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Why are the molecules of life always left- or right-handed?

Cornelia Meinert
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How did life begin?

There can hardly be a greater question. With the rapid progress in the field of molecular biology and the discovery of the structure of DNA, which revealed life's building blocks at a molecular level, our vision of life and its origin have been constantly challenged. It is widely accepted that Earth was formed about 4.5 billion years ago and that life must have appeared on the early Earth anywhere between 4.1 and 3.8 billion years ago (Javaux, 2019). However, one of the oddest aspects of life on Earth which puzzles chemists, biologists and physicists alike, is nature's choice of using only one of two possible mirror images for building up its molecular machinery. Each of the monomers (sugars and amino acids) constituting life's biopolymers, primarily nucleic acids and proteins, have a mirror image twin. Just like our left hand mirrors our right hand, but can never be superimposed on the same space, amino acids and sugars exist in both left- and right-handed forms.

Proteins—the workhorse in all living cells—are made up of hundreds of thousands of amino acids, which are all left-handed. While ribose, the chiral sugar subunit upon

which nucleotides build the structure of RNA and DNA is always right-handed. This phenomenon of selecting only one molecular handedness is called *homochirality* of life or *biomolecular asymmetry*. If you synthesise amino acids and sugars in the laboratory, you will always get equal amounts of left and right. Since life does not (and could not) work with a mixture of both, the question is: how and why did life select left-handed amino acids and right-handed sugars?

While several potentially prebiotic routes towards the synthesis of biological building blocks have been reported (Miller, 1953; Powner et al., 2009; Xu et al., 2020), none of them account for the chiral symmetry breaking inherent to all biopolymers. Theories developed to explain the ultimate cause of homochirality on Earth include random mechanisms, i.e. undirected processes that lead to the appearance of biomolecular asymmetry by stochastic fluctuations with a 50:50 chance—like flipping a coin. Alternative theories emphasise the possible role of an inherently chiral bias of external origin (Evans et al., 2012). Circularly polarised light (CPL) appears to be one of the most promising candidates for such true-chiral force, as it can generate absolute molecular asymmetry.

Life's handedness might stem from our sun's stellar birth cluster

The enrichment of naturally occurring L-amino acids found in carbonaceous meteorites (Cronin and Pizzarello, 1997)—the remnants of space rocks that occasionally hit Earth and did so in large numbers during the heavy bombardment period shortly after Earth was formed—offers the sole example of asymmetry outside of the biosphere and has raised the hypothesis of a possible link between astrochemical evolution and the origin of homochiral biomolecules. Indeed, a molecular cloud, of the sort in which our Solar System was formed, may have also caused a left-handed preference for amino acids. The radiation of a nearby star within such a dusty star-forming cluster can scatter on dust particles resulting in high degrees of CPL that interacts differently with two mirror images of a chiral molecule. Stellar CPL is arguably the most compelling

argument to explain the molecular asymmetry of meteoritic amino acids and has been detected in the active sites of several star-forming regions (Kwon et al., 2013).

Our former studies on the interaction of 'chiral photons' with organic molecules successfully demonstrated: i) the *enantioselective photolysis* of racemic amino acids by circularly polarised synchrotron light (Meinert et al., 2014) and ii) the *asymmetric photochemical synthesis* of amino acids from solely one carbon- and one nitrogen-containing molecules by simulating interstellar environments (de Marcellus et al., 2011). Both approaches are based on circular dichroic transitions, and we have been developing state-of-the-art synchrotron radiation circular dichroism and anisotropy spectroscopy with our collaborators at ASTRID2 (Aarhus University, Denmark) (Meinert et al., 2012). Our recent discovery that besides amino acids the central chiral unit of RNA, ribose, also forms readily under simulated

comet conditions (Figure 1) (Meinert et al., 2015), provided further evidence that interstellar photosynthetic processes during protoplanetary disc formation can trigger the synthesis of life's building blocks. It remains to be proven whether meteoritic sugars carry the biological signature of the right-handed form. However, it is widely accepted that comets and other small bodies, such as asteroids and interplanetary dust particles, have survived impact events and delivered huge amounts of these extra-terrestrial organic molecules to Earth (Oró, 1961) and possibly also to exoplanets. Interstellar ice chemistry cannot be expected to reflect prebiotic chemistry itself. However, the chemical reactions formed under low temperature and low pressure conditions triggered by ultraviolet CPL radiation could have shaped the prebiotic chemical networks of the early Earth by providing the starting portfolio of enantiomer-enriched products from which biosynthetic pathways evolved on the early earth.

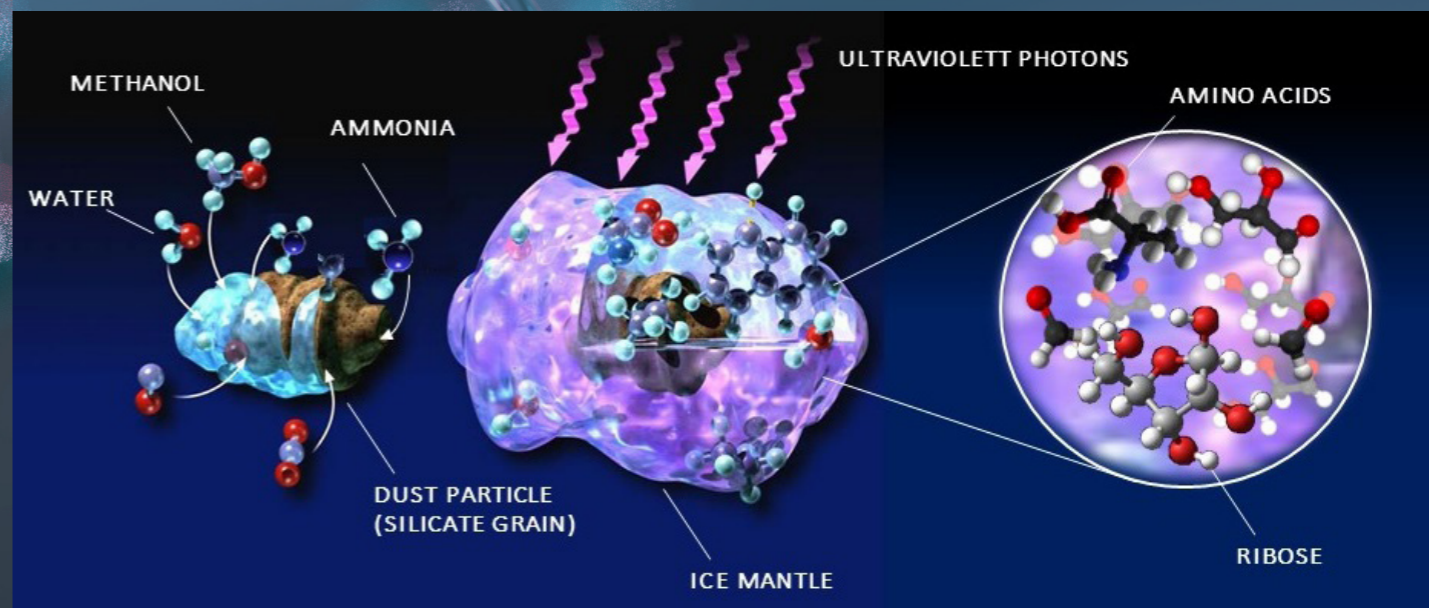


Figure 1: Deep-space amino acids and ribose may reveal clues about the origins of life. Interstellar dust particles (IDP) covered with thin ice layers containing molecules such as H_2O , CH_3OH , and NH_3 (left). IDP with a thick ice layer irradiated by UV radiation (middle). UV processing of these analogues represents a template of the evolution of interstellar ices in molecular clouds.



Photo: The A-LIFE team. Left to right: Postdoc Dr Jana Bockova, PhD student Adrian Garcia, PI Dr Cornelia Meinert, ASTRID2 collaborator and visiting scientist Dr Søren V. Hoffmann, PhD student Raphaël Pepino, and ASTRID2 collaborator and visiting scientist Dr Nykola C. Jones.

The asymmetry of life: towards a unified view of the emergence of biological homochirality

The significance of the A-LIFE project arises due to the current lack of experimental demonstration that the biomolecular single-handedness of the building blocks of the complex trinity—DNA/RNA, proteins and lipids—can simultaneously and asymmetrically be synthesised by a universal physical selection process. Our aim is, therefore, to develop a synergistic methodology to build a unified theory for the origin of all chiral biopolymers, from rich interstellar ice chemistry as nurseries for the formation of life's chiral monomers, with special emphasis on their stereoselective evolution in cometary and meteoritic matter, to their accumulation and amplification on the early Earth. The successive systems will be experimentally simulated in chemical reactors combining novel circularly polarised laser and synchrotron sources with experiments on how life's building blocks assembled



Figure 3: Japan's Hayabusa 2 spacecraft (left) and NASA's OSIRIS-REx probe (right) will bring back precious samples from the near-Earth asteroids Ryugu and Bennu to shed light on the origins of the Solar System and life on Earth.

themselves into homochiral functioning macromolecular systems allowing them to exhibit biological behaviour. Our laboratory data on the 'chirality-transfer' from CPL to molecules of prebiotic relevance, combined with advanced analyses of extra-terrestrial samples (Figure 2), including those from the current asteroid sample return missions OSIRIS-REx and Hayabusa 2 (Figure 3), will afford a visionary step forward in our understanding of the formation of pristine organic molecules and the origin of biomolecular asymmetry.

Looking beyond Earth

If the bias towards left-handed amino acids and right-handed sugars originated in space, it most likely extends across other places in our Solar System where environmental conditions allow prebiotic chemistry to evolve, such as beneath the surface of Mars, or in the oceans under the icy crusts of Enceladus and Europa. We are therefore convinced that our current research on understanding plausible pathways for

the origin of homochiral life will directly contribute to our understanding of the indispensable properties of life on Earth, as well as inform our search for life on other worlds through the use of molecular chirality as a key biosignature in current and future space exploration studies.

Moreover, we would like to reach out to the general public with this fascinating research and positively impact teaching and higher education programmes on the origin of life and evolution, as well as attracting young people towards physical and natural sciences.

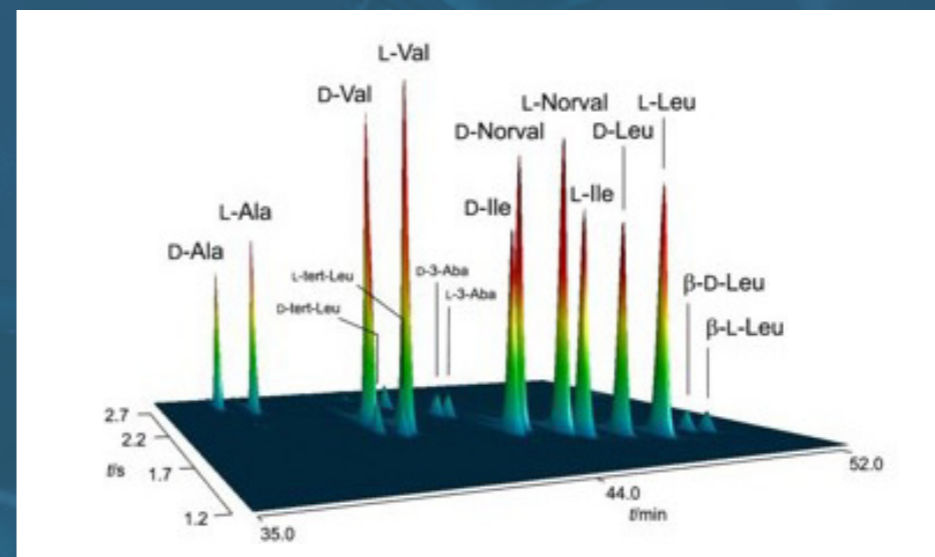


Figure 2: Chiral resolution of amino acid enantiomers in a sample of the Murchison meteorite using GCxGC-TOFMS.

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SUMMARY

The ERC Starting Grant project "A-LIFE" aims to understand the origin of life's homochirality—the exclusive use of one chiral molecule over its mirror image in all extinct life forms. Experiments on the chirality transfer from circularly polarised light to matter combined with data from current space missions will build a unified theory for the origin of all chiral biological building blocks.

PROJECT LEAD PROFILE

Cornelia Meinert holds a PhD in chemistry (Germany) and started her independent research career in 2013 as a CNRS Research Scientist at the Institute of Chemistry of Nice. She is Executive Councillor of the SFE and ISSOL Society. Her work combines astrochemistry with state-of-the-art analytical methods. She enjoys working in an interdisciplinary research team with excellent collaborators and supportive mentors.

PROJECT PARTNERS

The ALIFE project is based at the University Côte d'Azur and the Centre National de la Recherche Scientifique, CNRS. Collaboration partners include groups from the synchrotron SOLEIL (France) and ASTRID2 at Aarhus University (Denmark), the W.M. Keck Laboratory at the University of Hawaii (USA), and NASA's Goddard Space Flight Center (USA).

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