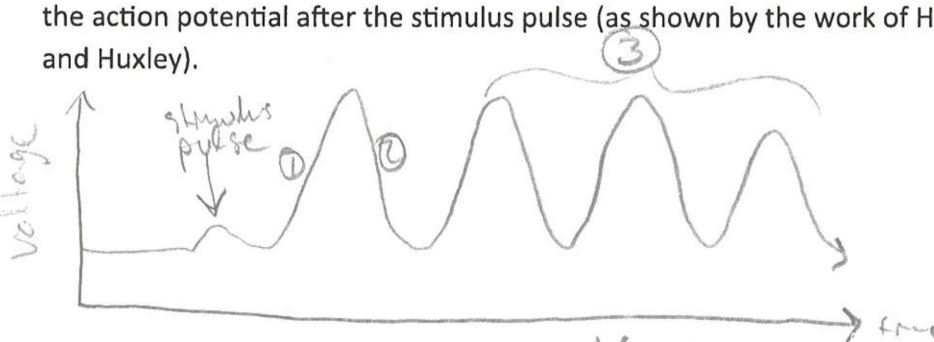


Trajectories outside the attractor spiral inwards until they reach the behavior of the attractor:



5.

a. (5 pts) Sketch the time series for voltage in the neuron model (also known as the action potential). Describe what's happening in the neuron in the three stages of the action potential after the stimulus pulse (as shown by the work of Hodgkin and Huxley).



If the stimulus pulse ~~is large enough~~ will cause the action potential to rise 1 until the resistance (or recovery) current brings it back down 2. If the pulse is large enough, this will trigger a train of action potentials 3.

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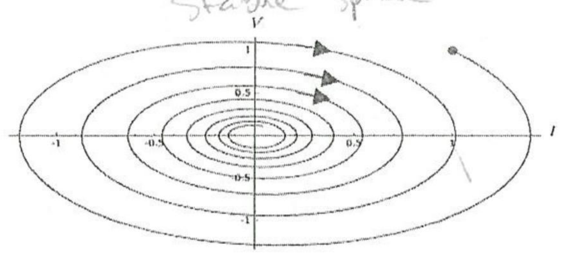
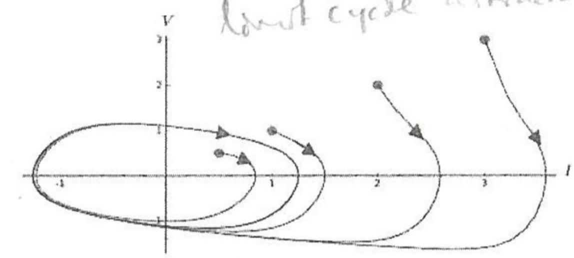
b. (6 pts) Match each set of electronics/neuron differential equations below to a generalized trajectory graph and name the type of equilibrium point. If you are not sure of the name of the type of equilibrium point, describe it verbally for partial credit. Note that we may have let some parameters equal 1 or 0 to simplify and that we sometimes use I where the literature uses w. In each graph, one or more trajectories start at the large point indicated.

Differential Equations	Trajectory Graph	Equilibrium Type
i. $I' = V$, $V' = -I$ no res.	D	center / neutral equilibrium
ii. $I' = V$, $V' = -I \boxed{-gV}$ linear resistance	A	stable spiral
iii. $I' = V$, $V' = -I \boxed{+gV}$ neg. res.	C	unstable spiral
iv. $I' = V$; $V' = -I - \boxed{(V^3 - V)}$ n-shaped res.	B	limit cycle attractor
v. $I' = V, V' = -I + V(1-V)(V-a) + I_{ext}$ for large constant current	B	limit cycle attractor
vi. $I' = V, V' = -I + V(1-V)(V-a) + I_{ext}$ for small or no constant current	A	stable spiral

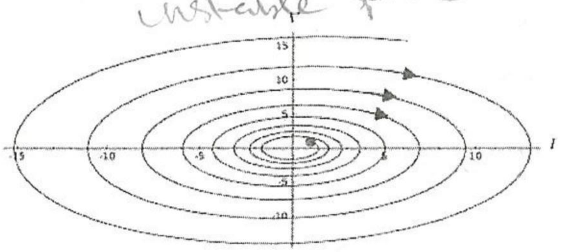
A. stable spiral



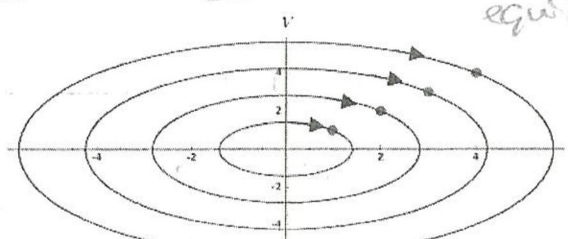
B. limit cycle attractor



C. unstable spiral



D. center / neutral equilibrium



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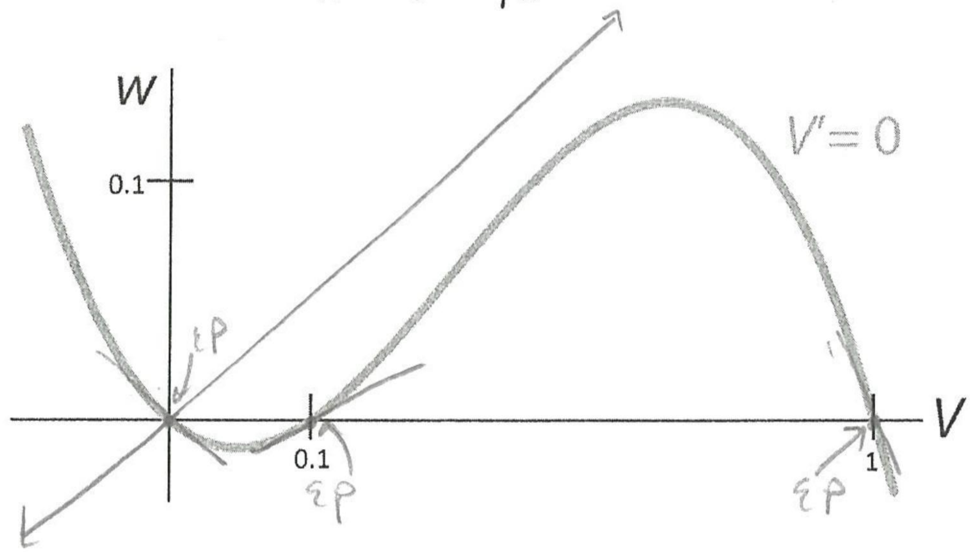
6. Drugs that block potassium channels are used to treat several diseases. They cause an increase in γ (gamma), which is the resistance of the potassium channel.

$$V' = \frac{1}{\epsilon}(V(1-V)(V-a) - w + I_{ext}$$

$$w' = V - \gamma w$$



a. (2 pts) Use the differential equations provided to determine the equation for a w'-nullcline for a large γ (such as $\gamma = 10$). Sketch it on the state space graph with V-nullcline provided. $w' = V - 10w$

$0 = V - 10w$

$10w = V$

$w = \frac{1}{10}V$

$\boxed{w = 0.1V}$

b. (6 pts) Label the equilibrium point(s) of the system and determine the type of each. (V, w) EP

$(0,0) \longrightarrow$ stable (neg. slope)

$(0.1, 0) \longrightarrow$ unstable (pos. slope)

$(1, 0) \longrightarrow$ Stable (neg. slope)

linear stability analysis

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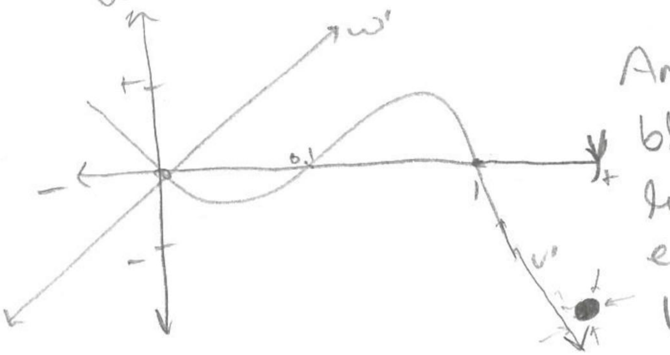
c. (3 pts) An overdose of potassium channel blockers can cause a failure of the action potential to return to its resting value. Use the diagram to explain this.



An overdose of K^+ channel blockers would result in a low 'w' value in the equations

$V' = \frac{1}{\varepsilon}(V(1-V)(V-a) - w + I_{ext})$ and $w' = V - \gamma w$

meaning on the graph that the point would be at a very high V value and low w value. If the point was somewhere like the dark, large one shown above, this past the second stable equilibrium point, and therefore would not be able to return back to its original resting value

7. (6 pts) Suppose

$$X' = 0.5X(t-0.4) + 2X(t-0.1) + 5X(t)$$

and $\boxed{X = 2 \text{ for all values of } t \le 0.}$ Using Euler's method with a step size of 0.1, approximate the value of X at time $t = 0.3$ (that is, $X(0.3)$).

$x(t) = x(t^{old}) + x'(t^{old}) \cdot \Delta t$

$t = 0$: $x'(0) = 0.5(2) + 2(2) + 5(2)$
$= 1 + 4 + 10 = 15$

$x(0.1) = 2 + 15(0.1) = 3.5$

$t = 0.1$: $x'(0.1) = 0.5(2) + 2(2) + 5(3.5)$
$= 1 + 4 + 17.5 = 22.5$

$x(0.2) = 3.5 + 22.5(0.1) = 5.75$

$t = 0.2$: $x'(0.2) = 0.5(2) + 2(3.5) + 5(5.75)$
$= 1 + 7 + 28.75 = 36.75$

$x(0.3) = 5.75 + 36.75(0.1) = \boxed{9.425}$