BIO/AMS 332: Computational Modeling of Physiological Systems — Homework 1

Instructions

- **You must work on this assignment independently.** You are welcome to make use of the class notes, lectures, and resources published online, but you may not discuss the problems with anyone other than the instructors (including the teaching assistant). Please note that prohibited discussion includes all forms of communication. Also note that all responses must be your own; direct copying from *any* source (including the class notes) is strictly forbidden. Your assignment must be accompanied by a statement that explains all resources that were used in the completion of any aspect of the assignment.
- **The use of past solutions to any problem set or exam for this class is strictly forbidden. This prohibition includes any material published on course sharing sites such as Chegg or CourseHero.**
- This assignment is in two parts: Part A requires you to given written definitions or explanations of key concepts from the module, while Part B requires you to apply these concepts.
- Your submitted work may either be completed by hand or type-written; if you choose to do work by hand, ensure that all your work is clearly legible. Work that is overly difficult to read will not be graded.
- All written answers should be given in complete sentences, and in your own words. You are encouraged to include sketches and/or equations to support your explanations, but responses of a sketch or equation without an accompanying explanation will not be given full credit. While points will not be deducted for minor grammatical errors, work that contains an excessive number of errors in grammar and/or spelling may be penalized.
- All mathematical responses should use a consistent and well-defined choice of notation. Problems that require manipulation of mathematical expressions must include enough work that the logic of your work can be followed by someone with an understanding of the underlying math but who is not familiar with the given problem.
- Your assignment should be submitted as a single PDF file including all responses in the correct order. If your work has been done by hand, Adobe Scan (`https://acrobat.adobe.com/us/en/mobile/scanner-app.html`) is recommended for scanning and converting your work into the appropriate form.

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Part A: Defining concepts.

1. Provide a one sentence definition of each of the following classes of protein:
   (a) Enzyme.
   (b) Receptor.
   (c) Transcription Factor.
2. Provide a one sentence definition of each of the following aspects of cellular physiology:
   (a) Anabolism.
   (b) Catabolism.
   (c) Transport.
3. Provide a detailed description (1-2 paragraphs) of each of the following cellular physiological processes:
   (a) Signal Transduction.
   (b) Transcription.
   (c) Translation.
4. Provide a brief description (2-3 complete sentences) of each of the following mathematical concepts:
   (a) System of ordinary differential equations.
   (b) Null cline.
   (c) Stationary point.
5. Provide a detailed description (1-2 paragraphs) of the following computational method:
   (a) The Forward Euler Algorithm.

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Part B: Applying concepts.

1. Consider the following model for the expression of a single gene:

$$\frac{d[X_{prot}]}{dt} = \omega[X_{rna}] - \chi_{prot}[X_{prot}] \qquad \frac{d[X_{rna}]}{dt} = \mu - \chi_{rna}[X_{rna}]$$

   (a) Explain these equations. Be sure to define each term and variable, and provide an explanation of the functional form for each term.

   (b) Find all null clines of the system, and plot them on plane of $[X_{rna}]$ vs $[X_{prot}]$.

   (c) Find all possible steady states of the system and highlight them on the plot made in (b).

   (d) What is the biological significance of your result? Under what circumstances might a gene evolve to have this sort of regulatory structure?

2. Proteins *lan* and *huang* are both transcription factors that control their own production as obligate auto-activators, and both bind DNA without any cooperativity. Protein *lan* is blue and protein *huang* is yellow.

   (a) Write a system of ordinary differential equations that may be a reasonable model for this system. Be sure to clearly define each term and variable, and provide an explanation of why the functional form you have chosen for each term is appropriate.

   (b) Find all possible steady states of the system, and provide conditions on the parameters necessary for each to exist.

   (c) Explain your results from (b) using two annotated plots, one showing the null clines of *lan* RNA and protein and the other showing the null clines of *huang* RNA and protein.

   (d) Under what conditions would you expect cells that contain the genes for both *lan* and *huang* to be (i) blue; (ii) yellow; (iii) green; or (iv) colorless.

3. Consider a general model for an auto-regulatory gene:

$$\frac{d[X_{prot}]}{dt} = \omega[X_{rna}] - \chi_{prot}[X_{prot}] \qquad \frac{d[X_{rna}]}{dt} = \mu\left(\frac{[X_{prot}]^h}{(K_{1/2})^h + [X_{prot}]^h}\right) - \chi_{rna}[X_{rna}]$$

   (a) Demonstrate why cooperative binding, represented by $h > 1$ is necessary for this system to have two equilibrium states (*i.e.* two stable stationary points).

   (b) Explain why cooperative binding alone does not guarantee the existence of two equilibrium states.

   (c) Will a model of this form always have at least one equilibrium state? Explain your answer.

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