Origin of Biomolecular Chirality. Analysis of Frank's Model

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Frank's model for biochemical L-D stereoselection is examined and approximate analytical solutions of its generalized form are deduced, extending earlier results of Frank and Tennakone.

Introduction

The fact that L-amino acids and and D-sugars are ubiquitous constituents of living organisms whereas D-amino acids and L-sugars are present in minor amounts and/or in exceptional cases, has puzzled scientists over a long period of time [1]. Various approaches towards the explanation of this phenomenon were offered (see [2 – 8] and the references cited therein). Frank [9] proposed one of the first plausible kinetic models for a chemical process which, starting with a racemic mixture of L- and D-species, leads to the elimination of one and the dominance of the other enantiomer. Frank's model is based on the system of coupled differential equations

$$dn_L/dt = k_1 n_L - k_2 n_L n_D \,, \qquad (1\,a)$$

$$dn_D/dt = k_1 n_D - k_2 n_D n_L \,, \qquad (1\,b)$$

where n_L and n_D denote the molar amounts of the L- and D-enantiomers, respectively, and k_1 and k_2 are positive constants.

Equations (1) are compatible with the chemical reactions

$$\mathrm{L} + \mathrm{A} \rightarrow 2\mathrm{L} \,, \qquad (2)$$

$$\mathrm{D} + \mathrm{A} \rightarrow 2\mathrm{D} \,, \qquad (3)$$

$$\mathrm{L} + \mathrm{D} \rightarrow \mathrm{A}' \,, \qquad (4)$$

where A and A′ symbolize some achiral substances, the amount of A being assumed to be always large compared to that of the enantiomers.

We shall later extend the above mechanism by a further pair of enantiomeric reactions:

$$\mathrm{L} + \mathrm{D} \rightarrow \mathrm{A}'' + \mathrm{D} \,, \qquad (5)$$

$$\mathrm{L} + \mathrm{D} \rightarrow \mathrm{A}'' + \mathrm{L} \,, \qquad (6)$$

where A″ denotes another achiral substance.

From (1) it immediately follows that

$$n_L - n_D = (n_{L0} - n_{D0}) \exp(k_1 t) \,, \qquad (7)$$

where n_{L0} and n_{D0} are the values of n_L and n_D at $t = 0$.

The difference between n_{L0} and n_{D0} is traditionally ascribed to chance fluctuations [9]. Recently Klemm [2] put forward a similar, yet more trustable argument. According to [2], L-D stereoselection might have occurred simultaneously in several mutually isolated regions, resulting in the dominance of the L form in some and of the D form in other regions. Eventually these regions merged causing the extinction of one enantiomer. The number of isolated regions with the L and D form dominant, might have been slightly different due to some biased influences (e. g. the electroweak interactions or, more precisely, the weak neutral currents).

The energy differences between enantiomers caused by weak neutral currents have been recently estimated (see [10 – 12] and the references cited therein). In the case of biomolecules these energy differences are very small and imply only a minute excess of the more stable enantiomer (10^6 molecules per mole). This is much less than 10^{12} molecules per mole, which is the average difference between the number of enantiomers in a racemic mixture due to random fluctuations. As a consequence of this, weak neutral current arguments cannot be directly employed within Frank's model.

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Generalization of Frank's Model

Another way to include the electroweak bias into Frank's model is to assume that the rate constants k_1 and k_2 have slightly different values in (1 a) and (1 b). This again can be viewed as a consequence of weak neutral current interactions [13] and applies to all enantiomeric chemical reactions.

Hence the rate constant $k'_{1\mathrm{L}}$ of the reaction (2) will be somewhat different than the rate constant $k'_{1\mathrm{D}}$ of its enantiomeric counterpart (3). In addition to the achiral reaction (4), whose rate constant is k_2, we may include into the consideration also two enantiomeric reactions (5) and (6). Their rate constants will be denoted by $k'_{2\mathrm{L}}$ and $k'_{2\mathrm{D}}$, respectively.

The kinetic scheme consisting of the reactions (2)–(6) implies the system of differential equations

$$\mathrm{d}n_\mathrm{L}/\mathrm{d}t = k_{1\mathrm{L}} n_\mathrm{L} - k_{2\mathrm{L}} n_\mathrm{L} n_\mathrm{D}\,, \tag{8 a}$$

$$\mathrm{d}n_\mathrm{D}/\mathrm{d}t = k_{1\mathrm{D}} n_\mathrm{D} - k_{2\mathrm{D}} n_\mathrm{D} n_\mathrm{L}\,, \tag{8 b}$$

which in an obvious way generalizes Frank's model (1). Here $k_{1\mathrm{L}} = k'_{1\mathrm{L}} n_\mathrm{A}$, $k_{1\mathrm{D}} = k'_{1\mathrm{D}} n_\mathrm{A}$, $k_{2\mathrm{L}} = k_2 + k'_{2\mathrm{L}}$ and $k_{2\mathrm{D}} = k_2 + k'_{2\mathrm{D}}$.

The special case of (8) in which $k_{2\mathrm{L}} = k_{2\mathrm{D}}$ was previously examined by Tennakone [14] and Mason [3].

In the subsequent sections we derive approximate analytical expressions for the solutions of (8) and establish some of their asymptotic properties.

It will be assumed that the rate constants $k_{1\mathrm{L}}$ and $k_{1\mathrm{D}}$ as well as $k_{2\mathrm{L}}$ and $k_{2\mathrm{D}}$ have very close numerical values. We define therefore the parameters g_1 and g_2 via

$$k_{1\mathrm{L}} = (1 + g_1)\, k_{1\mathrm{D}}\,,$$
$$k_{2\mathrm{L}} = (1 + g_2)\, k_{2\mathrm{D}}\,.$$

According to model calculations of Tranter [13], the g values for pairs of enantiomeric reactions (taking place at room temperature) are of order 10^{-13}. Anyway, the conditions

$$|g_1| \ll 1\,; \quad |g_2| \ll 1$$

will be well satisfied.

Solution of Generalized Frank's Model

As already pointed out, the initial values of n_L and n_D are subject to random (and thus unpredictable) fluctuations. In order to stress the effect of the electroweak bias, we shall set $n_{\mathrm{L}0} = n_{\mathrm{D}0} = n_0$. The examination of the system (8) with the initial conditions $n_{\mathrm{L}0} \neq n_{\mathrm{D}0}$ will be the subject of a subsequent study.

At this point it is instructive to compare solutions of Frank's model (1) with those of its generalized version (8). A typical result of this kind is presented in Figure 1.

We proceed now to solve (8) by an iterative method. Assume first that $k_{1\mathrm{L}} = k_{1\mathrm{D}} = k_1$ and $k_{2\mathrm{L}} = k_{2\mathrm{D}} = k_2$. Then (8) reduces to Frank's model (1). Because of (7), $n_\mathrm{L} = n_\mathrm{D}$ holds for all values of t, and from either (1 a) or (1 b) we arrive at

$$\mathrm{d}n/\mathrm{d}t = k_1 n - k_2 n^2\,,$$

whose solution leads to the zero'th order approximation

$$n_\mathrm{L}^{(0)} = n_0 \exp(k_{1\mathrm{L}}\, t)\, F_\mathrm{L}\,, \tag{9 a}$$

$$n_\mathrm{D}^{(0)} = n_0 \exp(k_{1\mathrm{D}}\, t)\, F_\mathrm{D}\,, \tag{9 b}$$

where

$$F_\mathrm{L} = \{1 + (n_0 k_{2\mathrm{L}}/k_{1\mathrm{L}})[\exp(k_{1\mathrm{L}} t) - 1]\}^{-1}\,,$$
$$F_\mathrm{D} = \{1 + (n_0 k_{2\mathrm{D}}/k_{1\mathrm{D}})[\exp(k_{1\mathrm{D}} t) - 1]\}^{-1}\,.$$

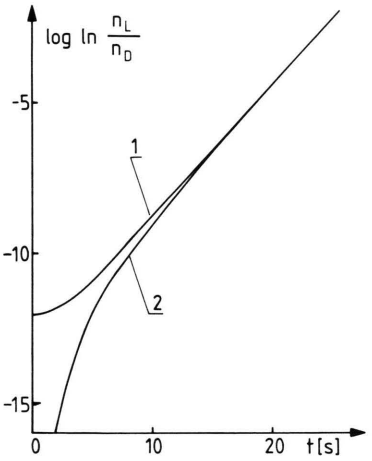

Fig. 1. Comparison of Frank's model, curve 1 based on (1), with its generalization, curve 2 based on (8). Curve 1: $n_{\mathrm{L}0} = 1 + 10^{-12}$, $n_{\mathrm{D}0} = 1$, $k_1 = 1\ \mathrm{s}^{-1}$, $k_2 = 0.1\ \mathrm{s}^{-1}\,\mathrm{mol}^{-1}$; Curve 2; $n_{\mathrm{L}0} = n_{\mathrm{D}0} = 1$, $g_1 = 1 \cdot 10^{-13}$, $g_2 = -1 \cdot 10^{-13}$, $k_{1\mathrm{L}} = 1\ \mathrm{s}^{-1}$, $k_{2\mathrm{L}} = 0.1\ \mathrm{s}^{-1}\,\mathrm{mol}^{-1}$.

We mention in passing that already $n_L^{(0)}$ and $n_D^{(0)}$ approximate the solutions of (8) better than the expressions proposed in [13].

Substituting (9b) instead of n_D in (8a) we arrive at the first order approximation

$$n_L^{(1)} = n_0 \exp(k_{1L} t)\, F_D^{1+g_2}. \qquad (10\,a)$$

In a fully analogous manner we get

$$n_D^{(1)} = n_0 \exp(k_{1D} t)\, F_L^{1-g_2}, \qquad (10\,b)$$

where the fact $(1+g_2)^{-1} \approx 1 - g_2$ was used.

The second order approximation for n_L could be found by substituting (10b) into (8a) and solving the differential equation thus obtained. This will be much faciliated by changing the term $\exp(k_{1D} t)$ in (10b) into $\exp(k_{1L} t)$. Then

$$n_L^{(2)} = n_0 \exp(k_{1L} t) \exp[(1 - F_L^{-g_2})/g_2].$$

Since g_2 is close to zero, we can use the limit

$$(1 - x^{-h})/h \to \ln x \quad \text{if} \quad h \to 0$$

and thus transform the above expression into

$$n_L^{(2)} \approx n_0 \exp(k_{1L} t)\, F_L.$$

Similarly we obtain

$$n_D^{(2)} = n_0 \exp(k_{1D} t) \exp[(F_D^{g_2} - 1)/g_2] \approx n_0 \exp(k_{1D} t)\, F_D.$$

Bearing in mind (9), we see that our second order approximation essentially coincides with the zero'th order approximation. This clearly justifies our method of approximation and indicates its rapid convergence.

Discussion

For large values of t, $n_L^{(1)}$ and $n_D^{(1)}$ behave asymptotically as

$$n_L^{(1)} \approx n_0^{g_2} (k_{1D}/k_{2D})^{1+g_2} \exp[(g_1 - g_2)\, k_{1L} t], \qquad (11\,a)$$

$$n_D^{(1)} \approx n_0^{-g_2} (k_{1L}/k_{2L})^{1-g_2} \cdot \exp[-(g_1 - g_2)\, k_{1D} t]. \qquad (11\,b)$$

From (11) is evident that if the difference $g_1 - g_2$ is positive, then $n_L^{(1)}$ exponentially increases and $n_D^{(1)}$ exponentially decreases and vanishes with increasing t. If $g_1 - g_2$ is negative, then the behaviour of $n_L^{(1)}$ and $n_D^{(1)}$ for large t is opposite. These properties of $n_L^{(1)}$ and $n_D^{(1)}$ are obeyed no matter how minute are the numerical values of the parameters g_1 and g_2. Since g_1 and g_2 are not subject to chance fluctuations and remain constant over considerably long periods of time, we conclude that the generalized Frank's model exhibits a simple mechanism by which electroweak interactions *could* influence the biochemical L-D stereoselection in nature.

From the present study, however, one cannot see how these electroweak interactions are coupled with the other relevant effect in Frank's model – namely the random fluctuation of the concentrations of the enantiomeric species. We hope to resolve this problem in the future.

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