A nonlinear autocatalysis of a chiral substance is shown to achieve homochirality in a closed system, if the back-reaction is included. Asymmetry in the concentration of two enantiomers or the enantiometric excess increases due to the nonlinear autocatalysis. Furthermore, when the back-reaction is taken into account, the reactant supplied by the decomposition of the enantiomers is recycled to produce more and more the dominant one, and eventually the homochirality is established.

PACS numbers:

Natural organic molecules associated with living matters usually have two possibilities in their stereocategories, in a right-handed form ($R$) or in a mirror-image left-handed form ($S$). These two forms are called enantiomers, and the molecules are said to be chiral. Chiral molecules are optically active to rotate the direction of polarization of plane polarized light. From the energetic point of view, these two enantiomers can exist with an equal probability, but the life on earth utilizes only one type: only levorotatory ($L$)-amino acids (or S) and dextrorotatory ($D$)-sugars (or R). This symmetry breaking in the chirality is called the homochirality.

The origin of this unique chirality has long intrigued many scientists. In order to find the physical origin of this homochirality, initial asymmetry in the primordial molecular environment has to be created by chance or engendered determinately by external or internal factors, such as the parity breaking effect in the weak interactions. The asymmetry in circularly polarized light, or adsorption on optically active crystals, may depend on the concentrations $R$ and $S$ at time $t$ vary in proportion to the present amount of the reactants $A$ and $B$ as

$$\begin{align*} \frac{dR}{dt} &= k_R(A_0 + R_0 + S_0 - R - S)(B_0 + R_0 + S_0 - R - S) \\ \frac{dS}{dt} &= k_S(A_0 + R_0 + S_0 - R - S)(B_0 + R_0 + S_0 - R - S). \end{align*}$$

Here we first neglect the back reaction from ($S$)-C or ($R$)-C to A and B. Later, the effect of back reaction is shown to be very important in achieving the complete homochirality.

Frank has shown theoretically that an autocatalytic reaction of a chemical substance with an antagonistic process can lead to an amplification of enantiomeric excess (ee) and to homochirality. Many theoretical models are proposed afterwards, but they are often criticized as lacking any experimental support. Recently, asymmetric autocatalysis of pyrimidyl alkanoal has been studied intensively. The enhancement of ee was confirmed, and its temporal evolution was explained by the second-order autocatalytic reaction. But only with the nonlinear autocatalysis, chirality selection is not complete and the value of ee stays less than unity. Here we show that the complete homochirality is achieved by the back-reaction to recycle the reactant. If the rate of back reaction is small, it takes a long time before the homochirality is achieved.

We consider a chemical reaction such that substances $A$ and $B$ react to form substance $C$. Though reactants $A$ and $B$ are achiral, the product $C$ happened to be chiral in two enantiometric forms; $R$-isomer ($R$)-C and $S$-isomer ($S$)-C.

$$\begin{align*} A + B &\equiv (R)-C \\ A + B &\equiv (S)-C \end{align*}$$

In the experiment by Soai et al., one provides a small amount of enantiomers with concentrations $R_0$ and $S_0$ respectively in the reactants of concentrations $A_0$ and $B_0$. Instead of the open flow system considered by Frank, we assume a closed conserve system such that concentrations $R$ and $S$ at time $t$ vary in proportion to the present amount of the reactants $A$ and $B$ as

$$\begin{align*} \frac{dr}{dt} &= k_r(1 - r - s) \\ \frac{ds}{dt} &= k_s(1 - r - s) \end{align*}$$

where the reaction rate coefficient $k_{r,s} = k_{R,S}(B_0 + R_0 + S_0)$ may depend on $r$ and $s$.

Since both enantiomers are equivalent except the handedness, the time evolution should be symmetric in $r$ and $s$. The chirality of the system can be brought about through the asymmetry of the initial concentrations $r_0$ and $s_0$ of two enantiomers, ($R$)-C and ($S$)-C. In the fol-
lowing we study the temporal variation of the enatiometric excess measured by

\[ \Omega = \frac{r - s}{r + s}. \]  

(4)

**Non-Autocatalytic Case**

If the reaction is not autocatalytic, the reaction coefficients are simply constant as \( k_r = k_s = k \). Then the ratio of the two equations (3) gives \( \frac{dr}{ds} = 1 \), which defines the trajectory in the \( r-s \) space. It is easily solved as \( r - s = r_0 - s_0 = \text{const} \). The time evolution of enantiomers is depicted in the flow diagram in Fig.1(a). The flow is on the line with a unit slope, and terminates on a point of crossing the diagonal line \( r + s = 1 \); the reaction stops because the reactant \( A \) is consumed up in a closed system. The diagonal line \( r + s = 1 \) is in fact a set of stable fixed points.

\[ \frac{dr}{ds} = \frac{r^2}{s^2} \]  

(6)

which is easily solved to give the trajectory in the \( r-s \) space as \( 1/r - 1/s = 1/r_0 - 1/s_0 = \text{const} \). The time evolution is depicted in the flow diagram Fig.1(b). Below the diagonal \( r = s \), the flow bends down, whereas above the diagonal the flow bends up. The final concentrations \( r_\infty \) and \( s_\infty \) should satisfy the relation \( r_\infty + s_\infty = 1 \). Then the final value of the ee is determined by the initial value \( \Omega_0 \) and the amount of the input \( r_0 \) (or \( s_0 \)) as

\[ \Omega_\infty = r_\infty - s_\infty = \text{sgn}(\Omega_0) \left( \sqrt{1 + \frac{r_0^2}{s_0^2} \left( \frac{1 - \Omega_0}{\Omega_0} \right)^2} - r_0 \frac{1 - \Omega_0}{|\Omega_0|} \right) \]  

(7)

FIG. 1: Flow diagrams in \( r-s \) space. (a) Nonautocatalytic, (b) linearly autocatalytic, (c) nonlinearly autocatalytic and (d) nonlinearly autocatalytic with backward reactions (\( \lambda/k = 0.1 \)).

The ee decreases since the numerator \( r - s \) in \( \Omega \) remains constant whereas the denominator \( r + s \) increases in time. Actually, the equation is easily solved, and ee is obtained as \( \Omega = (r_0 - s_0)/(1 - (1 - r_0 - s_0)e^{-2kr}) \). The ee decreases from the initial value \( \Omega_0 = (r_0 - s_0)/(r_0 + s_0) \) to the asymptotic value \( \Omega_\infty = r_\infty - s_\infty \), which should be very small if the initial amounts \( r_0 = R_0/(A_0 + R_0 + S_0) \) and \( s_0 = S_0/(A_0 + R_0 + S_0) \) are small. This corresponds to racemic mixtures.

**Linearly Autocatalytic Case**

If the reaction is autocatalytic in the first order, the reaction coefficient is linearly proportional to the product concentrations as \( k_r = kr \) and \( k_s = ks \). In this case, the ratio of two rate equations gives \( \frac{dr}{ds} = r/s \), which is easily solved as \( r/s = r_0/s_0 = \text{const} \). The time evolution is depicted in the flow diagram Fig.1(b). The flow is radial from the origin and trivially the ee does not change even as the reaction proceeds,

\[ \Omega = \frac{r - s}{r + s} = \frac{r_0 - s_0}{r_0 + s_0} = \Omega_0 \]  

(5)

as first notified by Frank.\(^2\)

**Nonlinearly Autocatalytic Case**

If the reaction is autocatalytic in the higher order, the reaction coefficient depends nonlinearly on the product; for the second order autocatalysis, for example, \( k_r = kr^2 \) and \( k_s = ks^2 \). In this case, the ratio of two rate equations gives

\[ \frac{dr}{ds} = \frac{r^2}{s^2} \]  

(6)

FIG. 1: Flow diagrams in \( r-s \) space. (a) Nonautocatalytic, (b) linearly autocatalytic, (c) nonlinearly autocatalytic and (d) nonlinearly autocatalytic with backward reactions (\( \lambda/k = 0.1 \)).

The ee decreases since the numerator \( r - s \) in \( \Omega \) remains constant whereas the denominator \( r + s \) increases in time. Actually, the equation is easily solved, and ee is obtained as \( \Omega = (r_0 - s_0)/(1 - (1 - r_0 - s_0)e^{-2kr}) \). The ee decreases from the initial value \( \Omega_0 = (r_0 - s_0)/(r_0 + s_0) \) to the asymptotic value \( \Omega_\infty = r_\infty - s_\infty \), which should be very small if the initial amounts \( r_0 = R_0/(A_0 + R_0 + S_0) \) and \( s_0 = S_0/(A_0 + R_0 + S_0) \) are small. This corresponds to racemic mixtures.

**Homochirality by Back Reaction**

From the previous analysis we found that the ee amplification takes place with a nonlinear or higher-order autocatalytic chemical reaction. However, the final chirality is not complete. The ee is smaller than 100%, even if the initial composition \( r_0 = 0.051 \) and \( s_0 = 0.049 \), the final ee is \( \Omega_\infty = 19\% \). For example, with the same initial ee as \( \Omega_0 = 2\% \), if one starts with \( r_0 = 0.051 \) and \( s_0 = 0.049 \), the final ee is \( \Omega_\infty = 26\% \) according to eq.(6), whereas with the initial values \( r_0 = 0.00051 \) and \( s_0 = 0.00049 \), then \( \Omega_\infty = 98\% \).

A simple back reaction process is incorporated into the rate equation (3) as

\[ \frac{dr}{dt} = kr^2 (1 - r - s) - \lambda r \]  

\[ \frac{ds}{dt} = ks^2 (1 - r - s) - \lambda s \]  

(8)

with a rate constant \( \lambda \) of the back reaction. Now the flow diagram in \( r-s \) space changes from Fig.1(c) to (d).
The diagonal line \( r + s = 1 \) is no more a set of infinitely many stable fixed points. Instead, there are seven fixed points in the flow diagram, Fig.1(d). The trivial fixed point at the origin \( O: (r_o, s_o) = (0, 0) \) is stable. On the \( r- \) axis there are two fixed points: \( U_1: (1 - \sqrt{1 - 4\lambda/k})/2, 0) \) is unstable and \( S_2: (1 + \sqrt{1 - 4\lambda/k})/2, 0) \) is stable. There are analogous points on the \( s- \) axis as the unstable fixed point \( U_2: (0, 1 - \sqrt{1 - 4\lambda/k})/2 \) and the stable fixed point \( S_3: (0, 1 + \sqrt{1 - 4\lambda/k})/2 \). On the diagonal line, \( r = s \), there are two other unstable fixed points: \( U_3: ((1 - \sqrt{1 - 8\lambda/k})/4, (1 - \sqrt{1 - 8\lambda/k})/4) \) and \( U_4: ((1 + \sqrt{1 - 8\lambda/k})/4, (1 + \sqrt{1 - 8\lambda/k})/4) \).

If the rate of back reaction \( \lambda \) is small, \( U_{1,2,3} \) are close to the origin \( O \), and \( U_4 \) and \( S_{1,2} \) are close to the diagonal line \( r + s = 1 \). Then the flow diagram looks similar to Fig.1(c). However, there is a big difference in the flow diagram Fig.1(c) and (d). In Fig.1(c) the diagonal line \( r + s = 1 \) is a set of infinitely many fixed points. On this line, neither \( r \) nor \( s \) varies in time. On the contrary, in Fig.1(d) there are only three stable fixed points: \( O \) and \( S_{1,2} \). The trivial fixed point \( O \) corresponds to the structureless or lifeless world, without the chemicals (\( R \)-C) or (\( S \)-C). Its basin of attraction is a small region enclosed by curves connecting \( O \) and \( U_{1,2,3} \). If the the primordial environment allows some chemical system to reach exterior of this basin, chemical complexes with chirality can be produced. The nonlinear autocatalysis amplifies the ee, and afterwards the back reaction process selects only one type of a chiral component.

The time evolution of the concentration of each component \( r \) is depicted in Fig.2. The initial ee is as small as \( \Omega_0 = 0.01% \) with \( r_0 = 0.00050005 \) and \( s_0 = 0.00049995 \). If there is no back reaction \( (\lambda = 0) \), then in the early stage reactant concentrations increase as \( r \approx r_0/(1 - r_0t) \) and \( s \approx s_0/(1 - s_0t) \), and tend to diverge at times \( 1/r_0 \) and \( 1/s_0 \) respectively. Before the divergence, the shortage of the reactant \( A \) leads to the saturation of \( r \) and \( s \), as \( r \approx r_\infty (1 - e^{-2kt}) \) and \( s \approx s_\infty (1 - e^{-2kt}) \). The final amounts \( r_\infty \) and \( s_\infty \) are finite and nonzero. The ee is amplified to \( \Omega_\infty = 7.9% \) which is less than unity.

If there is a small but a finite back reaction process with \( \lambda = 0.0002 \), both \( r \) and \( s \) increase again and approach close to the values corresponding to the unstable fixed point \( U_4 \). Then the component which has a slight advantage, \( r \) in Fig.2, starts to dominate, and the other chiral type extinguishes gradually. The substance (\( S \)-C) decomposes and supplies the reactant \( A \) which is consumed to increase its enantiomer (\( R \)-C). The reactant \( A \) is, so to say, recycled. Eventually, the complete homochirality with \( \Omega = 100% \) is achieved.

We have shown theoretically that in a closed chemical system, the nonlinear autocatalysis amplifies the initial small enantiometric excess. But eventually, the simple back reaction promotes the decomposition of less abundant enantiomer to the reactant, which is recycled to produce the more abundant type. Through this recycling process, the complete homochirality can be achieved.

The ratio of the forward and the backward reaction rates, \( k \) and \( \lambda \), is related to the equilibrium concentration or the yield. Therefore, a system with a yield less than unity might have sufficiently large back reaction rate to achieve complete homochirality in experimental time scales. But if the rate of back reaction is too large and the forward reaction is autocatalytic, the system might be trapped into the basin of attraction of the origin and the reaction can not proceed. On the contrary, when the rate of back reaction is too small, the enantiometric amplification can take place, but the final selection of chirality should take a long time. This might be the reason that the previous experiments by Soai et al. are well fitted by a model with only the forward autocatalytic reaction. To observe the effect of back reaction, one might have to wait a long time, depending on the back-reaction rate. Otherwise one has to search appropriate chemical systems with proper reaction constants.

If one considers spatial dependence of the chemical reaction, further complications arise in the process of chirality selection. Initial productions of enantiomers actually take place randomly in space and time. The nonlinear autocatalysis promotes the chemical reaction around these initial enantiomers, and the reaction fronts propagate and expand. When fronts of different enantiomers meet with each other, the competition should take place between them. This competition of enantiomers in space is an interesting future research subject.

---

* Electronic address: yukio@rk.phys.keio.ac.jp

† Electronic address: hyuga@rk.phys.keio.ac.jp
1 W.A. Bonner, Topics Stereochem. 18, 1 (1988).
2 B.L. Feringa, and R.A. van Delden, Angew. Chem. Int. Ed. 38, 3418 (1999).
3 S.F. Mason and G.E. Tranter, Proc. R. Soc. Lond. A 397, 45 (1985).
4 D.K. Kondepudi and G.W. Nelson, Nature, 314, 438 (1985).
5 W. J. Meiring, Nature, 329, 712 (1987).
6 J. L. Bada, Nature 374, 594 (1995).
7 J. Bailey, A. Chrysostomou, J.H. Hough, T.M. Gledhill, A. McCall, S. Clark, F. Ménard, and M. Tamura, Science 281, 672 (1998).
8 R.M. Hazen, T.R. Filley, and G.A. Goodfriend, Proc. Natl. Acad. Sci. 98, 5487 (2001).
9 F. C. Frank, Biochimi. Biophys. Acta 11, 459 (1953).
10 H. Wynberg, Chimica 43, 150 (1989).
11 K. Soai, S. Niwa, and H. Hori, J. Chem. Soc. Chem. Commun. 982 (1990).
12 K. Soai, T. Shibata, H. Morioka, and K. Choji, Nature 378, 767 (1995).
13 I. Sato, D. Omiya, K. Tsukiyama, Y. Ogi, and K. Soai, Tetrahedron Asymmetry 12, 1965 (2001).
14 I. Sato, D. Omiya, H. Igarashi, K. Kato, Y. Ogi, K. Tsukiyama, and K. Soai, Tetrahedron Asymmetry 14, 975 (2003).