Homochirality as Prerequisite for the Origin of Life
R. Pohl

First presented as a poster at the Conference ‘Extraterrestrial Life – Beyond our expectations?’ Vienna, April 21st-22nd, 2012

I would like to thank the ‘EXO-Life’ forum Professor Dr. Maria G. Firneis and Mag. Johannes Leitner for their support.
Motivation

- Homochirality - - what is it all about?

- Take the left / left hand of your neighbour and shake
- Do the same with the right / right hand

- What is the result when you try to shake with your
  - Left hand your neighbour's right hand
  - Right hand your neighbour's left hand?

- We now have established the term ‘handedness’

- We transfer these findings to chemical molecules like
  - Amino acids
  - Sugars (e.g. pentoses)
Chirality of amino acids

- We see the principle picture of an amino acid having four different ligands at one carbon atom.
- This construction makes the C*-Atom optical active.
- Two different molecules of the same formula are existing, behaving like picture and mirror picture.
Chirality of pentoses

- We see a sugar molecule where three carbon atoms having each four different ligands at one carbon atom
- It exists DDD-Ribose where LLL Ribose is its mirror picture

\[
\begin{align*}
\text{D-Ribose} & : & \begin{array}{c}
\text{O} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{CH}_2\text{OH}
\end{array} & \quad & \begin{array}{c}
\text{O} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{CH}_2\text{OH}
\end{array} \\
\text{L-Ribose} & : & \begin{array}{c}
\text{O} \\
\text{OH} \\
\text{HO} \\
\text{HO} \\
\text{CH}_2\text{OH}
\end{array} & \quad & \begin{array}{c}
\text{O} \\
\text{OH} \\
\text{HO} \\
\text{HO} \\
\text{CH}_2\text{OH}
\end{array}
\end{align*}
\]
Synthesis of molecules is always racemic, which means that they result in equal concentrations of each chiral isomer (enantiomer).

Living matter is different:
- proteins contain almost exclusively L-amino acids
- while only D-sugars appear in RNA and DNA

Figure 1: L- and D- Alanine

Figure 2: L- and D- Ribose
Alpha-helix and beta-sheets (seen below) are the most common secondary structures of proteins.
Both are based on a strictly homochiral origin, because otherwise no regular organization is possible.
That means either L-amino acids or D-amino acids can form these structures.
Homochirality as Prerequisite for the Origin of Life

Organization of Life

Quartärstruktur

Tertiärstruktur

Sekundärstruktur

α-Helix

β-Faltblatt

Primärstruktur

Tyr-Lys-Ala-Ala-Val-Asp-Leu-Ser-His-Phe-Leu-Lys-Glu-Lys
Asp-Trp-Trp-Glu-Ala-Arg-Ser-Leu-Thr-Thr-Gly-Glu-Thr-Gly-Tyr-Pro-Ser
The common (furanosyl) form of RNA (fRNA) may have replaced the pyranosyl form (pRNA), in spite of the fact that pRNA has a stronger and more selective base-pairing system.

When one of the (D)-ribopyranosyl units at any position of a homochiral (D)-tetramer is replaced by a corresponding (L)-unit, the rate of oligomerization is reduced by about two orders of magnitude.
To describe the occurrence of an imbalance between left and right handed molecules the enantiomeric excess (ee), is used, where

\[ ee = \frac{(L-D)}{(L+D)} \]

Discussions of how an imbalance could have originated here on Earth producing an ee was often debated with the question of whether life was preordained to be based on D-sugars and L-amino acids or whether this happened by chance.

This implies that a life form based on the opposite chirality might have been just as likely at the beginning.
More than 60 years ago, Frank developed a mathematical model for an autocatalytic reaction mechanism for the evolution of homochirality (Frank 1953; Calvin 1969).
An autocatalytic reaction has been reported to verify the considerations of Frank (Soai et al. 1995), applied to amino acids (Klussmann, 2007 and Blackmond, 2012).
In the Salt-Induced Peptide Formation (SIPF) reaction a preference for the L-form of several amino acids was suggested. A survey of several amino acids was performed but the results were not satisfactory for all tested amino acids (Fitz et al. 2007).
Saghatelian et al. (2001) reports a chiroselective peptide replicator resulting in about 70% diastereomeric excess at low concentrations. The increasing diastereomeric excess expressed as

\[ \text{ee Diast.} = 100 \cdot \frac{(T_{LL} + T_{DD}) - (T_{DL} + T_{LD})}{T_{Total}} \]

show a function of time signifying amplification of homochiral products.
Enantiomeric excess

- Takahashi et al. (2009) reported on the influence of synchrotron-radiation on amino acids and circular polarized light from space as origin of terrestrial homochirality. This has been considered tentatively by Bailey already (1998).
- Unfortunately in the case of alanine the D-alanine is produced slightly more than the L-form. So maybe on another planet a D-amino acid / L-sugar world could be established.

CD spectra of DL-alanine films after CPL irradiation: L induced CPL [orange (2 mWh) and red (10 mWh)]; D-handed CPL (light blue and blue).
Enantiomeric excess

- An extraterrestrial origin of chirality is strongly debated. But this is only exporting the problem!
- Racemic mixtures of amino acids may be turned by catalytic processes on the surface of minerals (Hazen, 2010).

- The discovery of an excess of chiral organic compounds in the Murchison meteorite supports this view.
- Burton described 2012 the ee in materials from CI, CM and CR carboneous chondrites, however, only up to 18 % for selected amino acids.
Selective absorptions are feasible. Hazen, 2007, confirmed these results by demonstrating that D-aspartate binds to the calcite surface, which is a prerequisite of chiral selection.

The D- enantiomer, which requires significantly less calcite surface relaxation and aspartate distortion, is favoured by 8 kcal/mol. This is until today the largest known enantiospecific effect. This mechanism could concentrate L-forms in the solution close to the crystals.
RNA World first

- It might be imagined that all of the components of RNA were available in some prebiotic pool.
- These components assembled towards replication, evolving polynucleotides' without the prior existence of any evolved macromolecules (Robertson 2010).
- What other genetic systems might have preceded the RNA World? How could they have “invented” the RNA World?
LUCA was a protoeukaryote, with a RNA genome inherited from its progenote ancestor.
On the theoretical side, there has been an explosion of computer simulations and analytical models for complex collective behaviours of prebiotic chemical mixtures. Most of the popular versions tend to be variations of Eigen’s original Hyper-Cycle Concept (Eigen and Schuster 1977).

Eigen’s earlier model (1971) envisages a population of replicating polynucleotide’s that draw on a limited supply of activated mononucleotides to produce additional copies of themselves.
Using a code, in which each letter (and word spacing) is represented by a quintet of binary symbols.
The information content amounts to $v_m=125$ bits, allowing for about $4 \times 10^{37}$ alternatives. Evolution is very efficient near the critical value $1 – q$ of about $\sim 1/v_m$ which with $v_m=125$ amounts to $q = 0.992$.
The example left shows the catastrophic nonsense at $q$ of only 0.985.

<table>
<thead>
<tr>
<th>No. of generation</th>
<th>Best sentence</th>
<th>No. of mistakes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TAKE ADVANTAGE OF MISTAKE</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>TAKF !DVALTAGE OF MISTAKE</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>TALF ADVALTACE OF MISTAKI</td>
<td>5</td>
</tr>
<tr>
<td>20</td>
<td>DAKE ADUALEAGE OF MJUTAKE</td>
<td>6</td>
</tr>
<tr>
<td>40</td>
<td>TAKE ADVONTQCU OF MFST!ME</td>
<td>7</td>
</tr>
<tr>
<td>71</td>
<td>TAKEB ?VALTAGI LV MIST!KE</td>
<td>8</td>
</tr>
</tbody>
</table>

71 generations for $q=0.97$ (error rate 3%)

?AMEBADTIMOACFHQEBA!STBMF 18
For the Eigen model it was absolutely necessary that the chirality of the components, which were reduplicated, must be in the range of more than 99% purity in order to avoid lethal errors.

None of the foregoing methods and processes can provide such single chirality.
Summary and Outlook

- Life did not emerge in a single step.

- In chemical evolution, the first formation of a self-replicating molecule was probably one of the most critical bottlenecks.

- This was overcome only with a very low probability.

- We know little of the abiotic ingredients and prebiotic chemistries present on the primitive Earth.

- Various theories about the mechanisms of enantiomeric excess processes have been presented and their potential mechanisms could be:
Summary and Outlook

Mechanisms proposed:

- ‘Metabolism-first’ models, such as the iron-sulphide world hypothesis
- ‘Membrane-first’ lipid-world scenarios
- ‘Peptide-first’ models and
- ‘Genetics-first’ hypotheses such as in the RNA and pre-RNA world scenarios.

Closely connected with all theories is the question of the homochirality origin, or why bio-molecules display the same perfect spatial pattern.

The beauty of the ‘simple’ idea pre-RNA/RNA first is, that life started by using a self-sufficient replicator and that it needs only one of such successful event.

Therefore, the present-day life would originate from a single molecule only. However, this idea does not explain at all, why L-amino acids and D-sugars were chosen.
The conclusion I would draw is, that despite a large amount of both theoretical and experimental efforts put into the problem, the emergence of homochirality is agreed to be a necessity in our bioorganic world but remains an open question.
References (a small selection)


References (a small selection)

Fitz D. et al.(2007), Possible origins of biohomochirality, Current Chemical Biology (1), Bentham Science Publishers Ltd., pp.41-52


Jaakkolaa S. et al. (2008), Cause of chirality consensus, Current Chemical Biology, 2, pp.153-158


