Question 1

Enzyme-catalyzed reactions are often approximated via a Michaelis-Menten rate term. Here, write down the set of elementary chemical reactions that exactly describe an enzyme catalyzed reaction (below). Also, calculate the individual reaction event propensity, ***c***, for each reaction; use bulk rate constants of k_1 = 1E9$M^{-1}s^{-1}$, k_{-1} = 314s^{-1}, k_2 = 1s^{-1} and a V_{system} = 1E-15L.

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \xrightarrow{k_2} E + P$$

R1. E + S -> ES c1 = 1E9/M/s * 1/[(6E23#/mole)(1E-15L/system)] ~= 1/#/s

R2. ES -> E + S c2 = 314/s

R3. ES -> E + P c3 = 1/s

[Please note the units on c1. # implies units of "number of unique reaction event combinations." This will be multiplied by h to cancel out the /# units.]

Question 2

Consider a set of elementary chemical reactions (below). Reaction 1 occurs. In the Gibson-accelerated Next Reaction method, which of the remaining reactions need their next reaction event times updated? For each updated reaction, will the updated reaction time be earlier (E), later (L)?

			Update?	E or L?
Reaction 1:	A + B →	C + D	**_Fresh__**	**_n/a or E_**
Reaction 2:	C + D →	E	**___Y___**	**___E___**
Reaction 3:	A + B →	E	**___Y___**	**___E___**
Reaction 4:	A + C →	E	**___Y___**	**Either, depends**
Reaction 5:	E →	A + B	**___N___**	**___N___**
Reaction 6:	E →	C + D	**___N___**	**___N___**

[Please note that the impact on reaction will depend on the current abundances of A and C. E.g., if A and C are initially present at numbers 5 and 5, respectively, then reaction 4 will occur later. Or, if A and C are initially present at numbers 6 and 4, respectively, then reaction 4 will occur earlier.]

Questions 3

For this question you need to choose the simulation method that would best provide the desired results for each situation. You have four options to choose from. Option 1 is a continuous approximate method (e.g., Euler's method). Option 2 is either of the original Gillespie algorithms for computing the exact behavior of a coupled chemical system (i.e., the Direct and First Reaction methods). Option 3 is the Gibson-accelerated Next Reaction Method. Option 4 is some other method

For each situation, choose the best option and briefly justify your choice.

Situation 1. A 1000 liter batch reactor is using several engineered microorganisms to convert cellulose to glucose and then ferment the glucose to ethanol. You need to compute the yield of ethanol as a function of time.

Use a continuous method (option 1). Timing of individual reaction events unlikely to matter. Plus, lots of reaction events will be occurring in a system of this volume.

Situation 2. Your kid sister wants to engineer a strain of skin bacteria that can produce two fragrances (roses and mint). She plans to use a light-controlled genetically encoded latch to allow users of the bacteria to set their odor by exposure to sunlight. Specifically, the bacteria are supposed to produce mint odor by default. But, if users walk in sunlight for 15 minutes then the bacteria should instead produce a rose odor (and continue to produce a rose odor for the next 12 hours, independent of whether or not the user remains in the sun). You've just made a brand new genetically encoded latch but are unsure how long the latch will accurately maintain its state.

Timing of individual reaction events is essential to explore spontaneous switching of latch. Latch system is unlikely to be fully coupled. So, choose option 3, Gibson-accelerated Next Reaction method should be worth it.

Situation 3. The National Institutes of Health has hired you to make the world's most physically accurate model of a human embryonic stem cell. They are particularly insistent that you develop a model that can track the physical position of each molecule inside the cell as a function of time.

The methods developed in 20.181 this term don't account for the physical location / spatial position of the molecules. Need a different method (Option 4).

Situation 4. You need to model a many-reaction chemical system in which the execution of any one reaction impacts the substrate abundances for all other reactions in the system.

The system is fully coupled, so there would be no expected acceleration via Gibson's method. In fact, Gibson's method may actually be more expensive relative to Gillespie's original methods. Go with option 2 (Direct method).