

## A QUALITATIVE DYNAMIC PICTURE OF THE CHEMICAL KINETICS FOR PHOTOSYNTHESIS

FRANCESCA MAGNABOSCO <sup>a</sup> AND FRANCO CARDIN <sup>a\*</sup>

**ABSTRACT.** In this article the photosynthetic process is described from a qualitative dynamic point of view. After a brief and mesoscopic description of the chemical process, the related chemical reactions will be discussed by a mathematical point of view at a mesoscopic level, in agreement with the chemical kinetics theory. The behavior of the concentrations of all the chemical species involved in this process will be described and some new interesting relations among the kinetic constants will be found.

### 1. Introduction

The purpose of this paper is to describe one of the most important process for life in our planet: the conversion of solar energy into photochemical energy necessary to turn water and carbon dioxide into sugar and oxygen. The *chlorophylline photosynthesis* can be summarized with the rough chemical relation  $6\text{CO}_2 + 6\text{H}_2\text{O} + \text{energy} \longrightarrow \text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2$ , behind which there is a complex net of chemical reactions. It is not easy to find a complete and unitary description of these reactions at a mesoscopic scale: we have therefore summarized synthetically them in Section 2 by recalling, in an economic and hopefully clear way, as we found them in various articles and books (Govindjee and Rabinowitch 1969; Nelson and Cox 2014; *Fotosintesi clorofilliana* 2018).

Since the 60s a complete chemical theory that explains thoroughly this process has been developed: this theory provides two systems, called *Photosystem I* (PSI) and *Photosystem II* (PSII), in which the conversion of sunlight into energy takes place (Kok 1959; Hiroshi *et al.* 1963). This energy catalyzes reactions such as the splitting of water into oxygen (one of the final substances) and ions  $\text{H}^+$ , followed by an electron transport chain and by a synthesis of new chemical species which lead to the production of the other final substance, the sugar (Baltimore *et al.* 2000).

Afterwards, by using the chemical kinetics theory, this process will be rewritten as a system of 15 non linear ordinary differential equations that will be solved using a reduction technique based on the notion of *first integral*. This allows us to decrease the dimension of the differential system: the more first integrals are known, the more the size of the space is reduced. With some other considerations on asymptotically attractive surfaces, explicit

solutions will be obtained for all the equations, thus the behavior of the concentration of every chemical species involved will be fully described. After this, we will point out that our approach allows us to establish interesting new relations among the kinetic constants of the reactions. This is rather important, since as it is well known the value of the involved kinetic constants is largely unknown (Hallen and Rundberg 2000; Cardin and Moro 2007; Rubin and Riznichenko 2014).

## 2. The chemical model for the photosynthesis

**2.1. A brief history.** The description of the photosynthetic process has taken several years to be satisfactorily completed even though many microscopic and quantum aspects are not yet well understood. First important results were obtained in 1957 by Robert Emerson (Emerson 1957, 1958) and his co-workers who announced the discovery of the *enhancement effect*, also called *Emerson effect*, which occurs in the oxygen evolution when the light absorbed by a photosystem (afterwards identified with Photosystem I) is added to the light absorbed by another photosystem, the Photosystem II. This assumption had been confirmed by the large amount of experiments that Emerson concluded (Emerson and Rabinowitch 1960), and it suggested the new idea that *two* light reactions must occur in *two* photosystems. In 1960 Govindjee and Rabinowitch (Govindjee *et al.* 1960a; Govindjee *et al.* 1960b) concluded some experiments that suggested the presence of different spectral forms of chlorophyll *a* (Chl *a*) in the two photosystems. The longer wavelength forms (absorbing at wavelengths greater than 685nm) were found only in one photosystem, whereas the shorter wavelength forms (absorbing around 670nm) were found mostly in the other photosystem.

In 1960, Hill and Bendall (Hill and Bendall 1960) published an important paper in which they presented a representative scheme for photosynthesis which, in a modified form, is now known as the *Z-scheme*. This model, entirely based on thermodynamic arguments, described the idea of the two light reactions, but the concept of two photosystems, based on enhancement effect, was added later (Govindjee and Govindjee 2000). Due to some experiments performed by Duysens *et al.* (Duysens *et al.* 1961), it was suggested that the long wavelength forms of Chl *a* should be predominant in Photosystem I (PSI), whereas the other system, Photosystem II (PSII), should contain more short wavelength forms of Chl *a* and other accessory pigments.

In the following years this model has been improved, but the concept of two photosystems and two light reactions remains strongly settled (Govindjee and Krogmann 2004; Govindjee *et al.* 2017).

**2.2. Description of photosynthesis.** The entire process takes place in the *chloroplasts*, helical structures enclosed by a double layer of membrane. The inner part of this membrane, the *stroma*, contains the *thylakoids* where the central part of photosynthesis, called *light-dependent reactions*, occurs. This step needs to be catalysed: an external boost must be provided to the system, and this boost comes from the sunlight energy. When the light-dependent reactions are over then the *light-independent reactions* (or *dark reactions*) are triggered into the stroma.

**2.2.1. Light-dependent reactions.** Along the thylakoids membrane there are two multiprotein complexes: *Photosystem I* and *Photosystem II*. Their function is to absorb sunlight and

turn it into chemical energy. Both photosystems have two related components: the *antenna* which contains light absorbing pigments, and the *reaction center* formed by proteins clusters and molecules of Chl *a*. Studies have confirmed that each photosystem contains about 3000 pigments (Govindjee 1975). Different pigments absorb different wavelengths among the spectrum of the visible, and at each wavelength correspond a different amount of energy, in agreement with Planck's Law  $E = \frac{hc}{\lambda}$ , where  $c$  is the light speed,  $h$  is the Planck constant and  $\lambda$  the wavelength. This stored energy is transported through the molecules until it reaches the reaction center, where the real photosynthetic process begins. Here, the energy excites the electrons in chlorophyll molecules which pass from their fundamental state to an highly unstable state. These molecules, now excited, have to return to their initial state yielding their excited electron to some acceptors, triggering an electron transport chain. This loss of one electron by chlorophyll molecules must be immediately repaired.

What follows is a schematic description of what happens step by step:

*Photosystem II*: the reaction center of PSII is mostly formed by Chl *a* that absorbs maximum wavelengths of 680nm (orange light), hence these molecules are called P680. The energy here stored after the photons absorption is enough to allow one electron for each molecule to pass to the next orbit (we say that the electron has done a *quantum leap*). The P680 molecule passes to its excited state P680\* but, because of its high instability, the electron involved in the quantum leap is transferred to another molecule. Now, the oxidized molecule P680<sup>+</sup> recovers its missing electron from water molecules that split into ions H<sup>+</sup> and oxygen O<sub>2</sub>, releasing electrons. Thus, the chlorophyll molecule returns to its original state P680, whereas oxygen is produced and then released in the external environment.

*First electrons transport chain*: electrons released by P680\* are collected from the electron carriers that bring them to the reaction center of Photosystem I (PSI).

*Photosystem I*: the photons absorption occurs as in PSII with the only difference that in PSI the chlorophyll molecules are able to absorb wavelengths of 700nm, therefore called P700. Here, the oxidized molecules P700<sup>+</sup> replace their missing electron with the ones released by PSII and transported by the first electron transport chain, reducing into their initial state P700.

*Second electrons transport chain*: electrons released by P700\* are transported by the electron carriers into the site where the reduction of NADP<sup>+</sup> into NADPH occurs.

*ATP synthesis (or Phosphorylation)*: along the thylakoids membrane there is an enzyme called ATP-synthase whose task is to allow for the transition of ions H<sup>+</sup> produced during hydrolysis from the inner of the membrane to the external. This allows the synthesis of ADP and P<sub>i</sub> into ATP.

**2.2.2. Light-independent reactions.** These reactions, also called *Calvin cycle*, occur even in absence of light, unlike the light dependent reactions, and they need an input of carbon dioxide CO<sub>2</sub> from the external to be triggered. CO<sub>2</sub> molecules then react with ions ATP, NADPH (produced during the light-dependent reactions) and water, releasing a 3-carbon sugar (G3P) and regenerating ADP, NADP<sup>+</sup> and ions H<sup>+</sup>. The 3-carbon sugar produced, whose chemical formula is C<sub>3</sub>H<sub>7</sub>O<sub>6</sub>P, is the starting point for the synthesis of other carbohydrates. Some of this G3P is used to continue the cycle, but some other is available for molecular synthesis and is used to make fructose diphosphate. The fructose diphosphate is then used to make glucose, sucrose, starch and other carbohydrates.

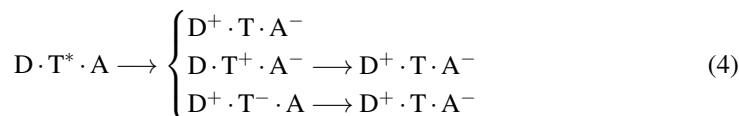
**2.3. Chemical reactions of Photosynthesis.** In 1963 Kamen (Kamen 1963) suggested a description of the photosynthetic process as a partition into three Eras (reactions written in a box will be the definitive ones):

- (1) Era of Radiation Physics:  $10^{-15}$  sec to  $10^{-6}$  sec during which excitation processes, physical migration and trapping of excitation energy occur. The related chemical reactions are the following:



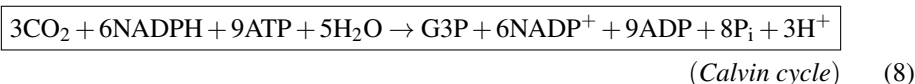
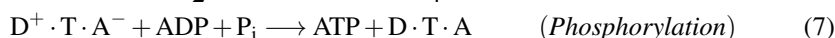
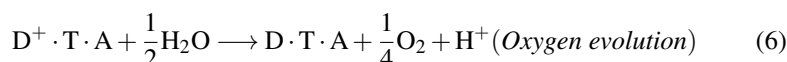
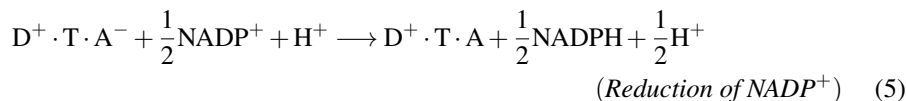
where Chl are the chlorophyll molecules at their initial state, whereas  $\text{Chl}^*$  the excited molecules. Reaction (3) describes the phenomenon of fluorescence that occurs when excited chlorophyll molecules return to their initial state releasing a photon with a wavelength ( $\nu'$ ) that, in general, has nothing to do with the one that excited the molecules ( $\nu$ ). Generally, only 3% of stored energy is used by fluorescence.

- (2) Era of Photochemistry:  $10^{-10}$  to  $10^{-3}$  sec in which processes as separation of charges or primary oxidant-reduction reactions occur. The primary redox reactions can be expressed in three different ways, as below:



where D stands for "donor", A for "acceptor" and T for "energy trap" (that correspond to the PSI or PSII reaction center). Nevertheless, these reactions can't be considered as true chemical reactions, but they only represent the transfer of electrons between a donor and an acceptor, with the mediation of the reaction center that provides the necessary energy for this transition.

- (3) Era of Biochemistry:  $10^{-4}$  to  $10^{-2}$  sec in which electron carriers and enzyme are involved, leading to oxygen evolution and  $\text{CO}_2$  fixation. The chemical reactions are the following:

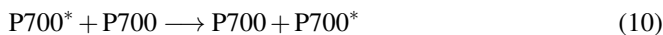


As said above, acceptors A donors D and energy traps T will not be treated as common chemical species and the chemical reactions will be rewritten in such a way as to omit the

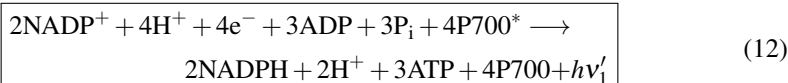
writing of these fictitious substances. An observation has now to be done about the Era of Radiation Physics. If reaction (1) describes the process of absorption, the other two describe the opposite phenomenon in which the excited molecules return to their initial state. Reactions (2) and (3), together, provide the energy necessary to trigger the remaining part of photosynthetic process. They also describe the phenomenon of fluorescence that requires about the 3% of the available energy. In the model that will be here described, reactions (2) and (3) will be included into the main reactions (from (5) to (8)). The same will be done for reaction (7), as it occurs by exploiting the energy released by reaction (5).

**2.4. Analysis of reactions.** From a mesoscopic point of view, the chemical reactions presented above will be now analyzed one by one.

**NADP<sup>+</sup> REDUCTION:** in the term  $D^+ \cdot T \cdot A^-$  on the left hand side of reaction (5) an electron is missing from the donor while the acceptor has an extra one. After the reaction has occurred, the donor is still missing an electron ( $D^+$ ) whereas the acceptor has turned back to its initial state (A). The extra electron must have been released and immediately used by the reaction, thus an electron must be added among reagents. As this reaction occurs in Photosystem I, that contains mainly molecules of chlorophyll P700, reactions (1) to (3) can be rewritten in this way:

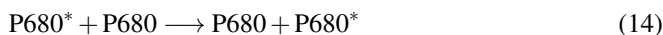


The two reactions (10) and (11) can be joined into equation (5), that describes the NADP<sup>+</sup> reduction and that supplies the energy necessary to trigger the phenomenon of phosphorylation, whose reaction can be more easily reformulated as  $ADP + P_i \longrightarrow ATP$ . This will be incorporate into eq. (5) as well, thus the final reaction, after a proper balancing, will be the following:

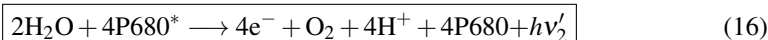


where  $v'_1$  indicates the frequency of fluorescence radiation emitted by chlorophyll P700.

**OXYGEN EVOLUTION:** by the same arguments as above, the presence between reagents of the term  $D^+ \cdot T \cdot A$  and of the term  $D \cdot T \cdot A$  among the products can be replaced with the writing of one electron between the products of reaction (6). As this reaction occurs in Photosystem II, where the presence of P680 predominates, equations (1) to (3) assume the following aspect:



and the overall reaction for oxygen evolution becomes



CALVIN CYCLE: reaction (8) does not need any manipulation because it shows up already in a proper form.

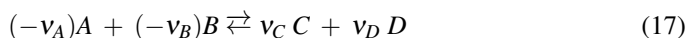
Hence, we have written a system of chemical reactions that describes mesoscopically the photosynthetic process and this system will be subsequently revisited from a mathematical point of view, according to chemical kinetics theory.

### 3. Chemical Kinetics Theory

This theory has the purpose to describe the dynamic of a set of chemical reactions in a reactive system, under proper conditions. The system under consideration has to be closed, homogeneous, isothermic (with a fixed temperature  $T$  which in our case correspond to the environment one) and in mechanic equilibrium.

The fundamental parameters in the description of a reactive system are the concentrations  $[\alpha] := \frac{n_\alpha}{V}$  of the several chemical species  $\alpha$  involved in at least one of the reactions, where  $n_\alpha$  represents the number of moles involved in the system, and  $V$  is the volume. These concentrations must be considered as time-dependent functions  $[\alpha]_t$  where the dependence on time is uniquely determined by the variation of  $n_\alpha$ , being the volume supposed to be constant.

**3.1. One reaction model.** The easier situation of a single reaction will now be taken in consideration. Let's consider the following reaction



By convention, the stoichiometric coefficients of reagents  $\nu_A$  and  $\nu_B$  are supposed to be negative, whereas the products coefficients  $\nu_C$  and  $\nu_D$  are positive. This allows to write the conservation law in the form

$$\frac{\Delta n_\alpha}{\nu_\alpha} = \frac{\Delta n_\beta}{\nu_\beta} \quad (18)$$

that reduces to one the number of unknown functions, simplifying considerably the analysis of the problem.

We can now define the *extent of reaction*  $\zeta(t) := \frac{n_\alpha(t) - n_\alpha(0)}{\nu_\alpha}$  as the variable that describes the variation of the number of moles of a chemical species respect to its initial state, scaled with its stoichiometric coefficient. This quantity is completely independent from the choice of the chemical species  $\alpha$ , thanks to the conservation law (18), and it allows to define the *concentration referred to the extent of reaction*

$$c(t) := \frac{\zeta(t)}{V} \quad (19)$$

that will be used to describe the time dependence of the concentrations as follows:

$$[\alpha]_t = [\alpha]_0 + \nu_\alpha c(t) \quad (20)$$

where  $[\alpha]_0$  is the initial concentration of the species  $\alpha$ . Hence, it is sufficient to specify the time dependence of the concentration  $c(t)$  to determine the evolution of the kinetic process through the concentrations of the chemical species. With this purpose, it is convenient to define the *reaction rate*  $v(t)$  as the time derivative of the concentration referred to the

extent of reaction  $c(t)$ . This quantity might be defined also through the variation of the concentration of one species  $\alpha$ , accordingly to eq. (20):

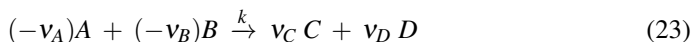
$$v(t) := \frac{dc(t)}{dt} = \frac{1}{v_\alpha} \frac{d[\alpha]_t}{dt} \quad (21)$$

We can assume that the reaction rate, in fixed thermodynamic conditions, depends only on instant concentrations of reagents and products:  $v(t) = f([A]_t, [B]_t, [C]_t, [D]_t)$ . The *kinetic law*  $f$  is characterized by the reaction under consideration and its determination is purely phenomenological. Taking into account both eq. (20) and eq. (21), we can write  $\dot{c}(t) = f([A]_0 + v_A c(t), \dots, [D]_0 + v_D c(t)) = F(c(t))$  that is an ordinary differential equation of first order, with initial condition  $c(0) = 0$ . The knowledge of the kinetic laws for a system of chemical reactions is necessary to provide information about the course of the reactions. In this mesoscopic description there are no general methods to determine such functions, that could be deduced experimentally or through a molecular description, but this is beyond the purpose of the paper.

In our mesoscopic description, we will consider irreversible reactions that proceed until at least one of the reagents vanishes, since it has been empirically observed that for this kind of reactions the kinetic laws can assume simpler forms. Sometimes, but not necessary, the reaction rate might be directly proportional to reagents concentrations powers

$$v(t) = f([A]_t, [B]_t, [C]_t, [D]_t) = k[A]^{m_A} [B]^{m_B} \quad (22)$$

with  $m_A$  and  $m_B$  the *orders of reaction* respectively of reagent  $A$  and  $B$ , whereas their sum is called *global order of reaction*. The coefficient  $k$  is called *reaction rate constant* and it depends on the thermodynamic conditions of the system. Usually it is written as follows:



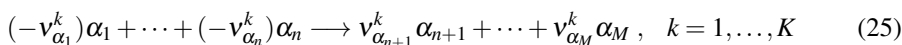
There is no relation between the orders of reaction and the stoichiometric coefficients since these are not uniquely defined, whereas the orders of reaction are fixed parameters, experimentally determined. To simplify our discussion, we will consider unitary the order of reaction of every reagent involved in our chemical system.

Consider now the chemical reaction  $A + B \rightarrow P$  to which we can associate the kinetic law  $v = k[A]_t[B]_t$ , then according to eq. (21) the related differential equations can be written as follows, being  $v_A = v_B$

$$\frac{d[A]_t}{dt} = \frac{d[B]_t}{dt} = v_B \frac{dc(t)}{dt} = -k[A]_t[B]_t \quad \frac{d[P]_t}{dt} = v_P \frac{dc(t)}{dt} = k[A]_t[B]_t \quad (24)$$

**3.2. Many reactions model.** Considering now the situation of a system with more than one chemical reaction depending one to each other, we want to describe the corresponding system of ordinary differential equations obtained from the kinetic law of each reaction.

A system with  $K$  chemical reactions is given, involving  $M$  reactive species that will be indicated with  $\alpha_m$  for  $m = 1, 2, \dots, M$  and each species has its stoichiometric coefficient  $v_{\alpha_m}^k$  for  $k = 1, 2, \dots, K$  related to the  $k$ -th reaction.



where if the  $m$ -th chemical species does not react in the  $k$ -th reaction then its coefficient  $v_{\alpha_m}^k$  is vanishing. The convention according to which the reagents coefficients are negative and the products ones are positive still holds.

Through the definition of the concentration  $c_k(t)$  according to eq. (19), we can obtain a time dependent function for the concentrations of every chemical species involved in the system  $[\alpha_m]_t = [\alpha_m]_0 + \sum_{k=1}^K v_{\alpha_m}^k c_k(t)$  where  $m = 1, 2, \dots, M$  and the initial concentrations are supposed to be known.

Deriving  $[\alpha_m]_t$  with respect to the time, it can be noticed that each reaction contributes independently of the others to determine the rate of change of the concentration of the  $m$ -th chemical species

$$\frac{d[\alpha_m]_t}{dt} = \sum_{k=1}^K \left( \frac{d[\alpha_m]_t}{dt} \right)_k \quad (26)$$

where  $\left( \frac{d[\alpha_m]_t}{dt} \right)_k = v_{\alpha_m}^k v_k(t)$ , according to equations (21).

#### 4. The differential equations of Photosynthesis

Before proceeding in the description of the differential system for the photosynthesis, it is necessary to introduce some notions that will be useful for future considerations.

**4.1. Einstein model on the radiation-matter interaction (Moro 2007).** Consider a system of  $N$  isolated molecules that admit only two energy levels  $E_0$  (fundamental state) and  $E_1$  (excited state) and that interact with each other through an electromagnetic radiation of frequency  $\nu$  and energy density  $\rho(\nu)$ . Three processes might occur: the *absorption*, *spontaneous emission* or *stimulated emission* of a photon with energy  $h\nu$  ( $h$  is the Planck constant) that implies the transition of one molecules through the two energy levels available.

If *spontaneous emission* occurs it means that one molecules passes from the excited state  $N^*$  to its fundamental state  $N$  with emission of a photon, independently from any radiation. The reaction is:  $N^* \rightarrow N + 1 \text{ photon}$ . Since the conservation principle holds, here in the form  $N(t) + N^*(t) = \text{cost}$ , applying the chemical kinetic to the previous reaction, we obtain the differential equation  $\frac{dN}{dt} = -\frac{dN^*}{dt} = -A_{21}N^*$  with  $A_{21}$  the reaction rate constant for spontaneous emission.

*Absorption* occurs when one molecule at its fundamental state  $N$  absorbs one photon. The reaction is:  $N + n \text{ photons} \rightarrow N^* + (n - 1) \text{ photons}$ , which is related to the differential equation  $\frac{dN}{dt} = -B_{12}N\rho(\nu)$  where  $\rho(\nu)$  represents the energy density of the electromagnetic radiation.

It might occur also the *stimulated emission* that is exactly the revers process of absorption. Its reaction is:  $N^* + (n - 1) \text{ photons} \rightarrow N + n \text{ photons}$ . The related differential equation has the form  $\frac{dN}{dt} = B_{21}N^*\rho(\nu)$ .

The sum of the contributions of these three different processes gives a differential equation that describes the Einstein model:

$$\frac{dN}{dt} = -A_{21}N^* - B_{12}N\rho(\nu) + B_{21}N^*\rho(\nu') \quad (27)$$

**4.2. Kinetic of Photosynthesis.** Applying all the considerations made so far to the chemical reactions written in Section 1, we will now discuss the kinetic of the photosynthesis. To



this aim, we have to consider equations (13), (9), (16), (12), (8) and we have to associate to each of them the reaction rate constant  $k_i$  with  $i = 1, \dots, 5$ . The variation of chlorophyll concentration is regulated by Einstein model, since these molecules are involved in processes of absorption and emission of photons. It must be remarked also that a conservation law must hold in the form

$$\frac{d}{dt} ([\text{Chl}] + [\text{Chl}^*]) = 0 \quad (28)$$

This can be rewritten as  $[\text{Chl}] + [\text{Chl}^*] = 3000$ , being 3000 the average number of molecules in every photosystem, as it has been established during the large amount of experiments that have been led in the 60s. Adapting eq. (27) to the chlorophyll concentration we obtain the following differential equation

$$\frac{d[\text{Chl}]}{dt} = -A_{21}[\text{Chl}^*] - B_{12}[\text{Chl}]\rho(v) + B_{21}[\text{Chl}^*]\rho(v') \quad (29)$$

where if we replace the generic term "Chl" with [P680] or [P700] and  $v, v'$  with  $v_1, v'_1$  or  $v_2, v'_2$  then it describes the variation of chlorophyll molecules in Photosystem II or I respectively. Since the two formulations are totally equivalent, we keep studying the general form (29) for which we will find a solution, suitable for both the photosystems PSII or PSI. By exploiting the conservation law, this differential equation can be rewritten as a function of only [Chl] as follows

$$\frac{d[\text{Chl}]}{dt} = \underbrace{3000(-A_{21} + B_{21}\rho(v'))}_{c_1} - [\text{Chl}] \underbrace{(-A_{21} + B_{21}\rho(v') + B_{12}\rho(v))}_{c_2} \quad (30)$$

with initial condition  $[\text{Chl}]_0 = 3000$  since initially all the chlorophyll molecules are at their fundamental state. Solving the Cauchy problem thus obtained, we find the following expression for the concentration of Chl

$$[\text{Chl}]_t = \frac{c_1}{c_2} - e^{-c_2 t} \left( \frac{c_1}{c_2} - 3000 \right) \quad (31)$$

with the constants  $c_1$  and  $c_2$  that depend on the photosystem under consideration. Through this expression for [Chl], we can easily deduce the concentration of excited chlorophyll molecules [P680\*] and [P700\*], in agreement with the conservation law seen above.

$$[\text{Chl}^*]_t = 3000 - [\text{Chl}]_t = \left( 3000 - \frac{c_1}{c_2} \right) (1 - e^{-c_2 t}) \quad (32)$$

To have a clearer idea of the course of these concentrations it is necessary to establish a sign for the two coefficients  $c_1$  and  $c_2$ . We can immediately observe that the concentration of a chemical species, in general, must be positive and, in this particular case, less or equal than 3000. If we suppose  $c_2 = 0$  then the differential equation (30) becomes  $[\text{Chl}] = c_1$  whose solution is  $[\text{Chl}]_t = c_1 t + 3000$  but taking the limit for  $t \rightarrow \infty$  we have that  $[\text{Chl}] \rightarrow \pm\infty$  and this is not acceptable. Whereas, if  $c_1 = 0$ , then [Chl] remains constant with respect to time but this means that there is no excitation of any molecule and this is not our case. If we suppose, instead, that  $c_1 = 3000c_2$  then from eq. (31) we deduce that  $[\text{Chl}]_t = 3000$  for every  $t$  but we have already seen that this can not happen, since it would mean that no excitation of molecules occurs. When  $c_2 < 0$  then, taking the limit for  $t \rightarrow \infty$  of eq. (31), it results that  $[\text{Chl}]_t \rightarrow \pm\infty$  and, again, this case has to be excluded. The only situation that remains possible is that  $c_2 > 0$ : in this case the limit for  $t \rightarrow \infty$  of the concentration  $[\text{Chl}]_t$

is  $c_1/c_2$  that is a finite quantity. We can deduce that  $c_1$  must be positive too, since  $[\text{Chl}]_t$  must be greater than 0 for every  $t$ .

For the remaining reactions ((16), (12), (8)) we can directly apply the chemical kinetic theory presented in Section 2. In order to do this we have to define the kinetic laws that, supposing unitary the orders of reaction of every chemical species and according to (22), can be written as below, where  $v_1$  and  $v_2$  are not considered since they concern reactions (9) and (13) which have been treated above by the means of Einstein model.

$$\begin{aligned}v_3(t) &= f_3 = k_3[\text{H}_2\text{O}][\text{P680}^*] \\v_4(t) &= f_4 = k_4[\text{NADP}^+][\text{H}^+][\text{e}^-][\text{ADP}][\text{P}_i][\text{P700}^*] \\v_5(t) &= f_5 = k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}]\end{aligned}\quad (33)$$

Hence, from eq. (26), it can be obtained a system of differential equations with 11 unknown concentrations ([P680], [P680\*], [P700] and [P700\*] are already known)

$$\frac{d[\text{H}_2\text{O}]}{dt} = -2k_3[\text{H}_2\text{O}][\text{P680}^*] - 5k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}] \quad (34)$$

$$\frac{d[\text{O}_2]}{dt} = k_3[\text{H}_2\text{O}][\text{P680}^*] \quad (35)$$

$$\frac{d[\text{e}^-]}{dt} = 4k_3[\text{H}_2\text{O}][\text{P680}^*] - 4k_4[\text{NADP}^+][\text{H}^+][\text{e}^-][\text{ADP}][\text{P}_i][\text{P700}^*] \quad (36)$$

$$\frac{d[\text{ADP}]}{dt} = -3k_4[\text{NADP}^+][\text{H}^+][\text{e}^-][\text{ADP}][\text{P}_i][\text{P700}^*] + 9k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}] \quad (37)$$

$$\frac{d[\text{P}_i]}{dt} = -3k_4[\text{NADP}^+][\text{H}^+][\text{e}^-][\text{ADP}][\text{P}_i][\text{P700}^*] + 8k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}] \quad (38)$$

$$\frac{d[\text{ATP}]}{dt} = 3k_4[\text{NADP}^+][\text{H}^+][\text{e}^-][\text{ADP}][\text{P}_i][\text{P700}^*] - 9k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}] \quad (39)$$

$$\frac{d[\text{NADP}^+]}{dt} = -2k_4[\text{NADP}^+][\text{H}^+][\text{e}^-][\text{ADP}][\text{P}_i][\text{P700}^*] + 6k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}] \quad (40)$$

$$\frac{d[\text{NADPH}]}{dt} = 2k_4[\text{NADP}^+][\text{H}^+][\text{e}^-][\text{ADP}][\text{P}_i][\text{P700}^*] - 6k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}] \quad (41)$$

$$\begin{aligned}\frac{d[\text{H}^+]}{dt} &= 4k_3[\text{H}_2\text{O}][\text{P680}^*] - 2k_4[\text{NADP}^+][\text{H}^+][\text{e}^-][\text{ADP}][\text{P}_i][\text{P700}^*] \\ &\quad + 3k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}]\end{aligned}\quad (42)$$

$$\frac{d[\text{CO}_2]}{dt} = -3k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}] \quad (43)$$

$$\frac{d[\text{G3P}]}{dt} = 3k_5[\text{CO}_2][\text{NADPH}][\text{ATP}][\text{H}_2\text{O}] \quad (44)$$

where the initial concentrations at  $t = 0$ , corresponding to the instant of time in which the first photon absorption occurs, are

$$\begin{aligned}[\text{H}_2\text{O}]_0 &= h_0; [\text{CO}_2]_0 = b_0; [\text{ADP}]_0 = adp_0; [\text{P}_i]_0 = p_0; [\text{NADP}^+]_0 = nadp_0 \\ [\text{O}_2]_0 &= [\text{e}^-]_0 = [\text{H}^+]_0 = [\text{NADPH}]_0 = [\text{ATP}]_0 = [\text{G3P}]_0 = 0\end{aligned}\quad (45)$$

Such a choice of initial data is reasonable since it is necessary to provide the system with a certain amount of water and carbon dioxide so that the entire process occurs, whereas substances as ADP,  $\text{P}_i$  and  $\text{NADP}^+$  can be already found inside the system so they must have

a positive initial concentration. All the remaining substances are products of the process and for them an initial positive concentration is not required, thus we can assume it to be zero.

Denote with  $X : \mathbb{R}^{15} \rightarrow \mathbb{R}^{15}$  the vector field to which our dynamics is associated  $\dot{x}(t) = X(x)$ . This ode system corresponds to the equations (34)-(44) and to the further four equations for [P680], [P680\*], [P700] and [P700\*] which are summarized jointly by equation (29) on the basis also of the conservation law (28). Four of these concentrations are already known from (31) and (32), whereas an explicit expression for the remaining eleven concentrations is still to be found. In order to do this, we can find some first integrals which will reduce the dimension of the system.

By equations (43) and (44) it is clear that  $\frac{d[CO_2]}{dt} + \frac{d[G3P]}{dt} = 0$  from which the relation

$$[CO_2] + [G3P] = [CO_2]_0 + [G3P]_0 = b_0 \tag{46}$$

Other similar relations hold among equations (40)-(41) and (37)-(39)

$$[NAPD^+] + [NADPH] = nadp_0 \quad [ADP] + [ATP] = adp_0 \tag{47}$$

By these first integrals we can avoid studying ADP, NADP<sup>+</sup> and G3P concentrations since they can be more easily deduced from [ATP], [NADPH] and [CO<sub>2</sub>].

We can now study the concentration of every remaining chemical species.

ELECTRON CONCENTRATION: from the chemical reactions describing the photosynthetic process, it can be noticed that electrons are involved in a mechanism of production and consumption, respectively by reactions (16) and (12). Therefore we can assume vanishing the component  $X_{[e^-]}([H_2O], \dots)$  of the vector field  $X$  associated to the electrons concentration. This stationary condition for  $[e^-]$  proposes an expression for the unknown  $[e^-]$  belonging to the surface, which is a local attractor for the solutions, obtained as a graph of the following function  $g$ :

$$[e^-] = g([H_2O], \dots) = \frac{k_3 [H_2O] [P680^*]}{k_4 [NADP^+] [H^+] [ADP] [P_i] [P700^*]} \tag{48}$$

It can be proved that this is a local attractor by computing its Taylor series of first order  $X_{[e^-]} = -2k_4 [NADP^+] [H^+] [ADP] [P_i] [P700^*] ([e^-] - g) + O_2$ . Since  $k_4 > 0$  and every concentration is a positive quantity, the coefficient is negative. Therefore if the electron concentration  $[e^-]$  is above the surface  $g$  then  $\frac{d[e^-]}{dt} < 0$ , otherwise if  $[e^-] < g$  then  $\frac{d[e^-]}{dt} > 0$ . Hence the electron concentration converges towards the surface  $g$ , which must be a local attractor.

In the approximation  $X_{[e^-]} = 0$  the differential equations associated to  $[H^+]$ ,  $[ATP]$  and  $[NADPH]$  become:

$$\begin{aligned} \frac{d[H^+]}{dt} &= 2k_3 [H_2O] [P680^*] + 3k_5 [CO_2] [NADPH] [ATP] [H_2O] \\ \frac{d[ATP]}{dt} &= 3k_3 [H_2O] [P680^*] - 9k_5 [CO_2] [NADPH] [ATP] [H_2O] \\ \frac{d[NAPDH]}{dt} &= 2k_3 [H_2O] [P680^*] - 6k_5 [CO_2] [NADPH] [ATP] [H_2O] \end{aligned} \tag{49}$$

from which the first integral

$$2 \frac{d[ATP]}{dt} - 3 \frac{d[NAPDH]}{dt} = 0 \tag{50}$$

NADPH CONCENTRATION: with the same arguments as above, we can obtain an expression for [NADPH] by assuming vanishing its component of the vector field  $X$ . Hence [NADPH] belongs to the local attractive surface obtained as the graph of the following function  $m$ :

$$[\text{NADPH}] = m([\text{H}_2\text{O}] \dots) = \frac{k_3 [\text{H}_2\text{O}] [\text{P680}^*]}{3k_5 [\text{CO}_2] [\text{ATP}] [\text{H}_2\text{O}]} \quad (51)$$

According to eq. (50)

$$[\text{ATP}] = \frac{3}{2} [\text{NADPH}] = \sqrt{\frac{k_3 [\text{P680}^*]}{2k_5 [\text{CO}_2]}} \quad (52)$$

By equations in (47) then  $[\text{ADP}] = adp_0 - [\text{ATP}]$  and  $[\text{NADP}^+] = nadp_0 - [\text{NADPH}]$ .

The approximation  $X_{[\text{NADPH}]} = 0$  allows to rewrite some differential equations as follows:

$$\frac{d[\text{H}^+]}{dt} = 3k_3 [\text{H}_2\text{O}] [\text{P680}^*] \quad \frac{d[\text{H}_2\text{O}]}{dt} = -\frac{11}{3} k_3 [\text{H}_2\text{O}] [\text{P680}^*] \quad (53)$$

$$\frac{d[\text{P}_i]}{dt} = -\frac{1}{3} k_3 [\text{H}_2\text{O}] [\text{P680}^*] \quad \frac{d[\text{CO}_2]}{dt} = -k_3 [\text{H}_2\text{O}] [\text{P680}^*] \quad (54)$$

From these new expressions, a lot of new first integrals can be easily identified which let now to study explicitly  $[\text{H}^+]$ ,  $[\text{P}_i]$ ,  $[\text{CO}_2]$  and  $[\text{O}_2]$ :

$$\begin{aligned} \frac{11}{3} \frac{d[\text{H}^+]}{dt} + 3 \frac{d[\text{H}_2\text{O}]}{dt} &= 0 & -11 \frac{d[\text{P}_i]}{dt} + \frac{d[\text{H}_2\text{O}]}{dt} &= 0 \\ -\frac{11}{3} \frac{d[\text{CO}_2]}{dt} + \frac{d[\text{H}_2\text{O}]}{dt} &= 0 & \frac{d[\text{O}_2]}{dt} + \frac{d[\text{CO}_2]}{dt} &= 0 \end{aligned} \quad (55)$$

WATER CONCENTRATION: by the differential equation related to water in eq. (53) we have to solve the following Cauchy problem, after denoting with  $h(t)$  the water concentration:

$$\begin{cases} \dot{h}(t) = -\frac{11}{3} k_3 h(t) [\text{P680}^*] \\ h(0) = h_0 \end{cases} \quad (56)$$

which solution is  $h(t) = h_0 e^{\alpha(t + \frac{1}{c_2} e^{-c_2 t} - \frac{1}{c_2})}$ , being  $\alpha = -\frac{11}{3} k_3 (3000 - \frac{c_1}{c_2})$ . It can be noticed that taking the limit for  $t \rightarrow +\infty$  then  $h(t) \rightarrow 0$  as the constant  $\alpha$  defined above is negative. With this explicit solution for water concentration, the concentrations of ions  $\text{H}^+$ ,  $\text{P}_i$  and  $\text{CO}_2$  can now be deduced by relations in (55):

$$[\text{H}^+] = \frac{9}{11} (h_0 - [\text{H}_2\text{O}]) \quad (57)$$

$$[\text{P}_i] = p_0 - \frac{1}{11} (h_0 - [\text{H}_2\text{O}]) \quad (58)$$

$$[\text{CO}_2] = b_0 - \frac{3}{11} (h_0 - [\text{H}_2\text{O}]) \quad (59)$$

By combining eq.(59) with the first integrals related to  $\text{O}_2$  and G3P, we also have

$$[\text{O}_2] = [\text{G3P}] = \frac{3}{11} (h_0 - [\text{H}_2\text{O}]) \quad (60)$$

**4.3. Discussion.** We will now discuss the results obtained so far.

**4.3.1. Chlorophyll concentration at the fundamental or excited state.** Before photon absorption occurs, all the chlorophyll molecules in both the photosystems are at the fundamental state, whereas during light exposition these molecules begin to change their state into the excited one. Since during the photosynthetic process, emission phenomena occur, some excited molecules return to their initial state but since this happens with a very low rate, the number of molecules at the fundamental state has to be almost vanishing. All of these facts are summarized by the two equations (31) and (32) that supply an idea for the number of excited and not excited molecules that will be found in the system at the end of the entire process:  $\lim_{t \rightarrow +\infty} [\text{Chl}^*] = 3000 - \frac{c_1}{c_2} \simeq 3000$ ,  $\lim_{t \rightarrow +\infty} [\text{Chl}] = \frac{c_1}{c_2} \simeq 0$ .

**4.3.2. Water  $H_2O$ .** We have provided the system with the minimum water quantity,  $h_0$ , necessary to conclude the process, hence it should be completely spent by the process. One would expect that water concentration will be vanishing and in fact  $\lim_{t \rightarrow +\infty} h(t) = 0$ , where  $h(t)$  is the explicit solution for water concentration, clearly always positive as it is an exponential function.

**4.3.3. Oxygen  $O_2$ .** Oxygen is one of the final products of photosynthesis which is released by the splitting of water in the first step of the process. By taking the limit for  $t \rightarrow +\infty$  of eq. (60) we can deduce that, supplying an initial water concentration  $h_0$ , only 3/11 of it will be transformed into oxygen whereas the remaining water concentration will be available for the other reactions. Equation (60) is consistent with the fact that we are dealing with chemical concentrations, in fact it must hold that  $[\text{CO}_2]_t \geq 0$  for every  $t > 0$  and, as the water concentration is decreasing in time, this condition is always verified.

**4.3.4. Ions  $H^+$ .** Ions are released during the splitting of water but then they are immediately consumed from reaction (12). During the same reaction half of them is regenerated (half of the quantity of ions that react in (12) is returned), but ions are also released by Calvin Cycle. Therefore this concentration, that has a vanishing initial value, is increasing, as proved by eq. (57) whose limit for  $t \rightarrow +\infty$  means that 9/11 of initial water concentration is used for the production of ions. The consistency of equation (57) can be justified with the same arguments of oxygen concentration.

**4.3.5. Electrons.** Electrons are produced after the splitting of water, but then they are immediately consumed from reaction (12) to convert  $\text{NADP}^+$  into  $\text{NADPH}$  and to combine ADP with  $P_i$  into ATP. Therefore their concentration must remain almost vanishing into the system, and in fact  $\lim_{t \rightarrow +\infty} [e^-] = 0$ .

**4.3.6. Phosphate  $P_i$ .** In reaction (12) 3 phosphate molecules react with 3ADP and other substances, releasing 3ATP. The Calvin Cycle will then use 9ATP and one molecule of phosphate to create the 3-carbon sugar G3P, releasing eight  $P_i$  molecules. This suggests two facts: the phosphate concentration must be decreasing in time, and the relation  $3v_5 = v_4$  must hold as the Calvin Cycle uses three times the ATP produced by reaction (12). The decreasing of  $[P_i]$  is confirmed by equation (58) whose derivatives is  $\frac{1}{11} \frac{d[\text{H}_2\text{O}]}{dt} < 0$ . Equation (58) shows off also that the phosphate concentration inside the system at the end of the photosynthetic process will be  $p_0 - \frac{1}{11}h_0$ . This suggests that the initial concentration of

phosphate needed by the systems is, at least,  $\frac{1}{11}h_0$  otherwise the process can not proceed. To check the equality  $3v_5 = v_4$  the definition of the rate reaction given in eq. (33) and equations (48) and (51) must be reminded. By simple substitutions, it results  $k_3 = k_3$  which is always verified. Thus the relation between the two rate reactions is valid.

**4.3.7. Carbon dioxide  $CO_2$ .** Carbon dioxide is one on the fuel-substances of the photosynthetic process and it must be provided the system with a certain initial amount  $b_0$ . Since it is not produced by any reaction but it is only consumed, its concentration must be decreasing in time. This is confirmed by equation (59), by which  $\lim_{t \rightarrow +\infty} [CO_2] = b_0 - h_0 3/11$ . As before, the condition of consistency must hold. Here:  $b_0 \geq h_0 3/11$ , otherwise the process does not trigger.

**4.3.8. 3-carbon sugar G3P.** With oxygen, this is one of the final products of photosynthesis given by the Calvin cycle as a consequence of the reaction of  $CO_2$  with other substances as NADPH, ATP and  $H_2O$ . Therefore its concentration will increase and from eq. (60) we can deduce that  $3/11$  of initial water concentration convert into sugar.

**4.3.9. NADPH.** This chemical species is produced by reaction (12) but then it is totally consumed by the dark reaction to release sugar and  $NADPH^+$ . Since these two reactions occur in a small time interval, NADPH concentration can be considered overall vanishing, hence it should be  $[NADPH] \simeq 0$ . The equation (52) allows to rewrite the relation (51) as  $[NADPH] = \sqrt{\frac{2k_3}{9k_5} \frac{[P680^*]}{[CO_2]}}$  and, by all the considerations made so far about  $[Chl^*]$  and  $[CO_2]$ ,  $[NADPH] \rightarrow \sqrt{\frac{1000}{3} \frac{k_3}{k_5} \frac{1}{2b_0 - h_0}}$  that has to be vanishing. This is possible in two cases:  $k_5 \gg k_3$  or  $2b_0 \gg h_0$ . Since we want to supply the minimum carbon dioxide quantity  $b_0$  necessary to end the process, we can assume that  $b_0 \simeq \frac{3}{11}h_0$ , hence necessarily  $k_5 \gg k_3$  (further considerations about the reaction rate constants are difficult to find through this mesoscopic analysis of the process).

**4.3.10.  $NADP^+$ .** On the contrary of NADPH,  $NADP^+$  is consumed by reaction (12) but then released in the same quantity by Calvin Cycle. Thus its concentration remains overall constant and equal to its initial value  $nadp_0$ , as confirmed by the equation  $[NADP^+] = nadp_0 - [NADPH] \simeq 0$ .

**4.3.11. ATP.** This substance is released by reaction (12) and then consumed by Calvin Cycle to release sugar, ADP and phosphate. The behavior of ATP concentration is equivalent to the NADPH one, hence it has to be vanishing. Since relation (50) holds, then all the considerations above for NADPH are suitable for ATP too.

**4.3.12. ADP.** As  $NADP^+$ , this substance is used by reaction (12) and produced by Calvin Cycle. Since the equation  $[ADP] = adp_0 - [ATP]$  holds and  $[ATP]$  is vanishing, then  $[ADP]$  remains overall constant.

Finally, we have seen that the set of vanishing points for the vector field  $X$  is not a topologically discrete set, but a continuous and asymptotically attractive one, obtained by the intersection of the attractive surfaces found. Further investigations on the above setting, would allow to translate the given explanation into a more meaningful dynamic description, with a natural stationary input-output flow of reaction matter and energy.

## Acknowledgments

We are deeply indebted to Giorgio J. Moro for many enlightening discussions on the subject.

## References

- Baltimore, D., Berk, A., Darnell, J., Lodish, H., Matsudaira, P., and Zipursky, S. L. (2000). *Molecular Cell Biology*, 4th edition. W. H. Freeman.
- Cardin, F. and Moro, J. G. (2007). *Chimica and Matematica*. URL: <http://www.math.unipd.it/~cardin/BOOK-Chimica-Matematica.pdf>.
- Duysens, L. N. M., Amesz, J., and Kamp, B. M. (1961). "Two Photochemical Systems in Photosynthesis". *Nature* **190**(4775), 510–511. DOI: [10.1038/190510a0](https://doi.org/10.1038/190510a0).
- Emerson, R. (1957). "Dependence of yield of photosynthesis in long wave red on wavelength and intensity of supplementary light". *Science* **125**(3251), 746. DOI: [10.1126/science.125.3251.746](https://doi.org/10.1126/science.125.3251.746).
- Emerson, R. (1958). "Yield of photosynthesis from simultaneous illumination with pairs of wavelengths". *Science* **127**(3305), 1059–1060. DOI: [10.1126/science.127.3305.1058](https://doi.org/10.1126/science.127.3305.1058).
- Emerson, R. and Rabinowitch, E. (1960). "Red Drop and Role of Auxiliary Pigments in Photosynthesis". *Plant Physiology* **35**(4), 477–485. DOI: [10.1104/pp.35.4.477](https://doi.org/10.1104/pp.35.4.477).
- Fotosintesi clorofilliana* (2018). Enciclopedia Treccani. URL: [www.treccani.it/enciclopedia/fotosintesi-clorofilliana](http://www.treccani.it/enciclopedia/fotosintesi-clorofilliana).
- Govindjee (1975). *Bioenergetics of photosynthesis*. Academic Press.
- Govindjee, R., Thomas, J. B., and Rabinowitch, E. (1960a). "'Second Emerson Effect' in the Hill Reaction of Chlorella Cells with Quinone as Oxidant". *Science* **132**(3424), 421. DOI: [10.1126/science.132.3424.421](https://doi.org/10.1126/science.132.3424.421).
- Govindjee and Govindjee, R. (2000). *Photosynthesis and the "Z"-scheme*. URL: <http://www.life.illinois.edu/govindjee/textzsch.htm>.
- Govindjee, Ichimura, S., Cederstrand, C., and Rabinowitch, E. (1960b). "Effect of combining far-red light with shorter wave light on the excitation of fluorescence in Chlorella". *Archives of Biochemistry and Biophysics* **89**(2), 322–323. DOI: [10.1016/0003-9861\(60\)90063-1](https://doi.org/10.1016/0003-9861(60)90063-1).
- Govindjee and Krogmann, D. (2004). "Discoveries in Oxygenic Photosynthesis (1727–2003): A Perspective". *Photosynthesis Research* **80**(1-3), 15–57. DOI: [10.1023/B:PRES.0000030443.63979.e6](https://doi.org/10.1023/B:PRES.0000030443.63979.e6).
- Govindjee and Rabinowitch, E. (1969). *Photosynthesis*. Wiley.
- Govindjee, Shevela, D., and Björn, L. O. (2017). "Evolution of the Z-scheme of photosynthesis: a perspective". *Photosynthesis Research* **133**(1-3), 5–15. DOI: [10.1007/s11120-016-0333-z](https://doi.org/10.1007/s11120-016-0333-z).
- Hallen, D. and Rundberg, R. (2000). *Mathematical modelling of natural and artificial photosynthesis*. URL: <http://www.math.chalmers.se/Math/Grundutb/CTH/tma075/0405/ModellingPhotosynthesis.pdf>.
- Hill, R. and Bendall, F. (1960). "Function of the Two Cytochrome Components in Chloroplasts: A Working Hypothesis". *Nature* **186**(4719), 136–137. DOI: [10.1038/186136a0](https://doi.org/10.1038/186136a0).
- Hiroshi, T., Duysens, L. N. M., and Sweers, H. (1963). *Studies on Microalgae and Photosynthetic Bacteria: A Collection of Papers Dedicated to Hiroshi Tamiya on the Occasion of His 60th Birthday*. Japanese Society of Plant Physiologists, University of Tokyo Press.
- Kamen, M. D. (1963). *Primary Processes in Photosynthesis*. Academic Press. DOI: [10.1016/C2013-0-12206-4](https://doi.org/10.1016/C2013-0-12206-4).
- Kok, B. (1959). "Light Induced Absorption Changes in Photosynthetic Organisms. II. A Split-beam Difference Spectrophotometer". *Plant Physiology* **34**(3), 184–192. DOI: [10.1104/pp.34.3.184](https://doi.org/10.1104/pp.34.3.184).

- Moro, J. G. (2007). *Modello di Einstein*. URL: <http://www.chimica.unipd.it/giorgio.moro/pubblica/CII/Cap4.pdf>.
- Nelson, D. L. and Cox, M. M. (2014). *I principi di biochimica di Lehninger Sesta edizione*. Zanichelli.
- Rubin, A. and Ritznichenko, G. (2014). *Mathematical Biophysics*. Springer US. DOI: [10.1007/978-1-4614-8702-9](https://doi.org/10.1007/978-1-4614-8702-9).

---

<sup>a</sup> Università degli Studi di Padova  
Dipartimento di Matematica "Tullio Levi-Civita"  
Via Trieste 63, 35121 Padova, Italy

\* To whom correspondence should be addressed | email: [cardin@math.unipd.it](mailto:cardin@math.unipd.it)

Paper contributed to the workshop entitled "Mathematical modeling of self-organizations in medicine, biology and ecology: from micro to macro", which was held at Giardini Naxos, Messina, Italy (18–21 September 2017)  
under the patronage of the *Accademia Peloritana dei Pericolanti*

Manuscript received 17 February 2018; published online 30 November 2018



© 2018 by the author(s); licensee *Accademia Peloritana dei Pericolanti* (Messina, Italy). This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/) (<https://creativecommons.org/licenses/by/4.0/>).