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Chiral Symmetry Breaking in Nonequilibrium Systems

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Sensitivity of a nonequilbrium chemical system to small symmetry-breaking influences is analyzed in the context of chiral-symmetry breaking. For a hypothetical model system, with realistic kinetic constants, a reaction energy barrier difference of $\Delta E/kt = 10^{-17}$–10^{-15} is shown to be sufficient to have a strong chiral selectivity. This is in the range of the estimated energy differences between right- and left-handed molecules due to weak neutral currents.

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It is well known that *symmetry breaking* can occur in systems far from thermodynamic equilibrium.[1,2] In this note, we investigate the breaking of chiral symmetry in molecular synthesis, discuss the effects of small chiral influences on such processes, and obtain an order-of-magnitude estimate of the energy of interaction required to produce macroscopic chiral selection.

It has been shown that, depending on the symmetry that is broken, one can obtain the qualitative aspects of the symmetry breaking by obtaining the form of the bifurcation equations through group-theoretic methods[3]; such an analysis depends on the symmetry properties and not on the details, such as the exact nature of chemical kinetics, of the system. This procedure has been extended[4-7] to the consideration of the effects of small symmetry-breaking factors on the nature of bifurcation. It has been pointed out that nonequilibrium systems can become extremely sensitive and that this *sensitivity* may be characterized by general expressions.[8] This type of sensitivity can arise in several ways in dissipative structures.[9,10] Here we discuss such sensitivity in the context of chiral-symmetry breaking and illustrate the phenomenon using a simple model.

We consider the synthesis of a molecule that could be left- or right-handed in the absence of any chiral influence. When such a chemical system is near equilibrium both types of molecules will be produced in equal amounts. When the system is sufficiently far from equilibrium, however, there could result a state in which the concentrations of the left- and right-handed molecules are unequal.[11] We might expect such symmetry breaking, for instance, when there are autocatalytic effects.

Let $X \equiv (x_L, x_R, x_3, \ldots, x_n)$ denote the concentrations of the n reactants, x_L and x_R being the concentrations of the left- and right-handed species, respectively. For simplicity, we assume that the other molecules, $x_3, \ldots, x_n$, have no chirality. We denote the kinetics by $F(X, \lambda)$, λ being a parameter that denotes the nonequilibrium constraint on the system (typically, it is the concentration of one of the reactants that is maintained constant). The equation of the system is

$$dX/dt = F(X, \lambda). \tag{1}$$

Since we assume that F has no chirally selective kinetics, it must be covariant under the interchange of x_L and x_R. If we define a parity operator P, then $P(x_L, x_R, x_3, \ldots, x_n) = (x_R, x_L, x_3, \ldots, x_n)$, and we must have $PF(X,\lambda) = F(PX,\lambda)$. (Here we assume that λ is unaffected by P.) Thus F is covariant under the group $\mathcal{G} \equiv \{e, P\}$, e being the identity element. It follows that if X is a solution of Eq. (1) then PX is also a solution. When the system is near equilibrium the solution is symmetric, i.e., $PX = X$. The kinetics F could be such that when $\lambda < \lambda_c$ the steady-state solution is symmetric but, for $\lambda > \lambda_c$, the solution is asymmetric, i.e., $PX \neq X$; then Eq. (1) has two solutions, X and PX, that bifurcate at the critical value λ_c. If we denote the symmetric solution by X_S, then the bifurcating solution will be of the form[1,3] $X = X_s + \alpha X_A$, where X_A is the antisymmetric part, i.e., $PX_A = -X_A$. The "amplitude" α is determined by the bifurcation equation. The general form of this bifurcation equation may be determined from the condition that it must be covariant under the group $\mathcal{G}$ and that $\alpha = 0$ must be a solution.[3] In our case the group has only two elements and the covariance should be satisfied for $P\alpha = -\alpha$ and it is easy to see (see Ref. 3 for the general procedure) that the bifurcation equation is of the form

$$-A\alpha^3 + B(\lambda - \lambda_c)\alpha = 0. \qquad (2)$$

Here A and B are positive coefficients that can be computed from the kinetics F with the well-known methods of bifurcation theory (see Refs. 1 and 3, for example); their explicit form will be given below. For $\lambda > \lambda_c$, there are two nonzero solutions: $\alpha = \pm[(B/A)(\lambda - \lambda_c)]^{1/2}$; in one $x_L > x_R$ and in the other $x_R > x_L$. Which one of these states will be realized is not determined by the processes specified in Eq. (1). It is in this situation that small influences, which are normally ignored because their interaction energy is small, play a significant role.

We suppose now that there is a small perturbation present that alters the energies of the reaction intermediates in the synthesis reaction. Thus, taking the kinetic constants to have the Arrhenius form $K = Ce^{-E/kT}$, when E is the height of the reaction barrier the molecules must overcome, we suppose that the intermediates in the formation of the right- and left-handed products differ in energy by a small amount ΔE; thus $E_L = E_R + \Delta E$. Then the kinetic constants K_L and K_R will differ by a factor $e^{-g} \simeq 1 - g$ when $g \equiv (\Delta E/kT)$, as $\Delta E/kT \ll 1$. Thus $K_L = K_R(1-g)$.

Since $K_R \to K_L$ under parity inversion P, we must have $Pg = -g$. The equation of the system now contains the parameter g and is of the form

$$dX/dt = F(X, g, \lambda) \qquad (3)$$

and $PF(X,g,\lambda) = F(PX, -g, \lambda)$. Using this symmetry property of g one can show that[4-6] the corresponding bifurcation equation is of the form

$$-A\alpha^3 + B\alpha(\lambda - \lambda_c) + gC = 0. \qquad (4)$$

The effect of the symmetry-breaking perturbation g on the bifurcation diagram is shown in Fig. 1. Because of the chiral asymmetry in the kinetics the two branches are separated. As a consequence, as λ increases, depending on the sign of (gC), the system will evolve preferentially into one branch and not the other, unless there is a large enough fluctuation that knocks it to the other branch. The effectiveness of this macroscopic selection depends on the minimum separation

$$s = \tfrac{3}{2}(4Cg/A)^{1/3} = \tfrac{3}{2}(4C/A)^{1/3}(\Delta E/kT)^{1/3}.$$

The usual equilibrium factor $\Delta E/kT \ll 1$ appears here with an exponent $\frac{1}{3}$ because of the nonequilibrium nonlinearity in the system.

Since the fluctuations are inherent in a thermodynamic system, the effective chiral selectivity of g depends on the probability distribution of α. For almost all nonequilibrium systems (in particular the model we consider below) there is a critical slowing down and a separation of time scales.[2,12] For such systems we obtain an equation for the time evolution of α (the slow mode). To this equation we add a term $\epsilon^{1/2}F(t)$, representing the fluctuations, to obtain the Langevin

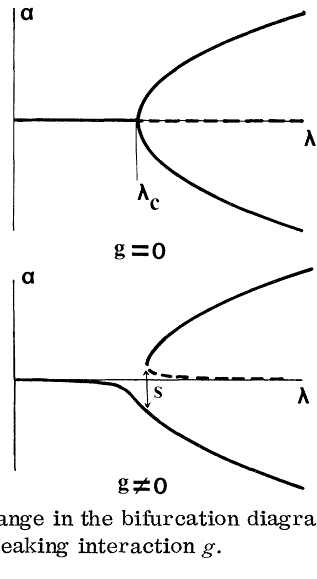

FIG. 1. Change in the bifurcation diagram due to symmetry-breaking interaction g.

equation:

$$d\alpha/dt = -A\alpha^3 + B\alpha(\lambda - \lambda_c) + gC + \epsilon^{1/2}F(t). \tag{5}$$

We assume that $F(t)$ is Gaussian white noise. The exact value of ϵ depends on the kinetics[13] but its order of magnitude is $(VN_A)^{-1}$, where V is the volume and N_A the Avagadro number. The probability distribution $P(\alpha)$ can now be obtained by use of the Fokker-Planck equation[14]:

$$P(\alpha) = N\exp\{[-\tfrac{1}{4}A\alpha^4 + \tfrac{1}{2}B(\lambda - \lambda_c)\alpha^2 + gC\alpha]/\tfrac{1}{2}\epsilon\}. \tag{6}$$

The maxima of this distribution correspond to the steady states of (5), which are the same as the solutions of the bifurcation equation. From this distribution the order of magnitude of chiral selection due to g can be obtained as follows. If λ passes through the critical point λ_c sufficiently rapidly in comparison with the branch-to-branch switching time, then the system will essentially remain on one branch and there will be very effective selection. If λ is varying very slowly, maximum switching will occur at the point of least separation. The probability of evolving into one of the branches depends on the relative time spent in that branch. We may take the value of $P(\alpha)$ at its maxima as the measure of the relative time spent in each branch. At the point where the separation s is minimum, $\lambda - \lambda_c = (AC^2/4)^{1/3}(3/B)g^{2/3}$. If α_1 and α_2 are the values of α at which P has its maxima, then it can be shown that $P(\alpha_1)/P(\alpha_2) = \exp(-2g^{4/3}\mathcal{C}/\epsilon)$ where $\mathcal{C} = \frac{27}{16}(4C^4/A)^{1/3}$, i.e., a term that depends on the kinetics. We can expect extremely good selection if the exponent $2g^{4/3}\mathcal{C}/\epsilon \sim 10$. With this criterion for observable effects we have the condition $\Delta E/kT \geqslant (5/\mathcal{C})^{3/4}(1/VN_A)^{3/4}$ where we have used the order-of-magnitude value of ϵ and the fact that $g = \Delta E/kT$.

To obtain a possible order of magnitude of $\mathcal{C}$, we consider the following scheme of reactions:

$$A + B \underset{K_{-1}}{\overset{K_1}{\rightleftharpoons}} x_{L(R)}, \tag{7a}$$

$$x_{L(R)} + A + B \underset{K_{-2}}{\overset{K_2}{\rightleftharpoons}} 2x_{L(R)}, \tag{7b}$$

$$x_L + x_R \xrightarrow{K_3} D. \tag{7c}$$

(Here, and in the equations below, $x_{L(R)}$ means that x_L could be replaced by x_R.) In this scheme the autocatalytic reaction (7b) is to be thought of rather as an effective reaction that represents a more complicated set of reactions. We assume that the concentrations of A and B are maintained constant by a suitable supply. Reaction (7c) denotes the removal of the products which, together with the supply of A and B, maintains the system far from thermodynamic equilibrium. Such a system is described by the kinetic equations

$$\frac{dx_{L(R)}}{dt} = K_1AB - K_{-1}x_{L(R)} + K_2x_{L(R)}AB - K_{-2}x_{L(R)}^2 - K_3x_Lx_R. \tag{8}$$

In this set of equations AB is the bifurcation parameter corresponding to λ. With the condition $K_3 > K_{-2}$, this scheme of reactions exhibits all the features discussed above. It is convenient to write Eq. (8) in variables $u \equiv (x_L - x_R)/2$ and $v \equiv (x_L + x_R)/2$. Solving the algebraic equations for the steady states $(dx_{L(R)}/dt = 0)$, one can easily see that there is a critical value $(AB)_c$, below which the steady state is symmetric, i.e., $u = 0$, and above which it is asymmetric, $u \neq 0$. The critical value is

$$(AB)_c = [s + (s^2 - 4K_2^2K_{-1}^2)^{1/2}]/2K_2^2$$

where

$$s = 2K_2K_{-1} + 4[K_{-2}^2K_1/(K_3 - K_{-2})].$$

For numerical estimates we give the following order-of-magnitude values for the kinetic constants: $K_1 \simeq 10^{-1}$ mole^{-1} s^{-1}, $K_{-1} \simeq 10^{-4}$ s^{-1}, $K_2 \simeq 10^{-4}$ mole^{-2} s^{-1}, $K_{-2} \simeq 10^{-4}$ mole^{-1} s^{-1}, and $K_3 \simeq 10^{-1}$ mole^{-1} s^{-1}. If we now introduce the symmetry-breaking term g, the kinetic constants for x_L and x_R will differ by a factor $1 - g$. To compute the chiral selectivity we need the coefficients A and C of Eq. (4). These can be obtained through the well-known methods of bifurcation theory (see, for example, Refs. 1, 7, and 8). The explicit expressions in terms of the kinetics F are

$$A = \frac{1}{3!}\sum_{i,j,k,l}^{n}\left(\frac{\partial^3F_l}{\partial x_i\,\partial x_j\,\partial x_k}\right)_0 \varphi_i\varphi_j\varphi_k\varphi_l^* + \sum_{i,j,k}^{n}\left(\frac{\partial^2F_l}{\partial x_i\,\partial x_j}\right)_0 h_i\varphi_j\varphi_k^*, \quad C = \sum_{k=1}^{n}\left(\frac{\partial F_k}{\partial g}\right)_0 \varphi_k^*.$$

Here F_k and X_k are the components of the vectors F and X of Eq. (3). φ_i and $\varphi_i{}^*$ are the null eigenvectors of the Jacobian matrix $F_{ki}{}^x \equiv \partial F_k/\partial X_i$ and its adjoint, respectively, evaluated for the symmetric steady states at the critical point, $g=0$, $\lambda=\lambda_c$. The subscript 0 denotes that all the derivatives are evaluated at $\lambda=\lambda_c$, $g=0$. It can be shown that

$$y_k \equiv \sum_{i,j} (\partial^2 F_k/\partial X_i\, \partial X_j)_0 \varphi_i \varphi_j$$

is orthogonal to φ^*. On the subspace orthogonal to φ^*, $(F^x)^{-1}$ is well defined and $h=(F^*)^{-1}y$. With these expressions $\mathcal{C}$ can be calculated. It is found that $\mathcal{C}\sim 10$ if the weak-interaction effect is included in K_1 and K_2, and $\mathcal{C}\simeq 10^{-2}$ if it is included only in K_2. In the vicinity of the critical value λ_c, the growth of α is slow (as can be easily checked) and diffusion keeps the system homogeneous over macroscopic volumes. Hence letting $V\sim 10^{-2}$ L, we obtain the condition for selection: $\Delta E/kT \geqslant 10^{-17}$ when $\mathcal{C}\sim 10$ and $\Delta E/kT \geqslant 10^{-15}$ when $\mathcal{C}\sim 10^{-2}$.

A possible source of the ΔE is the predicted weak-neutral-current energy difference between right- and left-handed molecules. (We are actually considering a ΔE between reaction intermediates. This should be at least of the same order of magnitude as ΔE for molecules.) Dimensional considerations lead to an estimate of $\Delta E \sim G\alpha^3 Z^5$,[15] where G is the Fermi coupling constant, α the fine-structure constant, and Z the atomic number of the chiral-center nucleus. Since ΔE must in reality vary with the degree of asymmetry, Hegstrom, Rein, and Sanders[15] define a molecular asymmetry factor η by $\Delta E = \eta G\alpha^3 Z^5$. Zel'dovich, Saakyan, and Sobel'man[16] estimate $\Delta E \simeq h\times 10^4\times(Z/100)^5 \simeq 7\times 10^{-33} Z^5$ erg, corresponding to $\eta\simeq 2\times 10^{-2}$. Hegstrom, Rein, and Sanders calculate ΔE for two specific molecular groups, finding $\Delta E\simeq 9\times 10^{-31}$ erg (for $Z=6$) and $\Delta E\simeq -9\times 10^{-33}$ erg (for $Z=16$) which correspond to $\eta=3\times 10^{-4}$ and $\eta=3\times 10^{-8}$, respectively; these authors note that η could be larger for other molecules. We note here that it is not necessary to assume that the chiral center is carbon; for example, for a reaction catalyzed by a metal ion complex the chiral center could be the metal ion, so that Z could be much larger: 45 for the case of rhodium, an important catalyst for chiral-specific reactions.[17] If we set $Z=45$ the estimates $\eta=2\times 10^{-2}$ and 3×10^{-4} correspond to values of $\Delta E/kT$ (for $T=300$ K) of 3×10^{-11} and 5×10^{-13}, respectively; for $Z=6$ we get $\Delta E/kT$ values 1×10^{-15} and 2×10^{-17}. On the other hand, estimates of $\Delta E/kT$ for macroscopic chiral interaction due to electric, magnetic, centrifugal, and gravitational fields give an upper bound of 10^{-17}.[18,19] These estimates, compared with the results of our calculation above, suggest that in spite of the extreme smallness of molecular weak neutral current effects, the possibility of their determining the macroscopic chirality of a system cannot be entirely ruled out.

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