

# Homochirality and the moment when life came about

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Many biomolecules are not mirror-symmetric. A particularly simple example are amino acids that can exist in two different enantiomers, the levorotatory (the L-form; the – form) and dextrorotatory (the D-form; the + form) forms, according to whether the plane of polarization of the incident polarized light is rotated to the right or to the left with respect to the direction of incidence of the light.

The amino acids in living matter occur almost always in the L-form. On the other hand, when amino acids are being synthesized in the laboratory, e.g. via the famous Urey-Miller experiment, a mixture of left and right handed amino acids are being produced. This is referred to as a racemic mixture of right and left handed molecules. When only one of the two enantiomers exists, one speaks of a homochiral state. Dead matter gradually loses its preferred handedness. This property, which depends on temperature, can sometimes be used as an approximate dating method. Thus, a preferred handedness of biomolecules is intimately related to the existence of life. It is this that connects the problem of homochirality to the origin of life.

## **Enantiomeric cross-inhibition: a serious problem?**

In an important paper Joyce et al. (1984) showed that template-directed oligomerization can only proceed efficiently in a homochiral environment. In a racemic environment the oligomerization quickly comes to a halt after forming only some dimers and a few trimers. This phenomenon is referred to as enantiomeric cross-inhibition, and it was long thought to be a serious problem to the idea of an RNA world. In a recent paper Sandars (2003) showed that enantiomeric cross-inhibition might not actually be a problem, but rather the key to producing a homochiral environment in which life can develop. In the following we shall describe this suggestion in some detail.

There are strong parallels with the idea by Frank (1953) according to which homochirality might be the result of two quite different processes, autocatalysis and some sort of mutual antagonism between molecules of opposite chirality. Frank's model was rather abstract, and not really related to any particular chemical reactions. The model of Sandars is more advanced in that hypothetical polymerization reactions were considered, but it too is only an idealization. The main problem is that in this context autocatalysis remains only a hypothesis. In fact, only a small number of autocatalytic processes are known so far. One of them is the reaction by Soai et al. (1995) in which pyrimidyl alkanol becomes enantiomerically enriched from the reaction of pyrimidine-5-carbaldehyde and diisopropylzinc. This reaction is not believed to be relevant in prebiotic chemistry, but it serves as a first example of an auto-catalytic reaction leading to homochirality. Furthermore, this process involves only monomers and dimers and is not able to form longer polymers as it is envisaged in the production of the first replicating molecules such as in the RNA world. Another interesting reaction is the Ghadiri reaction in which particular peptide chains can be replicated. Islas et al. (2004) showed that this reaction leads to the emergence of homochirality as well, but this only works for particular peptide chains and cannot be

generalized to longer peptide chains, as it would be required for the molecule to evolve into ever more complicated molecules via Darwinian evolution.

There is still another quite different proposal for producing homochirality within the framework of a peptide world. This model, which goes back to a recent paper by Plasson et al. (2004), is based on the fact that in peptides the epimerization rates on N-terminal residues are much higher than those on the C-terminal residues. In the following we contrast both approaches and discuss also the importance of considering the spatial extent of the systems where these reactions are to take place.

### **The essence of auto-catalytic models**

In order to appreciate the phenomenon of autocatalysis we consider here a simple model that captures the essentials of Frank's (1953) ideas. In this context, autocatalysis means that a molecule of one handedness makes more of itself by using building blocks from the substrate, S. However, with this effect alone both concentrations, [L] and [D], grow exponentially with time, but the enantiomeric excess would remain unchanged and equal to its initial value. Therefore, Frank assumed in addition some kind of antagonistic process resulting from a competition between left and right handed building blocks. Thus, one assumes that a reaction between L and D results in the production of achiral "waste" that we assume to be recycled back into the substrate. Such a system shows first of all that there is a possible racemic solution, but one can show that even a tiny imbalance can grow exponentially. This provides the basis for the statement that both autocatalysis and mutual antagonism are required for homochirality to emerge.

A non-vanishing growth rate means that the enantiomeric excess, e.e., will grow away from zero and, depending on the sign of the initial value of e.e., it will eventually get close to a homochiral state where  $|e.e.|=1$ . Indeed, there are steady homochiral solutions where either  $[D]=0$  or  $[L]=0$ . The evolution of e.e. is shown in Figure 1 for different initial values.

To illustrate what has happened, let us consider a simple numerical example. Start with an initial value of e.e. of 0.1, corresponding to  $[L]=0.367$  and  $[D]=0.3$  with a substrate concentration  $[S]=0.333$ . Assuming suitable model parameters, the amplification factor is then 33.3% for both fields. After a time  $t=1$  this would correspond to the increments  $\Delta[L]=0.12$  and  $\Delta[D]=0.10$ , respectively. This effect alone would lead to  $[L]=0.49$  and  $[D]=0.40$ , but e.e. would still stay at 0.10. However, with enantiomeric cross-inhibition we still have a uniform decrement of 0.11 for both fields, leading therefore to  $[L]=0.39$  and  $[D]=0.30$ , and thus  $e.e.=0.13$ , which means a considerable increase. The same steps are repeated many times until eventually  $e.e.=1$ .

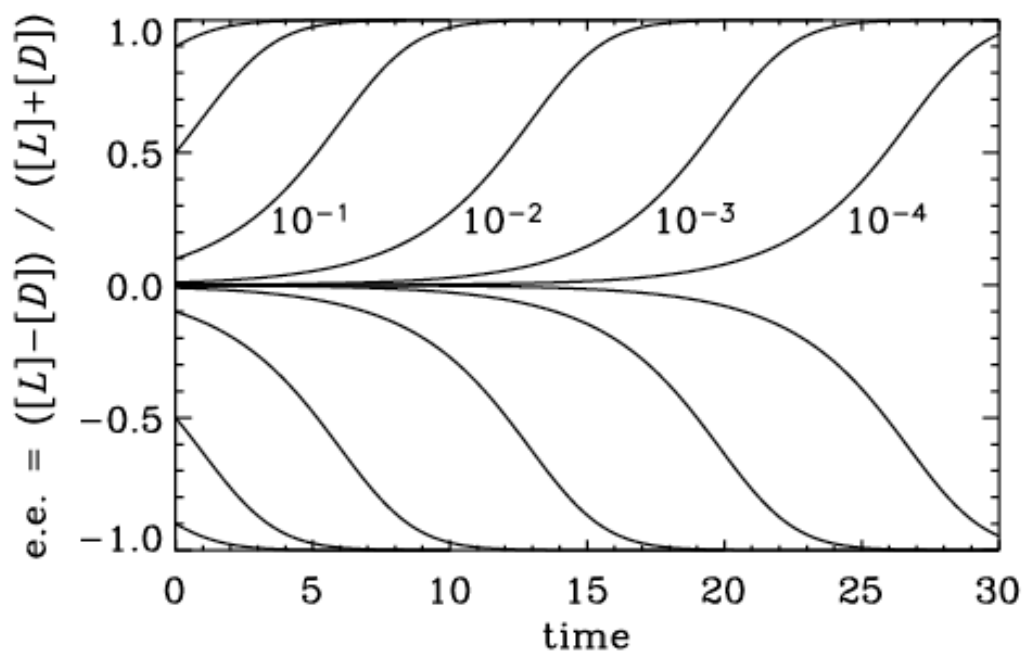


Figure 1: Evolution of the enantiomeric excess, e.e., for different initial values. The initial values of e.e. are indicated in most cases ( $\pm 10^{-4}$  ...  $\pm 10^{-1}$ ), except for e.e. =  $\pm 0.5$  and  $\pm 0.9$ .

Let us now highlight a difference in the directionality of polymerization between the polymerization model of Nilsson et al. (2005), where also achiral waste products contribute to the substrate, and the original one of Sandars (2003) and others after him. Sandars (2003) assumed that polymerization can proceed in either direction, which may indeed be possible in the polycondensation of peptide nucleic acids, but this is not the case in the polycondensation of RNA, where new monomers are only attached to the 3' end in the ribose sugar. Thus, the process is uni-directional. As a consequence, "semi-spoiled" compounds are already inactive, while in the Sandars model only compounds that are spoiled on both ends would be inactive. The same applies to the model of Brandenburg et al. (2005a), where we derived a reduced model consisting only of equations for the monomer concentrations, and to Brandenburg et al. (2005b), in which we considered a closed model where the inactive compounds were recycled back into the substrate. The polymerization process is represented pictorially in Fig. 2, where one can see how monomers begin to grow into longer chains, some of which can then be contaminated by a monomer of opposing chirality. The crossed-out chains represent polymers that can no longer grow.

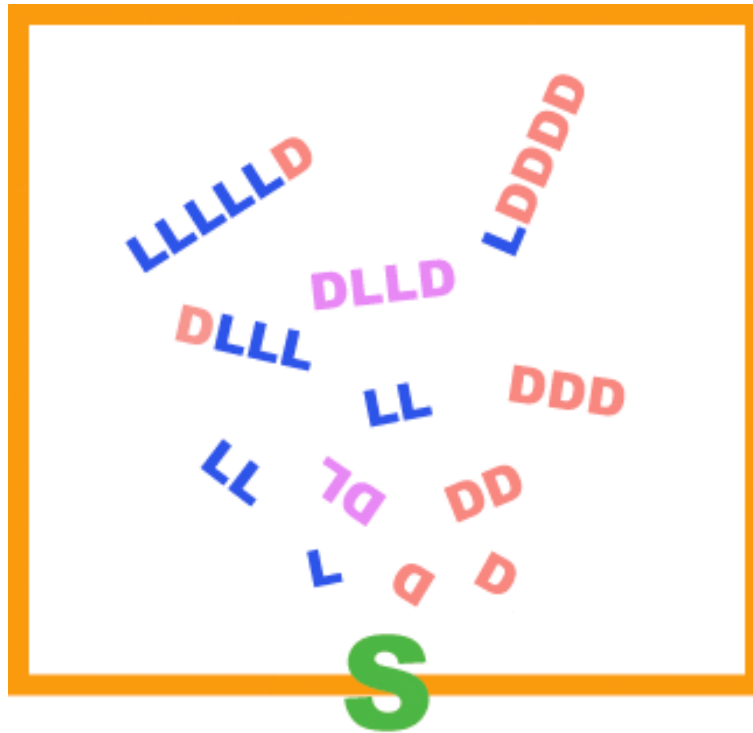


Figure 2: Polymerization process. In addition to a number of monomers, L and D, there are several isotactic dimers, LL and DD, as well as longer polymers. Semi-spoiled polymers such as LLLLLD and LDDDD can still polymerize on the unspoil end. Polymers such as LD and DLLD are dead and cannot polymerize further.

The reduced model of Brandenburg et al. (2005a) is of some interest because it has been used by Brandenburg & Multamäki (2004) to describe spatially inhomogeneous reactions where at some locations left-handed replicating molecules have begun to colonize the environment and right-handed ones at other locations. The main modifications necessary to include spatial extend to a chemical reaction model is to allow the concentrations to be not only functions of time, but also of space. Different spatial locations are coupled via diffusion and advection terms. Here,  $u$  is the velocity field of the solvent. If there is no advection, one only has diffusion which is far too small to establish spatially uniform homochirality over the Earth surface. However, some more or less strong fluid motions are likely to occur. In principle this model can also be applied to the motions in the deep biosphere, where life may have developed over long periods of time before ocean and atmosphere of the Earth became later habitable.

In Figure 3 we show the spatial evolution toward homochirality in a three-dimensional model where the fluid motions have been taken from simultaneously solving the equations of hydrodynamics with a forcing term included, modelling thus the effects of turbulence. In this model the typical time scale for achieving homochirality is the turnover time.

### **Homochirality within a peptide world**

It is worth noting that nucleic acid chemistry is sufficiently complicated and hard to envisage in a prebiotic environment that one should be open toward other potentially simpler mechanisms. One such mechanism was recently explored by Plasson et al. (2004) who used the fact that in dipeptides the epimerization rates, i.e. the

spontaneous change of chirality in one of the two amino acids, are different on the two ends. Epimerization occurs virtually only on the end with  $\text{NH}_2$ , i.e. on the N-terminal residue, and hardly at all on the end with  $\text{COOH}$ , i.e. the C-terminal residue.

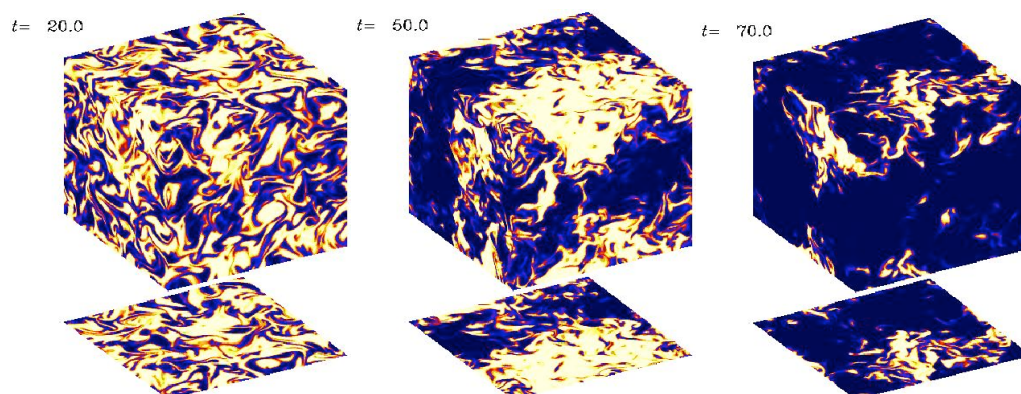


Figure 3: The spreading of homochiral regions in three dimensions. The dark (light) regions correspond to left (right) handed regions. The time  $t = 50$  corresponds here to about 2 turnover times. By the time  $t = 100$  (corresponding to 4 turnover times) the right handed life form went extinct.

It turns out that in the condensation to a dipeptide the handedness of what will become the second residue (C terminal) acts in a manner that is essentially equivalent to an autocatalytical conversion of an activated monomer of the opposite handedness into the same as that of the inducer. In other words, L induces the conversion of  $D^*$  into L and D induces the conversion of  $L^*$  into D. Thus, we can say that also the symmetry breaking described by the peptide model simulates autocatalytic behavior, although the molecules themselves do not possess catalytic activity. We note that there is also mutual antagonism, but in an explicitly productive manner without producing achiral 'waste' or degradation product. We will not go through the kinetics of these reactions, but let us stress that also in this model the linearized equations predict an instability of the racemic state.

## Conclusions

The main point of this work was to show that homochirality can emerge spontaneously and that the sense of handedness can turn to one of two possibilities, depending just on the details of the initial conditions. The chemistry would be the same if the chirality of all chiral molecules were reversed. This implies that, if there was a second genesis of life somewhere else in the Universe or even on Earth, it might well have been in such a way that the chirality of all chiral compounds was reversed simultaneously. Finding a second genesis of life is one of the great goals of astrobiology. Future missions to Mars do already allow for possibilities of determining the handedness of DNA molecules. However, even a positive detection of life on Mars, for example, even if it is now extinct, and of the same handedness as our live here on Earth, may not easily proof wrong the idea of a spontaneously growth of homochirality from an initially racemic environment. This is because of the possibility of transfer of life from Mars to Earth via impacts, and because of small-number statistics.

It should however be noted that there are a few stunning pieces of evidence pointing systematically into the direction of left-handed amino acids prevailing in some laboratory experiments, and in certain meteorite samples such as the Murchison

meteorite. The big contender in all these proposals is the possibility of contamination. This suggestion is supported by the fact that enantiomeric excess is mostly seen in those amino acids that are most prone to contamination. The only physical mechanism that could possibly distinguish between the two chiralities in exactly the right manner is the electroweak force, but the difference in binding energies is extremely tiny, even if the stereoselective difference is enhanced by four orders of magnitude. The latter has been suggested by the recent work of Plankensteiner et al. (2005), who appealed to the effects of certain more massive copper complexes that can produce chiral compounds. The mass ratio between copper and carbon enters with its fourth power in describing the energy difference, but even then the energy difference is still extremely weak. Thus, physically motivated mechanisms for producing a systematic bias in the initial enantiomeric excess are hard to believe, and it would therefore be an important goal to eliminate all possible effects of contamination in future laboratory experiments.

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