

FACTORS DETERMINING THE DIRECTION OF THE STEREO-SELECTION PROCESS IN THE GENERALIZED FRANK MODEL

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Abstract

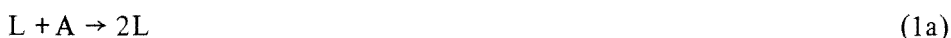
The Frank model for spontaneous chiral stereoselection of biomolecules is extended by taking into account the influence of electroweak effects on the rates of enantiomeric chemical reactions. Explicit analytical solutions of the respective differential equations are obtained, describing the behaviour of the generalized Frank model immediately after the beginning of the process, when the direction of the stereoselection is decided. The direction of the stereoselection is affected by both stochastic and deterministic factors, whose complex interrelations are examined.

1. Introduction

It is a well established fact that terrestrial organisms contain chiral (optically active) molecules and that only one series of enantiomers is present. Specifically, the biochemical processes in all known living organisms involve L- α -aminoacids and D-sugars, with an almost complete absence of their mirror-image counterparts (i.e. D- α -aminoacids and L-sugars). On the other hand, when living organisms and their products (especially enzymes) are excluded, then chiral substances are always formed as racemic mixtures, containing equal amounts of both enantiomeric forms. This striking stereochemical difference between living and non-living matter has puzzled the scientists since the middle of the last century [1]. Various experimental and theoretical approaches have been proposed for the explanation of this phenomenon [2–4], including some quite recent ones [5–35]. The theory put forward by Kondepudi and Nelson [15–20], based on a steady-state kinetic model, and the calculations of the electroweak parity-violating energy differences by Mason and Tranter [21–30] deserve to be particularly emphasized. For review and further references, see [2–4, 6–39].

From a theoretician's point of view, the problem is to explain the spontaneous creation of a homochiral system, starting from a racemic or achiral initial state, without the action of a chiral catalyst or any other external chiral influence. A closely related question is whether the direction of the evolution of the system towards one of the two possible homochiral end states is a matter of chance (and thus not predictable) or a result of some deterministic effects (and thus predictable). Frank [40] seems to be the first to propose a simple kinetic scheme resulting in a spontaneous stereoselection process. Frank's model was eventually further elaborated and extended [31–34,41–43].

In the original Frank approach [40], a pair of enantiomers L and D is produced in an autocatalytic process:



where A stands for a certain achiral substrate. The species L and D eliminate each other in a second-order reaction:



The rate constants of the reactions (1) and (2) are denoted by k_1 and k_2 . It is assumed that both (1a) and (1b) have equal rate constants and that the amount of the compound A does not change in the course of the process. Then, the time evolution of the concentrations of L and D is described by means of a pair of coupled differential equations

$$dn_L/dt = k_1 n_L - k_2 n_L n_D \quad (3a)$$

$$dn_D/dt = k_1 n_D - k_2 n_D n_L, \quad (3b)$$

from which immediately follows

$$n_D - n_L = (n_{D0} - n_{L0}) \exp(k_1 t). \quad (4)$$

Here and later, n_{D0} and n_{L0} denote the concentrations of D and L, respectively, at $t = 0$.

Equation (4) means that if in the initial moment there is a nonzero difference between the concentrations of L and D, then this difference will exponentially increase, resulting in a complete dominance of one stereoisomer. In particular, if $n_{D0} > n_{L0}$, then after some time only the species D will survive in the system. If $n_{D0} < n_{L0}$, then the dominant enantiomer will become L. The stereoselection process described

by Frank's model will occur whenever the initial conditions are asymmetrical, i.e. $n_{D0} \neq n_{L0}$. The direction of the process is determined by the sign of $n_{D0} - n_{L0}$ and is independent of its actual magnitude. If $n_{D0} \neq n_{L0}$ is a result of a random fluctuation in the initial moment (see appendix), then the sign of $n_{D0} - n_{L0}$ and therefore also the direction of Frank's stereoselection process is determined by pure chance.

A new dimension in the study of Frank-type stereoselection processes was achieved by the discovery of parity-violating energy differences (PVED) in molecules [44,45]. PVED is the energy difference between enantiomeric molecules. It is a result of the so-called weak neutral currents caused by electroweak interactions [46] between the electrons, protons and neutrons contained in a chiral molecule. For details on PVED, see [23,25] and the references cited therein.

PVED values are known for a variety of organic molecules including α -amino acids [24,28], polypeptides [22] and a carbohydrate [30]. In all cases examined, the PVED values are of the order 10^{-14} J mol⁻¹. These minute energy differences between enantiomers are difficult, but not impossible [47] to measure.

Not only stereoisomers, but also transition states of enantiomeric chemical reactions have their PVEDs [27], causing that enantiomers react with slightly different rates. If k_L and k_D are the rate constants of two enantiomeric chemical reactions (e.g. (1a) and (1b)), then according to the calculations of Tranter [27], $|k_D - k_L|/k_D$ is of order 10^{-13} in temperatures around 300 K.

Electroweak effects on chemical reactions induce a deterministic feature in Frank's model, implying that the direction of the stereoselection process may be influenced also by causal factors [31,32].

Bearing in mind the above arguments, a natural generalization of the equations (3) is [33,34]:

$$dn_L/dt = k_{1L} n_L - k_{2L} n_L n_D \tag{5a}$$

$$dn_D/dt = k_{1D} n_D - k_{2D} n_D n_L, \tag{5b}$$

where k_{1L} and k_{1D} , as well as k_{2L} and k_{2D} , differ slightly. The basic conclusion of the works [33,34] is that the direction of the stereoselection described by eqs. (5) is decided in the early stages of the Frank process and is the result of a delicate interplay between stochastic and deterministic effects. In [33,34], the behaviour of the solutions of (5) shortly after the initial moment has not been completely understood, and this issue is resolved in the present paper.

In this paper, we first examine a kinetic model which is a consistent and systematic generalization of eqs. (3) and (5), viz.:

$$dn_L/dt = e_L + f_{1L} n_L + f_{2L} n_D + g_{1L} n_L^2 + g_{2L} n_L n_D + g_{3L} n_D^2 \tag{6a}$$

$$dn_D/dt = e_D + f_{1D} n_D + f_{2D} n_L + g_{1D} n_D^2 + g_{2D} n_D n_L + g_{3D} n_L^2. \tag{6b}$$

As a matter of fact, eqs. (6) represent the most general Frank-type model involving chemical reactions of zeroth, first and second order. It is clear that (6) reduces to (5) by setting $f_{1X} = k_{1X}$, $g_{2X} = -k_{2X}$ and $e_X = f_{2X} = g_{1X} = g_{3X} = 0$; $X = L, D$. Along the lines of the previously discussed weak-neutral-current argumentation, we assume that there is only a very small difference in the values of the rate constants $e_L, f_{1L}, f_{2L}, g_{1L}, g_{2L}, g_{3L}$ and $e_D, f_{1D}, f_{2D}, g_{1D}, g_{2D}, g_{3D}$, respectively.

A method will be proposed, enabling the study of the time evolution of the difference $n_D - n_L$, as described by eqs. (6), shortly after the initial moment $t = 0$. Then the results obtained will be elaborated in detail for the special case of the Frank model (5), thus complementing the results of [33,34].

2. Solving equations (6)

We first transform eqs. (6) into a more convenient form [11] by introducing the (time-dependent) variables n , m and x as

$$n = n_D + n_L$$

$$m = n_D - n_L$$

$$x = n_D/n.$$

The values of the functions n and m for $t = 0$ will be denoted by n_0 and m_0 , respectively. Bearing in mind that $m = (2x - 1)n$, eqs. (6) become

$$\begin{aligned} d[nx]/dt = & e_L + [f_{1L}x + f_{2L}(1-x)]n + [g_{1L}x^2 + g_{2L}x(1-x) \\ & + g_{3L}(1-x)^2]n^2 \end{aligned} \quad (7a)$$

$$\begin{aligned} d[n(1-x)]/dt = & e_D + [f_{1D}(1-x) + f_{2D}x]n + [g_{1D}(1-x)^2 \\ & + g_{2D}x(1-x) + g_{3D}x^2]n^2. \end{aligned} \quad (7b)$$

Let the dimensionless parameters $\epsilon, \phi_1, \phi_2, \gamma_1, \gamma_2$ and γ_3 be defined by means of

$$\begin{aligned} e_L &= (1 - \epsilon/2)e & e_D &= (1 + \epsilon/2)e \\ f_{iL} &= (1 - \phi_i/2)f_i & f_{iD} &= (1 + \phi_i/2)f_i & i &= 1, 2 \\ g_{iL} &= (1 - \gamma_i/2)g_i & g_{iD} &= (1 + \gamma_i/2)g_i & i &= 1, 2, 3. \end{aligned}$$

Then, by adding and subtracting (7a) and (7b) and after a cumbersome calculation, one arrives at

$$\begin{aligned} dn/dt = & 2e + (f_1 + f_2)n + \frac{1}{2}(\phi_1 f_1 - \phi_2 f_2)m + \frac{1}{2}(g_1 + g_3)(n^2 + m^2) \\ & + \frac{1}{2}g_2(n^2 - m^2) + \frac{1}{2}(\gamma_1 g_1 - \gamma_3 g_3)mn \end{aligned} \quad (8a)$$

$$\begin{aligned} dm/dt = & \epsilon e + (f_1 - f_2)m + \frac{1}{2}(\phi_1 f_1 + \phi_2 f_2)m + (g_1 - g_3)mn \\ & + \frac{1}{4}(\gamma_1 g_1 + \gamma_3 g_3)(n^2 + m^2) + \frac{1}{4}\gamma_2 g_2(n^2 - m^2). \end{aligned} \quad (8b)$$

Now, we assume that the parameters ϵ , ϕ_i , $i = 1, 2$, γ_i , $i = 1, 2, 3$, are much smaller than unity (typical orders of magnitude are 10^{-13} [27]). The initial value of m must also be very small; taking $n_0 = 1$ mol, m_0 is estimated to be of the order 10^{-12} mol (see appendix). Therefore, if we are interested in the time dependency of the function m closely after the initial moment (when the direction of the stereoselection process will be decided anyway!), we may neglect the terms in (8) being proportional to m^2 , $m\phi_i$ and $m\gamma_i$. This results in

$$dn/dt = 2e + (f_1 + f_2)n + \frac{1}{2}(g_1 + g_2 + g_3)n^2 \quad (9a)$$

$$\begin{aligned} dm/dt = & \epsilon e + (f_1 - f_2)m + \frac{1}{2}(\phi_1 f_1 + \phi_2 f_2)n + (g_1 - g_3)mn \\ & + \frac{1}{4}(\gamma_1 g_1 + \gamma_2 g_2 + \gamma_3 g_3)n^2. \end{aligned} \quad (9b)$$

The noteworthy outcome is that (9a) does not depend on m and is therefore solvable by direct integration (which is especially easy if $e = 0$). Equation (9a) provides thus an explicit analytical expression for $n = n(t)$. When this function is substituted into (b), one can, at least in principle, integrate (9b) and deduce the required explicit analytical expression for $m = m(t)$. The solutions $n(t)$ and $m(t)$ thus obtained are applicable for near-zero values of t , i.e. they describe the early stages of the generalized Frank process. In particular, $m(t)$ may be used to predict the direction of the stereoselection.

Since the general expression for $m(t)$ depends on not less than fourteen parameters: e , f_i , g_i , ϵ , ϕ_i , γ_i , m_0 , n_0 , its investigation is a very tedious task and requires computer-aided studies. One example of this kind is described in the subsequent section.

3. Solving equations (5)

As already indicated, model (5) is a special case of model (6) when the only nonzero rate constants are $f_{1L} = k_{1L} = (1 - \phi/2)k_1$, $f_{1D} = k_{1D} = (1 + \phi/2)k_1$,

$g_{2L} = -k_{2L} = -(1 - \gamma/2)k_2$ and $g_{2D} = -k_{2D} = -(1 + \gamma/2)k_2$. Then, eqs. (9) reduce to:

$$dn/dt = k_1 n - \frac{1}{2} k_2 n \quad (10a)$$

$$dm/dt = k_1 m + \frac{1}{2} \phi k_1 n - \frac{1}{4} \gamma k_2 n^2. \quad (10b)$$

In order to solve (10a), rewrite it as

$$(k_1 n - \frac{1}{2} g_2 n^2)^{-1} dn = dt$$

and integrate. Direct calculation yields

$$(n/n_0)(k_1 - \frac{1}{2} k_2 n_0)(k_1 - \frac{1}{2} k_2 n)^{-1} = \exp(k_1 t),$$

i.e.

$$n = n_0 \exp(k_1 t) \{1 + \frac{1}{2} (k_2/k_1) n_0 [\exp(k_1 t) - 1]\}^{-1}.$$

Abbreviating $\exp(k_1 t)$ by T and $\frac{1}{2} (k_2/k_1) n_0$ by S , one obtains the following simplified form of the function $n(t)$:

$$n = n_0 T(1 - S + ST)^{-1}. \quad (11)$$

Substituting (11) back into (10b), we obtain

$$dm/dt = k_1 m + F(t),$$

where

$$F(t) = \frac{1}{2} \phi k_1 n - \frac{1}{4} \gamma k_2 n^2$$

and n is given by (11). Therefore,

$$m = m_0 T + T \int_0^t T^{-1} F(t) dt,$$

which after a lengthy calculation gives

$$m = m_0 T + \frac{1}{2} \phi n_0 T [k_1 t - \ln(1 - S + ST)] (1 - S)^{-1} - \gamma n_0 T(T - 1)S(1 - S + ST)^{-1}. \quad (12)$$

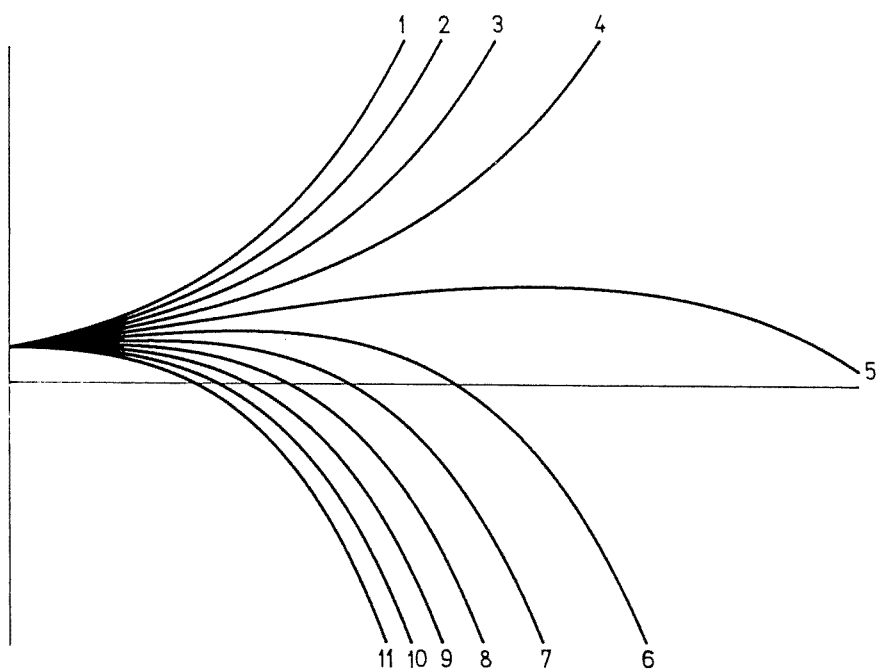


Fig. 1. The function $m(t)/m_0$ for $n_0 = 1, S = 0.1, \gamma = 0$. The curves 1, 2, ..., 11 correspond to $\phi/m_0 = 0, -1, \dots, -10$, respectively.

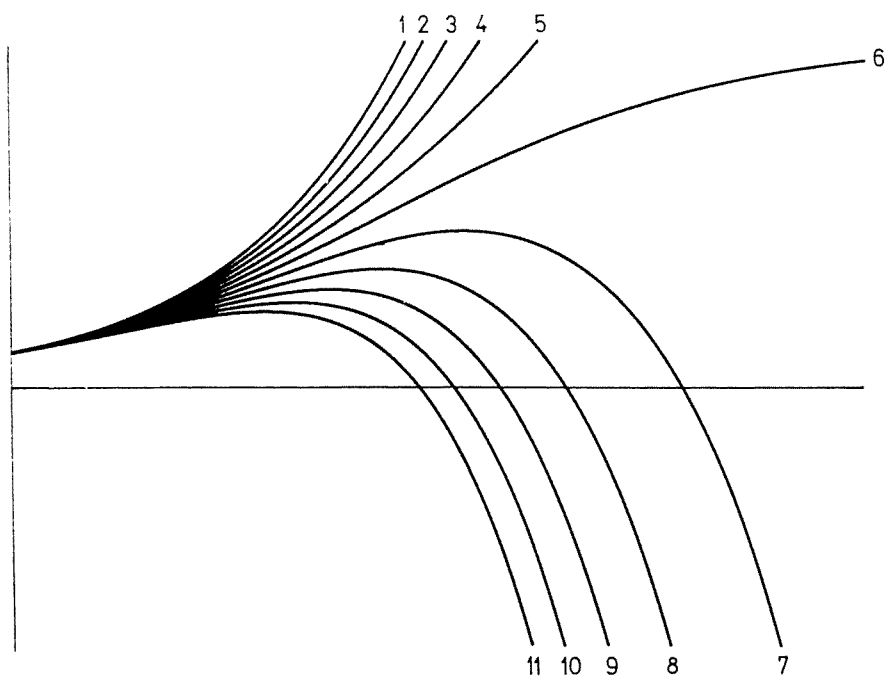


Fig. 2. The function $m(t)/m_0$ for $n_0 = 1, S = 0.1, \phi = 0$. The curves 1, 2, ..., 11 correspond to $\gamma/m_0 = 0, 1, \dots, 10$, respectively.

Equations (11) and (12) hold provided m_0 is much less than n_0 . Equation (12) reveals the way in which stochastic effects (represented by the variable m_0) combine with non-stochastic differences in the rate constants of enantiomeric reactions (represented by the parameters ϕ and γ) to determine the overall direction of the stereoselection. According to eq. (12), in the early stages of the generalized Frank process the time dependence of m is governed by two rate constants k_1 and k_2 , the initial concentrations of the enantiomers and their difference (n_0 and m_0) and two electroweak effects ϕ and γ ; the parameters ϕ , γ and m_0 are many orders of magnitude smaller than k_1 , k_2 and n_0 . The variety of cases which may occur in such a complex situation is illustrated in the examples given in figs. 1–7.

Figures 1 and 2 show the dependence of the function $m(t)$ on the parameters ϕ and γ , respectively. Suppose that $m_0 > 0$, i.e. that in the initial moment the dominating species is D. Then the interesting case is when the electroweak interactions favour the enantiomer L. This occurs when $\phi < 0$ and/or $\gamma > 0$. From figs. 1 and 2 we see that, depending on the ratio ϕ/m_0 and γ/m_0 , the direction of the stereoselection may be determined by either the random initial fluctuation (m_0) or by electroweak effects (ϕ, γ). If ϕ and γ have equal signs (fig. 3), then they necessarily act in opposite directions. From fig. 3, it is seen that the effect of γ will ultimately overpower the effect of ϕ .

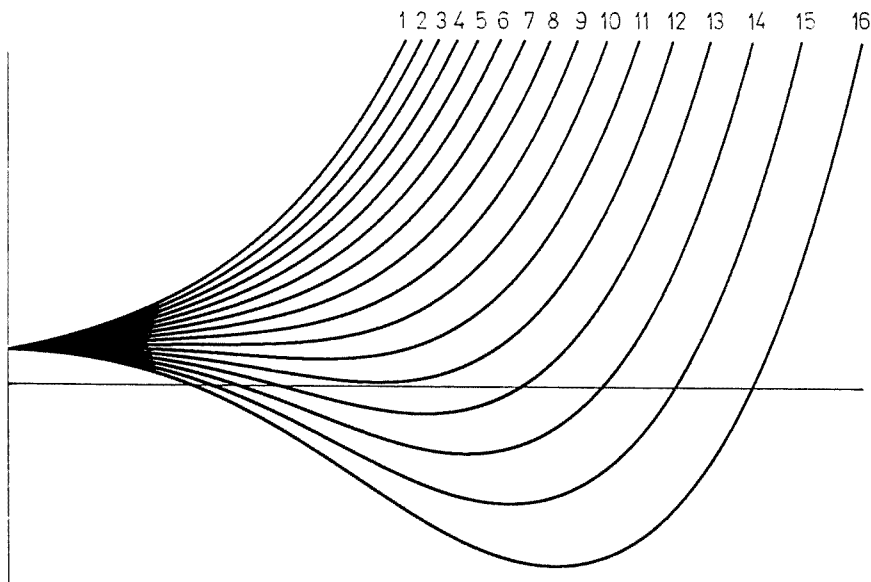


Fig. 3. The function $m(t)/m_0$ for $n_0 = 1$, $S = 0.1$, $\phi = \gamma$. The curves 1, 2, ..., 16 correspond to $\phi/m_0 = 0, -1, \dots, -15$, respectively.

Figures 4 and 5 show the case where ϕ and γ act in the same direction, either against the random initial fluctuation (fig. 4) or in line with it (fig. 5). Figures 6 and 7

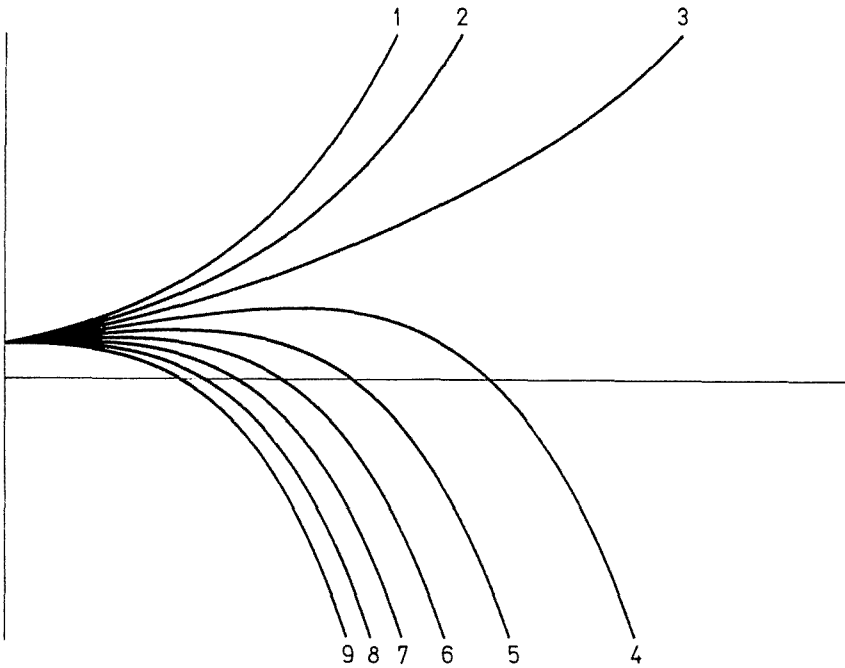


Fig. 4. The function $m(t)/m_0$ for $n_0 = 1, S = 0.1, \phi = -\gamma$. The curves 1, 2, ..., 9 correspond to $\phi/m_0 = 0, -1, \dots, -8$, respectively.

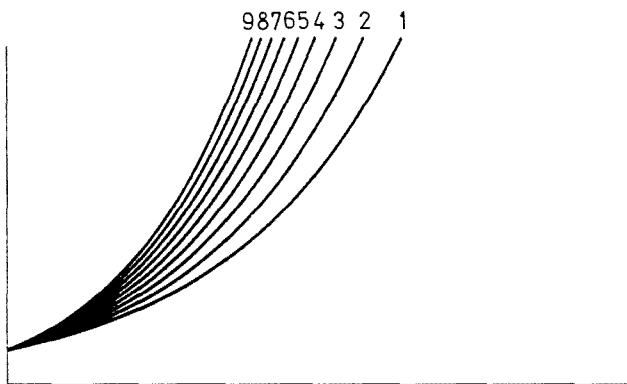


Fig. 5. The function $m(t)/m_0$ for $n_0 = 1, S = 0.1, \phi = -\gamma$. The curves 1, 2, ..., 9 correspond to $\phi/m_0 = 0, 1, \dots, 8$, respectively.

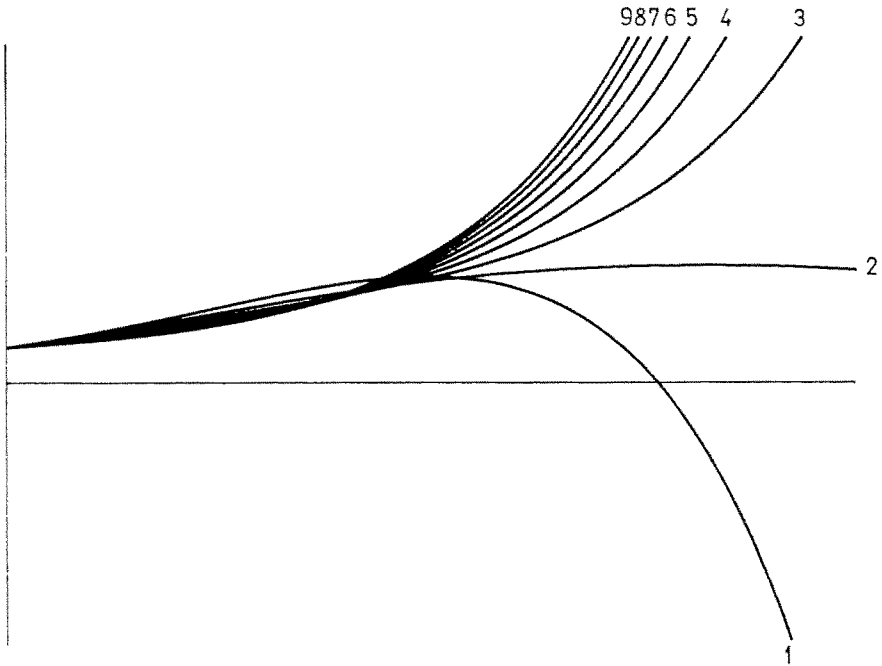


Fig. 6. The function $m(t)/m_0$ for $n_0 = 1$, $\phi = -2.5$, $\gamma = -2.5$. The curves 1, 2, ..., 9 correspond to $S = 0.1, 0.2, \dots, 0.9$, respectively.

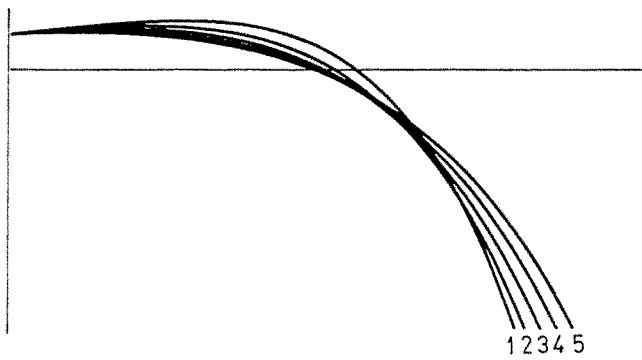


Fig. 7. The function $m(t)/m_0$ for $n_0 = 1$, $\phi = -4$, $\gamma = 4$. The curves 1, 2, ..., 5 correspond to $S = 0.1, 0.2, \dots, 0.5$, respectively.

illustrate the effect of the relative magnitude of the rate constants k_1 and k_2 . The dependence of $m(t)$ on the parameter S is quite sensitive to the values of ϕ and γ , as can be seen by comparing figs. 6 and 7.

4. Concluding remarks

The Frank model is certainly a drastic over-simplification of any stereoselection process which in reality could have occurred on the prebiotic Earth. Nevertheless, it demonstrates that such a process need not necessarily have a complicated mechanism and that it may be fully explicable by the long known laws of chemical kinetics. By taking into account the electroweak effects on the rates of chemical reactions, one can formulate generalized versions of the Frank model. Within these models, the direction of the stereoselection process is simultaneously influenced by both stochastic and deterministic factors. The complex interplay between these factors has been clarified in the present paper.

The fundamental problem in connection with the origin of homochirality in nature is whether the "choice" of L-aminoacids and D-sugars (instead of D-aminoacids and L-sugars) by terrestrial organisms was a result of pure chance or was a necessity. The Frank model cannot answer this question, but it provides arguments in favour of the deterministic or, at least, partially deterministic origin of the homochirality of biomolecules on the Earth.

Appendix

In this appendix, we demonstrate an elementary statistical result about racemic mixtures.

Consider a racemic mixture of species L and D, containing a total of N molecules. Then the difference between the numbers of D and L species, caused by random fluctuations, is about $\pm N^{1/2}$.

Proof

Denote by N_D and N_L the number of molecules D and L, respectively, in the mixture considered: $N_D + N_L = N$. What we actually prove is that the expected value of the square of the differences between N_D and N_L is equal to N .

Suppose that the enantiomers L and D are produced in a chemical reaction. There is a probability $p = 1/2$ that the molecule produced in an elementary step is D. The probability q of producing L is also equal to $1/2$. Then the probability that by producing a total of N molecules k of them are of type D is clearly

$$P(N, k) = \binom{N}{k} p^k q^{N-k} = \binom{N}{k} 2^{-N}.$$

In other words, $P(N, k)$ is the probability that $N_D = k$, i.e. that $N_L = N - k$, i.e. that $N_D - N_L = 2k - N$, i.e. that $(N_D - N_L)^2 = (N - 2k)^2$. The expected value of $(N_D - N_L)^2$ is thus

$$E[(N_D - N_L)^2] = \sum_{k=0}^N (N - 2k)^2 \binom{N}{k} 2^{-N}.$$

Transforming the summand on the right-hand side of the above equation as

$$\begin{aligned} (N - 2k)^2 \binom{N}{k} 2^{-N} &= N^2 \binom{N}{k} 2^{-N} - 2N(N - 1) \binom{N - 1}{k - 1} 2^{-(N - 1)} \\ &\quad + N(N - 1) \binom{N - 2}{k - 2} 2^{-(N - 2)} \end{aligned}$$

and applying the identity

$$\sum_{h=0}^M \binom{M}{h} 2^{-M} = 1$$

for $M = N$, $M = N - 1$ and $M = N - 2$, we immediately arrive at

$$E[(N_D - N_L)^2] = N^2 - 2N(N - 1) + N(N - 1),$$

i.e.

$$E[(N_D - N_L)^2] = N.$$

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