

Some properties of Calvin's model of spontaneous chiral amplification

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The kinetic scheme for spontaneous chiral amplification, put forward by Calvin, is examined and some of its general properties are established. Analytical solutions of Calvin's model are found in two important limiting cases, namely, when the system is open and the concentration of the substrate is constant, and when the system is closed.

In his seminal book on chemical evolution and the origin of life Melvin Calvin¹ also considered the possible mechanism for the formation of chiral (optically active) biomolecules from either achiral or racemic precursors. For this purpose Calvin proposed a simple kinetic scheme (see pp. 148-152 in ref. 1), which is explained in due detail in the subsequent section. In the meantime a variety of other kinetic models for spontaneous chiral amplification was elaborated²⁻¹⁰ but a pertinent analysis of the Calvin model was never undertaken. The aim of the present paper is to fill this gap.

Examination of the possible mechanisms by which a physico-chemical system can spontaneously evolve from a symmetric/racemic initial state into a monochiral terminal state was for a long time considered as an intriguing problem, connected with the elucidation of the origin of life, but with little or no relevance for "real-life" chemistry. Recent experimental achievements¹¹⁻¹⁶ have completely changed this situation. Especially important are the results reported by Dilip Kondepudi^{12,13,16} who demonstrated that an almost complete chiral amplification can be obtained under relatively easy and fully controllable laboratory conditions.

Bearing in mind that spontaneous chiral amplification is now within the grasp of experimental chemists, efforts to understand the underlying kinetics is a timely task. Spontaneous chiral amplification belongs among the so-called¹⁷ "chemical reactions with exotic behaviour", (which embrace also concentration oscillations, multistability and chemical chaos), whose theory is nowadays in great expansion¹⁸.

The Calvin model

The model proposed by Calvin assumes that in the reacting system the reactant is an enantiomeric pair A_L and A_D , between which a very rapid (instantaneous) racemization takes place:



Consequently, it can be assumed that at every moment the concentrations of A_L and A_D are equal, and are equal to the half of c_A , the total concentration of the species A.

Now, A_L is transformed into a chiral molecule L by mean of a relatively slow first order process (whose rate constant is k) and, simultaneously, by means of a much faster autocatalytic reaction (whose rate constants is k_{cat}):



In the precisely same way (with the precisely same rate constants) A_D reacts to yield a chiral species D, which is just the enantiomer of L:



Calvin's argument¹ was the following. In the initial moment only the compounds A_L and A_D are present in the system; because of the equilibration (α), the amounts of the species A_L and A_D are always equal. If by chance (or by some other reason) a molecule L is formed in the reaction (β'), then the autocatalytic reaction (γ') can start and the amount of L will rapidly increase in the system. At the same time the production of the other enantiomer, D, will have to wait until some D molecules are formed by the (slow) process (β''). Thus, after some time the system will become chiral

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with either partial or complete excess of the L-species.

If, on the other hand, the first molecule formed in the system were D, then the process (γ'') would be activated, resulting in a partial or complete excess of the D-enantiomer.

In this paper we perform a mathematical analysis of the Calvin model and establish its basic features as far as spontaneous chiral amplification is concerned.

Some general properties of the Calvin model

Calvin's original formulation pertains to chemical reactions occurring in a closed system¹. In this section, however, we assume that the process occurs in a continuously-fed stirred tank reactor (c.s.t.r.). A solution containing A_L and A_D (in equilibrium) is added to the tank and an equal volume of the reaction mixture, containing A_L and A_D (in equilibrium) as well as L and D, is simultaneously released from the tank. Then the time-evolution of the concentrations c_L , c_D and c_A (inside the c.s.t.r.) is described by the following system of differential equations:

$$dc_L/dt = \frac{1}{2} kc_A + \frac{1}{2} k_{cat} c_A c_L - k_{out} c_L \quad \dots (1)$$

$$dc_D/dt = \frac{1}{2} kc_A + \frac{1}{2} k_{cat} c_A c_D - k_{out} c_D \quad \dots (2)$$

$$dc_A/dt = k_{in} - kc_A - \frac{1}{2} k_{cat} (c_L + c_D) c_A \quad \dots (3)$$

The initial conditions are $c_A = c_{A0}$, $c_L = c_{L0}$ and $c_D = c_{D0}$ for $t=0$. Without loss of generality, throughout this paper it will be assumed that $c_{L0} \geq c_{D0}$.

Calvin's closed-system model is also described by the above equations when it is set $k_{in} = k_{out} = 0$.

The most important features of Calvin's model can be deduced without actually solving the differential equations (1)-(3). Subtracting (2) from (1) and introducing an auxiliary function $G = G(t)$

$$G = G(t) = \frac{1}{2} k_{cat} c_A - k_{out} \quad \dots (4)$$

one obtains

$$d(c_L - c_D)/dt = G(c_L - c_D)$$

from which it immediately follows

$$c_L - c_D = (c_{L0} - c_{D0}) \exp \left[\int_0^t G(t) dt \right] \quad \dots (5)$$

From Eq. (5) we conclude the following:

(i) If at the initial moment the system was racemic with respect to the enantiomers L/D (i.e. $c_{L0} = c_{D0}$), then the system will always remain racemic with respect to L/D (i.e., $c_L = c_D$ for all $t > 0$).

(ii) If at the initial moment there was a slight deviation from racemity (i.e. $c_{L0} > c_{D0}$), then this deviation will increase with time provided $G(t) > 0$, or will completely vanish if $G(t) < 0$.

Whereas Eq. (5) shows the time-evolution of the absolute value of the non-racemity of the system, a better information about what is really going on is gained from the so-called "enantiomeric excess" or "chiral polarization". This quantity is defined as^{11,19,20}

$$\eta = (c_L - c_D)/(c_L + c_D) \quad \dots (6)$$

and it measures non-racemity relative to the total amount of the enantiomers produced: its value is zero for racemic, and unity for monochiral states of the system considered. In systems in which chemical reactions take place, η is time-dependent. Its derivative with respect to t satisfies

$$d\eta/dt = 2(c_D dc_L/dt - c_L dc_D/dt)(c_L + c_D)^{-2} \quad \dots (7)$$

Substitution of (1) and (2) back into (7) yields

$$d\eta/dt = -2kc_A(c_L - c_D)(c_L + c_D)^{-2}$$

and by taking into account Eq. (5)

$$d\eta/dt = -2kc_A(c_{L0} - c_{D0}) \exp \left[\int_0^t G(t) dt \right] (c_L + c_D)^{-2} \quad \dots (8)$$

If $c_{L0} - c_{D0} > 0$, then the right-hand side of Eq. (8) is necessarily negative for all $t > 0$. Thus Eq. (8) implies a conclusion, valid for the most general version of Calvin's model:

(iii) The enantiomeric excess in the Calvin model monotonically decreases with time. Since already the initial value of η had to be close to zero, we see that the Calvin model has a quite low efficiency as far as chiral amplification is concerned.

(iv) If, exceptionally, the rate constant k is very small, then the right-hand side of Eq. (8) attains a near-zero value. Then the enantiomeric excess becomes time-independent and, as seen from Eqs (11) and (19), its value approaches unity.

A special case: Constant c_A

If the supply of the species A to the c.s.t.r. is large relative to its consumption in the reactions (β) and (γ), then it is legitimate to assume that c_A is time-independent.

If so, then the quantity G , given by Eq. (4), is a constant and Eq. (1) is rewritten as

$$\frac{1}{G} d \left(Gc_L + \frac{1}{2}kc_A \right) = \left(Gc_L + \frac{1}{2}kc_A \right) dt$$

which is straightforwardly integrated:

$$Gc_L + \frac{1}{2}kc_A = \left(Gc_{L0} + \frac{1}{2}kc_A \right) \exp(Gt)$$

i.e.

$$c_L = c_{L0} \exp(Gt) + (2G)^{-1} kc_A [\exp(Gt) - 1] \dots (9)$$

In full analogy to Eq. (9) one also has

$$c_D = c_{D0} \exp(Gt) + (2G)^{-1} kc_A [\exp(Gt) - 1] \dots (10)$$

From Eqs (9) and (10) we arrive at the following special cases of formulae (5) and (6):

$$c_L - c_D = (c_{L0} - c_{D0}) \exp(Gt)$$

$$\eta = \eta_0 \left[\eta_0 + \frac{kc_A}{G(c_{L0} - c_{D0})} (\exp(Gt) - 1) \right]^{-1} \dots (11)$$

Closed reacting system: The original Calvin model

If there is no influx into and no outflow from the c.s.t.r. (i.e. if $k_{in} = k_{out} = 0$), then we have special case of the closed Calvin system. Here $c_A + c_L + c_D = c_0$, and c_0 is time-independent. Then Eq. (3) can be written as

$$dc_A/dt = +kc_A - \frac{1}{2}k_{cat}(c_0 - c_A)c_A \dots (12)$$

A convenient way to solve Eq. (12) is to introduce an auxiliary (positive) constant λ ,

$$\lambda = k + \frac{1}{2}k_{cat}c_0 \dots (13)$$

and to seek for the function $c_A(t)$ in the form

$$c_A = C_{A0} \exp(-\lambda t) f(t); f(0) = 1. \dots (14)$$

When Eqs (13) and (14) are substituted back into (12) one arrives at

$$df/dt = \frac{1}{2}k_{cat}C_{A0} \exp(-\lambda t) f^2$$

from which $f(t)$ is readily obtained by integration:

$$f(t) = (1 - F)^{-1}$$

with $F = F(t)$ being another auxiliary function, defined as

$$F = F(t) = \frac{k_{cat}C_{A0}}{2\lambda} [1 - \exp(-\lambda t)].$$

Then

$$c_A = c_{A0} \exp(-\lambda t) (1 - F)^{-1}. \dots (15)$$

Combining Eq. (15) with (2) and (3) we find

$$c_L = [c_{L0} + (k/k_{cat})F] (1 - F)^{-1} \dots (16)$$

$$c_D = [c_{D0} + (k/k_{cat})F] (1 - F)^{-1}. \dots (17)$$

Equations (15)-(17) represent the complete solution of the original Calvin model¹ (pertaining to a closed reacting system). All properties of that model can be easily deduced from (15)-(17). For this purpose it is useful to observe that $F(t)$ is a monotonically increasing function of the variable t . Furthermore, $F(0) = 0$, $F(\infty) = k_{cat}C_{A0}/(2k + k_{cat}c_0) < 1$.

For instance, from Eqs (5) and (6) we calculate

$$c_L - c_D = (c_{L0} - c_{D0}) (1 - F)^{-1} \dots (18)$$

$$\eta = \eta_0 \left[\eta_0 + \frac{2(k/k_{cat})F}{c_{L0} - c_{D0}} \right]^{-1} \dots (19)$$

From Eqs (18) and (19) it is evident that the greatest chiral amplification in Calvin's model will be achieved when $k \rightarrow 0$. Then $F(\infty)$ is as close to unity as possible, and consequently, the right-hand side of Eq. (18), i.e. $c_L - c_D$ attains its greatest possible value. In the same time, if $k \rightarrow 0$, then η becomes time-independent and, besides, $\eta \rightarrow \infty$. This convenient limit case is just on what Calvin based the expectation of the success of his chiral amplification model¹.

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