Chirality and Life: what, why, how and who cares?

A diagram of left-handed and right-handed versions of the amino acid isovaline, found in the Murchison meteorite.NASA Image courtesy of NASA

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Why is life chiral?

- Compatibility: Biological systems require uniform chirality for their components to fit together and interact correctly, much like a glove only fits a specific hand.
- Function: Proteins, DNA, and RNA will not function properly or fold correctly if they contain a mixture of left- and right-handed molecules.
- Efficiency: A single handedness for molecules ensures that enzymes only need to process one type of molecular building block, preventing inefficiencies that would occur if they had to recognize and metabolize both forms.

How did chirality emerge?

- At some point a specific form of amino acid (left-handedness) became dominant, possibly due to extraterrestrial influences from meteorites, polarized light, or magnetic fields interacting with prebiotic chemistry, which then led to the preferential use of that handedness in the building blocks of life, such as proteins, creating homochirality. This selection process was amplified and perpetuated, as chiral molecules like enzymes can only interact with one specific handedness, preventing the other form from being incorporated.

- Once a bias toward one chiral form emerged, it was amplified through biochemical reactions. A "frozen accident"

When did Chirality

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Prebiotic World

Experimental Formation of Dipeptides From Racemic Mixture

"we discovered that the reaction favours heterochiral ligation ... We demonstrate, paradoxically, that this heterochiral preference provides a mechanism for enantio-enrichment in homochiral chains."

Deng, M., Yu, J. & Blackmond, D.G. Symmetry breaking and chiral amplification in prebiotic ligation reactions. Nature 626, 1019–1024 (2024). https://doi.org/10.1038/s41586-024-07059-y

Did Meteorites Bring in an Enantiomeric Excess?

The most common theory is that some were transformed by radiation from a certain kind of faraway neutron star. The UV, circular-polarized light from these stars hit the asteroids causing a disproportionately large number of L amino acids. Thus all life in our solar system would tend towards L aa.

Results From Asteroid Bennu (Collected by OSIRIS-REx)

"All chiral non-protein amino acids were racemic or nearly so, implying that terrestrial life's left-handed chirality may not be due to bias in prebiotic molecules delivered by impacts. "

Glavin, D.P., Dworkin, J.P., Alexander, C.M.O. et al. Abundant ammonia and nitrogen-rich soluble organic matter in samples from asteroid (101955) Bennu. Nat Astron 9, 199–210 (2025). https://doi.org/10.1038/s41550-024-02472-9

Scrambling of Chirality

the L handedness of aa may have been derived from a special group of aa,with an extra methyl group that prevented loss of their small excess of the L form by a process that can scramble the handedness of ordinary aas on prolonged heating. These aa were in Murchison and the excess can be amplified in water.

Levine M, Kenesky C, Mazori D, Breslow R (2008) Enantioselective synthesis and enantiomeric amplification of amino acids under prebiotic conditions. Org Lett10:2433–2436. Breslow R, Levine M (2006) Amplification of enantiomeric concentrations under credible prebiotic conditions. Proc Natl Acad Sci USA 103:12979–12980.

When did Chiralit[y] emerge[d]?

1 Prebiotic World

2 RNA world

Can Excess L Amino Cause D Sugars?

“We .. find that the geometry of sugars referred to D, as in D-ribose or D-glucose, is not an independent mystery. D-glyceraldehyde, the simplest sugar with a D center, is the basic unit on which other sugars are built. We find that the synthesis of glyceraldehyde by reaction of formaldehyde with glycolaldehydeis catalyzed under prebiotic conditions to D/L ratios greater than 1, to as much as 60/40, by a representative group of L-amino acids (with the exception of L-proline).

Breslow and Cheng. 2010. L-amino acids catalyze the formation of an excess of D-glyceraldehyde, and thus of other D sugars under credible prebiotic conditions. PNAS | | vol. 107 | no. 13 | 5723–5725

Experimental Formation of Dipeptides From Racemic Mixture

Aminoacylation using D-RNA may be inherently biased toward reactivity with L-amino acids, implying a deterministic path from a D-RNA World to L-proteins. Using a model system of self-aminoacylating D-ribozymes and epimerizable activated amino acid analogs, we test the chiral selectivity of 15 ribozymes. All of the ribozymes exhibit detectable selectivity, and a substantial fraction react preferentially to produce the D-enantiomer of the product. These results are consistent with the transfer of chiral information from RNA to proteins but do not support an intrinsic bias of D-RNA for L-amino acids. Different aminoacylation structures result in different directions of chiral selectivity, such that L-proteins need not emerge from a D-RNA World.. Kenchel, J., Vázquez-Salazar, A., Wells, R. et al. Prebiotic chiral transfer from self-aminoacylating ribozymes may favor either handedness. Nat Commun 15, 7980 (2024). https://doi.org/10.1038/

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Prebi

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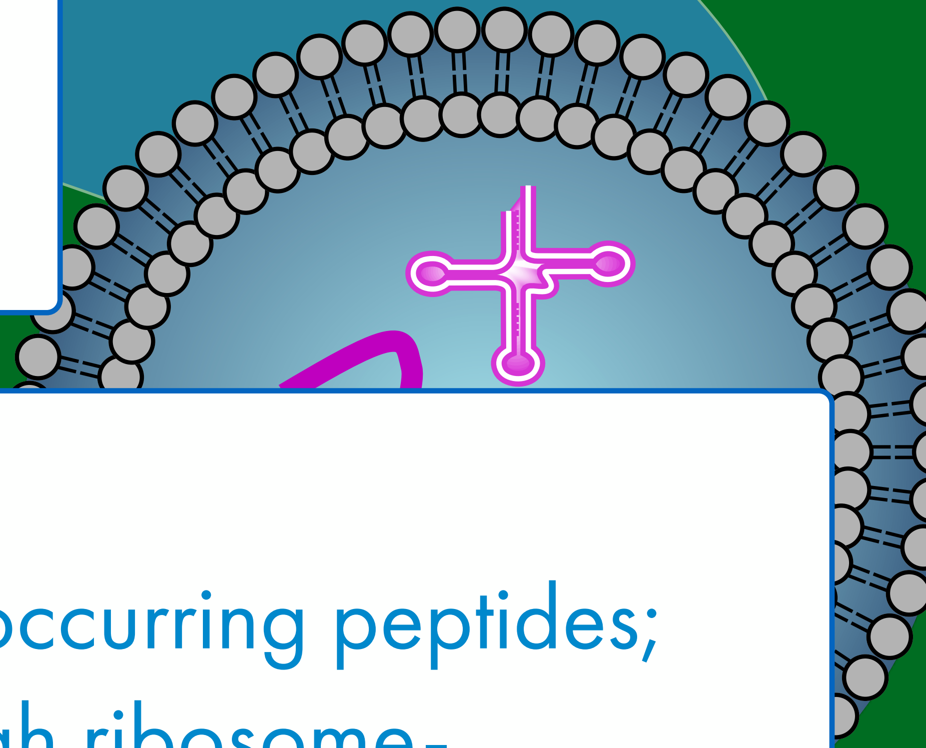
s coding and catalytic molecule)



Life Uses Some L Sugars and D Amino Acids

The presence and detection of D-amino acids in various organisms, along with their enzymatic conversion from L-amino acids, highlight their significance beyond their typical function in protein structure.

L-glucose is a an L-sugar that is not metabolized by humans. Can be used as Low-Calorie Sweetener Viking legacy) and bulking agent in food.

D-amino acids act as important biological signaling molecules, particularly in bacteria for regulating biofilm formation and peptidoglycan metabolism, and in animals, for example, D-serine's role in neurotransmission.

Epimerases and Isomerases

EC 5.1 Racemases and epimerases

This subclass contains enzymes that catalyse either racemization or epimerization of a centre of chirality. Sub-subclasses are based on the substrate: amino acids and derivatives (EC 5.1.1), hydroxy acids and derivatives (EC 5.1.2), carbohydrates and derivatives (EC 5.1.3), or other compounds (EC 5.1.99).

Coup

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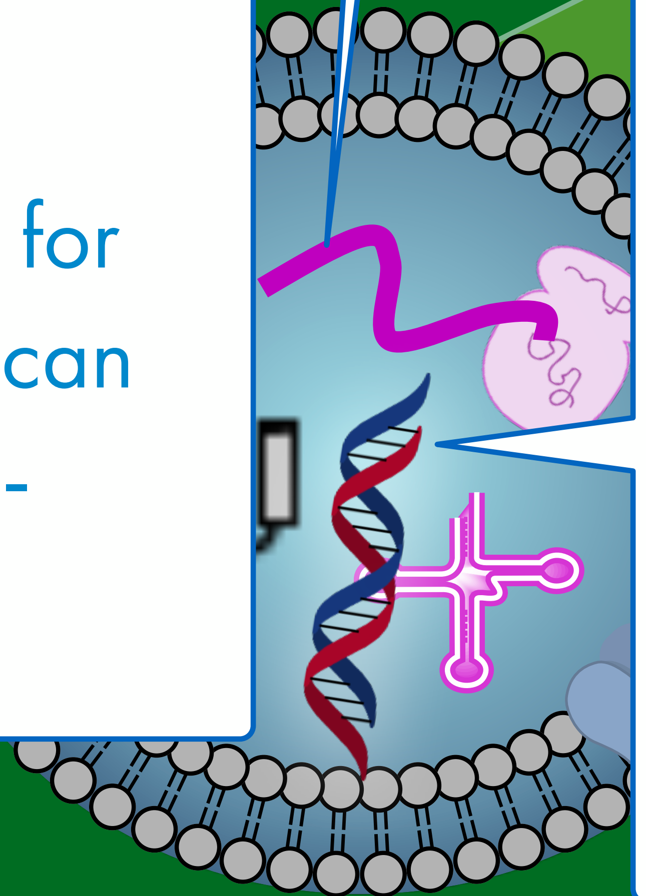

Mixed Proteins

Mixed proteins contain D aa. Some are naturally occurring peptides; these are in a variety of life, often produced through ribosome-independent synthetic pathways. For example, the cell walls of bacteria are made of peptidoglycans, which contain both D- and L-aa, antibiotics, such as gramicidin, tyrocidine, and valinomycin, are also non-ribosomally produced and contain mixtures of D- and L-amino acids. Animals: Mixed-chirality peptides called D-amino acid-containing peptides (DAACPs) have been discovered in many animal species, including humans. DAACPs function as signaling molecules or toxins.D-serine os found in the brain, where they act as important signaling molecules and neurotransmitterSynthetic peptides

Why do we (NASA) care?

aeronautics: novel materials?

Exploration issues:
For making products (drugs etc.)

Astrobiology

What is astrobiology?

a scientific discipline focused on three of humanity’s oldest and most profound questions.

Chirality has always been important for the first and last.