Monte Carlo Simulation of Photosynthesis

This is a very complex process to simulate.
It appears you did a lot of work to understand the chemistry.
I would have like to have seen much more detail regarding the
Monte Carlo method that you used; in particular your process
of determining parameters in that method. I would have also liked
to have seen much more modification of your model in the Adjustments
and Extensions section.

have a good break,

Dr. Conroy

Group 8

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Introduction

Photosynthesis is one of the fundamental processes of complex life. Without photosynthesis, there would be no life on the Earth. Photosynthesis is also the only process to transfer the solar energy to chemical energy we consume every day. We are interested in how the chemistry of this process works based on the available levels of light and the atmospheric composition. To investigate this process, we used a version of Monte Carlo simulation to explore the relationship between the inputs to the reaction and its overall production of glucose, which is used later in the metabolic pathway to produce more plant matter. Our model makes many simplifying assumptions, but still captures many important features of the large-scale reaction kinetics.

Our model examines the process of C3 photosynthesis, the version of the reaction common "to approximately 95% of Earth's plant biomass"[8], including many of the important food crops like rice and barley. In our model, we first looked for steady state solutions where the process runs without depletion of its chemical reserves, characteristic of the plant growing in optimal conditions. Then, we study the effects of perturbations to this this steady state to understand how this process is affected by different amounts of sunlight and different CO_2 and O_2 composition in the air by examining their impact on the rate of glucose production.

Background

In our first discussion meeting, our team decided to model dynamic system with Markov Chain concepts and simulate the model in Monte Carlo random walk. We considered many options including an artificial intelligence checker game, basketball season predictions, biochemical reaction simulation, and financial prediction in the stock market. After constructive discussion with Dr. Conroy, we decided to investigate a biochemical system, which is a relatively new field for most of us. To find proper subject to work on, we met and searched on pubmed article searching database and proposed several biological systems. Complex biological systems like the respiratory system and the phosphorylation process in ATP/ADP energy production were among our discussions because we wished to work on a biomedically important process which relates to our daily health. However, these systems are far more complicated to model than we previously conceived and so we looked for something that could be more easily simplified and modelled in the time frame we had. After some discussion, we agreed upon modelling photosynthesis, which while still complicated can be reduced to a simplified model without sacrificing its important dynamical behavior in response to external factors. Additionally, we felt that photosynthesis, owing to its enormous importance, would be a topic that many of our peers would have some familiarity with.

Photosynthesis. Photosynthesis is the process applied by plants and other organisms with chloroplasts to transform light energy into biochemical energy. This biochemical energy, in form of carbohydrate molecules such as sugars, are later used to drive all microscopic biological activities inside the organisms. These carbohydrate molecules are synthesized from carbon dioxide and water in our process of focus, photosynthesis.

In plants, photosynthesis consists of a series of light-dependent and light-independent reactions. The process begins when energy from sunlight is absorbed by proteins called reaction centers containing green chlorophyll. These proteins are held inside organelles called chloroplasts in plant leaf cells[10].

The pathway of photosynthesis inside chloroplasts is compartmentalized into three different spaces: extra-chloroplast intracellular space, stroma space, and granum space. To be specific, the chloroplast is enclosed by a membrane composed of a phospholipid inner membrane, a phospholipid outer membrane, and an intermembrane space. As shown in Figure 1, The inner membrane is folded into a network of flattened sacs called the thylakoid system that is suspended in the stroma, the aqueous fluid enclosed by the membrane. Stacks of thylakoids called grana contain the chlorophyll, which is responsible for the absorption of light, and are embedded within the stroma. The thylakoids have a shape of flattened disks and the grana have a shape of cylinders. The thylakoids are enclosed by the thylakoid membrane, and within the enclosed volume is the lumen or thylakoid space, another aqueous solution but with a much lower pH which is useful in driving reactions at the membrane. Integral and peripheral membrane protein complexes of the photosynthetic system are embedded in the thylakoid membrane.

FIGURE 1. Chloroplast Structure[2]

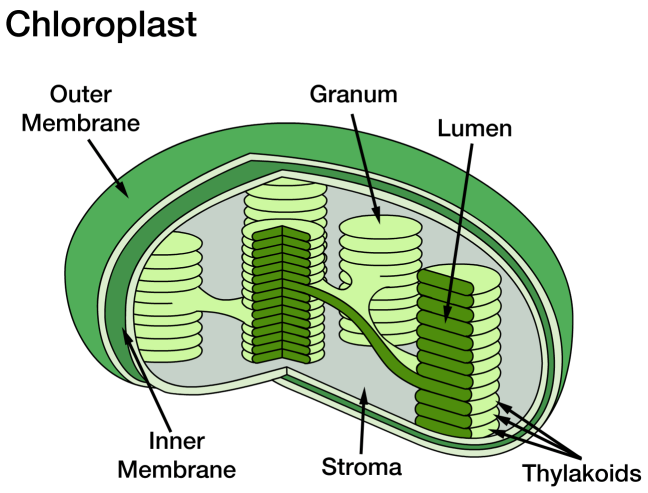
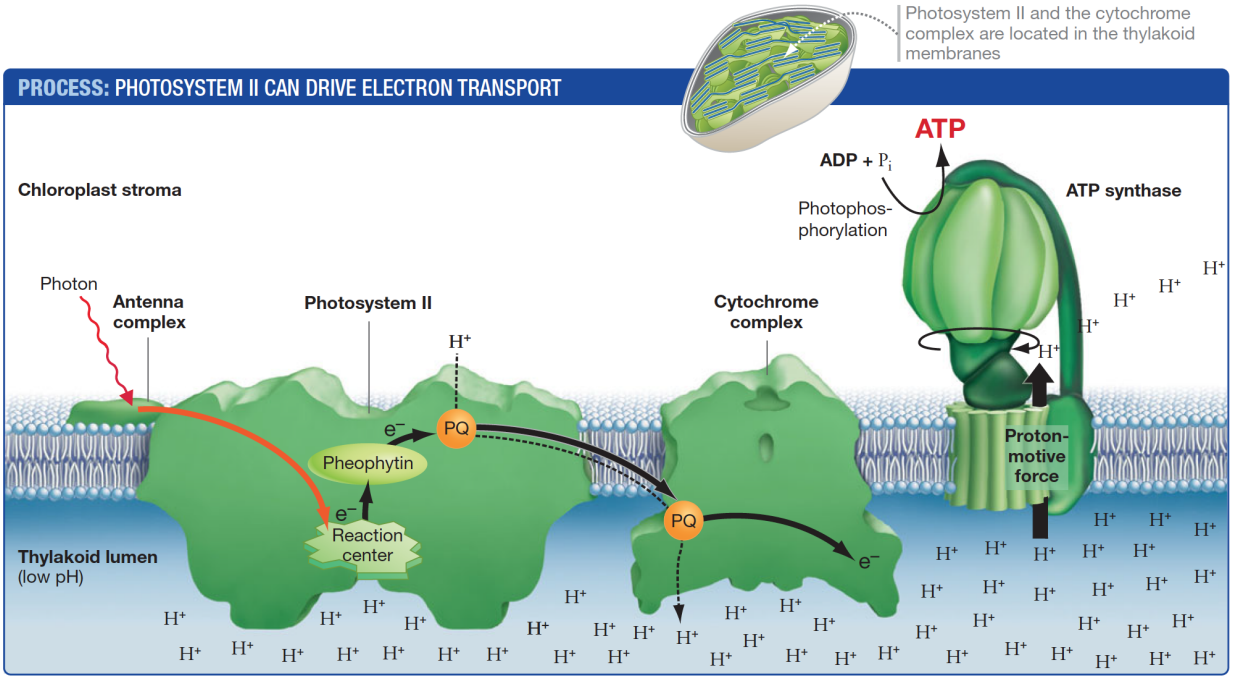


FIGURE 2. Electron Transport between Photosystem II and the Cytochrome Complex. Plastoquinone (PQ) carries electrons from photosystem II along with protons from the stroma. The cytochrome complex oxidizes plastoquinone, releasing the protons in the thylakoid lumen that drive ATP synthesis



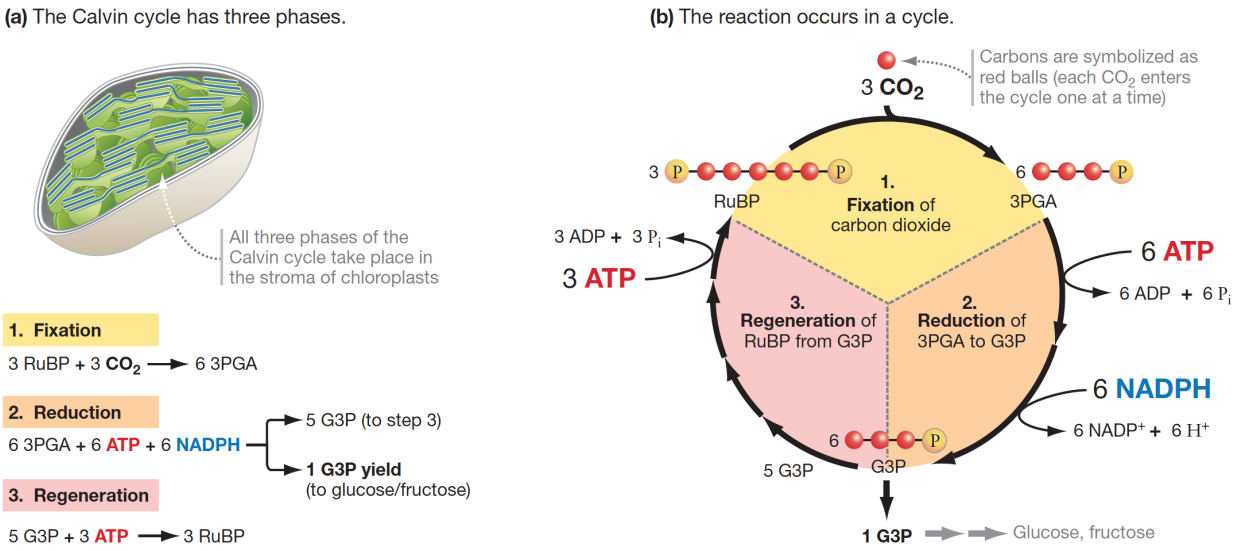
In the light-dependent reactions, or "light reactions", ATP and NADPH are synthesized when photons activate the reaction regions on the thylakoid membranes in the chloroplasts. ATP and NADPH are the chemical energy used later in the light-independent or "dark" reactions to drive the production of sugars from CO_2 and water. As shown in Figure 1, the lumen is the inside of the thylakoid membrane, and the stroma is outside the thylakoid membrane, where the light-independent reactions take place. The thylakoid membrane contains some integral membrane protein complexes that can catalyze the light reactions. There are four main protein complexes in the thylakoid membrane: Photosystem I (PSI), Photosystem II (PSII), Cytochrome b6f complex, and ATP synthase. These four complexes interact with each other to eventually create the products ATP and NADPH. The two photosystems absorb light energy through chlorophylls pigments. The light reactions begin in PSII, when the reaction center of PSII absorbs a photon, an electron in this chlorophyll molecule obtains a higher energy level and is transferred to another molecule creating a chain of reduction-oxidation reactions, called an electron transport chain (ETC). The ETC goes from PSII to cytochrome b6f to PSI, where the electron gets the energy from another photon and is transferred to the final electron acceptor, NADP. This drives oxygenic photosynthesis where water is photolyzed

and generates oxygen. ATP synthase then catalyzes Cytochrome b6f to create ATP in a process called photophosphorylation.

In summary, the composition of the light reactions forms the chemical equation:

$$2H_2O + 2NADP + 3ADP + 3P_i + light \rightarrow 2NADPH + 2H^+ + 3ATP + O_2 \quad (1)$$

FIGURE 3. Carbon Dioxide Is Reduced in the Calvin Cycle. The number of reactants and products resulting from three turns of the cycle are shown. Of the six G3Ps that are generated during the reduction phase, one is used in the synthesis of glucose or fructose and the other five are used to regenerate RuBP. The 3 RuBPs that are regenerated participate in fixation reactions for additional turns of the cycle

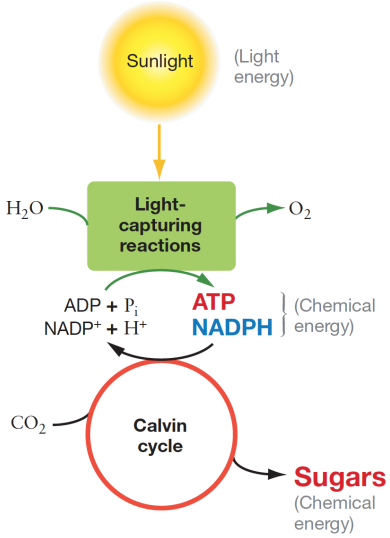


In the dark reactions, carbon is removed from the CO_2 in the air and turned into glucose in a process called the Calvin cycle. As shown in Figure 3, there are three phases in the Calvin cycle: fixation, reduction, and regeneration. First, in the fixation phase of the Calvin cycle, a CO_2 molecule is integrated into 1 of 2 three-carbon molecules (glyceraldehyde 3-phosphate or G3P), where it uses up 2 ATPs and 2 NADPHs, both produced in the light reactions. Next, the reduction phase, of the Calvin cycle is to regenerate RuBP. Costing 3 ATPs, 5 G3Ps produce 3 RuBPs. Since each CO2 molecule produces 2 G3Ps, 3 CO2 molecules produce 6 G3P molecules, of which 5 are used to regenerate RuBP, leaving a net gain of 1 G3P molecule per 3 CO2 molecules. Finally, in the regeneration phase, of 6 G3Ps produced, 5 are used to make 3 RuBPs, with only 1 G3P available for subsequent conversion to hexose. This requires 9 ATPs molecules and 6 NADPHs per 3 CO2 molecules[1].

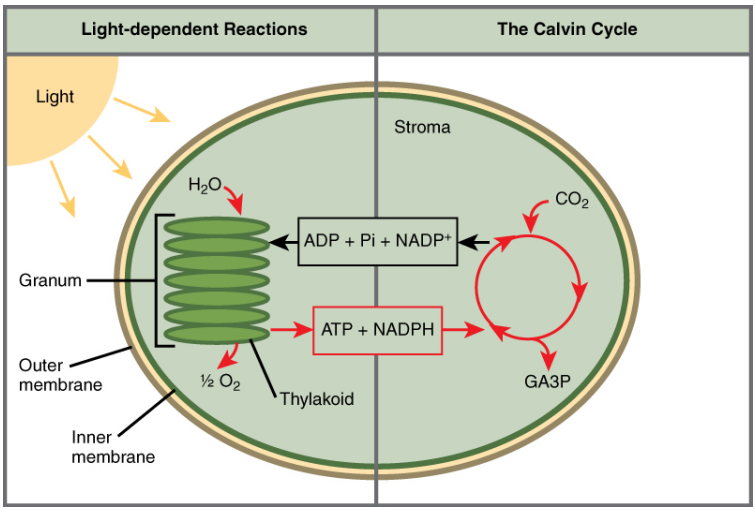
This complex series of reactions can by summarized as

$$3CO_2 + 9ATP + 6NADPH + 6H^+ \rightarrow C_3H_6O_3 - P_i + 9ADP + 8P_i + 6NADP + 3H_2O \tag{2}$$

FIGURE 4. In the light-capturing reactions of photosynthesis, light energy is transformed to chemical energy in the form of ATP and NADPH. During the Calvin cycle, the ATP and NADPH produced in the light-capturing reactions are used to reduce carbon dioxide to carbohydrate.



(A) Photosynthesis has two linked components



(B) Compartmentalization of photosynthesis

The combination of the light and dark reactions of photosynthesis is shown in Figure 4(a). In the light-capturing reactions of photosynthesis, light energy is transformed to chemical energy in the form of ATP and NADPH. During the Calvin cycle, the ATP and NADPH produced in the light reactions are used to reduce carbon dioxide to simple sugars. Figure 4(b) demonstrates the location each reaction takes place.

In summary, the entire photosynthesis reaction can be written in the simplified form:

$$6CO_2 + 6H_2O + light \rightarrow C_6H_{12}O_6 + 6O_2 \tag{3}$$

Similar and Related Modelling. The method that our model implemented is called Gillespie Algorithm initially discovered by Dan Gillespie in 1976[5]. Since popularized in 1977, the method has been implemented by many researchers in various fields across natural sciences such as chemistry and biology[9]. One of the interesting applications of Gillespie algorithm is exemplified in An implementation of the Gillespie algorithm for RNA kinetics with logarithmic time update by Eric C. Dykeman[4]. In this paper, Dykeman built KFOLD method upon Gillespie algorithm to select the samples of RNA molecules and predict folding kinetics. By using the Gillespie algorithm, the KFOLD method is able to compute a fixed number of changes at a low computational cost.

Different from the above method which implements Gillespie algorithm to compute for chemical substances, there are also applications in many other fields. In Temporal Gillespie Algorithm: Fast Simulation of Contagion Processes on Time-Varying Networks by Vestergaard Christian and Genois Mathieu[7], the Gillespie algorithm expands into the time-varying networks and deals with the probability under a time frame. Its very exciting to see that there emerged new areas where the Gillespie algorithm can be used.

Another related model is presented by Daniel Hallen and Robert Runberg, a mathematical modelling of natural and artificial photosynthesis[3]. In their setup, they used ordinary differential equations based on concentration of molecules to construct the model of natural photosynthesis, which is in contrast to our model since ours focuses on single molecules instead of the concentration. And for artificial photosynthesis, they modelled the part of photosynthesis II that has been constructed today but added missing parts with non existing molecules since there is no complete system of artificial photosynthesis. However, our project is mainly based on natural photosynthesis, so the artificial part in their model is less appealing for us. In their natural photosynthesis model, they described the dynamics of the complexes in terms of the dynamic probabilities of possible states of those complexes, which is an interesting part that differs from ours but also gets work.

Model

In order to simulate the complex dynamics of photosynthesis, we need to make many simplifying assumptions. While both the light and dark reactions are themselves a complex network of reactions catalyzed by an even more complex network of interacting proteins and enzymes, many of the underlying reaction rate coefficients are poorly understood. Rather than introduce a host of reaction parameters into our model, we consider the simplified two equation system

$$2NADP + 3ADP \xrightarrow{k_l} 2NADPH + 3ATP + O_2 \tag{4}$$

$$6CO_2 + 18ATP + 12NADPH + \xrightarrow{k_d} Glucose + 18ADP + 12NADP \tag{5}$$

These equations are slightly different than equations (1) and (2). In both equations, we've removed the hydrogen ion H^+, inorganic phosphate P_i, and water H_2O terms. These chemical species are in overwhelming abundance in all regions of the chloroplast and therefore play no role in limiting the rates of these reactions. We've also removed the explicit dependence on light from the reaction. Instead, we can think of the rate coefficient k_l as a function of the light intensity. Setting $k_l = 0$ effectively shuts off the light reaction allowing us to control the reaction rate quite efficiently.

We've also doubled the number of reactants and products in our dark reaction equation, Eq.(5). This allows us to ignore the complicated branching of G3P that occurs in the transition between the reduction and regeneration portions of the Calvin cycle and instead focus on the eventual output, glucose.

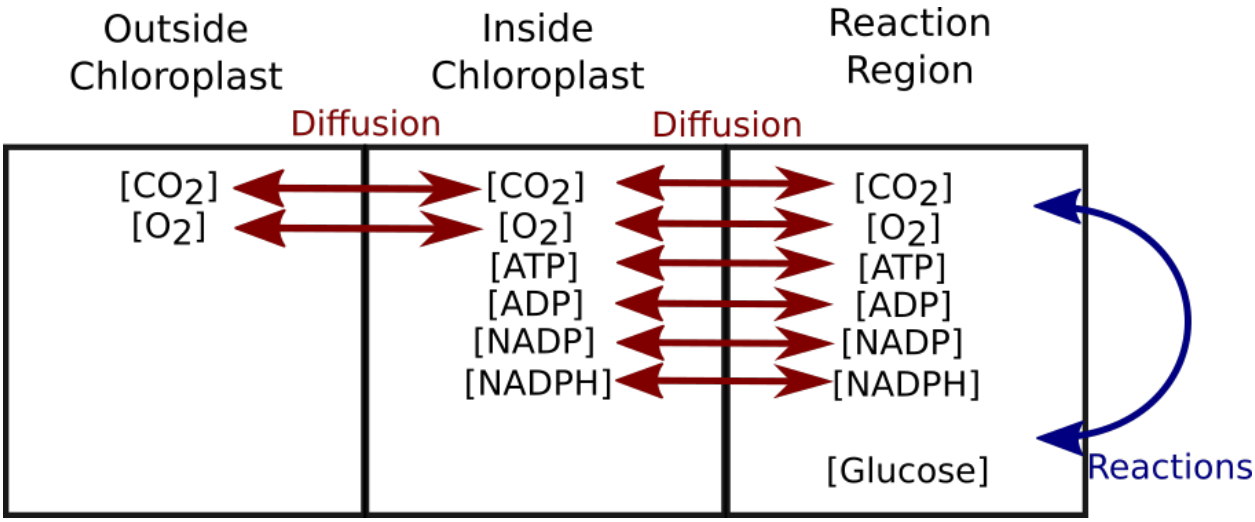
The stochastic simulation of the Gillespie algorithm is especially import for modelling biochemical reactions as the majority of biochemical reactions occur at very specific locations, usually on the membrane of some cell organelle. Typical reaction modelling uses differential equations and continuous concentrations as the dynamic variables. The nonlinearity of the resulting equations coupled with the inhomogeneous distribution of reaction sites contradicts the assumptions required for the continuous technique to be accurate, especially in limiting cases[5].

Here instead we consider the actual number of molecules as our dynamic variables. To enforce some approximation of the locality requirement, we also use a compartment model for the chloroplast as seen in Figure 6. In this model, we have subpopulations of the reactants in the different compartments and so we must also consider diffusion between the compartments.

This introduces the new model parameters K_m and K_r which are the diffusion coefficients across the chloroplast membrane (between inside and outside) between the interior and reaction regions, respectively. Additionally we consider the CO_2 and O_2 concentrations outside the chloroplast to be model parameters as they serve as a proxy for the makeup of the air the plant is growing in.

To develop our model we start from the typical differential equation model with the interpretation of these equations as instantaneous rate equations. By computing the individual reaction rates at each time step of interest and by assuming reactions occur as a Poisson process, we can generate a joint probability distribution over time intervals and reactions. We then draw an update interval and a particular reaction from this distribution and use them to update

FIGURE 6. Compartment Model of the Chloroplast



the number of reactants in the system. This process is repeated until we're satisfied with the output results.

Lets consider each piece of this process in turn. First we look at the rate calculation step. This comes from the normal differential equation reaction modelling. We denote the concentration of a reactant X as $[X]$. Then the reactions produce the following rate equations

Let

$$a_l = k_l \cdot [NADP] \cdot [ADP]$$

$$a_d = k_d \cdot [CO_2] \cdot [ATP] \cdot [NADPH]$$

then

$$\left.\frac{d[NADP]}{dt}\right|_r = -2 \cdot a_l + 12 \cdot a_d$$

$$\left.\frac{d[ADP]}{dt}\right|_r = -3 \cdot a_l + 18 \cdot a_d$$

$$\left.\frac{d[CO_2]}{dt}\right|_r = -6 \cdot a_d$$

$$\left.\frac{d[ATP]}{dt}\right|_r = 3 \cdot a_l - 18 \cdot a_d$$

$$\left.\frac{d[NADPH]}{dt}\right|_r = 2 \cdot a_l - 12 \cdot a_d$$

$$\left.\frac{d[O_2]}{dt}\right|_r = a_l$$

$$\left.\frac{d[Glucose]}{dt}\right|_r = a_d$$

These reactions all occur in the reaction region of Figure6. These differential equations then only represent a portion of the total change in concentration since diffusion is also changing the species count in a region. If we consider, say, ATP and it's diffusion, we have an additional rate equation

$$\Delta[ATP] = [ATP]_c - [ATP]_r$$

$$\left.\frac{d[ATP]_r}{dt}\right|_d = K \cdot \sqrt{\frac{T}{m_{ATP}}} * \Delta[ATP].$$

Here $\Delta[ATP]$ is a rough approximation of the concentration gradient between $[ATP]_r$, the ATP in the reaction region and $[ATP]_c$ the ATP in the body of the chloroplast. K is the overall diffusion coefficient which represents factors like the medium viscosity, membrane thickness, geometry of the boundary between regions, etc. T is the temperature of the cell and m_{ATP} is the mass of the ATP molecule. The equation says diffusion increases with temperature since molecules move more quickly, decreases with mass since heavy molecules move more slowly, and increases with the difference in concentration between any two regions. This equation is fairly correct for the diffusion in the chloroplast, though it's probably a poor approximation of the osmosis across the chloroplast membrane.

We won't repeat the remaining concentration equations here except to say they are identical in structure. We use two separate diffusion coefficients. One for diffusion across the chloroplast membrane and the other for diffusion insided the chloroplast.

We then set

$$D_X = \frac{d[X]}{dt}_d$$

as the instantaneous rate for the diffusion reaction for species X. The collection of these for each species as well as the light reaction rate a_l and the dark reaction rate a_d are collectively our reaction rates. For each reaction type, the mean time til that reaction occurs again is the inverse of the reaction rate. Since the rate at which anything will happen is simply the sum of all the reaction rates, which we'll denote by λ, we also can write the mean time until any reaction occurs as

$$\tau_m = \frac{1}{\lambda}$$

Then, under the assumption of a Poisson process, it's fairly straightforward to pick the next most likely reaction and the amount of time until the reaction occurs. For the time, we have

$$\tau = \frac{1}{\lambda} \log(\frac{1}{U_1})$$

for U_1 drawn uniformly from the unit interval. Likewise, if we denote the individual reaction rates as a_i we can select one based on the relative reaction rates by choosing a random variable

$$r = lambda * U_2$$

which gives for U_2 drawn uniformly from the unit interval. This gives us a random variable in the range $(0, lambda)$ which we can use to select the next reaction j by finding j such that

$$\sum_0^{j-1} \leq r \leq \sum_0^{j}$$

We then update the current time step, the number of reactants in all compartments, and go back to the beginning.

The update steps are performed by keeping matrices to store the reactant/reaction combinations as well as the number of molecules used in each reaction. Implementation details can be found in the appendix.

Results

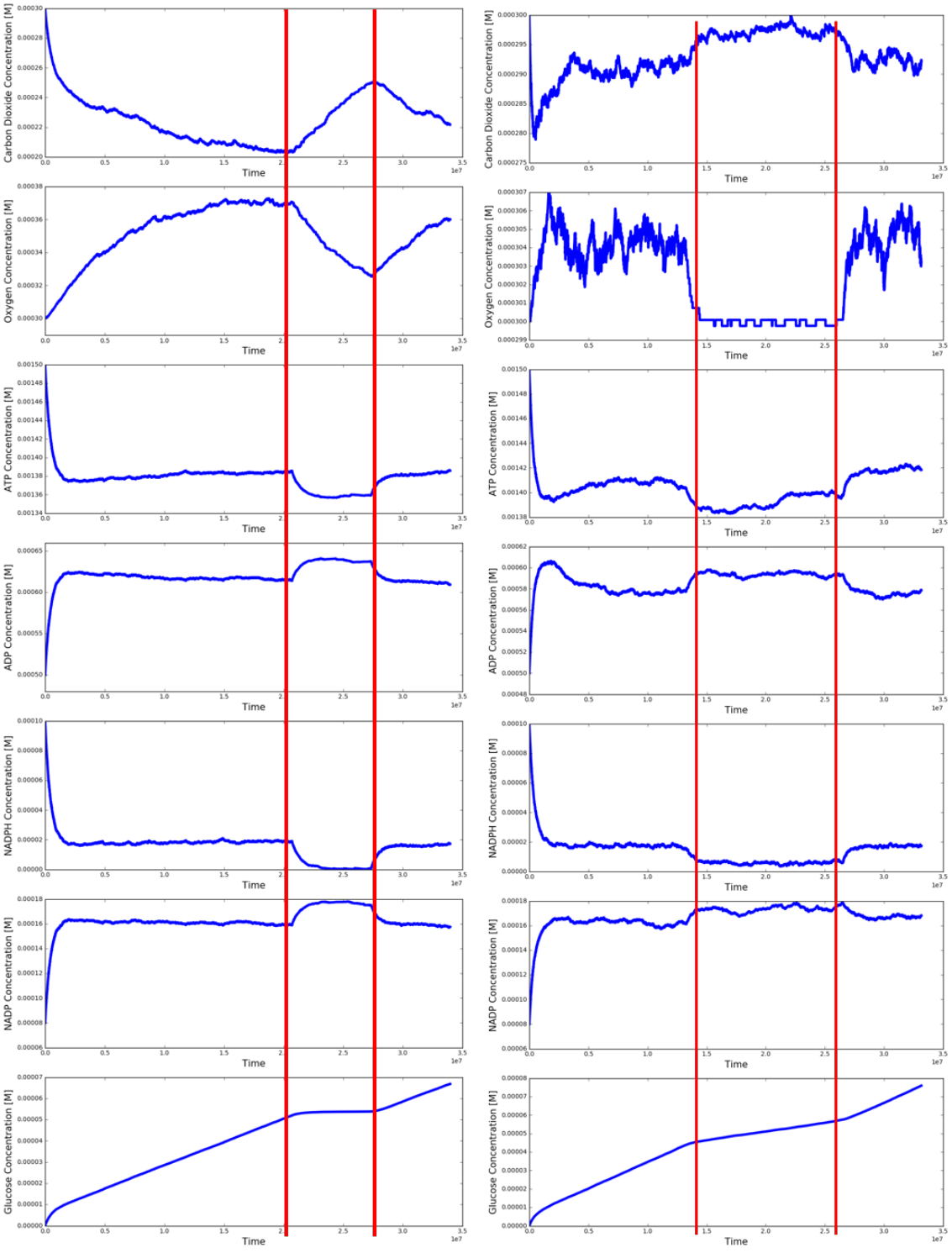
The first thing we sought to model was the normal operation of photosynthesis. We picked light and dark reaction rates to result in a steady state where none of the reactants hovered around zero. We then produced a single day/night cycle to see how the system responded.

Figure 7 (a) shows the model with very limited diffusion across both the chloroplast membrane and between the reaction and non-reaction areas of the chloroplast. This corresponds to the assumption that the diffusion rate of reactants is close to or smaller than the chemical reaction rates. This is not necessarily realistic, especially for the smaller molecules, but it produces easier to read graphs and gives us greater control over the state of the model. In the figure, we see a pretty rapid shift from the initial condition to a fairly stable steady state. The O_2 and CO_2 concentrations respond less strongly because even the relatively small diffusion constant affects them pretty strongly. This steady state is represented also by the linear slope in the glucose concentration indicating a consistent production rate. At the first red line, the light reaction was turned off to simulate the onset of night time (here relatively short). We can then see the rapid transition of all of the larger molecules to a new steady state with diffusion-limited production of glucose. Reintroducing the light source moves the system back into its previous steady state, as we would hope. This robustness to input and ability to reproduce the same state in response to the same inputs despite the any previous state history is a key feature of photosynthesis in the short term.

In figure 7(b) we see a result that mirrors that in the first subfigure, but with some important differences. Of particular not is much more rapid transitions between steady states for all the molecules. In the right ratio to the reaction rates, diffusion pushes the species concentrations in a semi- random way to their equilibrium position more rapidly. We also see the impact of diffusion on the glucose production. Even in the dark, glucose is still produced at a reasonable rate due to the reserves of chemical energy distributed throught the rest of the chloroplast.

These results, along with those presented in the following section, indicated that our model is qualitatively correct.

FIGURE 7. Normal photosynthesis, with and without diffusion



(A) Limited diffusion

(B) Abundant diffusion

Adjustments and Extenstions

Despite all the efforts we made to maximize the realistic accuracy of the photosynthesis system, we have to admit there are considerable amount of necessary assumptions we made to simplify our model. For example, we made the assumption that the concentrations of the CO2 and H2O are maintained inside intracellular space, which can be subject to realistic variations in different organisms and atmospheric pressures. Additionally, the concentrations of each reactants are different in stroma, intracellular space, and lumen space. However, we did accounts for the difference in concentrations of different process by adjusting our model and including the compartimization, which greatly resembles the real biological system. The introduction of diffusion decreases the error of the concentrations we used in each step of our simulations from the real concentrations in measurements.

Low Light Photosynthesis. Furthermore, we can extend the model and take into consideration the absence of light or the night environment. Before we change the light and dark rate, the reaction reaches its steady state with light rate = 200 and dark rate = 500. In this condition, based on the reaction all of the reactants are consumed up so no more glucose can be produced and therefore the reaction reaches the steady state. We then changed the set dark rate to 500 to mimic the night environment. As shown in the Fig.9, the concentration of glucose increases dramatically and goes beyond the previous steady state after the red line. This result proves our expectation that the dark reaction is initiated after we set dark rate to 500 and the glucose is being produced again because the products in the light reaction, namely the ADP, starts to react with NADP in the dark environment and produce glucose so that the concentration of glucose exceeds that of the previous steady state.

Calvin Cycle-limited Photosynthesis. For the condition that dark reaction is shifted off at the beginning, we firstly adjusted the light reaction rate = 500, then we shift the dark reaction on again with dark reaction rate = 500 as well. And we get the following graph. Before we shift dark reaction on, the simulation reached its steady state, which is the segment before the red line. In the steady state, the concentration of ADP and NADP almost hits zero level, and there is no glucose to be produced. After the dark reaction is shifted on, the concentration of ADP and NADP is precipitously increased and reaches to a new steady state in short time. While the concentration of NADPH and ATP just greatly decreases and also reaches to a new steady state in short time. Moreover, the concentration of glucose goes up as well as the concentration of oxygen does after the dark reaction is shifted on. These results make sense and reasonable since the glucose is rightly the production of dark reaction, so when dark reaction is present, glucose is present and accumulating as well. And for oxygen, since the simulation reached steady state before the dark reaction is shifted on, the system has consumed up ADP and NADP, then the concentration of oxygen is limited

since oxygen is the production of ADP plus NADP. While the dark reaction is shifted on, the concentration of ADP and NADP increases, so does the concentration of oxygen behave since ADP and NADP are present again and oxygen is accumulating as production.

Conclusion

From our exploration on modeling photosynthesis with Monte Carlos simulation, we learned about the dynamics of the photosynthesis in a mechanistic way. In our attempts, we learned to apply Gillespies Monte Carlos simulation, while adjusting the reaction constants calculation method in our discretion. More importantly, we managed to update our model and add more realistic elements into our model by many trials and errors based on the output we collected each time.

From our attempts, we successfully verified that our model can correctly simulate the photosynthesis and generate the values of all parameters needed to reach steady state in the normal condition. We also found that our model works well and can simulate the reactions of photosynthesis even in the extreme variations such as completely-dark and completely-bright variations.

Considering the potential application of our model to agricultural prediction and management, as well as the knowledge and skills we learned, we think our efforts are very worthwhile and rewarding.

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FIGURE 9. Low Light Photosynthesis and Transisition

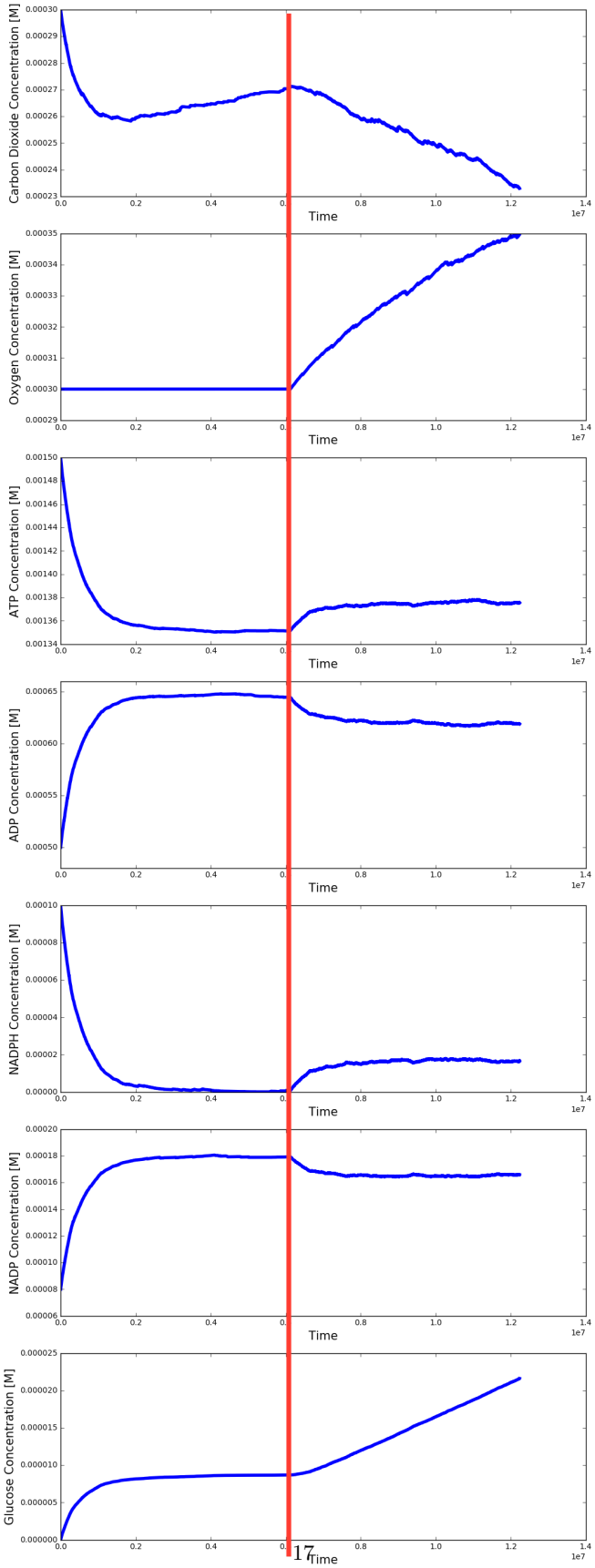

FIGURE 10. Calvin Cycle-limited Photosynthesis and Transition