What we (don't) know about origins of life

A biased sample of our ignorance about prebiotic chemistry and the origin of the first protocell

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Talk given at ECT Inaugural workshop on Nuclear Astrochemistry*
26 February - 1 March

CAVENDISH ASTROPHYSICS

LEVERHULME CENTRE FOR
LIFE IN THE UNIVERSE

What we don’t know
vs.
What *I* don’t know

Categories of Knowledge and Ignorance

What we know that we know	What we don't know that we know
What we know that don't we know	What we don't know that we don't know

main take-away:
There’s a lot we don’t know
(We need epistemic humility)

Preiner, M., Asche, S., Becker, S., Betts, H.C., Boniface, A., Camprubi, E., Chandru, K., Erastova, V., Garg, S.G., Khawaja, N. and Kostyrka, G., 2020. The future of origin of life research: bridging decades-old divisions. Life, 10(3), p.20.

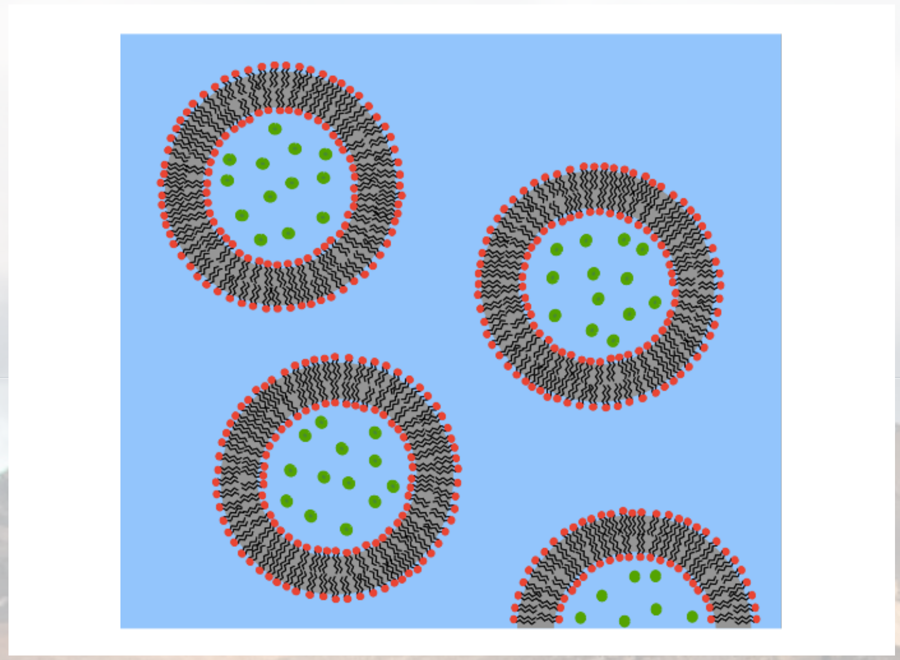
Assumptions

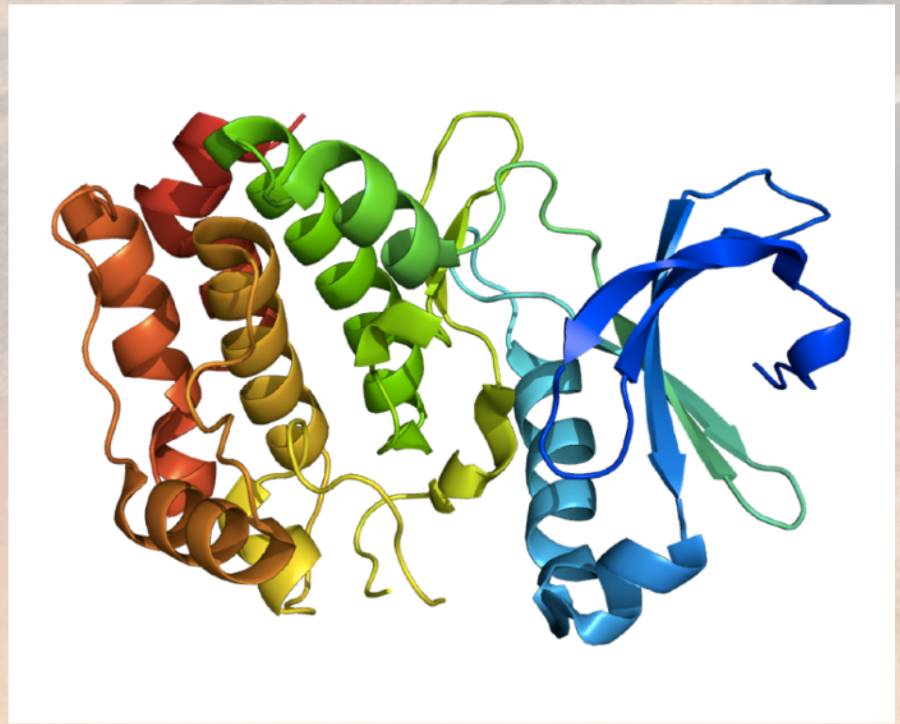
- Life is made of chemistry. *(Strong)*
- Origins of life is at its heart an organic chemistry problem. *(Strong)*
- Life started on Earth. *(Weak)*

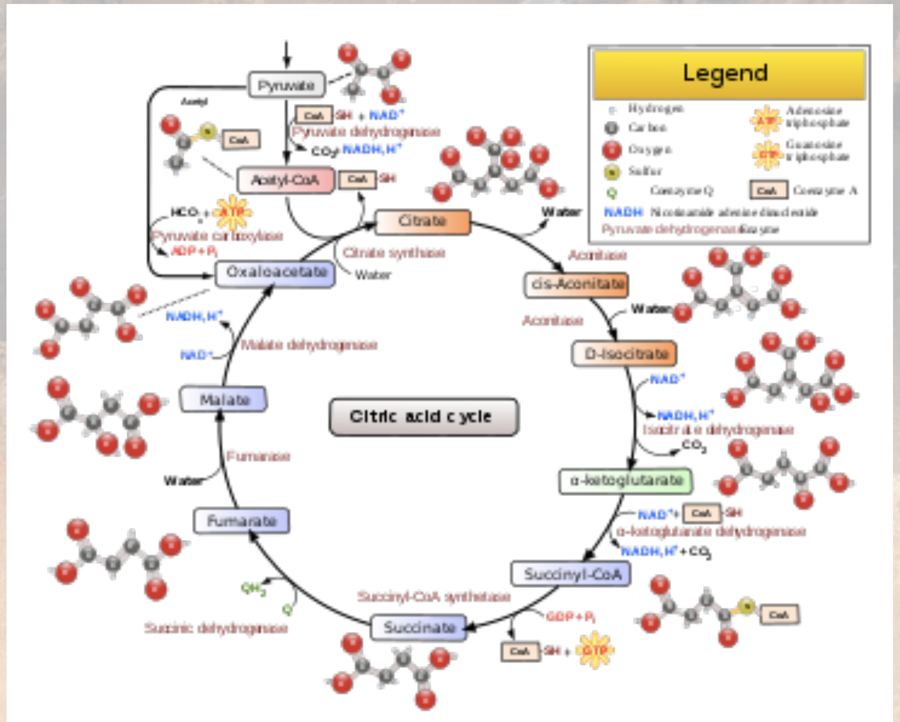
What we don’t know:

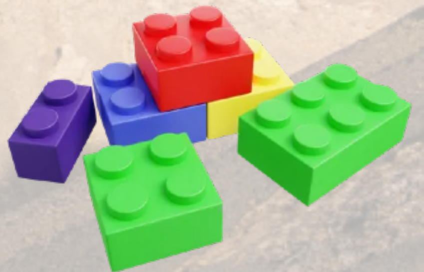
Same Molecules or Different Molecules?

Life as we know it needs four things:





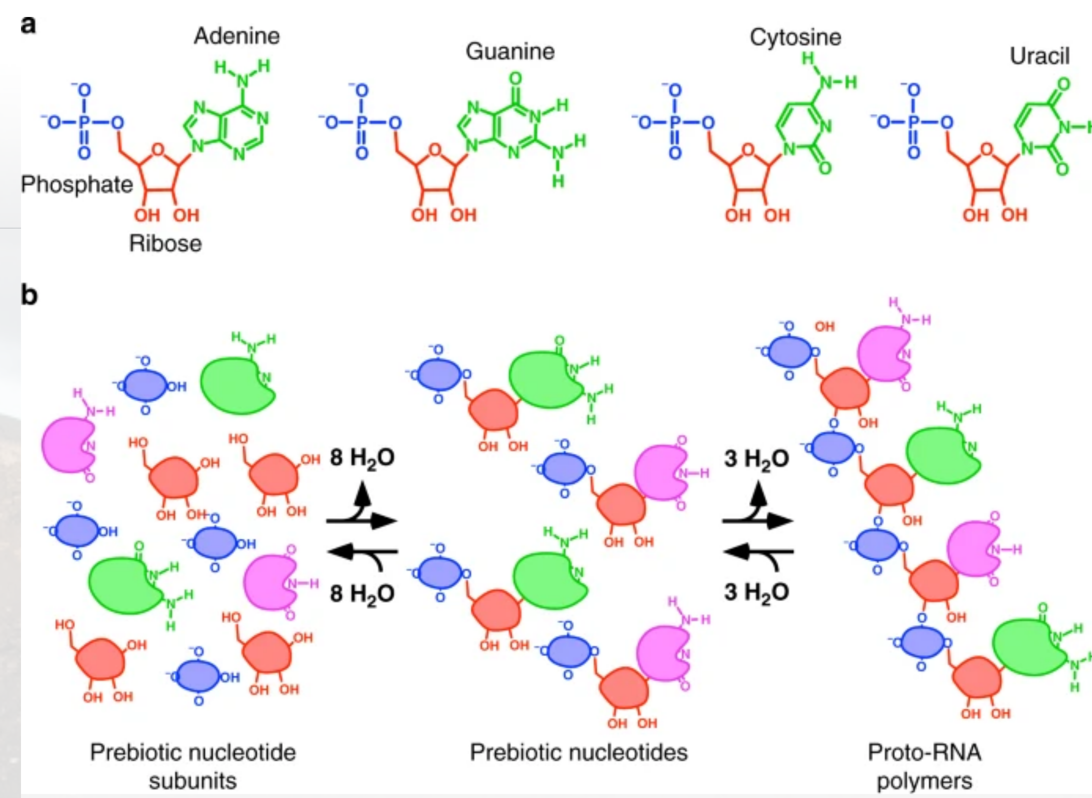




What we don’t know:

Same Molecules or Different Molecules?

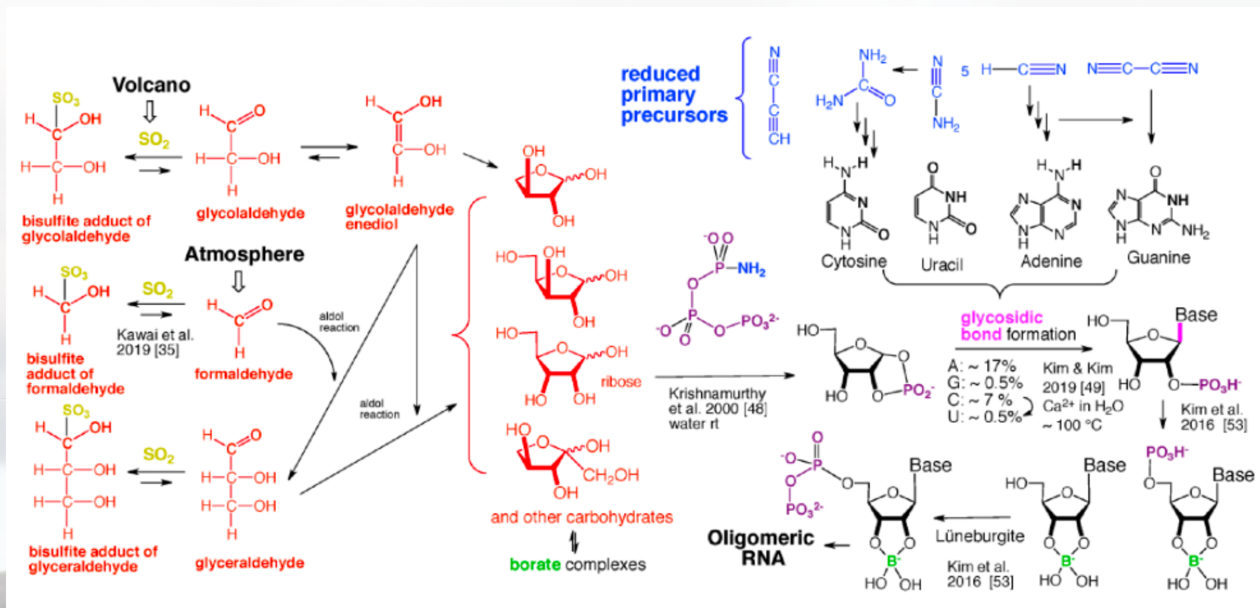
- If DIFFERENT, which ones?
- If DIFFERENT, how do we go from those molecules to the ones we know?
- If THE SAME, which ones came first?
- If THE SAME, how did they react without the molecular machinery of life?



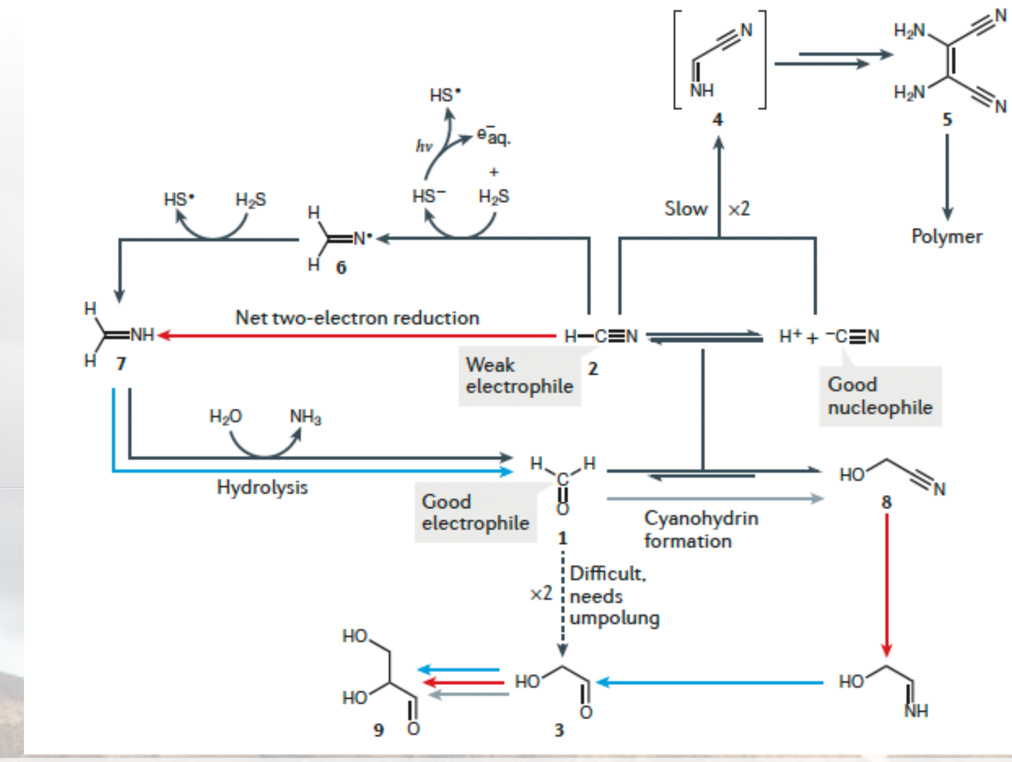
Hud 2018. Nature Communications, 9, 5171

Same Molecules, What we know:

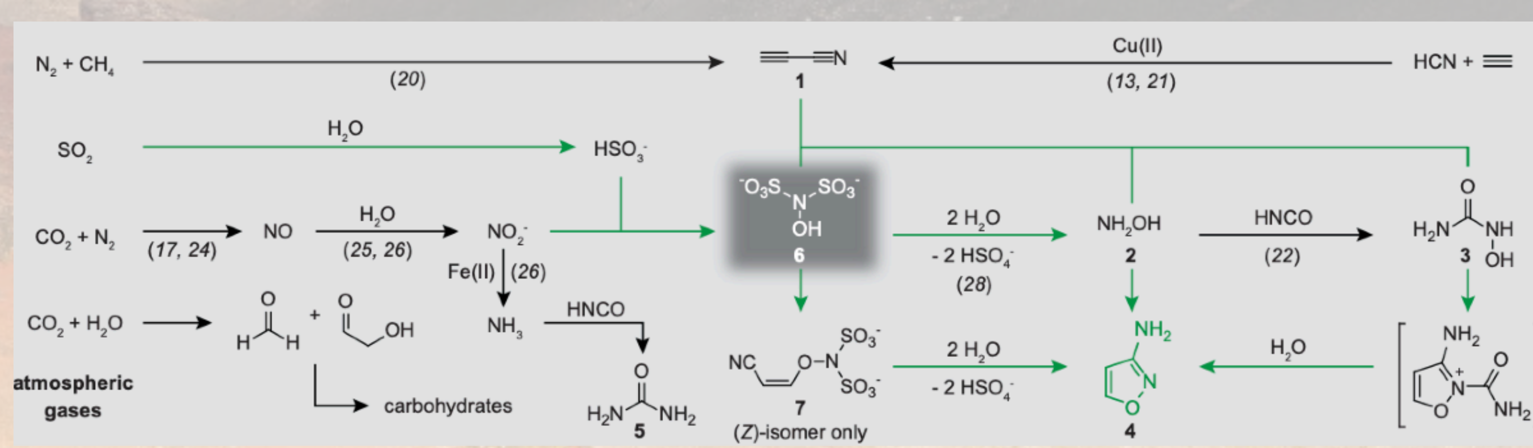
Some ways to make them in the lab



Benner, Kim, & Biondi, E., 2019. Life, 9, 84.



Sutherland, 2017.
Nature Reviews Chemistry, 1, 0012.



Becker et al. 2019. Science, 366, 76.

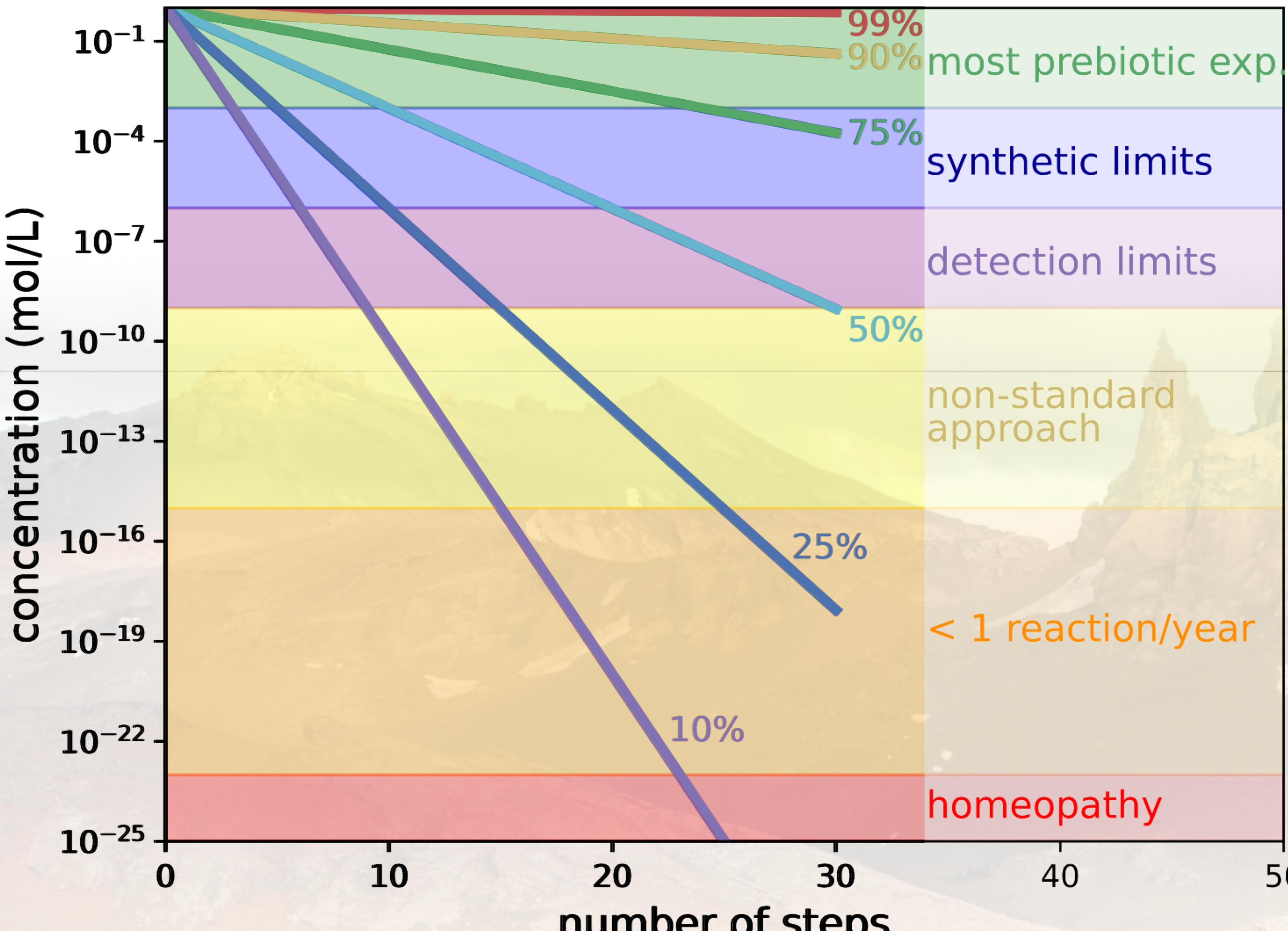
What we know:

Three Necessary Conditions for the Chemistry

1. Disequilibrium Chemistry
   - We need a source of energy — Environment-specific?
2. High-Yield Selective Chemistry
3. “Prebiotically Plausible” Chemistry

Why High-Yield Selective Chemistry?

The Arithmetic Demon



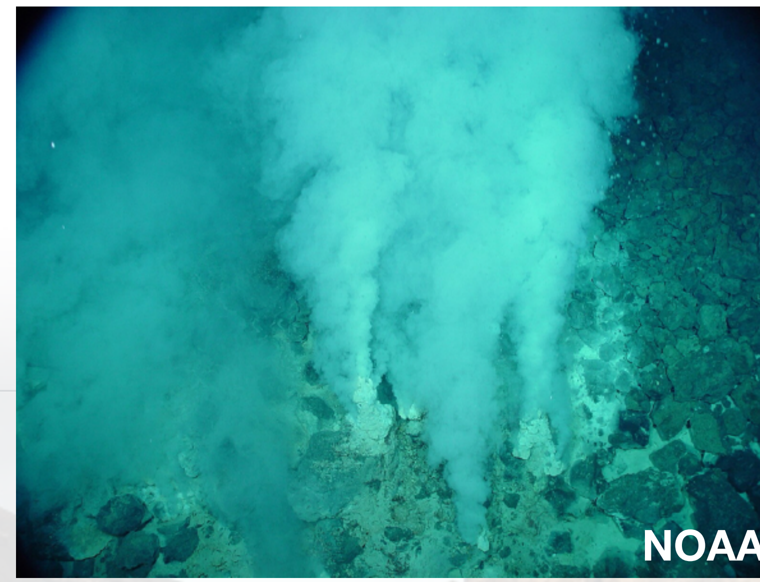
Ways through: ~~Few steps~~, high yield for each reaction, work-up.

Rimmer & White, "Do-Nothing Prebiotic Chemistry: The 'One-Nitrile' Revolution"
in prep for Accounts of Chemical Research

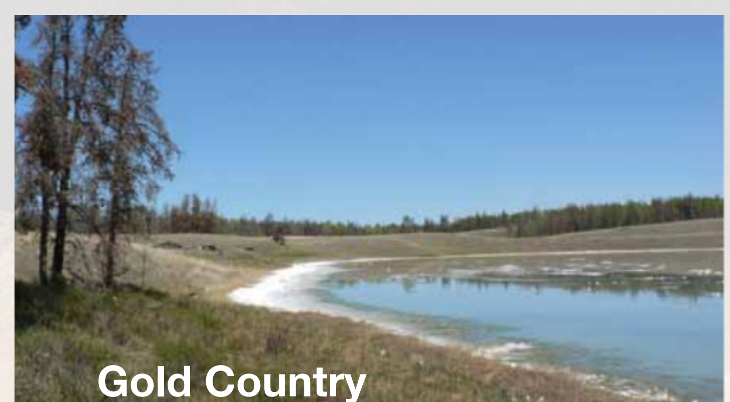
What we don’t know:

Where?

- Underwater hydrothermal vents.
  - Martin et al. 2008. Nature Reviews Microbiology, 6, 805.
- Surface hydrothermal vents.
  - Rimmer & Shorttle 2019. Life, 9, 12.
  - Rimmer & Shorttle. Life. *Submitted.*
- Alkaline lakes.
  - Toner & Catling 2019. CGA, 260, 124.
  - Toner & Catling 2020. PNAS, 117, 883.
- Underground.
  - Gold 1992. PNAS 89, 6045.
  - Sherwood Lollar et al. 2002. Nature, 416, 522.
- Basaltic glass.
  - Jerome et al. 2022. Astrobiology, 22, 629.
- Cosmic dust.
  - Walton et al. 2024. Nature Astronomy, 1.
- Giant impacts.
  - Chyba & Sagan, 1992. Nature, 355, 125.
  - Ferus et al. 2015. PNAS, 112, 657.
  - Todd & Öberg, 2020. Astrobiology, 20, 1109.
  - Anslow et al. 2023. PRS:A, 479, 20230434.
  - McDonald et al. *in prep.*



https://primordialscoop.org/2022/06/04/ribonucleic-acid-is-formed-by-percolating-ribonucleoside-triphosphates-through-basalt-glass/

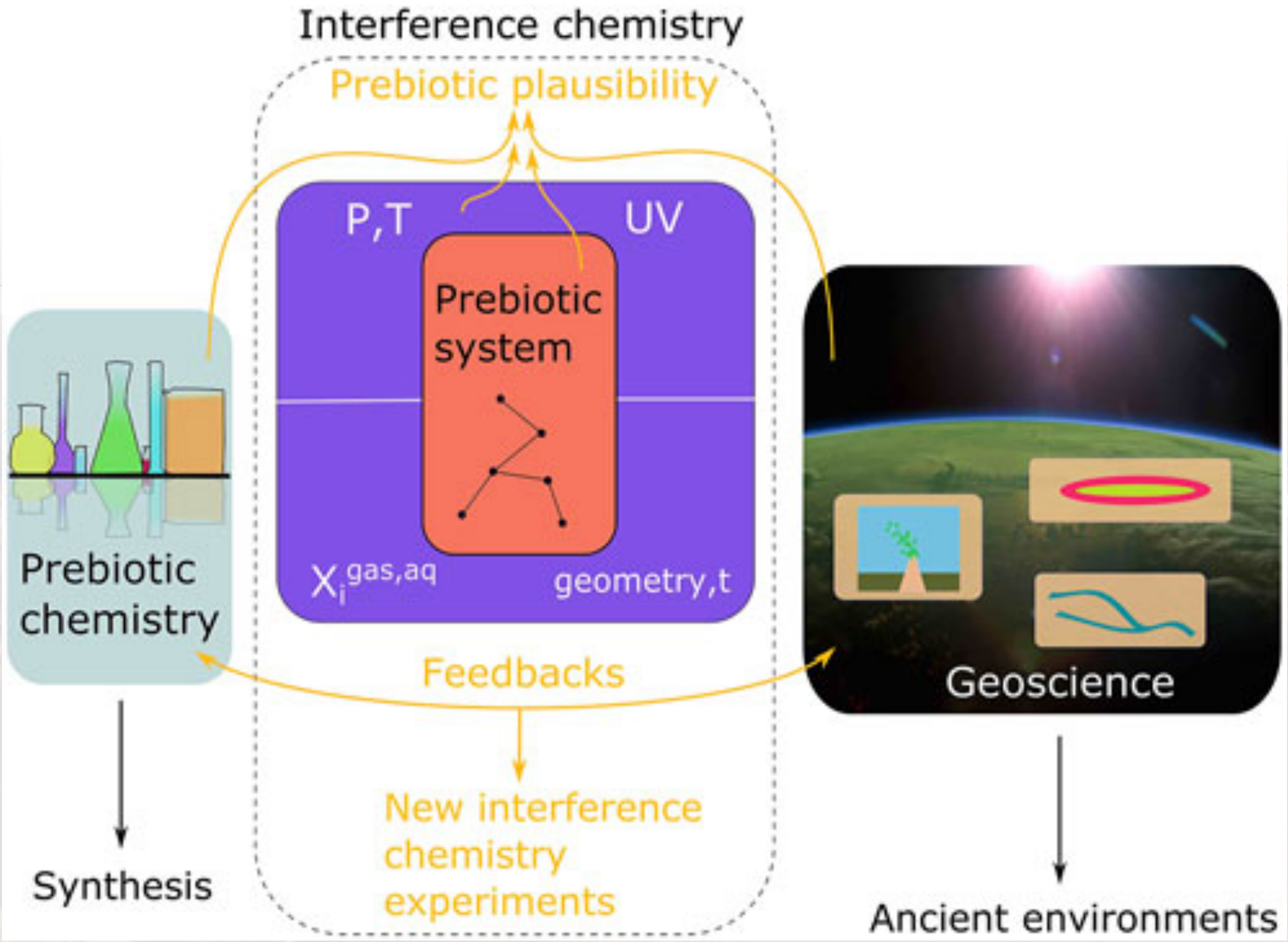


NASA Earth Observatory

What we can find out:

Connections between Chemistry and Geochemistry

- Chemical parameter space is effectively infinite.
- Possible environments are exceedingly diverse.
- If you can't make and test predictions, then it's not science.
- The **combination** of environment and chemistry ***can*** be tested!



Walton, C.R., Rimmer, P.B. and Shorttle, O., 2022. Can prebiotic systems survive in the wild? An interference chemistry approach. Frontiers in Earth Science, 10, 1011717.

Connections between Chemistry and Geochemistry

Interferences	Alkaline lake	Acid lake	Glacial brine	Alkaline vent	Acid vent	Shallow fresh-water	Seawater
pH (log units)	> 10 [A]	< 5 [D]	~ 5 [F]	~ 9 [H]	~ 3 [H]	~ 6 [O]	< 7 [T]
PO_4 (mM)	1000 [A]	< 1 [E]	< 10^{-3} [F]	< 10^{-3} [I]	< 10^{-3} [I]	0.05 [O]	< 0.1 [V]
SO_4	1000 [A]	1 [D]	50 [F]	0 [H]	0 [H]		10^{-3} [W]
HS-	0.1 [B]	10^{-4} [D]		0.05 [H]	1 [H]	10^{-3} [P]	10^{-6} [W]
$HSO3^-$						< 1 [P]	
$SO3^{2-}$						< 1 [P]	
Li	10 [B]	1 [D]	1 [F]	0.05 [H]	0.5 [M]	10 [Q]	0.05 [H]
B	1000 [A]	1 [D]	1 [F]	0.05 [J]	0.5 [M]	5 x 10^{-3} [R]	0.5 [X]
Cl	1000 [A]	10 [D]	1000 [F]	500 [H]	1000 [H]	0.1 [O]	500 [H]
Ca	10 [A]	0.1 [D]	100 [F]	50 [H]	50 [H]	0.5 [O]	50 [Y]
Mg	10 [A]	0.01 [D]	100 [F]	1 [H]	0 [H]	0.1 [O]	10 [Y]
K	1000 [A]	1 [D]	10 [F]	10 [H]	10 [H]	0.01 [O]	10 [H]
Na	10^4 [A]	10 [D]	1000 [F]	50 [H]	500 [H]	0.1 [O]	500 [H]
Br	100 [A]	0.01 [D]	1 [F]	1 [K]	0.5 [K]	0.01 [S]	1 [H]
DIC	1000 [A]	5 [D]	100 [F]	0 [L]	10 [J]	1 [T]	< 1 [T]
Fe(II)	5 x 10^{-4} [A]	0.1 [D]	0.5 [F]	< 10^{-3} [H]	50 [H]	0.1 [O]	0.1 [Y]
Si	1 [C]	10 [D]	0.5 [F]	0.1 [M]	10 [M]	0.1 [O]	1 [Y]
Wet/dry cycles				Mineral surfaces? Shallow variants only	Mineral surfaces? Shallow variants only		Aerosols? Evaporites?
UV irradiation							Near-surface only
Serpentinization	Hydrothermal end-members?		Hydrothermal interface?			Low temperature serpentinization?	Deep sea?
Exogenous material				Shallow variants only	Shallow variants only		Tidal variants?
Temperature (°C)	1-100	1-100	0-10 [G]	10-100 [N]	10-100 [N]	10-50 [U]	10-50 [Z]

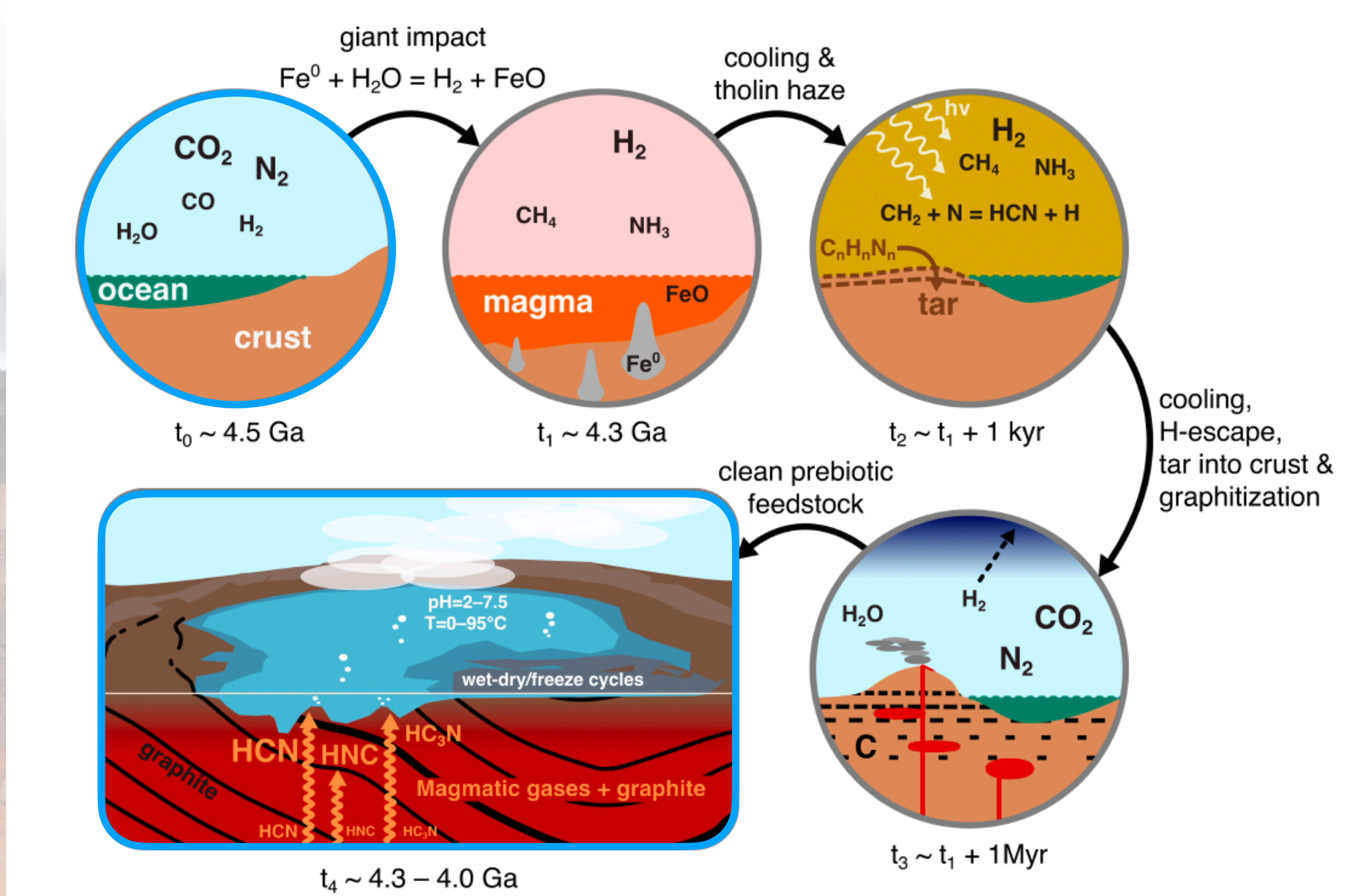
Notes: Maximum estimated concentrations in mM for each environment are rounded to nearest gradation (1 ← 5 → 10). Colour shading indicates where available constraints on a given environment are either especially uncertain (orange), or conversely based on dedicated experimental/theoretical studies of prebiotic conditions (green). DIC – Dissolved Inorganic Carbon, Fe(II) – dissolved ferrous iron. Additional references for acid and alkaline vent fluids in end-member compositions of Hodgkinson et al (2015) are as follows: (Kelley et al., 2001; Charlou et al., 2002; Douville et al., 2002). This compilation is not intended to be exhaustive. References cited from A-Z: **(Toner and Catling, 2020)**, B **(Visscher et al., 2020)**, C **(Zheng et al., 2016)**, D **(McCleskey et al., 2005)**, E **(Mulkidjanian et al., 2012)**, F (Lyons et al., 2019), G **(Harrison, 2009)**, H **(Hodgkinson et al., 2015)**, I **(Edmonds and German, 2004)**, J **(Lang et al., 2018)**, K **(Berndt and Seyfried, 1990)**, L **(Bradley et al., 2009)**, M **(Seyfried et al., 2011)**, N **(Barley et al., 2005)**, O **(Hao et al., 2017)**, P **(Ranjan et al., 2018)**, Q **(Dellinger et al., 2014)**, R **(Negrel et al., 2002)**, S **(Neal et al., 2007)**, T **(Morse and Mackenzie, 1998)**, U **(Rollinson, 2007)**, V **(Rasmussen et al., 2021)**, W **(Crowe et al., 2014)**, X **(Uppström, 1974)**, Y **(Jones et al., 2015)** Z **(Zahnle et al., 2007)**.

Strength of constraint	Based on dedicated experimental/theoretical studies of prebiotic conditions	Uncertain

Walton, C.R., Rimmer, P.B. and Shorttle, O., 2022. Can prebiotic systems survive in the wild? An interference chemistry approach. Frontiers in Earth Science, 10, 1011717.

Example: Cyanosulfidic Chemistry

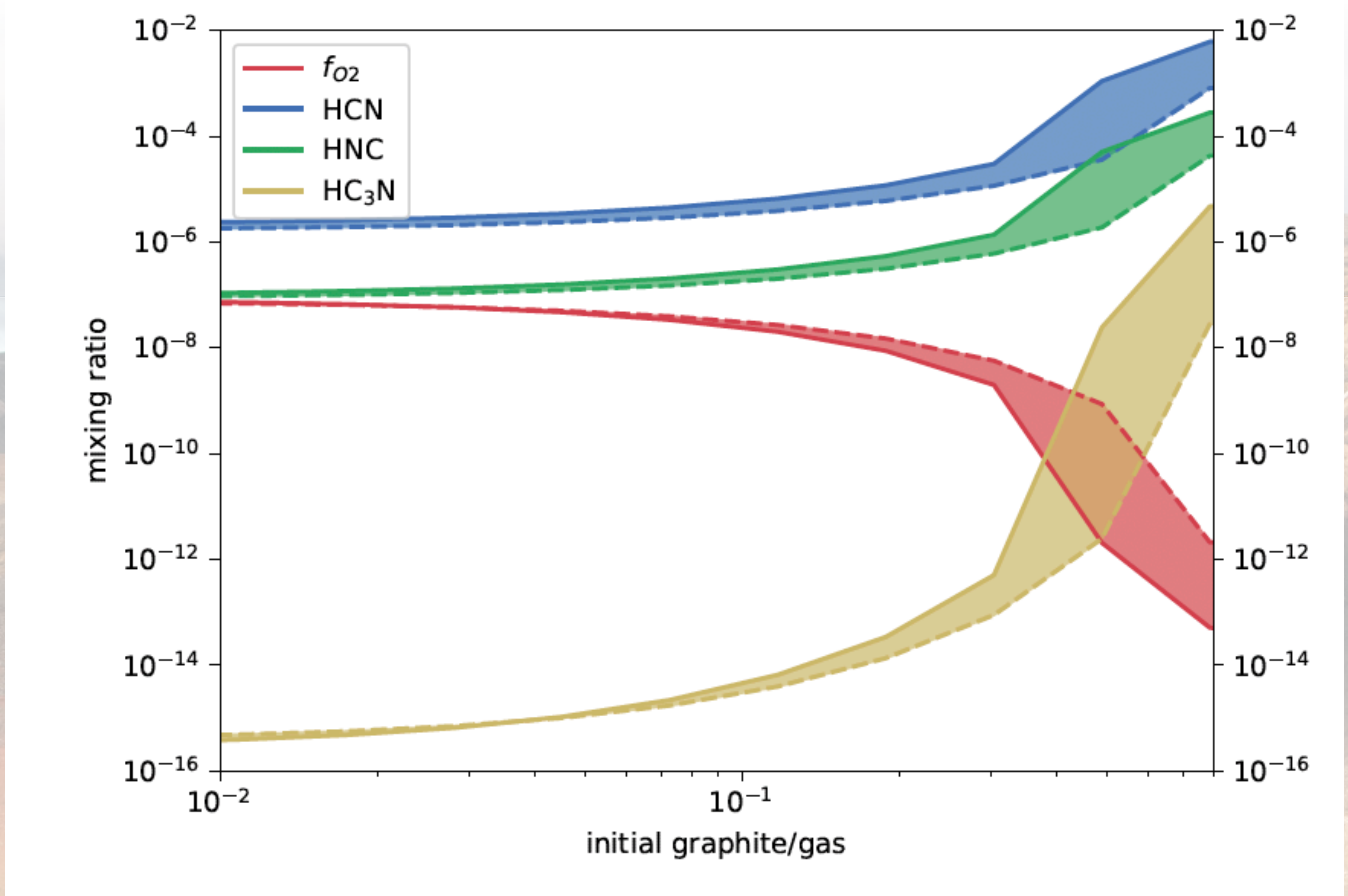
In a Surface Hydrothermal Vent



Zahnle, K., Schaefer, L. and Fegley, B. 2010. Earth's earliest atmospheres. Cold Spring Harbor Perspectives in biology, 2, a004895.

Example: Cyanosulfidic Chemistry

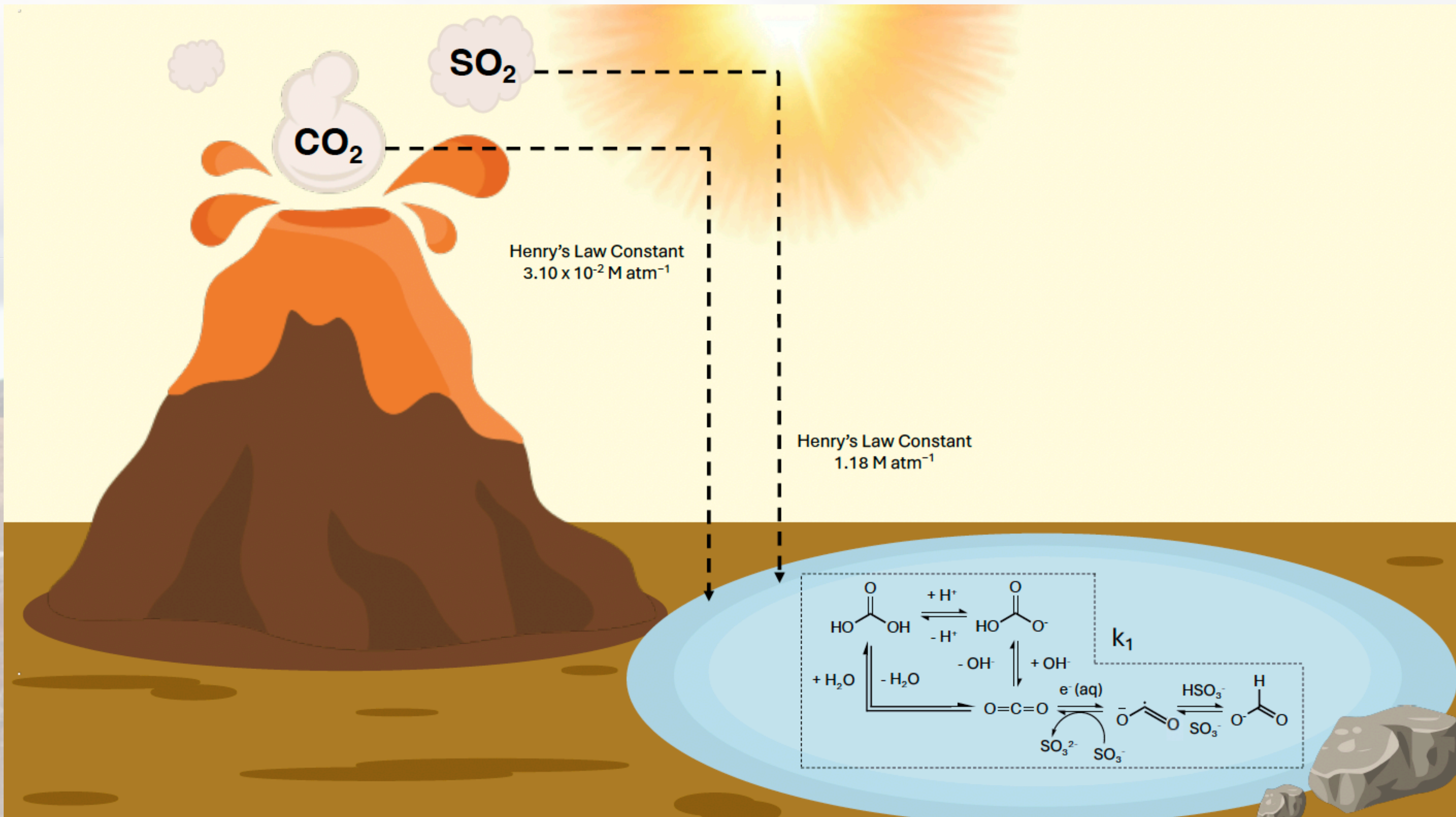
In a Surface Hydrothermal Vent



Rimmer, P.B. and Shorttle, O. A Surface Hydrothermal Source of Nitriles and Isonitriles. Life, *Submitted*.

Example: Carboxysulfitic Chemistry

In an Alkaline Lake

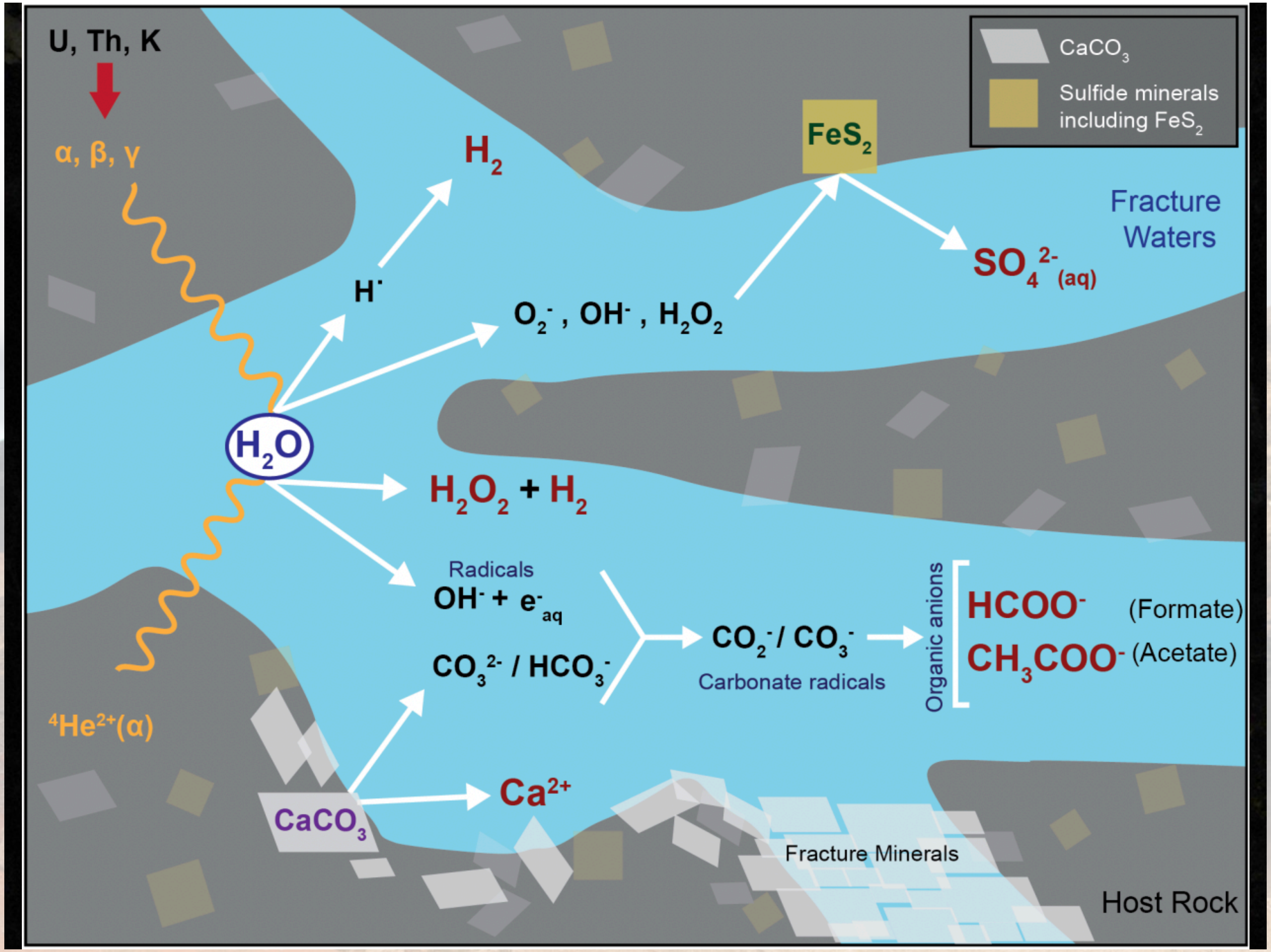


Skyla White

White, S., Liu, Z. and Rimmer, P.B. Shedding a Light on the Kinetics of the Carboxysulfitic Scenario. *in prep* for JACS.

Example: Radiolysis

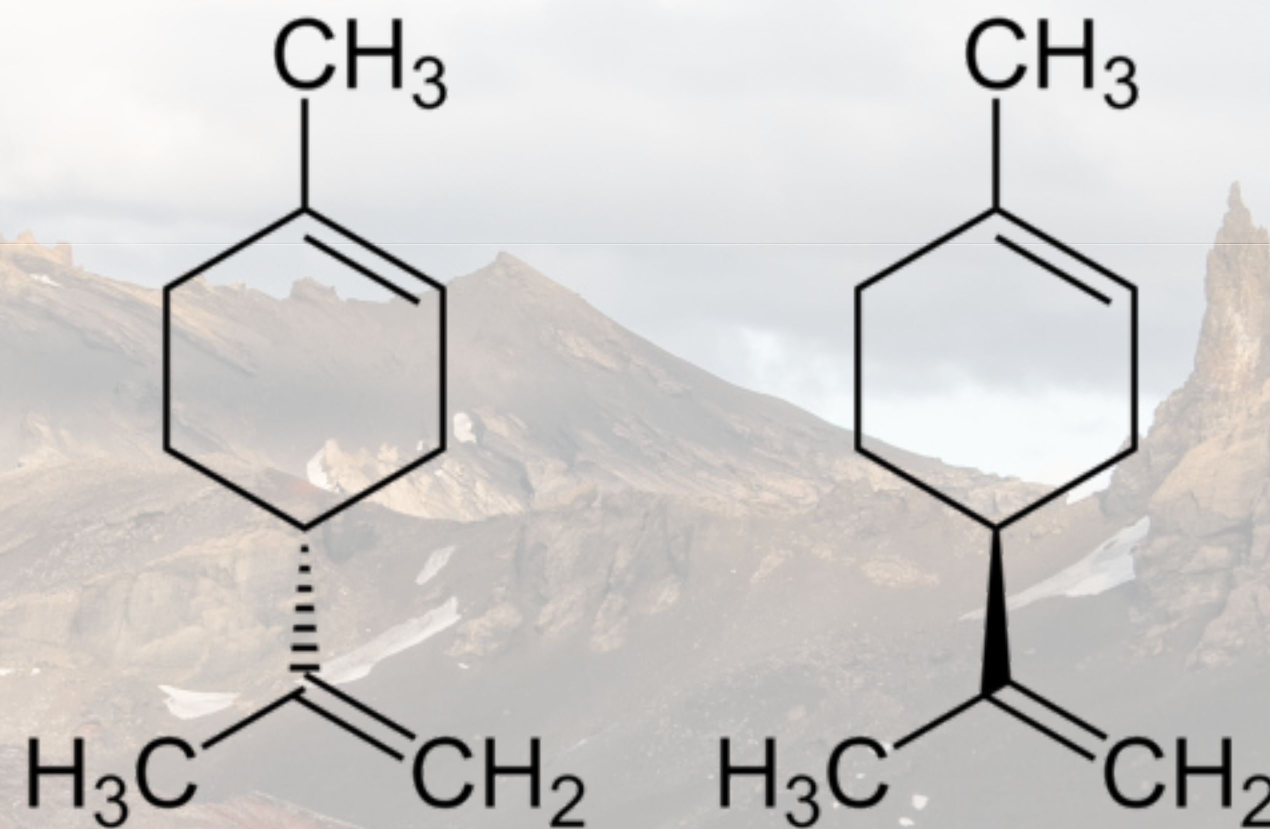
Underground



Lollar, B.S., et al. 2021. A window into the abiotic carbon cycle–Acetate and formate in fracture waters in 2.7 billion year-old host rocks of the Canadian Shield. Geochimica et Cosmochimica Acta, 294, 295.

What we don’t know:

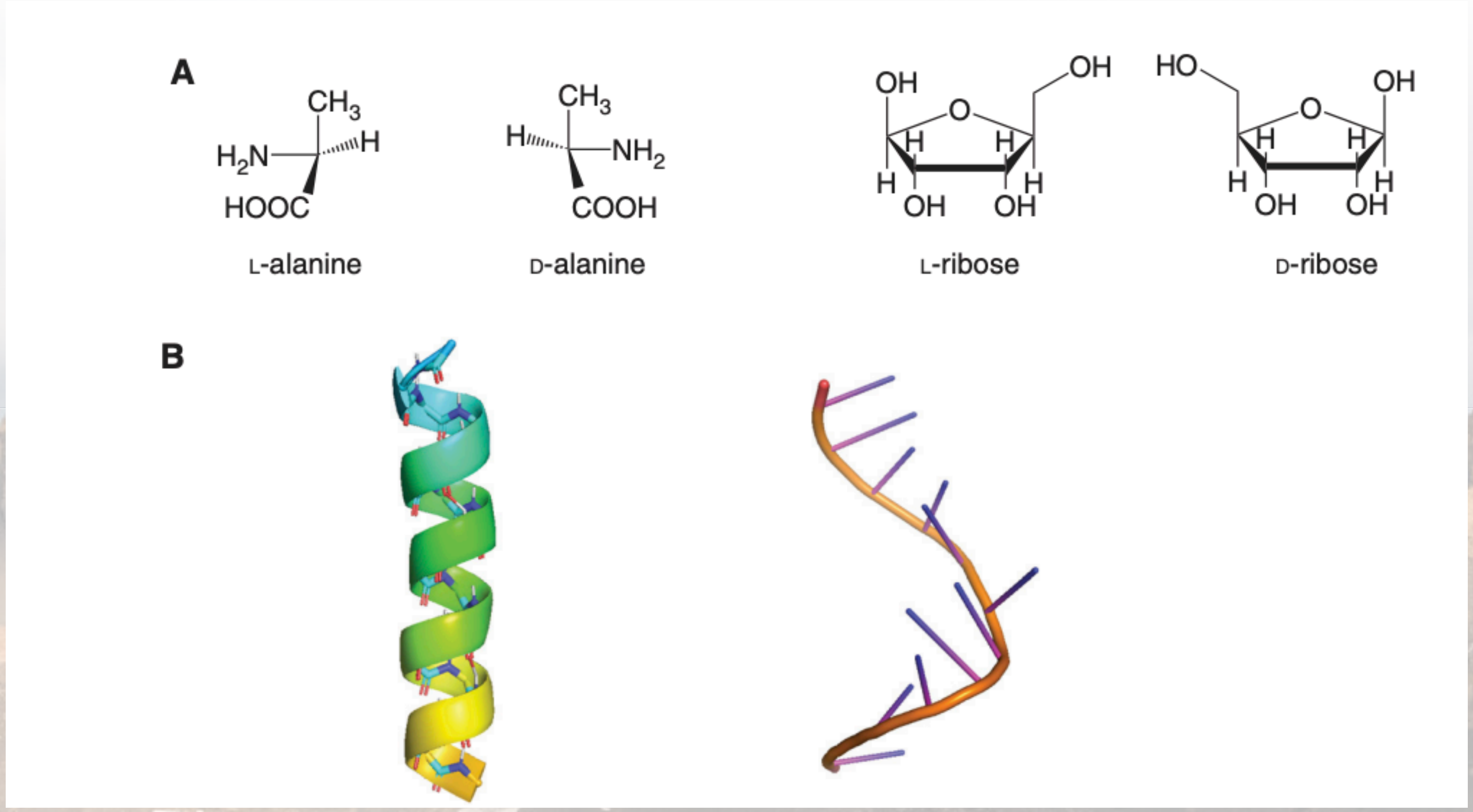
The problem of chirality



(L) (D)

What we don't know:

The problem of chirality



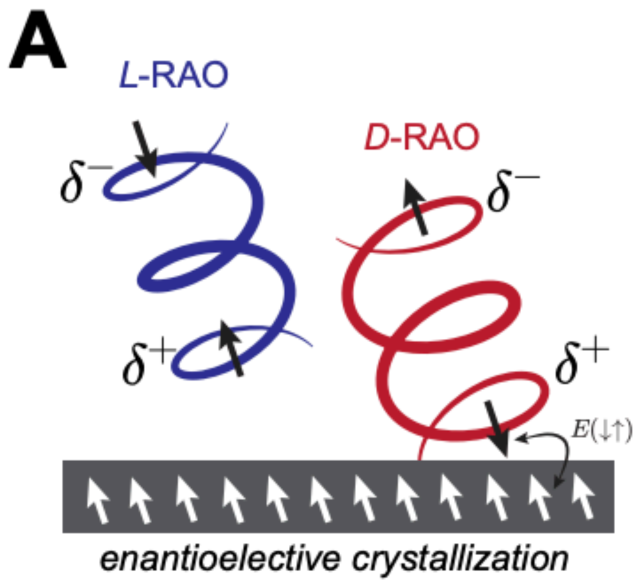
DON'T KNOW

Enantiomeric Excess → **DON'T KNOW** Amplification → Enantiomeric Purity

Blackmond, D.G., 2019. The origin of biological homochirality. Cold Spring Harbor Perspectives in Biology, 11, a032540.

Candidate Solution to Chirality:

Spin-Selective Chemistry on Magnetite

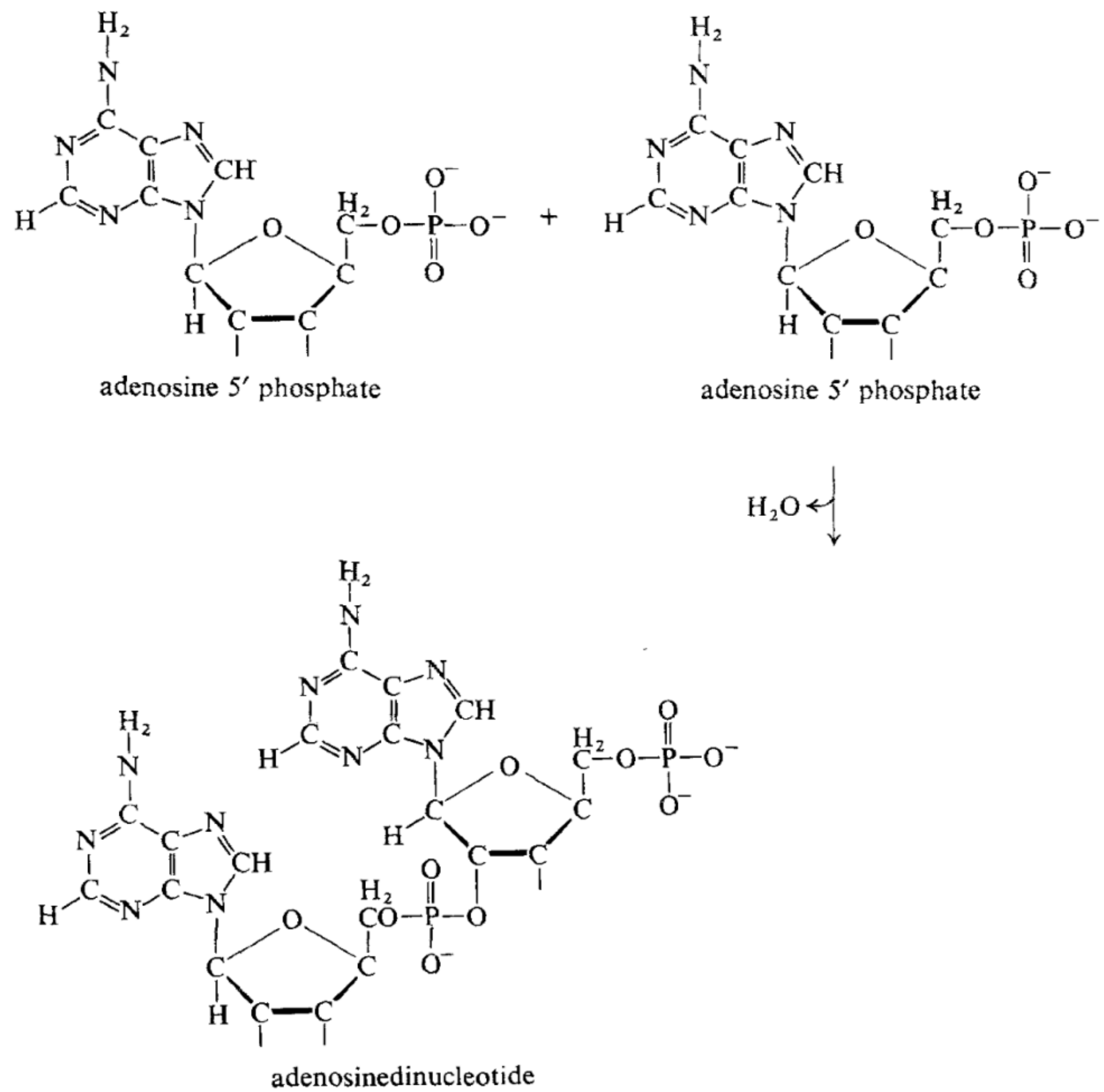


Ozturk, S.F., Liu, Z., Sutherland, J.D. and Sasselov, D.D., 2023. Origin of biological homochirality by crystallization of an RNA precursor on a magnetic surface. Science Advances, 9, eadg8274.

Ozturk, S.F., Sasselov, D.D. and Sutherland, J.D., 2023. The central dogma of biological homochirality: How does chiral information propagate in a prebiotic network? arXiv:2306.01803.

What we don’t know:

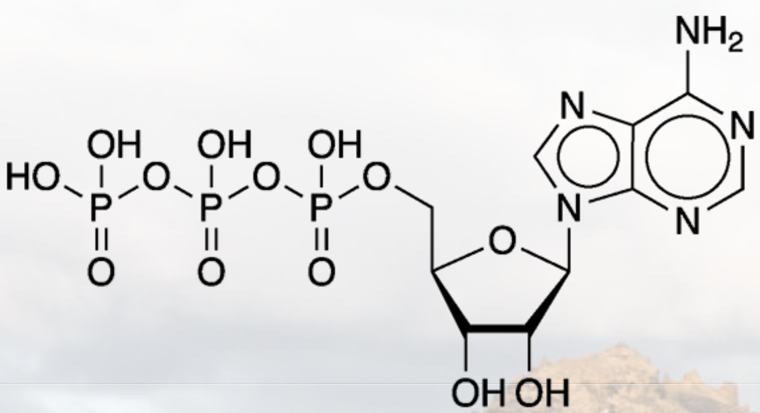
How these molecules link together without enzymes



Hulshof, J. and Ponnamperuma, C., 1976. Prebiotic condensation reactions in an aqueous medium: a review of condensing agents. Origins of life, 7, pp.197-224.

Candidate solution to activation and ligation:

Surface chemistry on basaltic glass [15]



+

100+ - long strands of RNA
Months-long stability

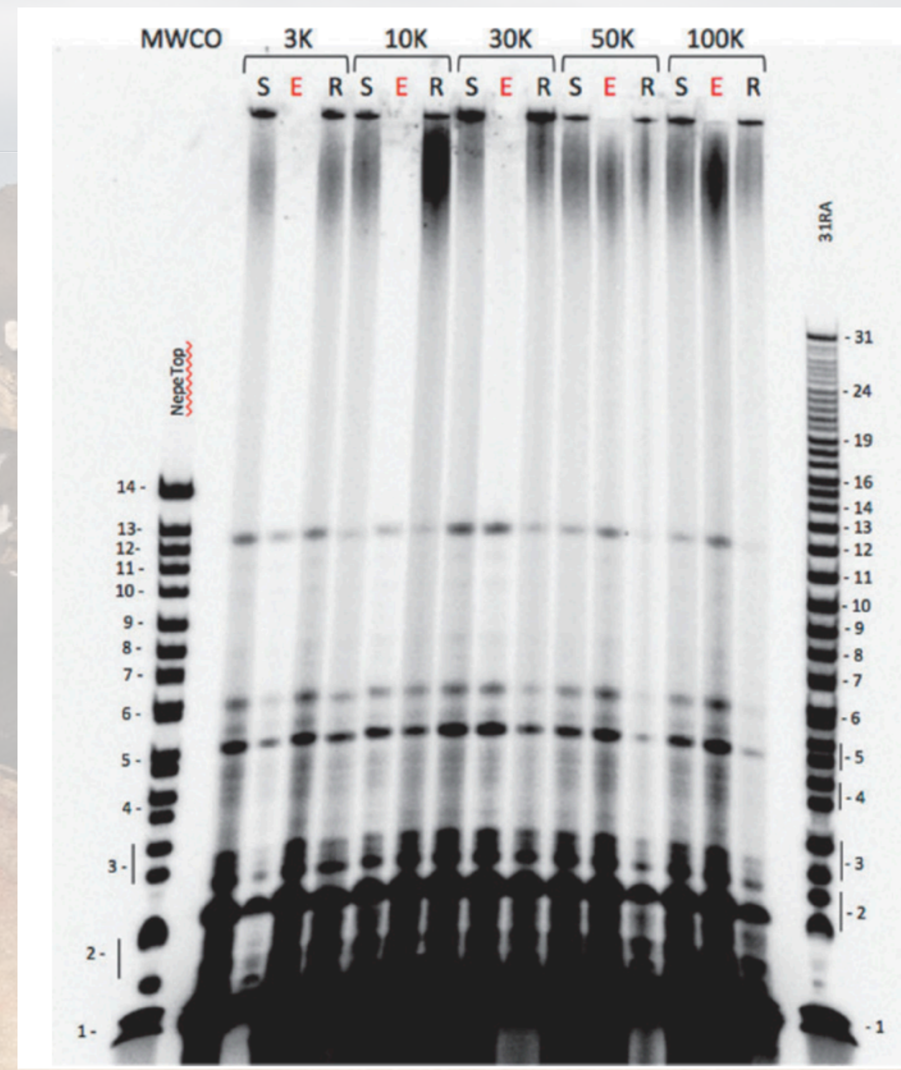


FIG. 3. Ultrafiltration of polyribonucleic acid formed on diabase. Shown are starting material (S), filter eluates (E), and filter retentates (R) with increasing MWCO filters. K = kDa. NEPETop and 31RA: partial alkaline hydrolysis of 14-mer and 31-mer RNA molecules. Sizes in nucleotides are on the sides. Twenty percent PAGE, 7M urea. MWCO, molecular weight cutoff.

Jerome, C.A., Kim, H.J., Mojzsis, S.J., Benner, S.A. and Biondi, E., 2022. Catalytic synthesis of polyribonucleic acid on prebiotic rock glasses. Astrobiology, 22(6), pp.629-636.

What I don’t know:

Steps from oligomers to protocells to life

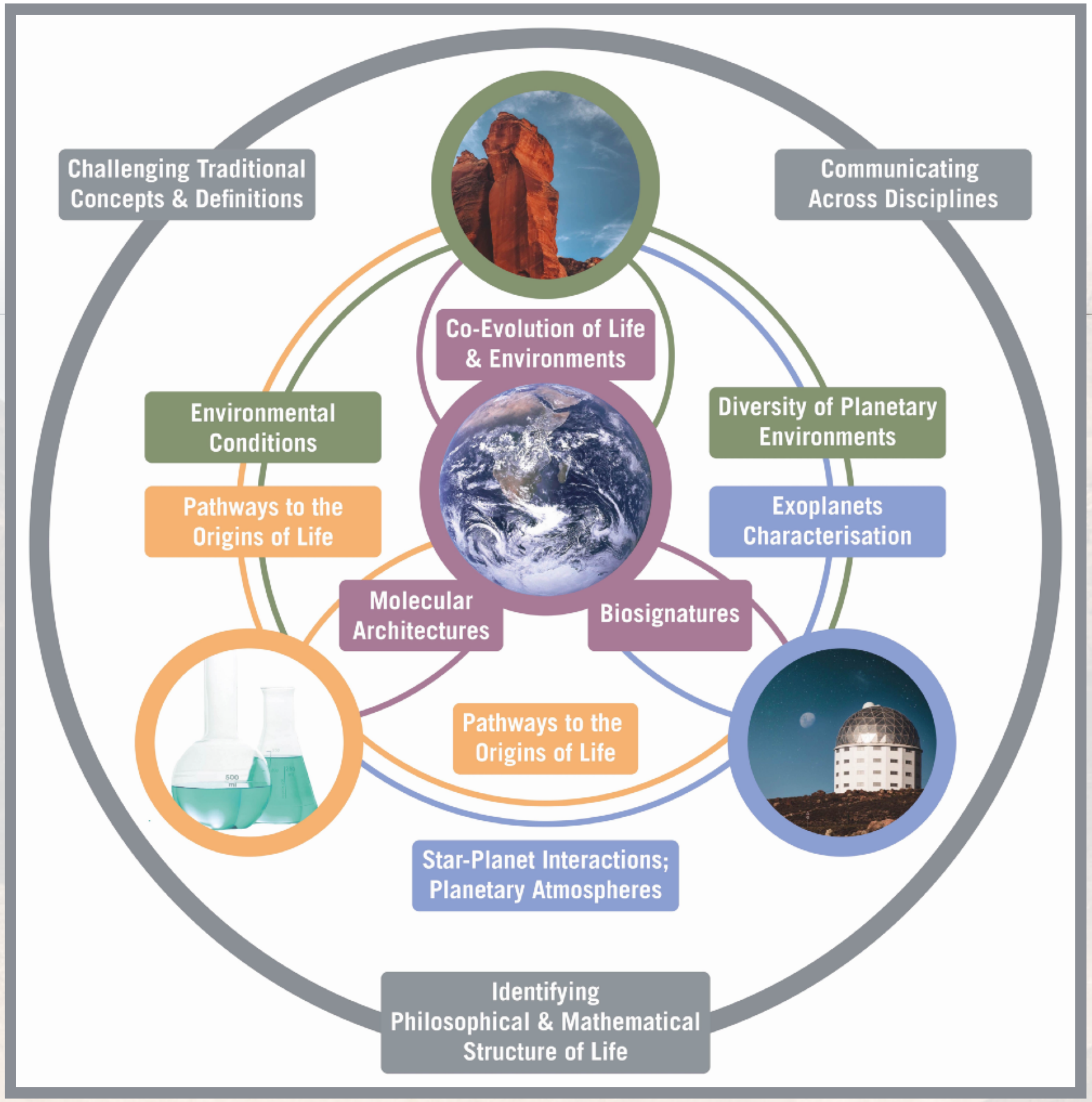
This is the field for biochemists, synthetic biologists and ecologists:

Invite, Listen, Learn, Connect

Leverhulme Centre for Life in the Universe

www.lclu.cam.ac.uk

- Centered at Cambridge (Departments of Astronomy, Chemistry, Earth Science, Philosophy, Physics, Theology, Zoology)
- Spokes at ETH-Zurich, Harvard, Princeton, University of Colorado, University College London
- Affiliated with Origins Federation
- Opening for 7 Postdocs
- Opening for 7 Summer Internships



Two things I've learned about next steps:

- Arethmetic Demon: Material Limit?

  Reaction-by-reaction outcome requires:

  $$Y \sim 1 - 1/S$$

  Rimmer & White, *in prep* for Accounts of Chemical Research

- Eigen Error Threshold: Formal (Informational) Limit?

  Replication-by-replication outcomes requires:

  $$F \sim 1 - 1/L$$

  Eigen, M., 1971. Selforganization of matter and the evolution of biological macromolecules. Naturwissenschaften, 58(10), pp.465-523.

Summary

What we know that we don't know:

- Which molecules
- What environment
- What energy source
- Origin of homochirality
- Activation and ligation chemistry
- Origin and nature of protocells.

What we know that we know:

- How to make many of the building blocks in the lab.
- Necessary conditions for prebiotic synthesis: disequilibrium, high-yield, selective.
- Candidate environments.
- Partial candidate solutions to some of what we don't know.
- How to combine environment and chemistry to test both.
- Eigen error threshold
- **That there's so much more that we don't know.** (Epistemic humility)