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Molecular Dynamics Simulations of Kinetic Models for Chiral Dominance in Soft Condensed Matter*

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A molecular dynamics model of binary racemic fluid mixtures, consisting of particles which only differ a little with respect to the pair attractions, shows that the isomerization kinetics in condensed states can act as a driver towards a phase separation and a symmetry break so that one of the species finally dominates. The model offers a possible explanation of the origin of biomolecular chirality.

Key words: molecular dynamics simulation, models for isomerization kinetics, origin of biomolecular chirality

The basic hypothesis in the present investigation is that the asymmetry of nature and the origin of biomolecular chirality could be caused by small differences in the packing effectiveness of chiral molecules in racemic mixtures of *condensed* fluids. This small differences in the packing effectiveness of homochiral molecules are ensured in a qualitative way in the Molecular Dynamics models, by that particles of the same type interact with a slightly more attractive pair potential than pairs of particles with different chirality. The small differences are carefully chosen in such a way that the mixture of the two species, A and B, are totally mixed and thus do not result in a phase separation in the condensed mixture without isomerization kinetics [1]. The small difference in the range of the intermolecular potentials will, however, slightly favor packing of species of the same kind, which shows up as small differences in the particle distribution functions, which are qualitatively equal to the corresponding differences observed for racemic mixtures of aminoacids [2]. The systems and the isomerization kinetics are implemented as described in [3]. A more detailed report can be found in [4].

The molecular dynamic isomerization model

The systems consist typically of N = 40000 Lennard-Jones particles in an equilibrium state with temperature, T, and number density, ρ, which corresponds to a condensed fluid. The potential parameters σ and ε in the Lennard-Jones potential

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$$u_{LJ}(r_{ij}) = 4\varepsilon\left[\left(\frac{\sigma}{r_{ij}}\right)^{12} - \left(\frac{\sigma}{r_{ij}}\right)^{6}\right] \quad (1)$$

give the unit of length and energy. Before the isomerization kinetics are started, all the particles interact with Lennard-Jones potentials, which for computational reasons are truncated (as usual) at an interparticle distance $r_{ij} = r(cut) = 2.5\sigma$, which means that the actual pair potential between two particles, i and j, at a distance r_{ij} is

$$u(r_{ij}) = u_{LJ}(r_{ij}) - u_{LJ}(r(cut)) \quad (2)$$

and the systems are equilibrated at the condensed fluid state $(kT/\varepsilon, \rho\sigma^3) = (2, 0.8)$. At the beginning of the kinetics half of the particles is (randomly) labeled A and the other half is labeled B and the range of interactions is changed so that two A-particles or two B-particles still interact with the same Lennard-Jones potential, but an A-particle interacts with a B-particle through a LJ-potential which is truncated at a shorter distance $r_{AB}(cut) < 2.5\sigma$. Three values of $r_{AB}(cut)$: 2.0σ, 2.25σ and 2.4σ, respectively, are investigated in the simulations.

The isomerization kinetics is divided into two parts: At first (I) some particles, at time t, are activated and then in the second part of the kinetics (II) the conversions of the activated particles might happen. Concerning the first part, I, three different kinds of activation kinetics are investigated. In the first model the kinetics are performed at particle collisions. The isomerization is performed when a pair energy, $u_{ij}(r_{ij}(t))$, at a high energy collision between particle i and j, at time t exceeds the activation energy, E. The kinetics can be described by the reaction scheme

$$A + A \Leftrightarrow A + B \Leftrightarrow B + B \quad (3)$$

where the activation energy, E_{AB}, for that an AB collision can convert either the A-particle to a B-particle or *vice versa* must be less than the corresponding activation energy, $E_{AA} = E_{BB}$, for that one of the particles in a collision of particles of the same kind is converted. This inequality describes the fact that the stereo specific conformational form of a species in a condensed fluid is better maintained in an environment of the same type of enantiomer molecules. This "collision induced activation model" can be further simplified and in the second model the activation and eventual conversion from one type to the other is simply performed whenever the potential energy, $u_i(t)$, of a particle exceeds the activation energy, E. This kinetics corresponds to the reaction scheme

$$A \Leftrightarrow B \quad (4)$$

The third model describes the isomerization as an "enzyme activated process" (EAP). Whenever a particle diffuses into an enzyme volume, a conversion might take place. In principle the enzyme activated process is just a further obstacle to the simple isomerization model, given by (4), in the sense that not only can the isomerization

only be performed for a certain (low) activation energy; but it will only take place at certain locations in the volume. The "enzymes" must of course not favor one of the species. In practice the enzymes are randomly placed spheres of the sizes equal to the particles, and whenever a particle diffuses into an enzyme sphere a conversion might take place (which corresponds to ignoring the activation energy barrier by setting it to minus infinity).

In the second part, II, of the kinetics (still at time t) the conversions of the active particles might take place. At this stage of the simulation the program contains a list of particles which fulfil an activation criterion either by that their intermolecular energy exceeds the activation barrier or by that the particles have diffused into enzymes spheres. The conversions of the activated particles are then performed on basis of the energy difference between the two states, ΔE: Let particle i at time t be an activated A-particle. The total potential energy of the particle,

$$u_{i,A}(\mathbf{r}^{\mathrm{N}}(t)) = \frac{1}{2}\sum_{j}^{N} u_{LJ}(r_{ij}(t)) - u_{LJ}(r_{ij}(cut)) \tag{5}$$

is calculated. In (5) $u_{LJ}(r_{ij}(cut))$ depends on the identity of particle i and j, and it is different for an AB-interaction and for an AA- or BB-interaction, as described above. At the same time also $u_{i,B}(\mathbf{r}^{\mathrm{N}}(t))$ is calculated, *i.e.* the potential energy of particle No. i if the particle identity is changed to a B-particle. The difference between the two intermolecular energies

$$\Delta E = u_{i,B}(\mathbf{r}^{\mathrm{N}}(t)) - u_{i,A}(\mathbf{r}^{\mathrm{N}}(t)) \tag{6}$$

is then used as a criterion for the conversion. In most of the simulations the exchanges are simply performed when $\Delta E < 0$. It models a MD excited "molecule" with two equal intramolecular energy states and exposed to an external medium force, given by ΔE. In the excited state at the saddle point even a small external medium force will bring it toward the state with smallest intermolecular energy. But the intramolecular state A or B must be chosen with a Boltzmann probability, if one describes the medium effect as a thermodynamic force on the chiral molecule, and in a set of experiments, the identity is changed with the normalized Boltzmann probability

$$p = \frac{e^{-\Delta E/kT}}{1 + e^{-\Delta E/kT}} \tag{7}$$

often used for kinetics in statistical physics [5]. All three kinetic models, (I), and for both exchange criteria, (II), are bistable, when the reactions take place in a condensed fluid, and give a total dominance of one of the species; but it is not possible to predict which species will dominate, nor when the dominance appears, even if one starts from the same configuration and uses different models or reaction rates! More than hundred experiments with different sizes (N), dimensions (2D, 3D), temperatures, densities, differences in pair energies ($r_{\mathrm{AB}}(cut)$ = 2.0σ, 2.25σ and 2.4σ) and start

configurations gave an equal number of dominance of each species within the statistical accuracy. Both conversion criteria are autocatalytic. They favor domains of particles with same identity and it is this quality which ensures the symmetry break. Figure 1 demonstrates this fact. The figure shows the time evolution of the order parameter

$$\eta \equiv \frac{N_A - N_B}{N_A + N_B} \tag{8}$$

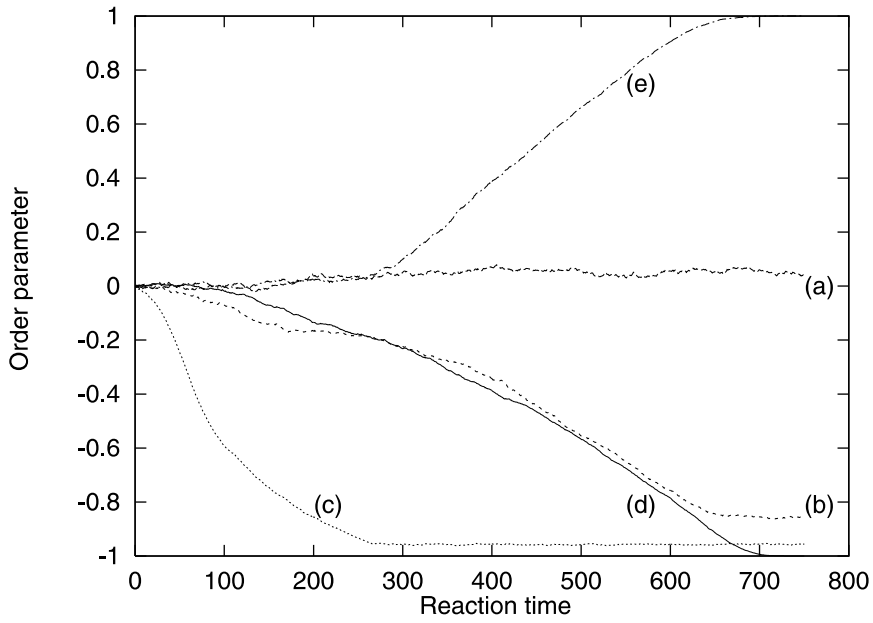

Figure 1. Order parameter, $\eta = (N_A - N_B)/(N_A + N_B)$, as a function of reaction time and using activation kinetics given by (2) and exchange kinetics given by (7). The reactions (a) – (d) are for $r_{AB}(cut) = 2.0\sigma$; and (e) are for $r_{AB}(cut) = 2.25\sigma$. The activation energy $E_{AB} = 3kT$ and different values of $E_{AA} = E_{BB}$. (a): $E_{AA} = E_{AB} + kT$; (b): $E_{AB} + 2kT$; (c): $E_{AB} + 3kT$; and (d): $E_{AA} = E_{BB} = \infty$.

for a 3D system of particles starting from the same configuration, but with different activation energies.

The bistability is manifested in two to three steps. What happen at first is that within a relatively short time the kinetics build up networks of micro-clusters of the two species due to the small energy gain by a conversion to a local environment consisting of particles of the same species. The diffuse percolating network of both species reminds of the early stage of spinodal decomposition in a critical mixture, but without conserved order parameter.

In the second part of the domain growth and kinetics driven phase separation there is a coarsening of diffuse subphases and the kinetics mainly take place in the interface zones. A species at an interface which is concave with respect to the same species will not be converted so easily as if its "own species" interface is convex. This is

simply due to the reacting particle having fewer nearest neighbors of its own kind when placed at a convex interface than a concave interface. But in some cases (especially in 2D) both species percolated the volume at early time of the evolution, and then the system can remain with both species in separated phases for a very long time. At first it might look as a mystery why one species after all is going to dominate the other in this case, since any percolating interface must contain convex as well as concave pieces. A picture of the interface between two percolating domains of A and B-particles explains, however, the phenomenon: Let this percolating interface be resolved in a sum of (concentration of a species) waves with different wavelengths. The kinetics will suppress all waves since the species will be removed from the convex top of its "home" phase and will be created at the concave bottom. But the kinetics will suppress the curvatures with the smallest wavelength, and for spinodal decompositions this coarsening will result in the final phase separation with equilibrium planar interfaces and with surface riplons with a non-critical power spectrum of frequencies. When this is not going to happen in the case of this kinetics driven separation, it is because the interfaces are established by the kinetics and the surface tension, γ, of the interfaces is very small due to the small difference in the potential energy of the two species with subphases of equal densities. This means that the kinetics driven phase separation in the second part of the time evolution has a structure with a *biased critical – like* behavior. It is biased because it suppresses the small wavelength fluctuations; but leaves the long wavelength fluctuations untouched, and it is critical-like due to the small surface tension. Thus, it is only a matter of time, even when the two percolating systems are fully separated, before a sufficiently big fluctuation breaks one of the connections between subdomains in one of the phases and then one of the species will dominate.

This explanation can be verified by starting from particle configurations with separated species in percolating subphases. The surface tension in these 2D and 3D systems with well defined interfaces can be calculated from the pressure tensor p_N and $p_T(z)$ normal and parallel to the interfaces [6].

$$\gamma = \int [p_N - p_T(z)]dz \tag{9}$$

The surface tension in a 3D system is almost zero, $\gamma\sigma/\varepsilon < 0.001$. The corresponding time evolution in 2D system (for illustrative reason) is demonstrated in Figure 2. Only the positions of the A-particle are shown in the figure, so the blank areas are filled with B-particles. The system is started with perfect separated species, and after a reaction time of 14500 (2.9×10^6 timesteps) the numbers of A-particles are reduced from 20000 to 15894 and the A-system seems to lose. The A-subsystem recovered, however, later and the configuration at the reaction time 56500 shows that the A-phase now percolates in both directions and with a droplet of a B-rich phase (due to the periodical boundaries the B-droplet are shown in three parts). This is the barrier for dominance and the last configuration shows the total dominance of the successful A-component at a somewhat later time and shortly after the remaining B-particles were converted.

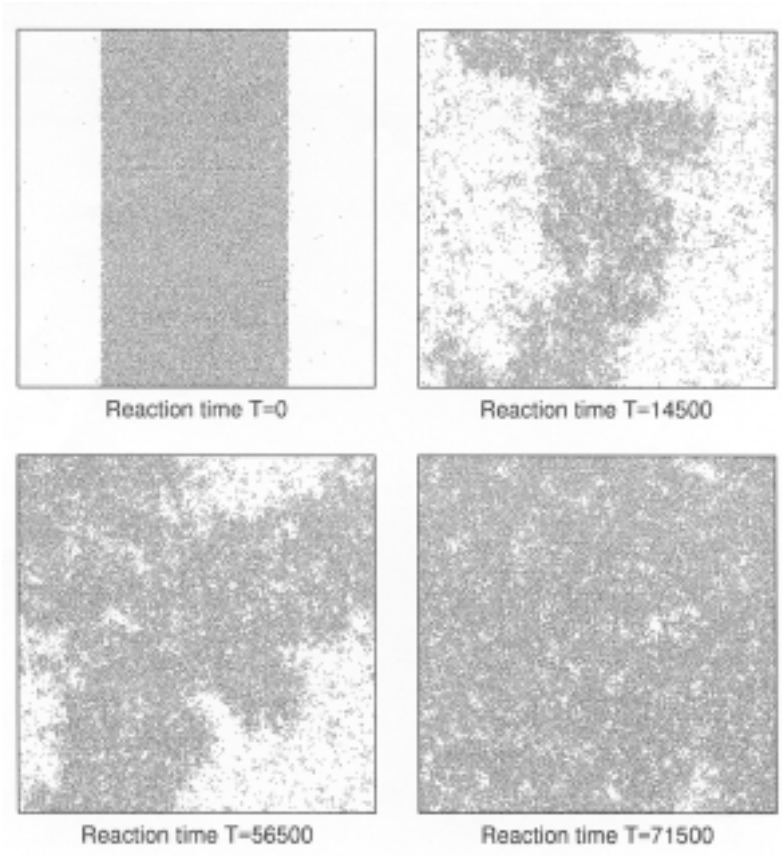

Figure 2. Particle configurations of the A-particles at different reaction times for a 2 dimensional system with activation kinetics given by (2) and conversion to minimum energy $\Delta E < 0$.

Discussion

The model offers a possible explanation of the origin of biomolecular chirality. The outcome: the symmetry break is robust with respect to the way the molecules are activated as well as the criteria for the conversion, and it indicates that the kinetic driven phase separation associated with the domain autocatalysis is not depending on the specific details in the MD model. It happens in condensed fluids in 2D as well as 3D, and for different temperatures, densities and for different degrees of packing effectiveness. It indicates a "generic" quality, as one should expect if this mechanism have been responsible for the symmetry break in nature, which means that the symmetry break have not appeared, due to a rare event; but is unavoidable in a condensed mixture of chiral biomolecules. The present model deviates from other models [7] for the symmetry break on a crucial point. Where other models introduce the symmetry break, necessary for the stereospecifique materials (*L*-aminoacids and/or *D*-glucose-like molecules) used in living organism, *via* a crystallization [8], or as

happen somewhere in the universe [9] and transported to the earth for further self-assembling [10], this model describes the purification as happens in soft condensed materials under pressure. The symmetry break is only the first step on a long route of self-assembling and it will be further supported by the weak parity violating forces [11], which constitutes a very small force difference between the two enantiomers asymmetry-centers. The gain in (Gibbs free) energy due to the packing effectiveness in a mixture of chiral molecules must increase with increasing pressure. One shall, however, expect that also the activation energy increases with increasing pressure. In order to obtain experimental evidence for the proposed mechanism of the symmetry break it might be necessary also to maintain a heigh isomerization rate, *e.g*. by use of stereo-neutral catalysis at solid surfaces.

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