Programming Interview

Question 1:

Using your own understanding write a 700-word essay on Biological Robustness and Fragility.

-In this essay define what is biological robustness and fragility.

-Give 1 example of robustness and 1 for fragility.

-Explain why biological robustness is integral part of survival.

-What are the consequences of fragility and how one could avoid it?

-Provide citations, where necessary, to justify your statements.

Question 2: Enzyme Kinetics

Enzymes are catalysts that help convert molecules that we will call substrates into other molecules that we will products. They themselves are not changed by the reaction. Within cells, enzymes are typically proteins. They can speed up biological reactions, sometimes by up to millions of times. They are also regulated by a very complex set of positive and negative feedback systems. Computational biologists are painstakingly mapping out this complex set of reactions. In this problem, we will model and simulate a simplified enzyme reaction.

An enzyme *E* converts the substrate *S* into the product *P* through a two-step process. First, *E* forms a complex with *S* to form an intermediate species *ES* in a reversible manner at the forward rate *k1* and reverse rate *k2*. The intermediate *ES* then breaks down into the product *P* at a rate *k3*, thereby releasing *E*. Schematically, we write

$$E + S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES \overset{k_3}{\rightarrow} E + P$$

8.1. Using the law of mass action, write down four equations for the rate of changes of the four species, *E*, *S*, *ES*, and *P*.

8.2. Write a code to numerically solve these four equations using the fourth-order Runge-Kutta method. For this exercise, assume that the initial concentration of *E* is 1 μM, the initial concentration of *S* is 10 μM, and the initial concentrations of *ES* and *P* are both 0. The rate constants are: *k1*=100/μM/min, *k2*=600/min, *k3*=150/min.

8.3. We define the velocity, *V*, of the enzymatic reaction to be the rate of change of the product *P*. Plot the velocity *V* as a function of the concentration of the substrate *S*. You should find that, when the concentrations of *S* are small, the velocity *V* increases

approximately linearly. At large concentrations of *S*, however, the velocity *V* saturates to a maximum value, *Vm*. Find this value *Vm* from your plot.

Question 3:

Read the below paper and write a report limited to 5 pages, including citations, figures etc. Reports beyond 5 pages will be rejected automatically.

The report should contain whether you think doppelganger effects are unique to biomedical data, and how you think it can be avoided in the practice and development of machine learning models for health and medical science.

Extra points are awarded if [1] you can find interesting examples in other data types e.g. imaging, gene sequencing, metabonomics. [2] Demonstrate clear understanding on how these doppelganger effects emerge from a quantitative angle, and [3] propose interesting and useful ways of avoiding or checking for doppelganger effects.