The Limits of Organic Life in the Solar System:
From Cold Titan to Hot Venus.

the foundation for applied molecular evolution
FAME

Full text provided by www.sciencedirect.com
SCIENCE DIRECT®

ELSEVIER

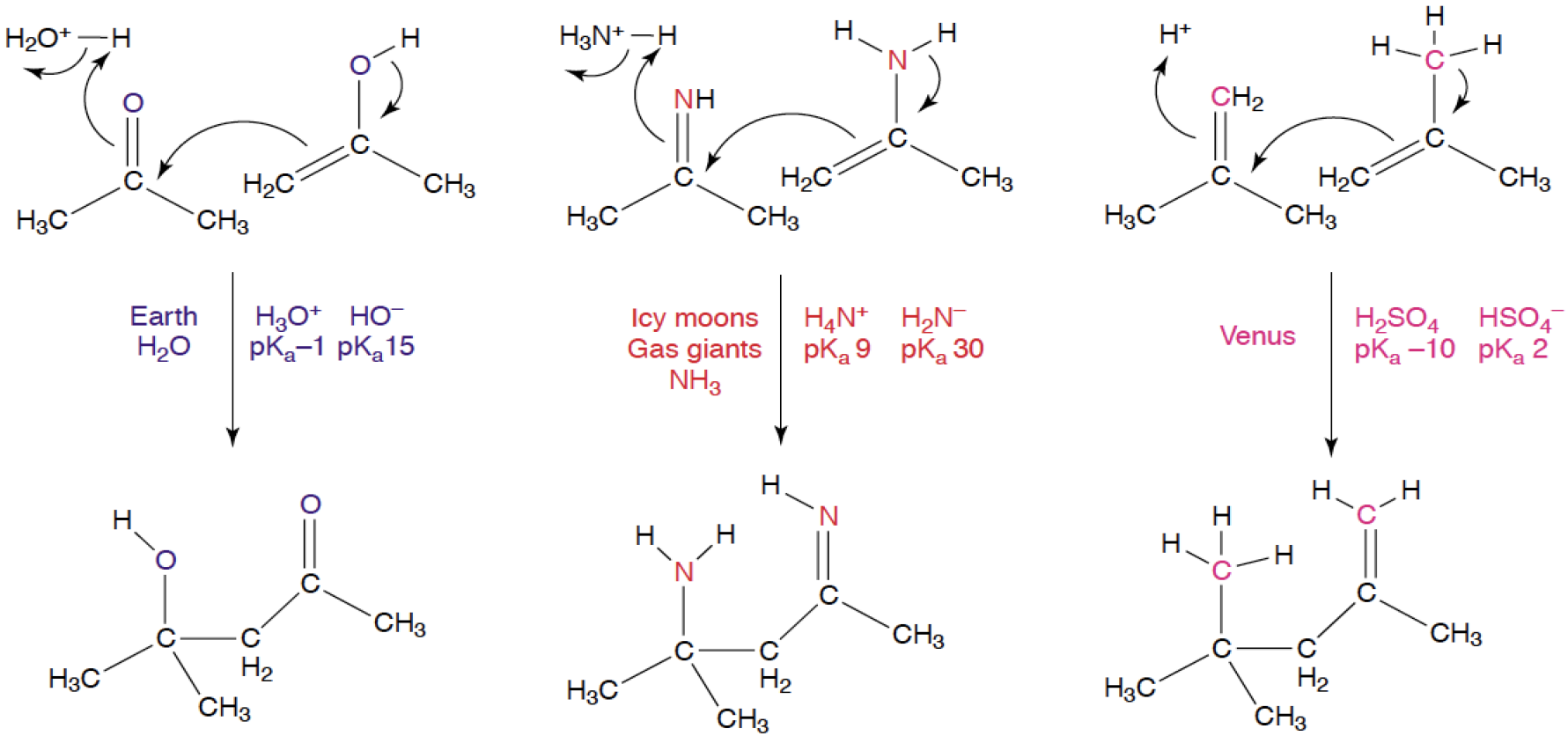
Is there a common chemical model for life in the universe?

Steven A Benner*, Alonso Ricardo and Matthew A Carrigan

Life, a chemical system capable of Darwinian evolution, may exist in a wide range of environments. These include non-aqueous solvent systems at low temperatures, or even supercritical dihydrogen– helium mixtures. The only absolute requirements may be a thermodynamic disequilibrium and temperatures consistent with chemical bonding. A solvent system, availability of elements such as carbon, hydrogen, oxygen and nitrogen, certain thermodynamic features of metabolic pathways, and the opportunity for isolation, may also define habitable environments. If we constrain life to water, more specific criteria can be proposed, …

Benner, S. A., Ricardo, A., Carrigan, M. A. (2004) Is there a common chemical model for life in the universe? *Curr. Opinion Chem. Biol.* **8**, 672-689.

We were not very creative. We took only small steps away from terran metabolism



Aldol reaction ≈
all of terran metabolism
Near neutral pH

At high pH
C=N replace C=O

At low pH
C=C replace C=O

Benner, S. A., Ricardo, A., Carrigan, M. A. (2004) Is there a common chemical model for life in the universe? *Curr. Opinion Chem. Biol.* **8**, 672-689.

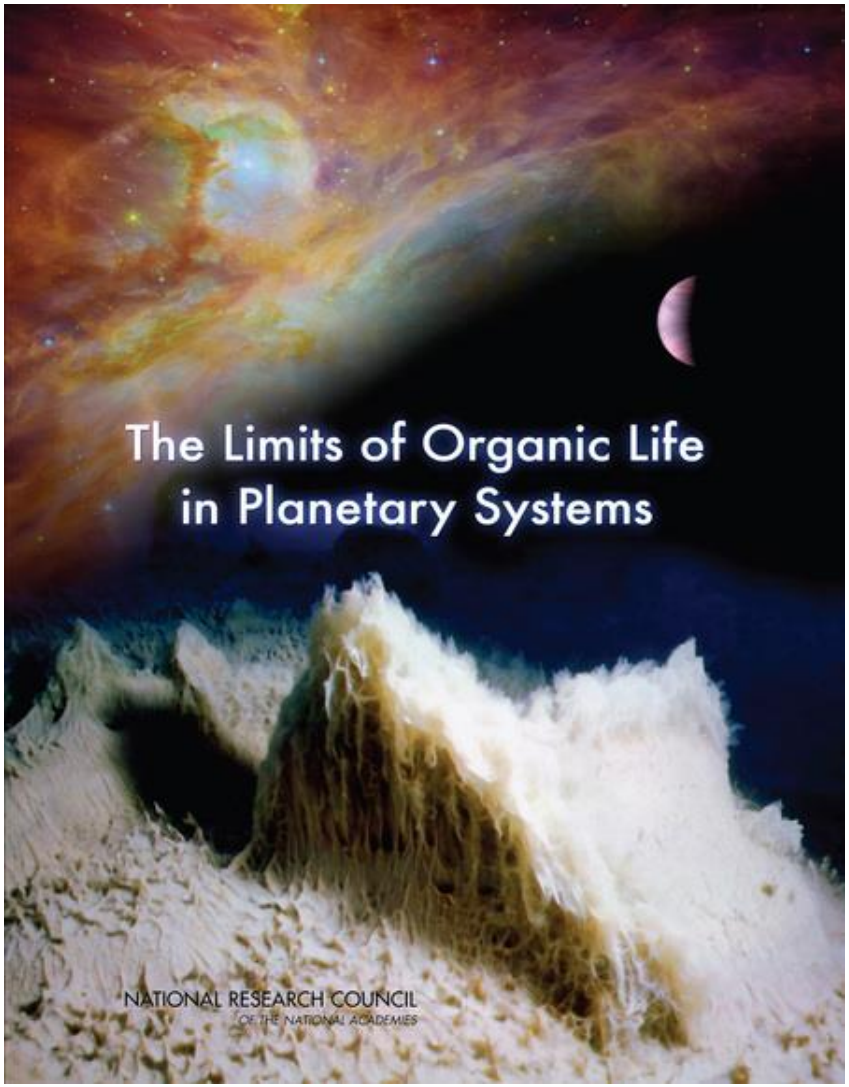
For my punishment, I was placed on a National Academies Committee …

Were I wrote a book with John Baross …

Anywhere there is …

- Energy (many places)
- Reduced carbon (many places)
- A solvent (many places)

… there can be life



For my punishment, I was placed on a National Academies Committee …

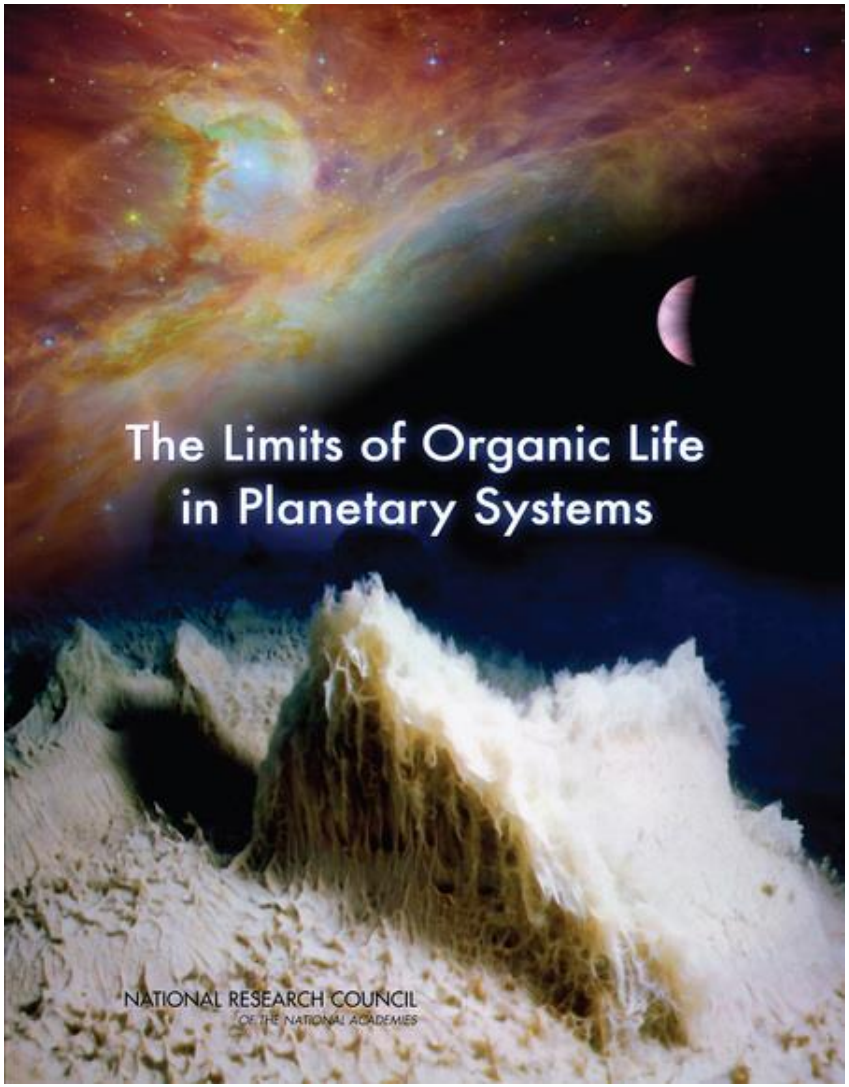
Were I wrote a book with John Baross …

Anywhere there is …

- Energy (many places)
- Reduced carbon (many places)
- A solvent (many places)

… there can be life

At least, that is what "the National Academy" (= Steve + John) said

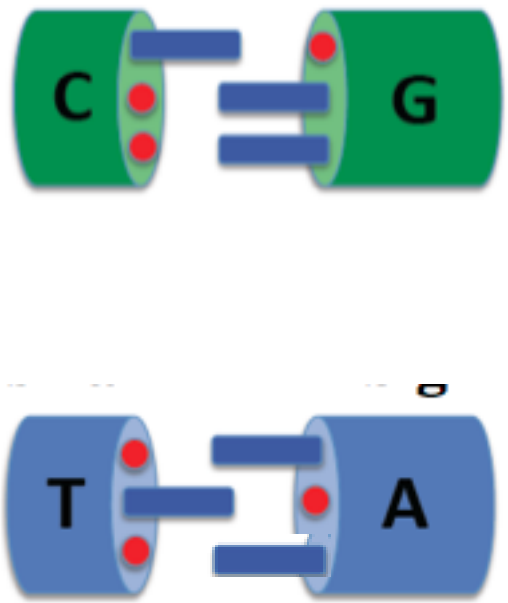


We understand water solvent best

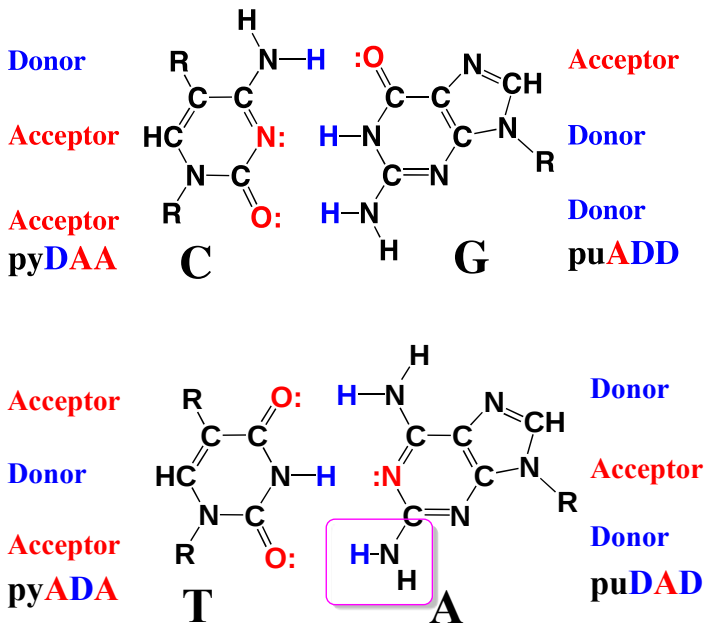
- We have ourselves examples of informational biopolymers that support Darwinian evolution in water (DNA, RNA)
- Synthetic Biology lets us as what *other* biopolymers might work

Here is what *your* informational biopolymers look like

In cartoon form



In molecular form



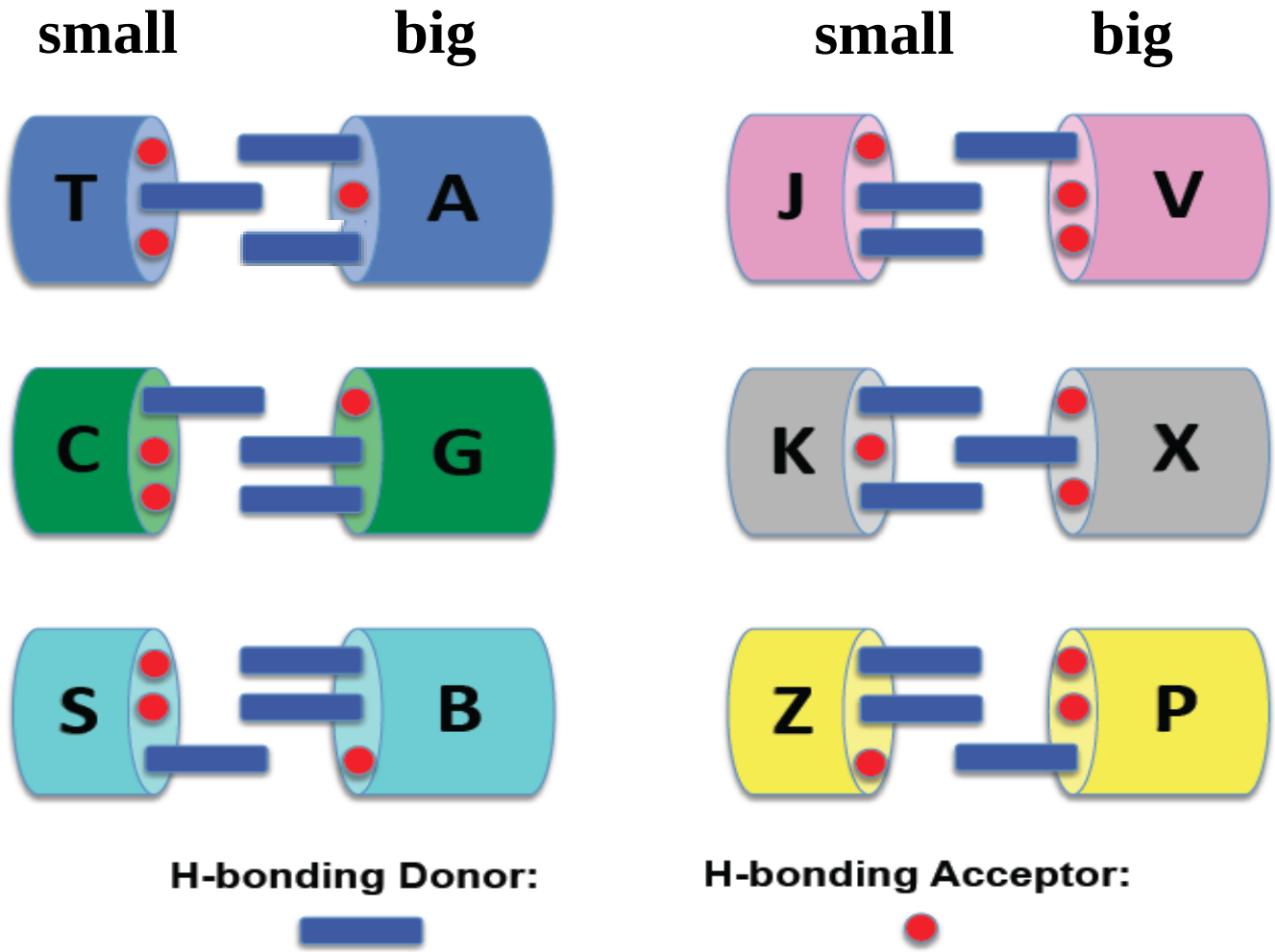
Size complementarity. Small things pair with big things

Hydrogen bond complementarity Hydrogen bond donors (**prongs**) match hydrogen bond acceptors (**holes**)

Make alternative DNA in the lab to see what works, and from that infer what might be found as we explore the cosmos

DNA with 12 letters is possible

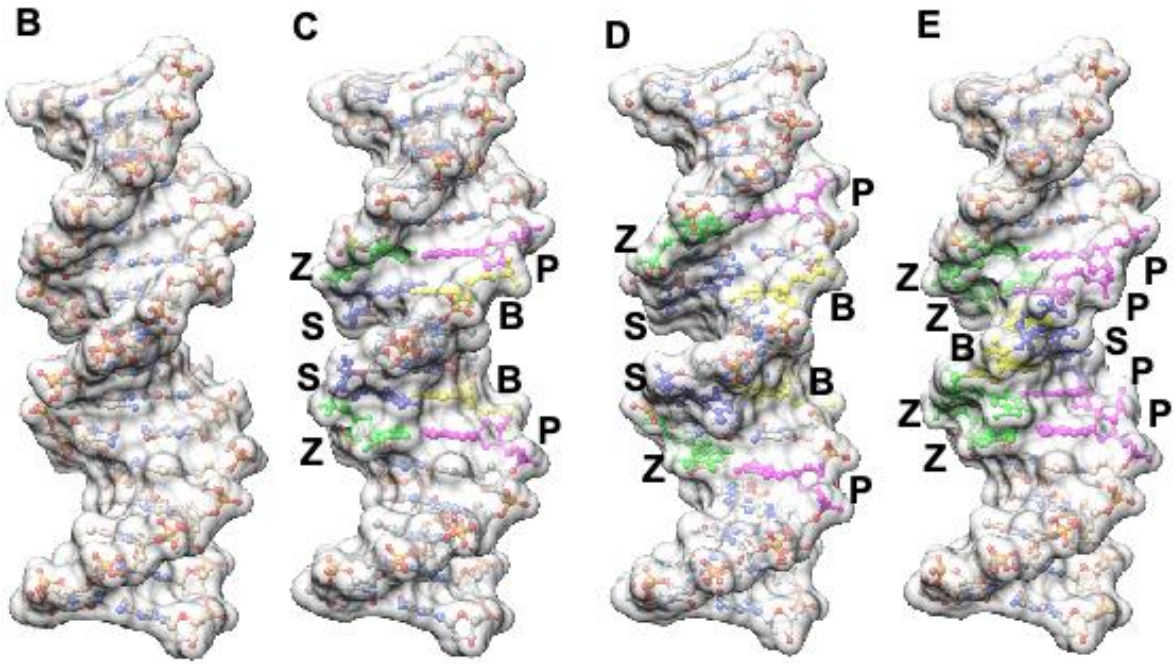
We ***know*** because we *synthesized* it, in the lab



Indeed, nucleobases tolerate significant structural changes

Alien DNA forms structures

We know because we *made* them, in the lab, and used them in diagnostics products worth $1.4 billion…



Hoshika, S., Leal, N. A., Kim, M.-J., Kim, M.-S., Karalkar, N. B., Bates, A. M., Watkins Jr., N. E., SantaLucia, H. A., Meyer, A.J., DasGupta, S., Piccirilli, J. A., Ellington, A. D., SantaLucia, J., Georgiadis, M. M., Benner, S. A. (2019) Hachimoji DNA and RNA. A genetic system with eight building blocks. *Science* **363**, 884–887.

This stores information better than 4-letter DNA. More profit.

This DNA can support evolution … to make anti-cancer drugs

What we can*not* change

Informational units must all have the same size and shape

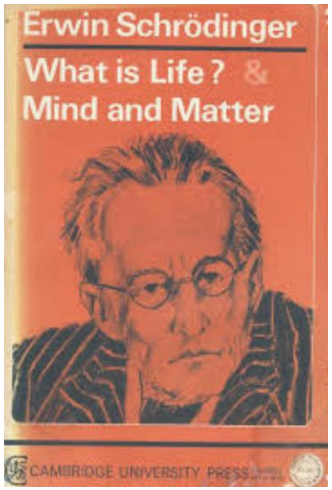
Interchanging units does not change the overall structure

Backbone supporting these units must have a repeated charge

Interchanging units does not change overall molecular properties

You can take these as experimentally validated statements

But they also have strong theoretical support



Schrödinger in 1943 knew nothing about DNA.
Simple binding cannot guarantee faithful information transfer. For that, need **phase transition physics**. For *that*, exchanged informational building blocks must all have similar size/shape. They must all fit an **aperiodic crystal structure**.

What we can*not* change

Informational units must all have the same size and shape

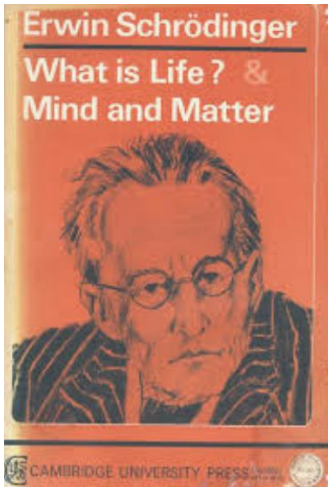
Interchanging units does not change the overall structure

Backbone supporting these units must have a repeated charge

Interchanging units does not change overall molecular properties

You can take these as experimentally validated statements

But they also have strong theoretical support



Schrödinger in 1943 knew nothing about DNA.
Simple binding cannot guarantee faithful information transfer. For that, need **phase transition physics**. For *that*, exchanged informational building blocks must all have similar size/shape. They must all fit an **aperiodic crystal structure**.

Alien DNA in H_2O may have 4, 6 or 8 units, but to support evolution, they must all have similar sizes/shapes.

That is a way to identify a *bio*-polymer in agnostic life finding

Another thing we can*not* change

Informational units must all have the same size and shape
Interchanging units does not change the overall structure

Backbone supporting these units must have a repeated charge
Interchanging units will not change overall molecular properties

To support evolution, a genetic system must be able to change information without changing physical behavior
Such as: solubility, molecular recognition rules, reactivity

Another thing we can*not* change

Informational units must all have the same size and shape
Interchanging units does not change the overall structure

Backbone supporting these units must have a repeated charge
Interchanging units will not change overall molecular properties

To support evolution, a genetic system must be able to change information without changing physical behavior
Such as: solubility, molecular recognition rules, reactivity

Such polymers are rare

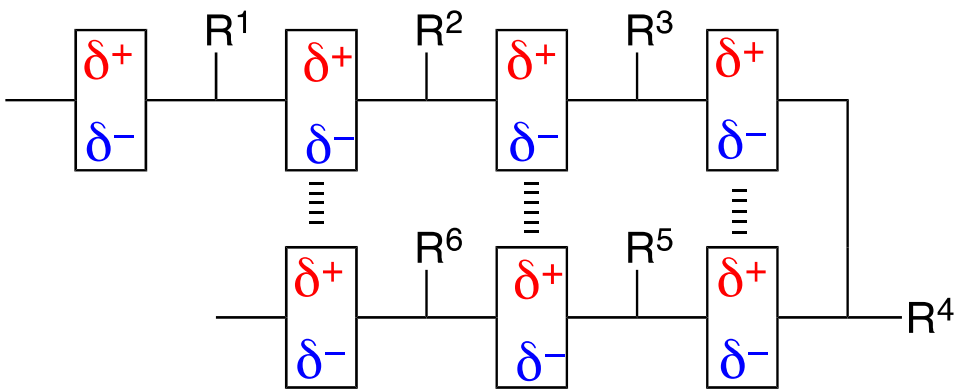
In proteins, physical behavior changes dramatically even with small changes in information content.
Protein molecules cannot support Darwinism.
Change one amino acid in hemoglobin, and it precipitates
The repeating charge lets the nucleotides change without risking precipitation, unproductive folding...

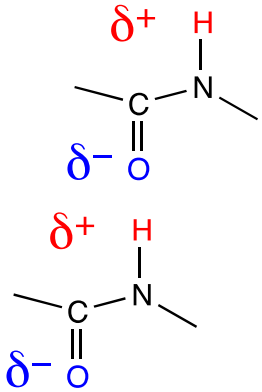
Sickle cell

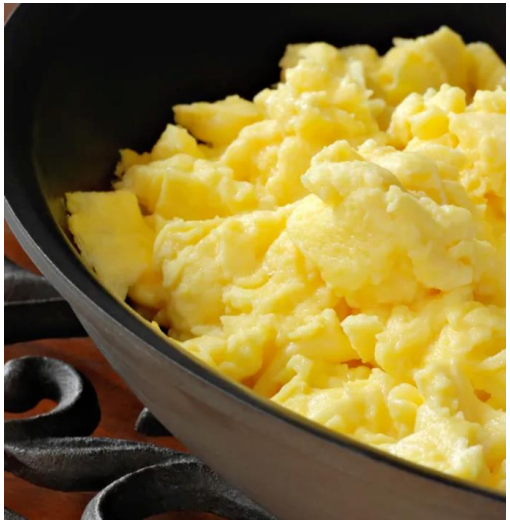
Alien DNA in H_2O may have 4, 6 or 8 units, but backbone may have a repeating positive or negative charge, but it must be a poly-electrolyte, universally, agnostically, in water.

The repeating charge repels

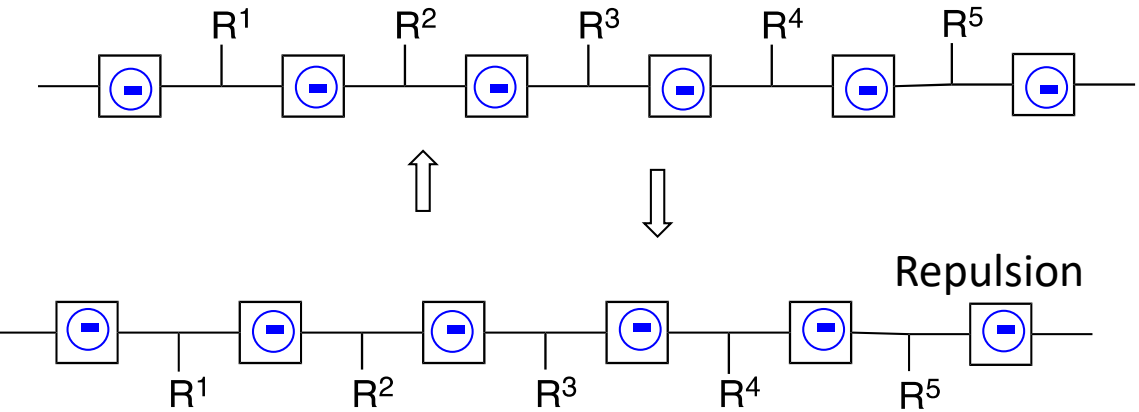
biopolymer can change information without precipitating







Precipitates no matter what the R groups are



Does not precipitates no matter what the R groups are

You do not want your informational biopolymer to become scrambled eggs.

Primordialscoop.org

Universal informational polymers in H_2O

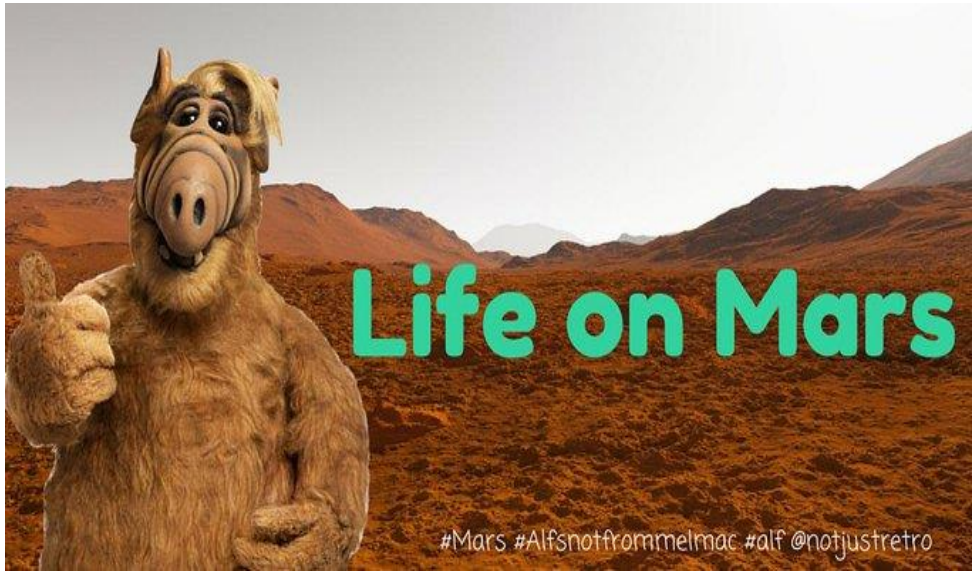
Found only in living systems; not produced without selective pressure enforcing two structural features

1. **Backbone with a repeating charge (polyelectrolyte theory of gene)**
2. **Informational units are size and shape interchangeable**

This forms the basis of an "Agnostic Life Finder" (ALF)

Repeating charge is very useful, as poly-anions (like *our* DNA) or poly-cations can be concentrated from *very* dilute solution in electrical fields

Špaček, J. (2021) "How the Agnostic Life Finder (ALF) Searches for Life on Mars". Primordial Scoop, 2021, e0211 . https://doi.org/10.52400/VNTE9601



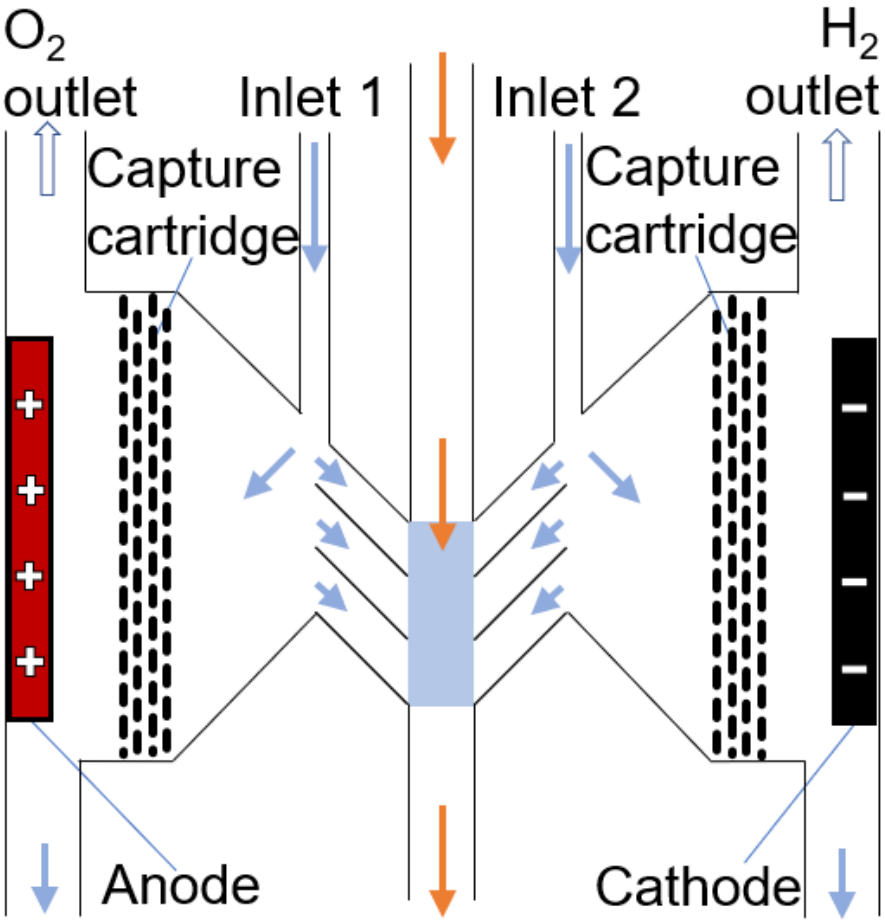
If we concentrate from Martian water poly-charged polymers assembled from units all with the similar size/shape, we have found Martian biology.

Essential for Darwinian evolution. Cannot be sustained without it.

ALF exploits poly-charge to remove any alien DNA from a flow of conditioned water

Jan Špaček designed ALF

www.primordialscoop.org



ALF extracts poly-anions and poly-cations in counter current free flow electrophoresis from flowing water mined for in situ resource utilization.

Low cost add-on to water mining to create fuel *in situ.*

Seeking instrument manufacturing partners.

sab@firebirdbio.com

What about *not* water

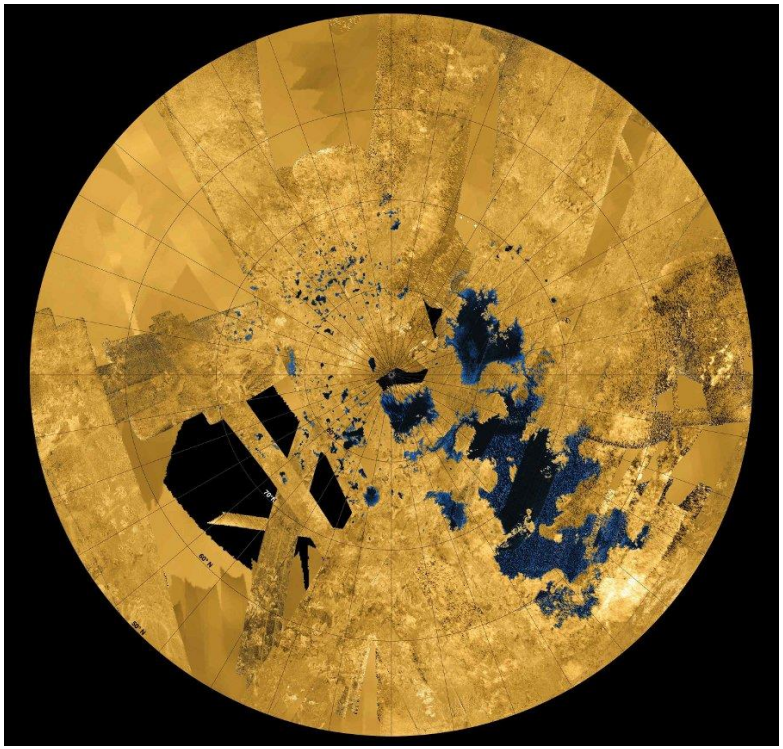
Informational units still must fit into an aperiodic crystal.

But the second requirement is only that physical properties must remain unchanged with changing information content.

In water we arrange for this by a repeating charge

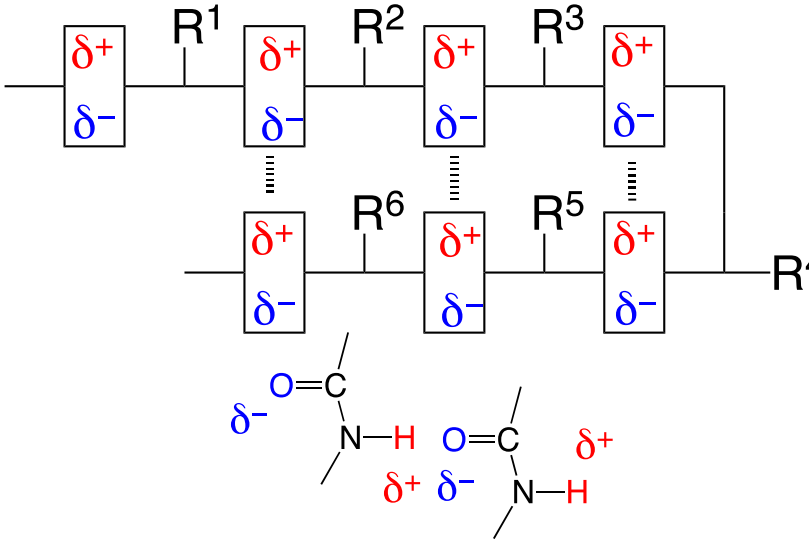
This certainly does ***not*** *work in methane (95 K, Titan)*

Are there alternatives?



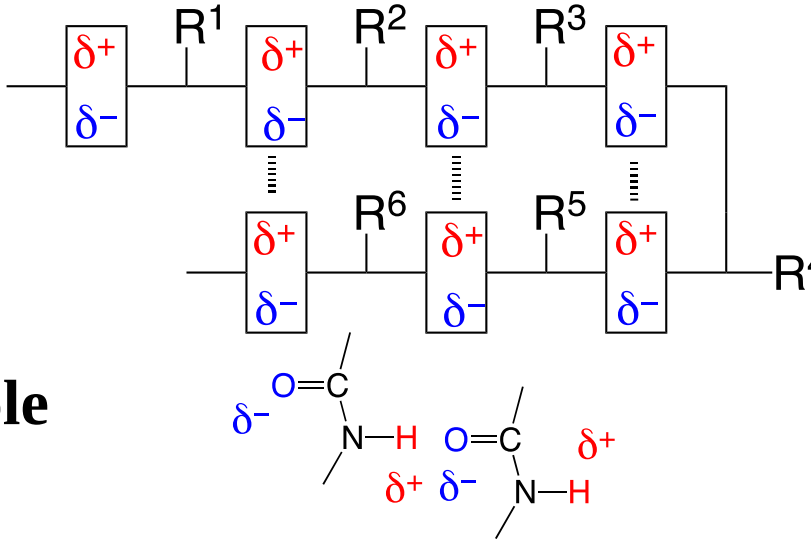
Get rid of repeating charge leaves a repeating dipole. This precipitates.

As in proteins. Alpha helices, beta sheets, the scrambled egg precipitate you ate this morning. They all form by interaction of the negative end of the amide dipole with the negative end.

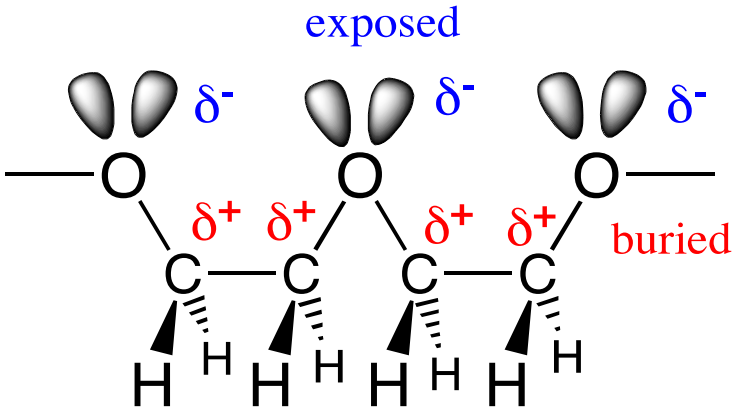


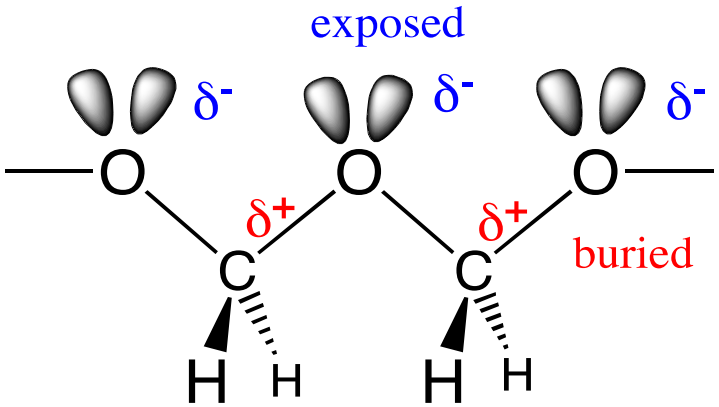
Get rid of repeating charge leaves a repeating dipole. This precipitates.

As in proteins. Alpha helices, beta sheets, the scrambled egg precipitate you ate this morning. They all form by interaction of the negative end of the amide dipole with the negative end.

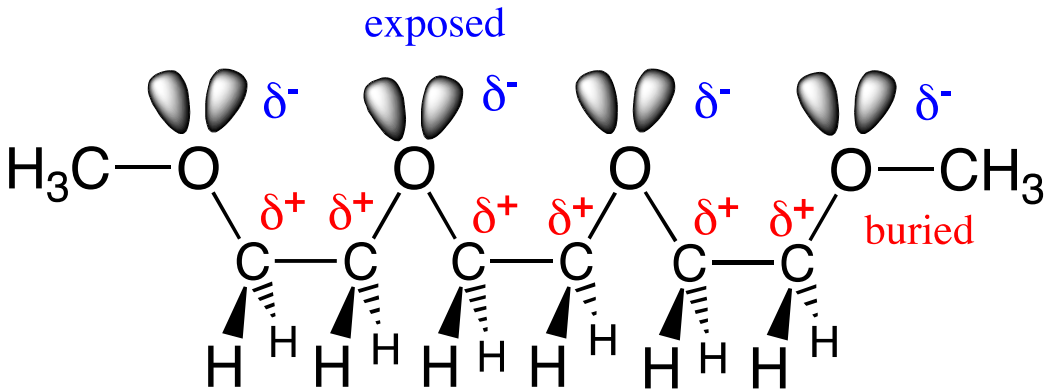


Maybe by burying one end of the dipole and exposing the other, the polymer cannot aggregate in hydrocarbon solvents?

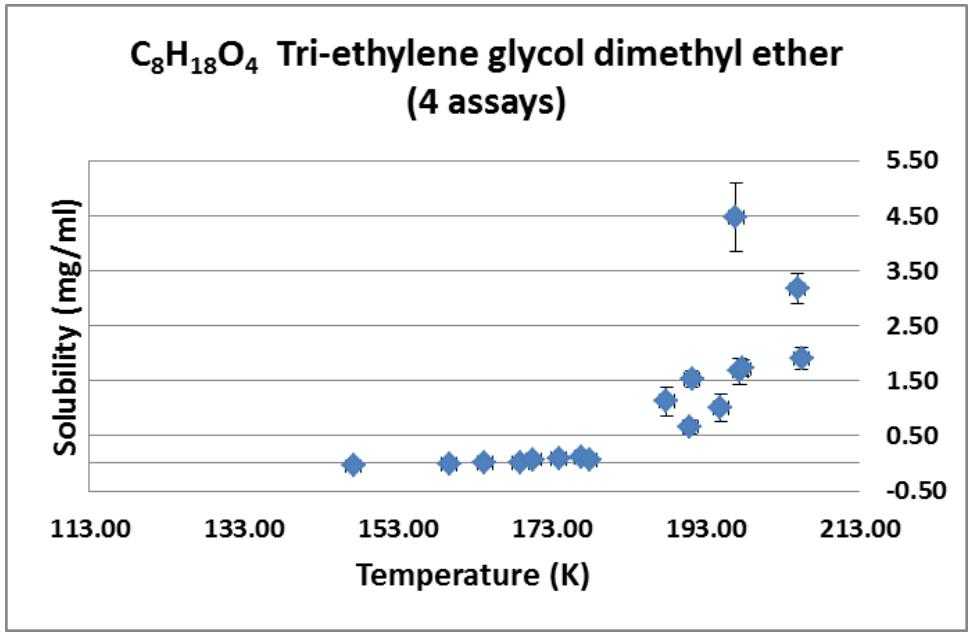




Polyethers dissolve in warm hydrocarbons, *but not human-cold hydrocarbons* cold



Hydrocarbon	Freeze	Boil
Methane	91 K	112 K
Ethane	89 K	184 K
Propane	**85 K**	**231 K**
Butane	135 K	273 K



A "warm big Titan"

McLendon, Opalko, Illangkoon, Benner (2015) Solubility of polymers in hydrocarbons at low temperatures. A model for potential genetic backbones on warm Titans. *Astrobiol.* **15**, 200-206.

Rob Hodyss, Pat Beauchamp
JPL Titan NAI
Jeff Opalko, Chris McLendon

Not much dissolves in liquid methane at 95 K

Hodyss, R., Choukroun, M., Sotin, C., Beauchamp, P. (2013) The solubility of 40Ar and 84Kr in liquid hydrocarbons: Implications for Titan's geological evolution. *Geophysical Research Letters*, *40*(12), 2935-2940.

Malaska, M. J., Hodyss, R. (2014) Dissolution of benzene, naphthalene, and biphenyl in a simulated Titan lake. *Icarus*, *242*, 74-81.

Stevenson, J. M., Fouad, W. A., Shalloway, D., Usher, D., Lunine, J., Chapman, W. G., Clancy, P. (2015) Solvation of nitrogen compounds in Titan's seas, precipitates, and atmosphere. *Icarus*, *256*, 1-12.

Benzene, naphthalene only micrograms per liter

Not much dissolves in liquid methane at 95 K

Hodyss, R., Choukroun, M., Sotin, C., Beauchamp, P. (2013) The solubility of 40Ar and 84Kr in liquid hydrocarbons: Implications for Titan's geological evolution. *Geophysical Research Letters*, *40*(12), 2935-2940.

Malaska, M. J., Hodyss, R. (2014) Dissolution of benzene, naphthalene, and biphenyl in a simulated Titan lake. *Icarus*, *242*, 74-81.

Stevenson, J. M., Fouad, W. A., Shalloway, D., Usher, D., Lunine, J., Chapman, W. G., Clancy, P. (2015) Solvation of nitrogen compounds in Titan's seas, precipitates, and atmosphere. *Icarus*, *256*, 1-12.

Benzene, naphthalene only micrograms per liter

Before Chemical Experiments (BCE). Benner et al. 2004.

"if life is an intrinsic property of chemical reactivity, life should exist on Titan. Indeed, for life not to exist on Titan, we would have to argue that life is *not* an intrinsic property of the reactivity of carbon-containing molecules under conditions where they are stable.

After Chemical Experiments (ACE). McClendon et al. 2015

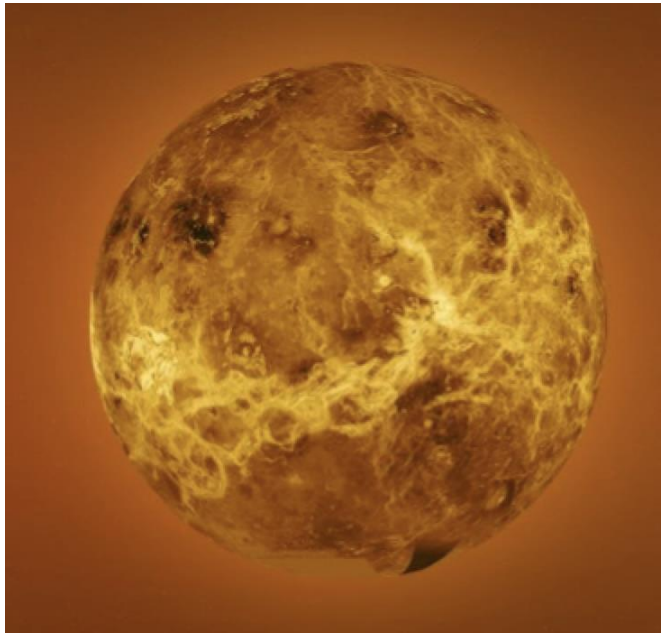
"All this would appear to diminish the likelihood that Titan holds a resident biosphere."

The first comment is quoted much more frequently than the second.

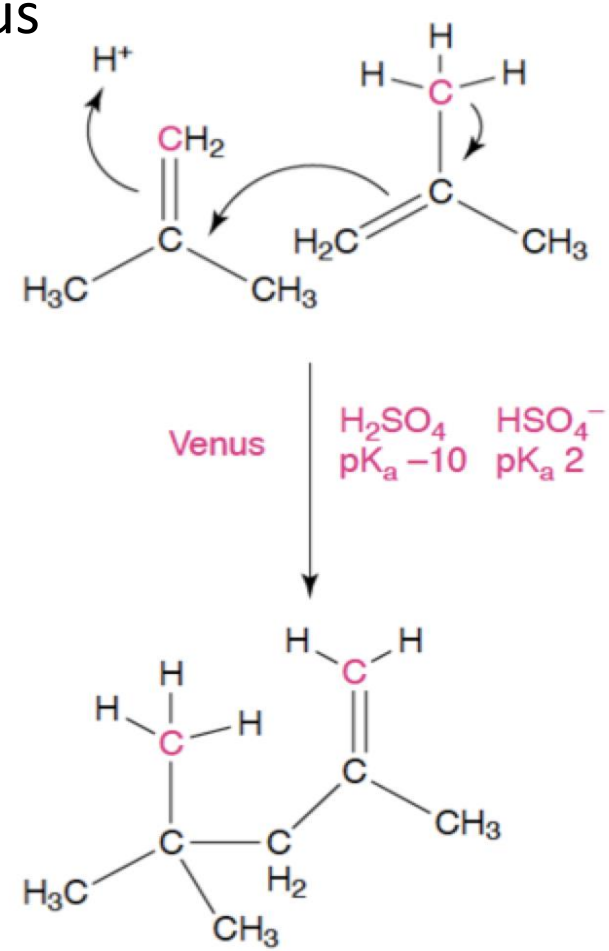
The National Academies Report required *solvents*, not *liquids*. Cryo liquids are bad solvents because they are cold.

Bains, W. (2004) Many chemistries could be used to build living systems. Astrobiology 4:137–167.

What about hot solvents?



Greaves et al. (2020)
Phosphine in Venus atmosphere?
A biosignature???



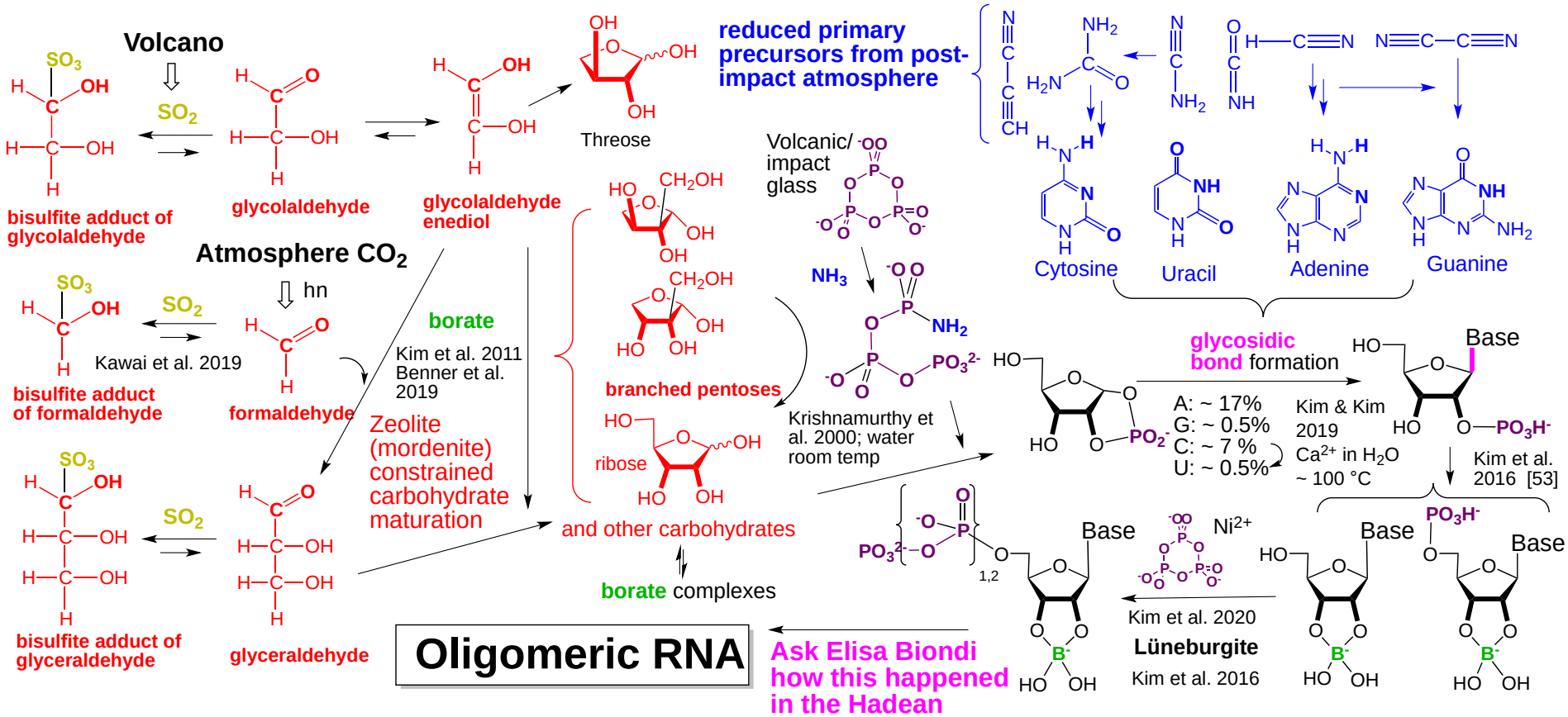
On Venus, our National Academy comments were anodyne

"Many authors have discussed possibility of life on Venus ... In strong acid, the C =C bond is reactive and can support a metabolism as an analog of the C=O unit. This type of reactivity is exemplified in some terran biochemistry. For example, acid-based reactions of the C=C unit have been used by plants as they synthesize fragrant molecules."

Replace C=O by C=C

Life is first about origins. Life may have emerged on Venus via a mechanism similar to Earth and Mars

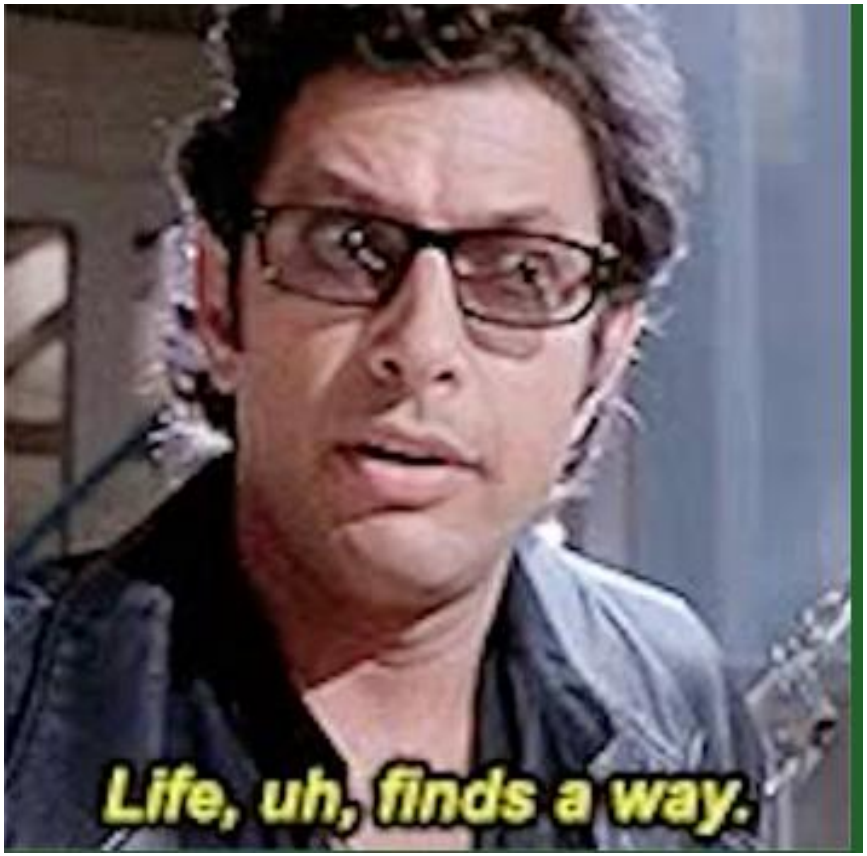
A well developed model suggests that formation of oligomeric RNA is an intrinsic outcome of an oxidized Hadean crust beneath a post impact atmosphere.



Benner, S. A., Kim, H.-J., Biondi, E. (2019) Prebiotic chemistry that could **not not** have happened. *Life* **9**(4), 84.

But after origin, life is about *persistence*.

On Earth, the RNA that emerged from an oxidized crust under a post-impact atmosphere has found a way to occupy all niches with energy and water.



On Earth, life had to find a way to survive poisoning by O_2.

On Mars, life had to find a way to survive cooling and loss of much atmosphere.

On Titan, life had to find a way to survive as a warm hydrocarbon solvent cools to bad cryosolvent.

On Venus, life had to find a way to survive replacement of H_2O by H_2SO_4 .

Notice the use of the word "replacement"

The "activity of water", phosphine, "biology in the gaps", and Earth-o-Centricity

"Activity of water" is a terracentric shorthand with unfortunate cultural history

- The Allan Hills meteorite caught NASA flatfooted in 1996.
- The public (and President Clinton) clearly wanted to know if Mars held life
- But the 1976 Viking life detection efforts were seen by some as causing the Mars program to have lost funding for over 20 years
- So NASA felt it needed a way to look for life without saying it was "looking for life"
- "Follow the water", "looking for habitability", these were some of the thoughts
- In a scientific culture, these things get a life of their own
- Then Tosca and Knoll used "water activity" as a metric to assess livability in "water plus"

Hallsworth *et al.* 2021. Talks from Rakesh on Monday, Mark Bullock on Wednesday.

The "activity of water", phosphine, "biology in the gaps", and Earth-o-Centricity

"Activity of water" is a terracentric shorthand with unfortunate cultural history

- The Allan Hills meteorite caught NASA flatfooted in 1996.
- The public (and President Clinton) clearly wanted to know if Mars held life.
- But the 1976 Viking life detection efforts were seen by some as causing the Mars program to have lost funding for over 20 years.
- So NASA felt it needed a way to look for life without saying it was "looking for life".
- "Follow the water", "looking for habitability", these were some of the thoughts
- In a scientific culture, these things get a life of their own.
- Then Tosca and Knoll used "water activity" as a metric to assess livability in "water plus".

Hallsworth *et al.* 2021. Talks from Rakesh on Monday, Mark Bullock on Wednesday.

Forget "water activity" as a metric for alien biology.

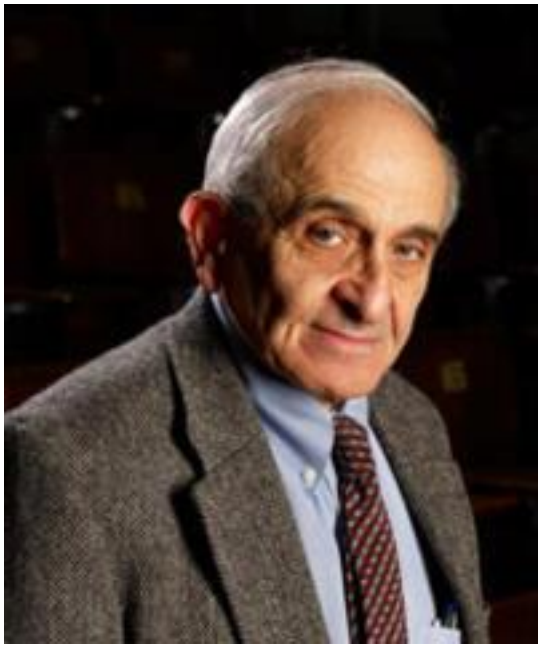
If life exists in a fluid where activity of water is low, it will have adapted to that activity.
RNA, other Schrödingerian polyelectrolytes work fine at high salt.

Problem with Venus cloud fluid is not that its water activity is low.

The problem is that the Venusian cloud fluid is not water.

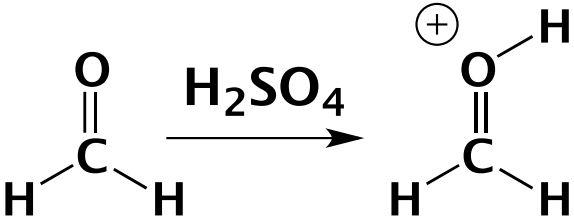
But the problem is worse

Strong H_2SO_4 is a fluid moves where "standard organic chemistry" does not offer good intuitions.



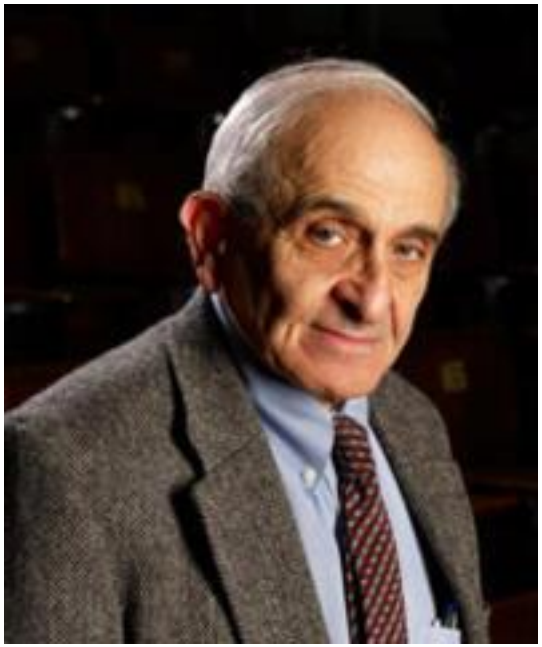
We asked Martin Saunders, who did the Nobel Prize-winning work on organic reactivity in strong acids: "What happens when you put formaldehyde in sulfuric acid?"

His answer: You get protonated formaldehyde



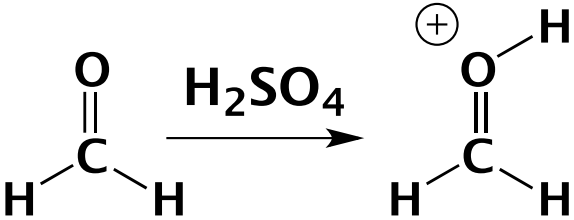
But the problem is worse

Strong H_2SO_4 is a fluid moves where "standard organic chemistry" does not offer good intuitions.



We asked Martin Saunders, who did the Nobel Prize-winning work on organic reactivity in strong acids: "What happens when you put formaldehyde in sulfuric acid?"

His answer: You get protonated formaldehyde

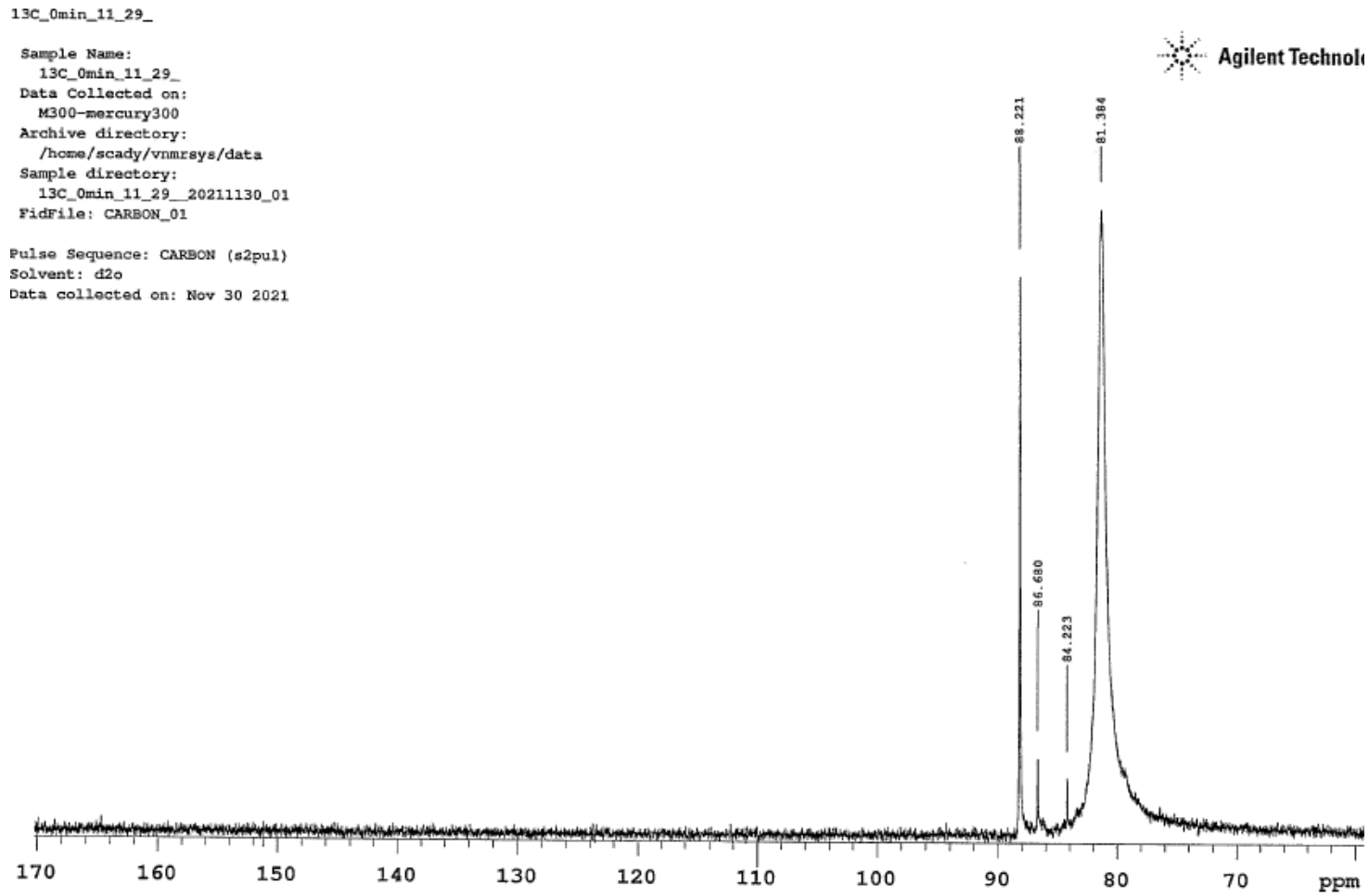


Jan Špaček's favorite game now is to get me to predict the outcome of an organic reaction in strong H_2SO_4, and then by experiment to show that my prediction is wrong.

So I went to work for Jan as his technician

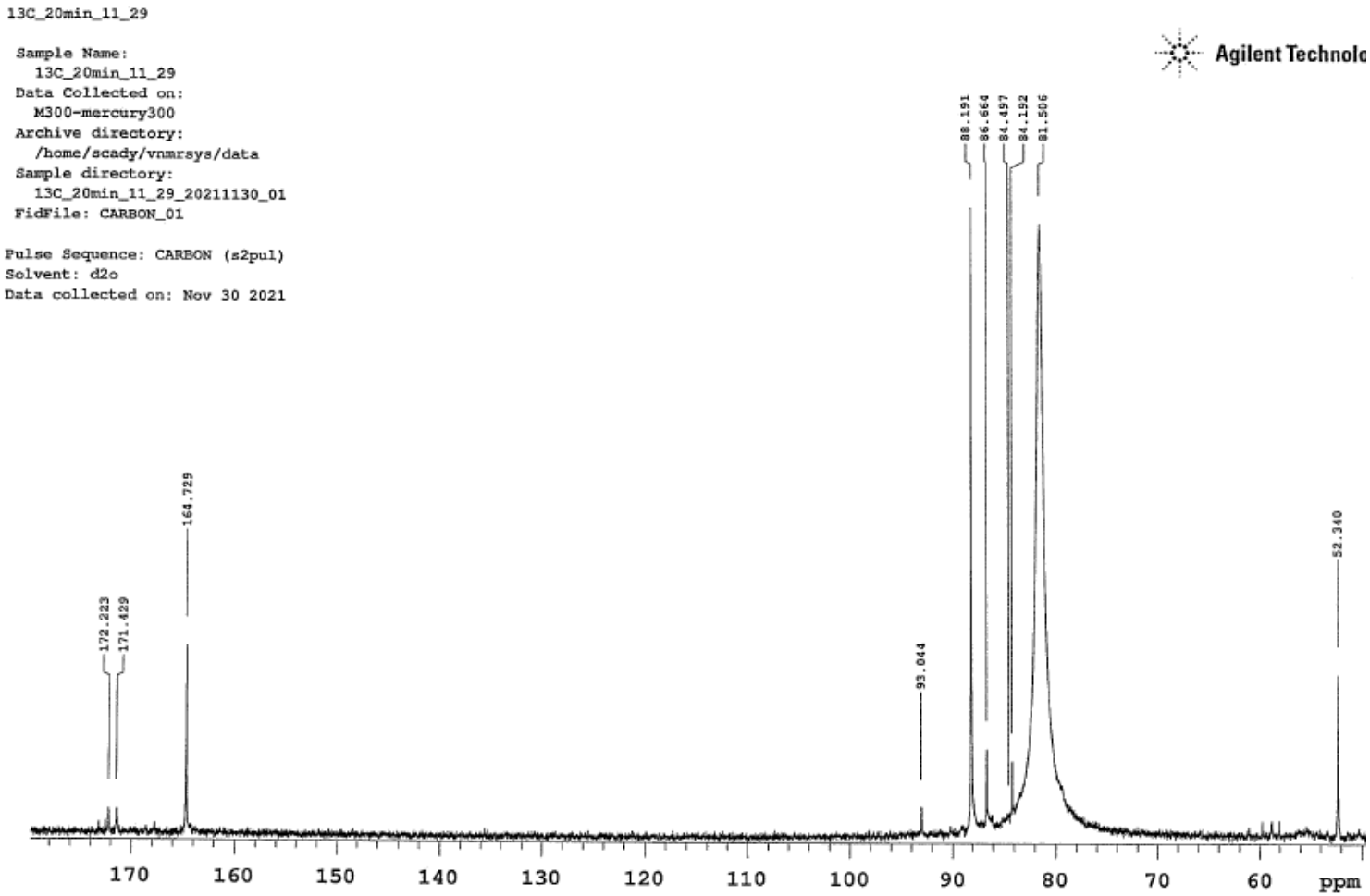
Experiments show that much more happens when HCHO is put in H_2SO_4

In 15 minutes, C-C bonds start to form.
Then, as Jan Špaček said on Monday, much much more happens.



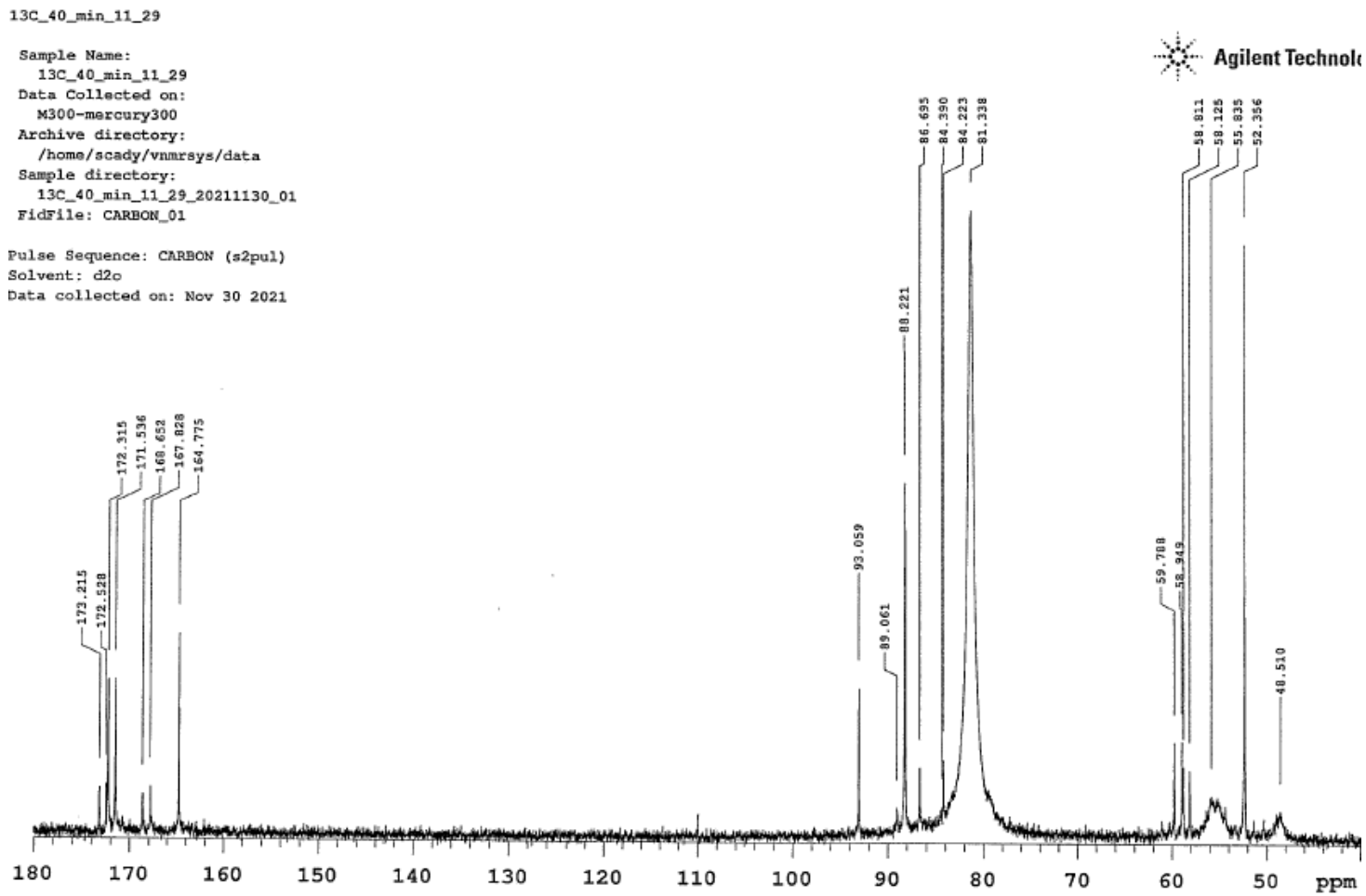
Experiments show that much more happens when HCHO is put in H_2SO_4

In 15 minutes, C-C bonds start to form.
Then, as Jan Špaček said on Monday, much much more happens.

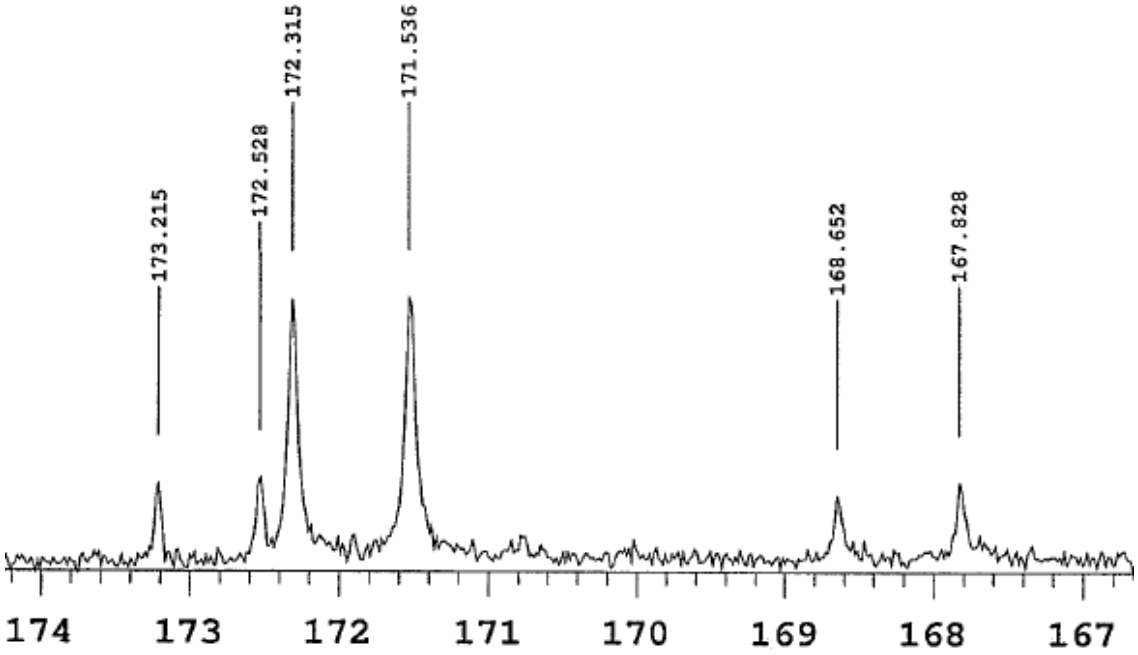


Experiments show that much more happens when HCHO is put in H_2SO_4

In 15 minutes, C-C bonds start to form.
Then, as Jan Špaček said on Monday, much much more happens.

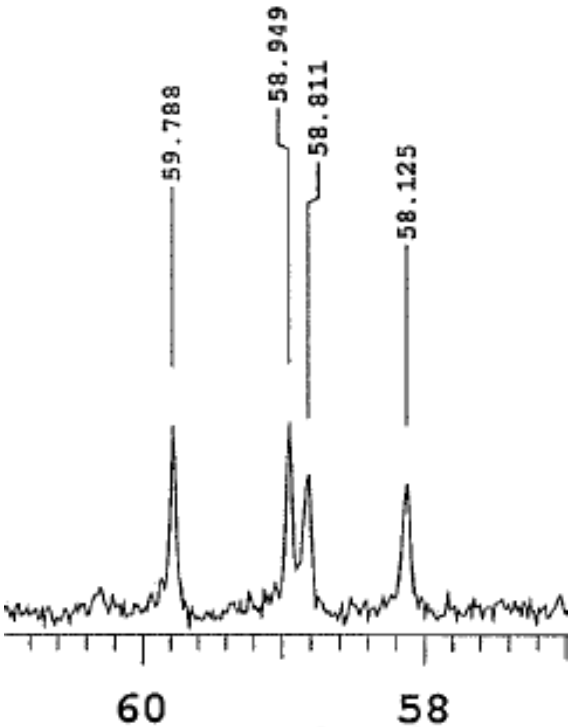


How do we know that C-C bonds form ^{13}C-^{13}C nmr coupling starting with $H^{13}CHO$



51.38 Hz

These two carbons are bonded

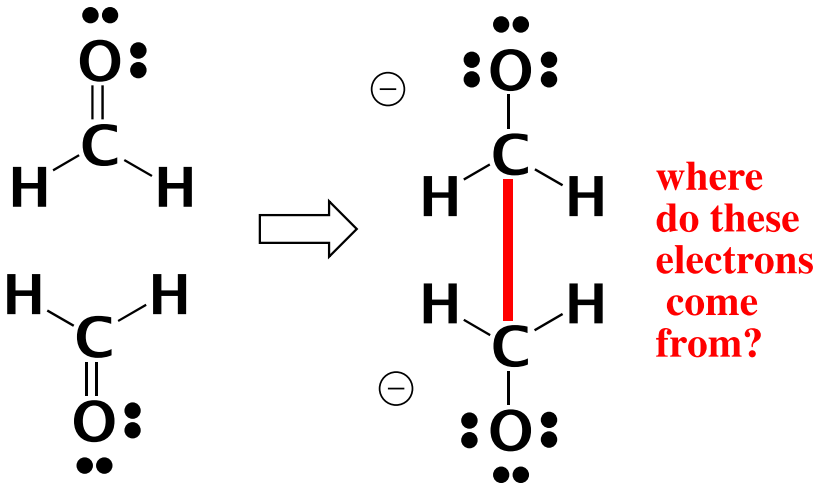


51.45 Hz

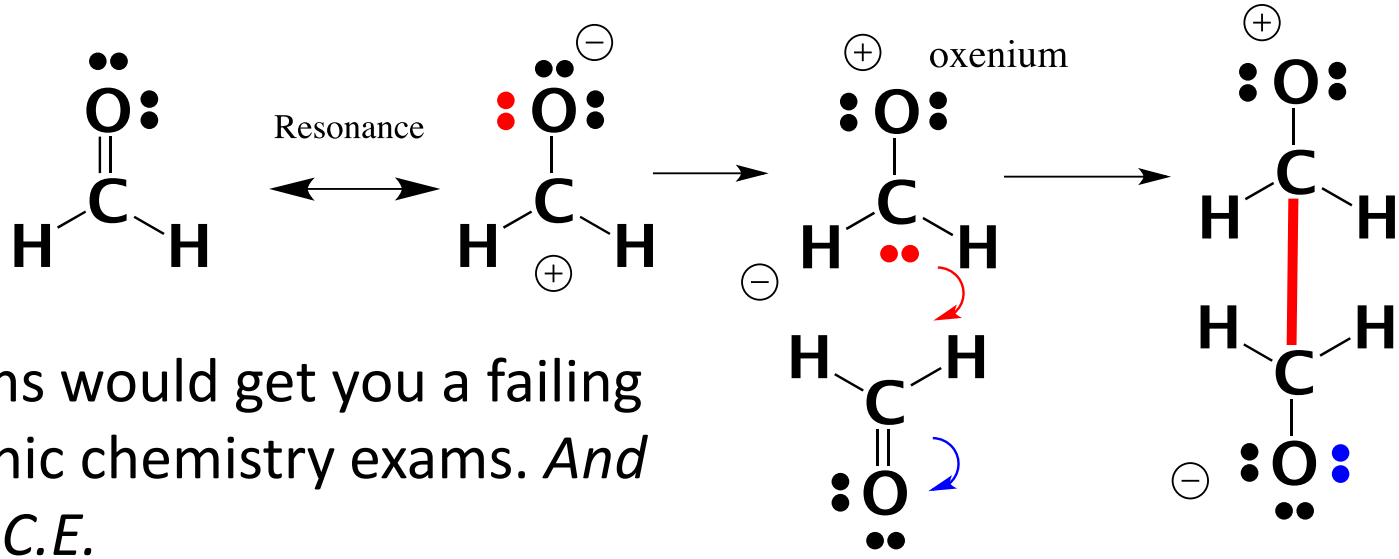
Why do these organic chemists get so excited by one lousy bond?

Why worry about $C_1H_2O_1 + C_1H_2O_1 \rightarrow C_2H_4O_2$??? *Get a life!*

Where do the bonding electrons come from?



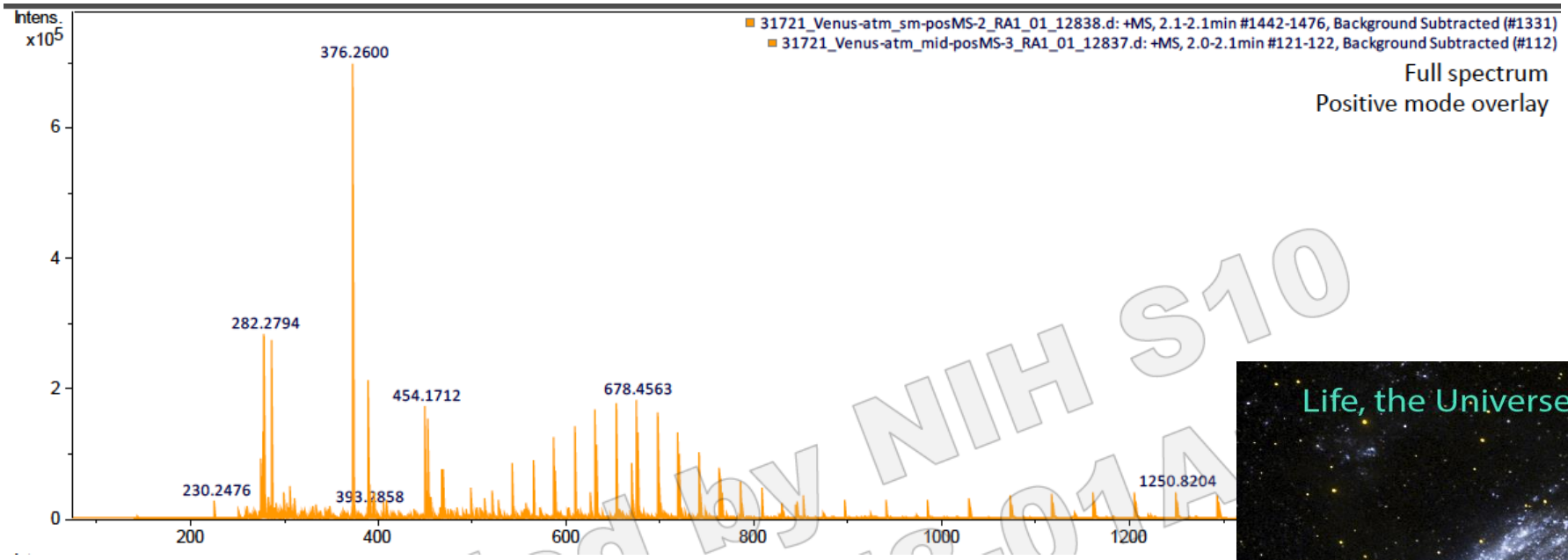
A parallel problem arises in reaction of single carbon species in alkaline conditions (the "formose reaction")



These mechanisms would get you a failing grade on an organic chemistry exams. *And yet it happens. A.C.E.*

Much more happens with HCHO in H_2SO_4

A polymer with an apparent repeating C_2H_4O unit, after neutralization, evidently with C-C bond formation.

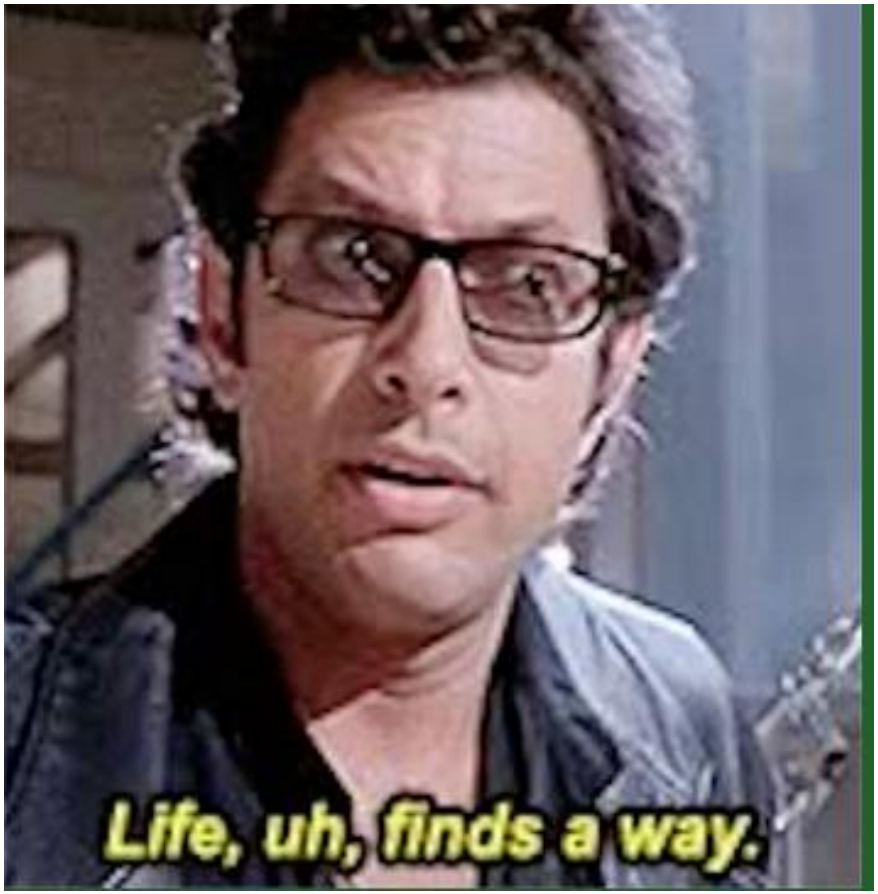


I do not think this is some contaminant, but not yet certain.

If you can get polymers, then you can get polymers with exchangeable units that fit a Schrödinger aperiodic crystal, and have a repeating charge.

Primordialscoop.org

On Venus, life had to find a way to survive the replacement of H_2O by H_2SO_4



Life's adaptability, is impressive, but a move from "standard" organic reactivity seems extreme (from our perspective as "ugly bags of mostly water).

On the other hand, the "non-standard" chemistry that occurs on Venus offers very alternative ways to "do" life, including informational polymers that meet necessary/sufficient structural requirements. We are only starting to explore these.

So what about phosphine?

Phosphine, the "activity of water", "Biology in the Gaps", and Earth-o-Centricity

Primordialscoop.org

Aristotle and the search for life on Venus

- Never throw good thought at uncertain data.
- But let us assume that PH_3 is there
- Greaves et al. write: "[All] the geological and photochemical routes we can think of are far too underproductive to make the phosphine we see." Hence … biology.
- To evaluate a "biology in the gaps" idea, one must ask about *fitness*.
- A first pass at "fitness" can be done by thermodynamics
- Terran organisms that make PH_3 are in environments rich in H and scarce in O.
- They grab scarce O from H_2O for use, throw away H *with two electrons* as PH_3.
- That is how PH_3 generation makes them fit In an environment where oxygen is scarce
- Now, the Venusian atmosphere is O-rich. It is poor in hydrogen *with two electrons.*
- Yes, Venusians might be able to extract H from H_2SO_4.
- A Venusian who throws away H (electrons) as PH_3 will not be attractive to mates.
- And not very fit over competitors who keep the scarce hydrogen for themselves.

If you want to talk about life, must talk about fitness, not mechanism

What have you seen today?

1. Universal agnostic biosignatures in water

If life is about information and evolution, only certain classes of biopolymers can support life in H_2O

- **polyelectrolytes**
- **building blocks that fit into a polyelectrolyte structure**

We have models for these to emerge on rocky planets

2. The Mars challenge is getting someone to look

3. challenge in cryosolvents is getting solubility

4. Venus offers two challenges

- **If terran-style life emerged, finding a way to continuously evolve to survive in its solvent *replacement.***
- **Getting rid of Earth-o-Centricity to build an understanding of organic chemistry that must be occurring on Venus.**

Elisa Biondi, Jan Špaček