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The limited Frank's chiral amplification model

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Frank's law of mass action-based model of chiral amplification is modified so as to avoid the unlimited increase in the concentration of one enantiomer. The basic features of this limited Frank model could be established without knowing the actual form of the solution of the respective system of differential equations. The model predicts two distinct time-evolutions of the system, one leading to complete monochirality and the other resulting in a racemic final state. The conditions for each of the two possible terminations of the process are established; they depend on the ratio of two certain rate constants and are independent of the initial composition of the system.

In 1953 Frank[1] proposed a simple kinetic scheme by which an almost racemic mixture (containing only a minute excess of a chiral molecule L over its enantiomer D) could spontaneously transform into a monochiral state (in which only the L form is present whereas the D species has completely vanished). By this he offered a possible and plausible solution of the long-existing problem of how monochirality of the biomolecules in the modern terrestrial life forms could have evolved from the racemic "primordial soup"[2,3]. Although Frank's model is only one of the several approaches put forward to rationalize the origin of the chirality of biomolecules (see refs 2-10 and the works quoted therein), it attracted and still attracts the attention of quite a few researchers (ref. 11 and the papers quoted therein). The importance of the Frank mechanism became clear after the discovery of the nonequivalence of the two enantiomeric forms of a molecule, caused by parity-violating effects in weak interactions. The slight thermodynamic bias in favour of one enantiomer, the so-called "parity-violating energy difference" (PVED)[12,13], could explain the small initial deviation from racemity, required for the success of Frank's chiral amplification mechanism[14,15]. In connection with this, the recently found examples of chiral biomolecules with exceptionally large PVEDs[16,17] might be of particular importance.

The Frank model assumes that the enantiomers L and D are capable of self-replication, cf. (α') and (α''). Although only a few years ago the existence of such chemical reactions seemed to be quite improbable[18], self-replicating molecules were recently obtained in laboratory[19,20]. Hence, an experimental realization of a Frank-type chiral amplification process may be expected in the foreseen future.

The Frank model consists of the chemical reactions (α', α'' and β) occurring in a homogeneous solution:

$$L + A \rightarrow 2L \qquad (\alpha')$$

$$D + A \rightarrow 2D \qquad (\alpha'')$$

$$L + D \rightarrow \text{precipitate} \qquad (\beta)$$

Applying to (α) and (β) the law of mass action and assuming that the concentration of the achiral species A is time-independent, the time-evolution of the concentrations n_L and n_D of the enantiomers L and D is described by the differential equations (1a) and (1b)

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

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

with the initial conditions $n_L = n_{L0}$ and $n_D = n_{D0}$ for $t = 0$. Without loss of generality, throughout this paper we will assume that $n_{L0} > n_{D0}$.

Equations (1a) and (1b) are readily solved[1]. The fundamental property of the solution is that if $n_{L0} - n_{D0} > 0$, then n_{L0} exponentially increases whereas n_{D0} exponentially decreases with increasing t. Consequently, no matter how small is the initial excess of [L] over [D], the system will eventually become monochiral. Whereas for $t \rightarrow \infty$, n_D vanishes, n_L unboundedly increases. This latter feature of the Frank model is clearly unrealistic. In order to avoid it we have extended the Frank model with an additional pair of enantiomeric reactions:

$$L + L \rightarrow \text{precipitate} \qquad (\gamma')$$

$$D + D \rightarrow \text{precipitate} \qquad (\gamma'')$$

Then instead of Eq. (1) we have

$$dn_L/dt = k_1 n_L - k_2 n_L n_D - k_3 n_L^2 \quad \ldots (2a)$$

$$dn_D/dt = k_1 n_D - k_2 n_L n_D - k_3 n_D^2 \quad \ldots (2b)$$

The solutions of Eq. (2) cannot unboundedly increase. Namely, for sufficiently large n_L, the right-hand side of (2a) will necessarily become negative-valued. Hence, if n_L is large, it must be a decreasing function of t. In other words, the function $n_L = n_L(t)$ is bounded from above.

The same conclusion is, of course, applicable also to the function $n_D = n_D(t)$.

In view of the above, we call the kinetic scheme consisting of the chemical reactions (α), (β) and (γ) the "*limited Frank model*". Its time-evolution is described by the system of differential equations (2a) and (2b).

Some properties of the limited Frank model

The finding of the functions $n_L(t)$ and $n_D(t)$ satisfying the differential equations (2a and 2b) seems to be a hard task. In what follows, however, we show that all the important properties of these functions can be deduced without knowing their actual analytical forms.

As usual in chemical kinetics (see, for instance, ref. 21), the system (2) is simplified by introducing the auxiliary dimensionless functions $x = x(\tau)$ and $y = y(\tau)$, where

$$\tau = k_1 t; \; x = (k_2/k_1) n_L; \; y = (k_2/k_1) n_D.$$

Then Eq. (2) is transformed into

$$dx/d\tau = x - xy - gx^2 \quad \ldots (3a)$$

$$dy/d\tau = y - xy - gy^2 \quad \ldots (3b)$$

where

$$g = k_3/k_2 \quad \ldots (4)$$

We have already demonstrated the validity of property 1.

Property 1—For all values of τ, $0 \leqslant \tau < \infty$, the functions $x(\tau)$ and $y(\tau)$ are bounded from above.

From Eqs (3a and 3b) we immediately see the following. If for a given fixed value of the variable τ, we know the values of the functions x and y, then we can compute the values of $dx/d\tau$ and $dy/d\tau$. Then from the known values of x, y, $dx/d\tau$ and $dy/d\tau$ we can compute $d^2x/d\tau^2$ and $d^2y/d\tau^2$. By continuing this argument we see that all derivatives of the functions x and y exist and are uniquely determined by x and y.

As a consequence of the above, if for a given value of τ, $x = y$, then $d^k x/d\tau^k = d^k y/d\tau^k$ for all values of $(k = 1,2,...)$. On the other hand, if for a given value of τ all the respective derivatives of the (analytical) functions $x(\tau)$ and $y(\tau)$ are equal, then these functions coincide for all values of τ, i.e., $x(\tau) \equiv y(\tau)$.

Conversely, if for a given value of τ, $x > y$, then for all values of τ, $x > y$. In other words: the functions x and y can never cross. Because the basic assumption of the Frank model is that at the initial moment there is a slight excess of one enantiomer over the other (conventionally, of L over D), we arrive at property 2.

Property 2—For all values of τ, $0 \leqslant \tau < \infty$, $x(\tau) > y(\tau)$.

Suppose that for a given fixed value of τ both $x(\tau)$ and $y(\tau)$ have very small (but positive) values, then the right-hand sides of Eqs (3a) and (3b) are necessarily positive-valued, i.e., x and y are increasing functions of τ. We thus obtain property 3.

Property 3—The functions $x(\tau)$ and $y(\tau)$ cannot simultaneously vanish. In particular, it is not possible to have both $x \to 0$ and $y \to 0$ when $\tau \to \infty$.

From property 1 it follows that for $\tau \to \infty$, both $x(\tau)$ and $y(\tau)$ have finite limit values. These limits are obtained by solving the equations $dx/d\tau = 0$ and $dy/d\tau = 0$. Using Eqs (3a and 3b) and bearing in mind property 3, we thus obtain property 4.

Property 4—Let $g \neq 1$. Then for $\tau \to \infty$ we have either (A) or (B):

(A) $x \to 1/g$ and $y \to 0$

(B) $x \to 1/(1+g)$ and $y \to 1/(1+g)$.

In connection with properties 3 and 4 it should be noted that the limit $\tau \to \infty$ is just a mathematical convenience. What we actually are interested in is the behaviour of the system when sufficient time has elapsed after the initial moment. As seen from Figs 1 and 2 the Frank system may practically reach its limit state quite soon after the start of the reactions.

In the subsequent section it is shown that the case $g = 1$ is exceptional, since, then the limited Frank model suddenly jumps from the evolution mode (A) to the evolution mode (B). Therefore the case $g = 1$ is studied separately.

The two evolution modes of the limited Frank model and their dependence on the parameter g

From property 4 we see that the limited Frank model has precisely two modes of evolution: (A)—resulting in a complete L-monochirality, and (B)—resulting in a fully racemic final state. We now establish the conditions needed for A and B.

Equations (3a and 3b) are rewritten as

$$dx/x = (1 - y - gx)d\tau \text{ and } dy/y = (1 - x - gy)d\tau.$$

Integration of these expressions yields

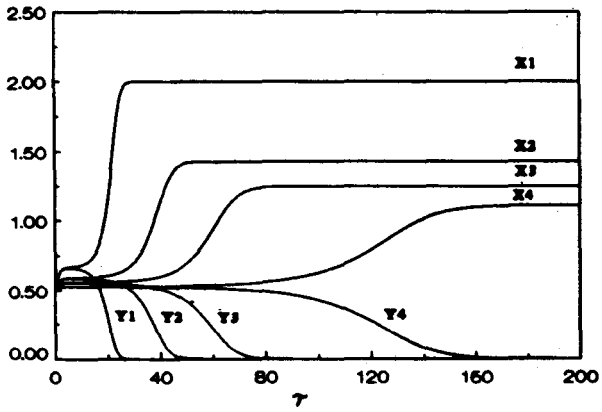

Fig. 1—The time-evolution of the limited Frank model for $g<1$; the curves x1,y1, x2,y2, x3,y3 and x4,y4 correspond to $g=0.5$, 0.7, 0.8 and 0.9, respectively; in all the cases the initial values of x and y are 0.5 and 0.499, respectively

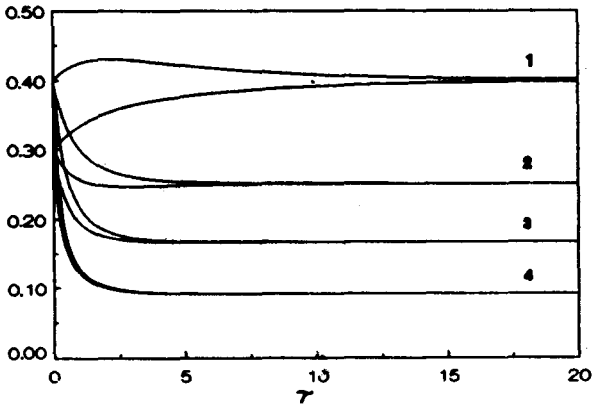

Fig. 2—The time-evolution of the limited Frank model for $g>1$; the pairs of curves 1, 2, 3 and 4 (x above, y below) correspond to $g=1.5$, 3, 5 and 10, respectively; in all the cases the initial values of x and y are 0.4 and 0.3, respectively

$$\ln(x/x_0)=\int_0^\tau (1-y-gx)\,d\tau \qquad \text{and}$$

$$\ln(y/y_0)=\int_0^\tau (1-x-gy)\,d\tau$$

from which

$$x/y=(x_0/y_0)\exp\left[(1-g)\int_0^\tau (x-y)\,d\tau\right] \qquad \ldots(5)$$

Because of the property 2, $x-y$ is positive for all values of τ. Consequently, the integral $\int_0^\tau (x-y)\,d\tau$ is necessarily positive-valued. When $\tau\to\infty$, this integral either tends to a finite constant C or becomes infinite.

If $\int_0^\infty (x-y)\,d\tau$ is finite, then for $\tau\to\infty$ the functions $x(\tau)$ and $y(\tau)$ must become asymptotically equal.

Consider first the case when the parameter g is less than unity.

Suppose that for $t\to\infty$, $\int_0^\tau (x-y)\,d\tau\to C<\infty$.

Then the limit value of the right-hand side of Eq. (5) is equal to $(x_0/y_0)\exp[(1-g)C]$. Because both (x_0/y_0) and $\exp[(1-g)C]$ are greater than unity, it follows that $\lim_{\tau\to\infty}(x/y)>1$. On the other hand, the finiteness of the integral $\int_0^\infty (x-y)\,d\tau$ implies that $\lim_{\tau\to\infty}(x-y)=0$, i.e., $\lim_{\tau\to\infty}(x/y)=1$, a contradiction. Hence, it must be $\int_0^\infty (x-y)\,d\tau=\infty$.

If $g<1$ and $\int_0^\infty (x-y)\,d\tau=\infty$, then for $\tau\to\infty$, the right-hand side of Eq. (5) tends to infinity. Consequently, $\lim_{\tau\to\infty}(x/y)=\infty$. Bearing in mind property 4, we see this latter limit value occurs only in the case (A).

Thus we conclude that the evolution mode (A) occurs if $g<1$. Consider now the case when the parameter g is greater than unity.

Suppose that for $t\to\infty$, $\int_0^\tau (x-y)\,d\tau\to\infty$. Then the right-hand side of Eq. (5) tends to zero. Consequently, $x/y\to 0$. This, however, is impossible, because by property 2, x/y cannot be less than one.

Therefore, if $g>1$, it must be $\int_0^\infty (x-y)\,d\tau=C<\infty$. Then, however, $x(\tau)$ and $y(\tau)$ become asymptotically equal for $\tau\to\infty$. Bearing in mind property 4, we see that this can occur only in the case (B).

Thus we conclude that the evolution mode (B) occurs if $g>1$. By this we arrived at our main result, i.e., property 5.

Property 5—The limited Frank mechanism leads to chiral amplification if, and only if the parameter g [given by Eq. (4)] is less than unity. If $g<1$, then the final state is (fully) monochiral. If $g>1$, then the final state is (fully) racemic.

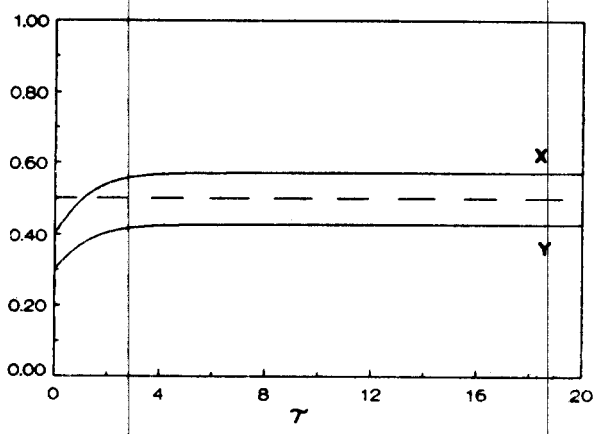

Fig. 3—The time-evolution of the limited Frank model for g = 1; the initial values of x and y are 0.4 and 0.3, respectively

The initial composition of the system (i.e., the values of n_{L0} and n_{D0}) as well as the numerical values of the rate constants k_1, k_2 and k_3 (except the ratio k_3/k_2) have no influence of the type of time-evolution of the system.

If $g < 1$, then the direction of the chiral amplification is fully determined by the difference between n_{L0} and n_{D0} (L-monochirality is achieved if $n_{L0} > n_{D0}$ and vice versa).

We see that the basic features of the original Frank model are preserved in its limited version, but only if the self-destruction reactions (γ) are less efficient than the reaction (β) of the mutual destruction of the enantiomers. Otherwise, no chiral amplification will occur.

The critical point in the limited Frank model (g = 1)

The discussion in the previous section reveals that when the parameter g is equal to unity, the limited Frank model has a specific behaviour. In view of property 5, $g = 1$ can be considered as a critical point of the Frank mechanism. If the value of g is monotonically varied from less than unity to greater than unity, then at $g = 1$ a sudden change in the type of the time-evolution of the system is observed. This is illustrated in Figs 1, 2 and 3. In these figures (especially in Figs 2 and 3) the initial values for the difference $x - y$ are chosen to be unrealistically large (since otherwise the curves $x(\tau)$ and $y(\tau)$ would lie too close to each other).

When $g = 1$, the solution of the limited Frank model is not difficult. First of all, from Eq. (5) we immediately obtain

$x/y = x_0/y_0$, i.e., $n_L/n_D = n_{L0}/n_{D0}$.

Hence, when $g = 1$, the ratio of the concentrations of the two enantiomers is time-independent. Because the initial composition of the system is assumed to only slightly deviate from racemity, we see that the system will always remain almost racemic.

For $g = 1$ Eqs (3a and 3b) can be rewritten as

$$d(x+y)/d\tau = (x+y) - (x+y)^2 \qquad \ldots (6a)$$

$$d(x-y)/d\tau = (x-y) - (x-y)(x+y) \qquad \ldots (6b)$$

This makes it possible to find $(x+y)$ from (6a) and using this solution to find $(x-y)$ from (6b). A tedious, but elementary calculation yields:

$$x(\tau) = \frac{x_0}{x_0+y_0} \cdot \frac{\exp(\tau)}{\exp(\tau) - [1 - 1/(x_0+y_0)]}$$

$$y(\tau) = \frac{y_0}{x_0+y_0} \cdot \frac{\exp(\tau)}{\exp(\tau) - [1 - 1/(x_0+y_0)]}$$

Note that for $\tau \to \infty$, $x \to x_0/(x_0+y_0)$ and $y \to y_0/(x_0+y_0)$. Only in the special case of $g = 1$, the limit values of $x(\tau)$ and $y(\tau)$ depend on the initial composition of the system.

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