

Craving continuity from cosmochemistry to cosmochemists

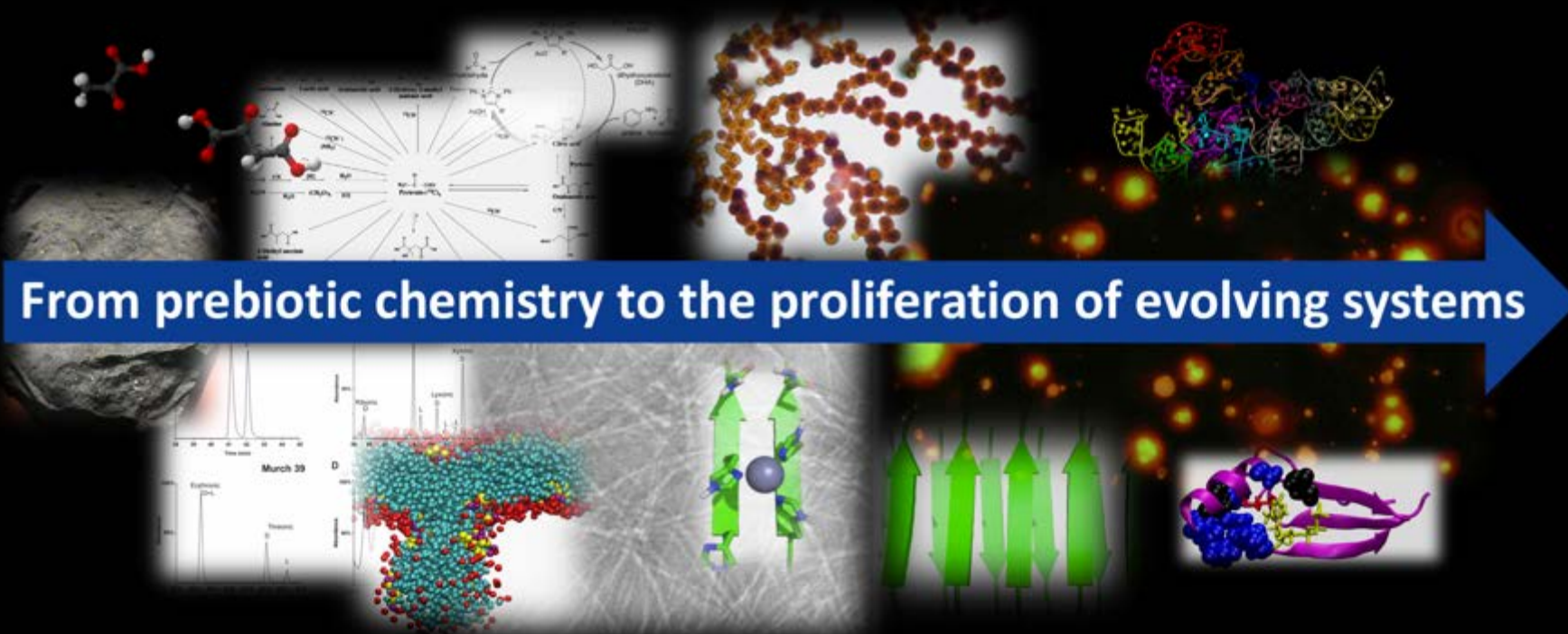


**Mark A. Ditzler, Center for the Emergence of Life, NASA Ames Research Center
February 27th 2019**

We ask fundamental questions

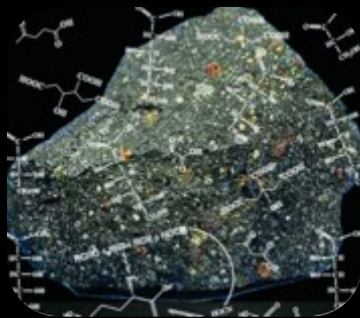
What processes drove the emergence and early evolution of life on Earth?

What is the potential for life to emerge in other habitable environments?

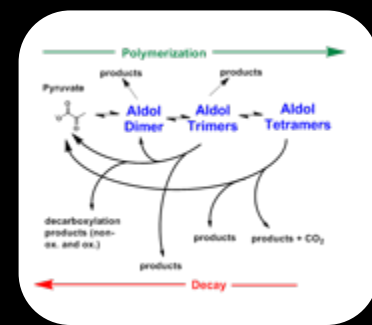


We are interdisciplinary

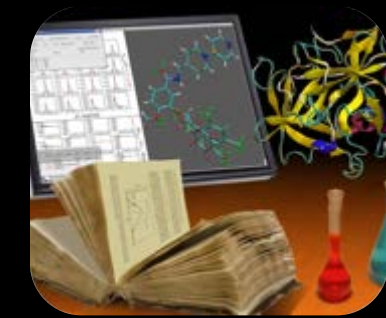
Cosmochemistry



Systems Chemistry



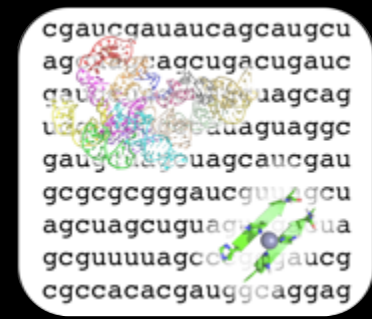
Molecular Modeling



In vitro Evolution



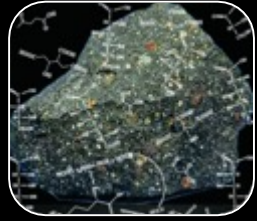
Bioinformatics



Synthetic Biology



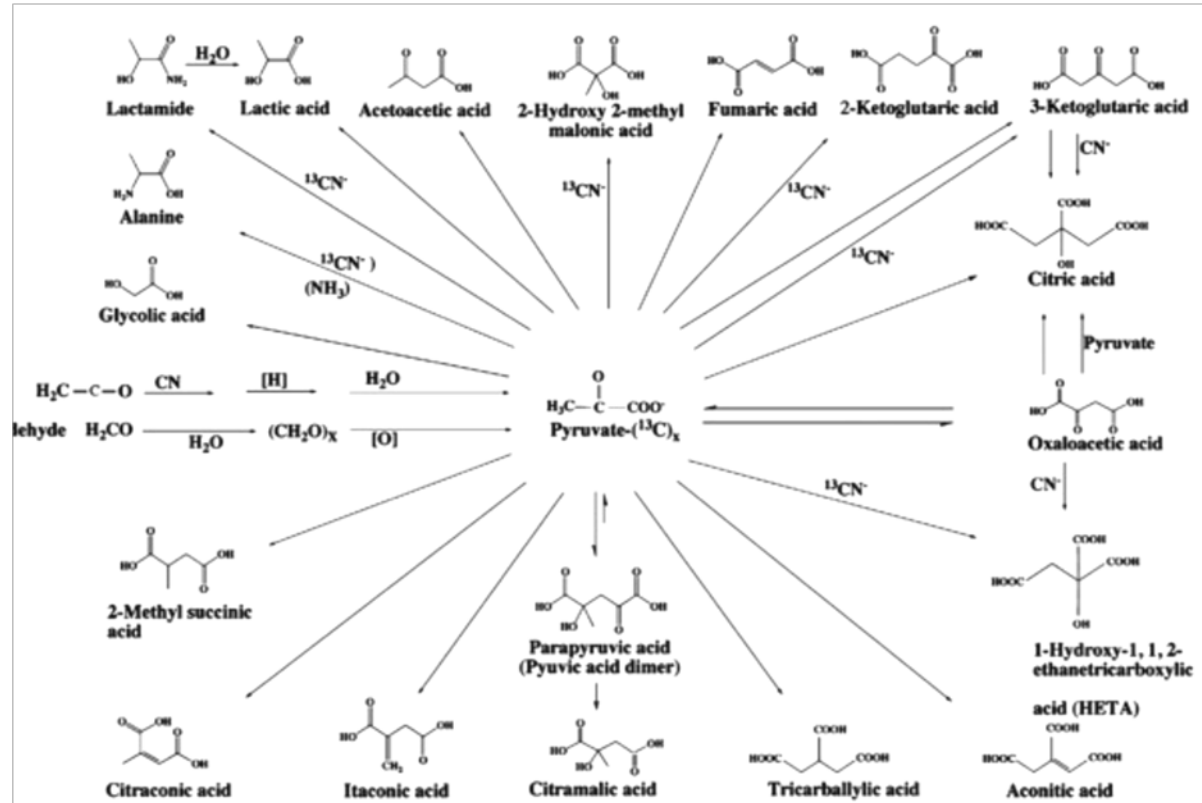
Potential proto-life pieces plop down from the sky



Tons of carbon per year rains down on the Earth (IDPs and meteorites)



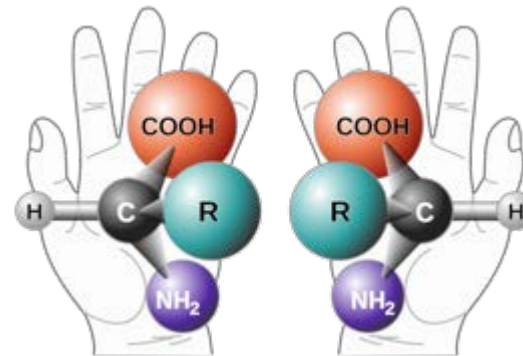
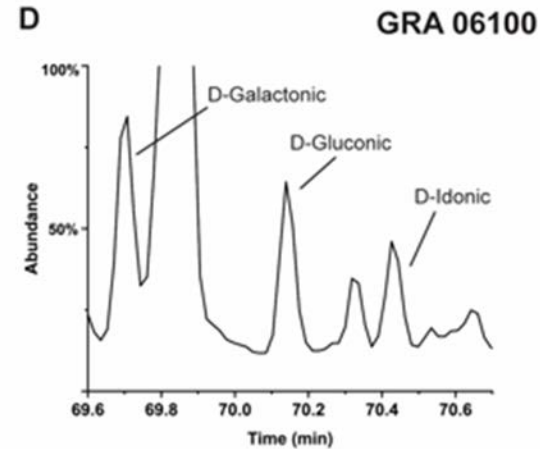
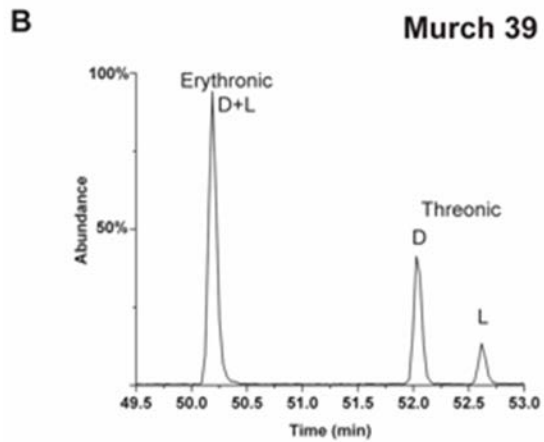
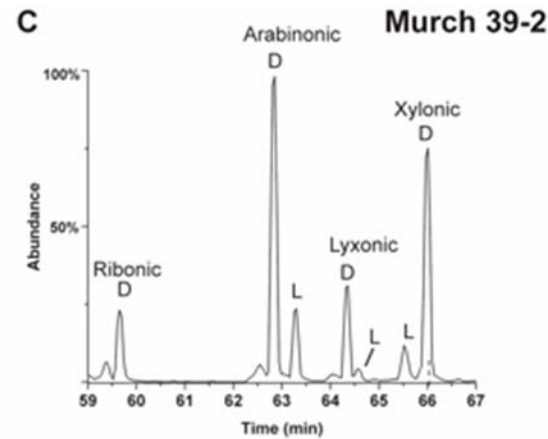
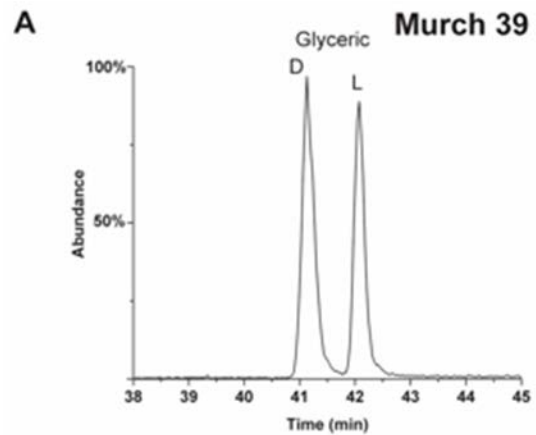
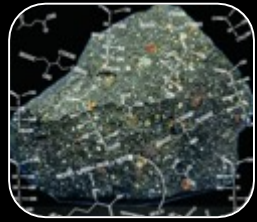
e.g. Murchinson



George Cooper

Cooper, G., Reed, C., Nguyen, D., Carter, M., & Wang, Y. (2011). Detection and formation scenario of citric acid, pyruvic acid, and other possible metabolism precursors in carbonaceous meteorites. *Proceedings of the National Academy of Sciences*, 108(34), 14015-14020.

Curiously, cosmochemistry can cause chiral preference



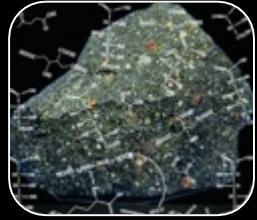
George Cooper



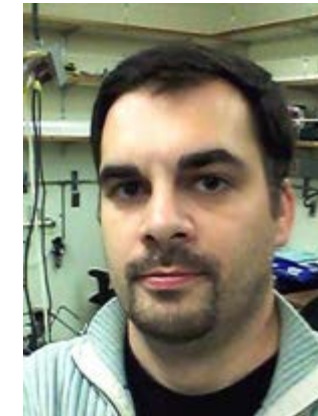
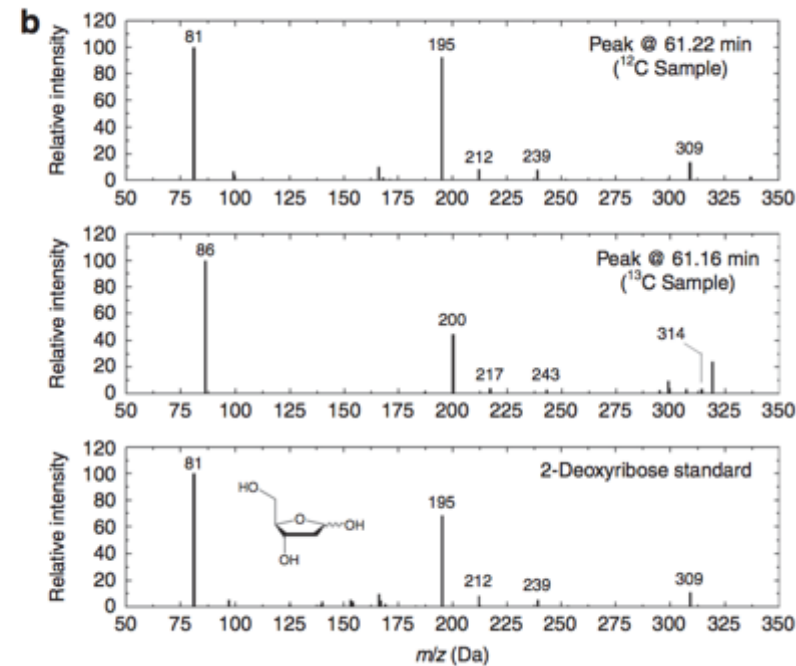
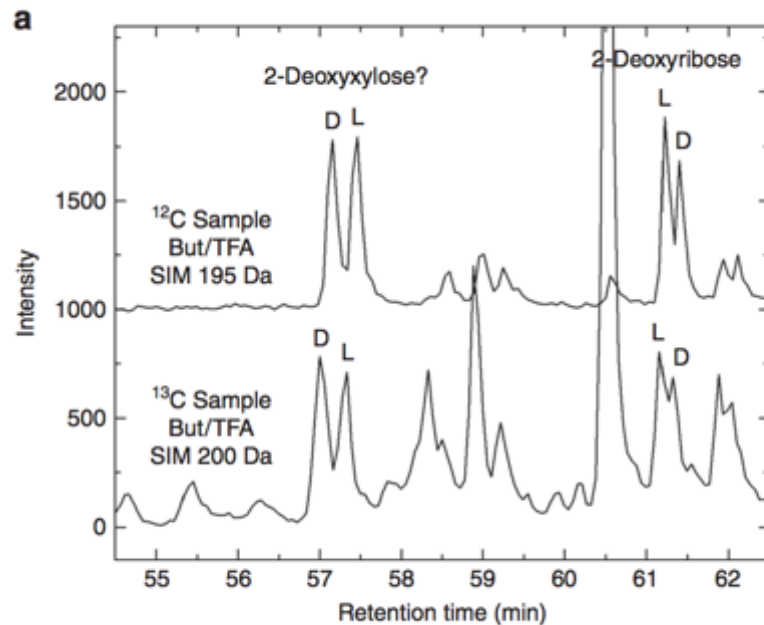
Andro Rios

Cooper, G., & Rios, A. C. (2016). Enantiomer excesses of rare and common sugar derivatives in carbonaceous meteorites. *Proceedings of the National Academy of Sciences*, 113(24), E3322-E3331.

Investigating irradiated ices indicates irrelevant “building blocks” can be identified



Deoxyribose: it is there but I doubt that's why we use it



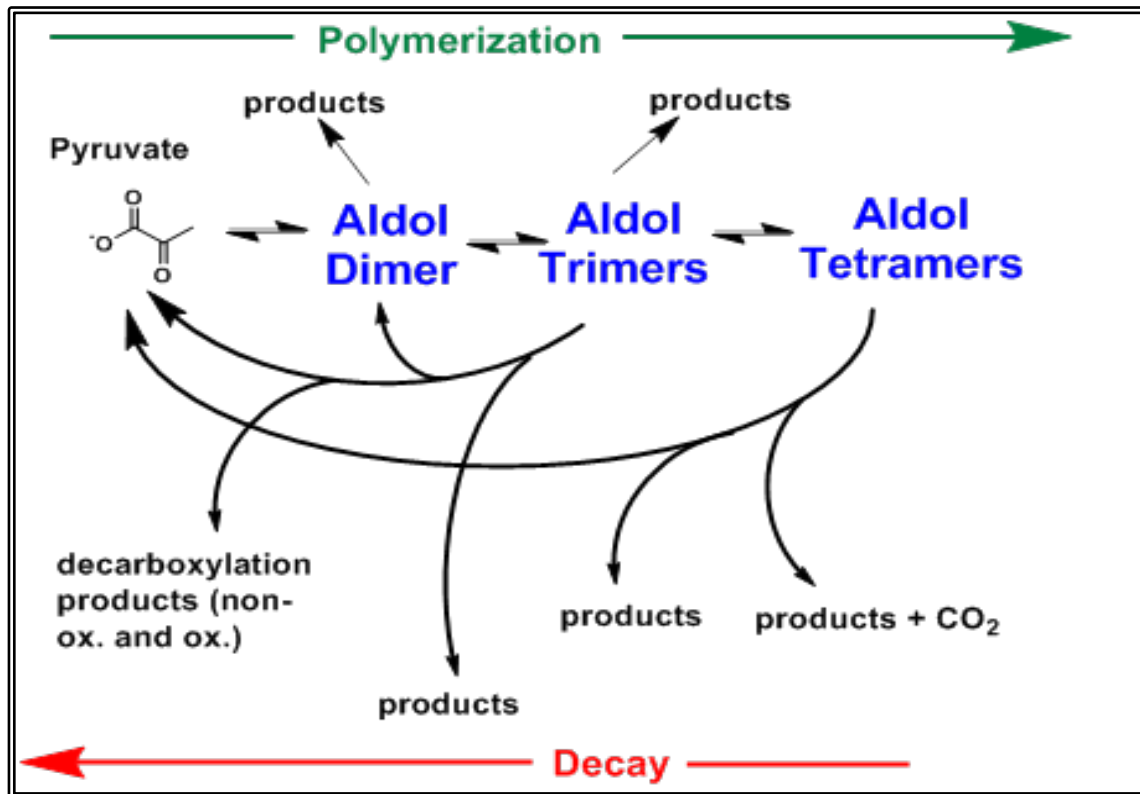
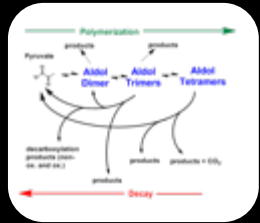
Michel Nuevo



Scott Sandford

Nuevo, M., Cooper, G., & Sandford, S. A. (2018). Deoxyribose and deoxysugar derivatives from photoprocessed astrophysical ice analogues and comparison to meteorites. *Nature Communications*, 9(1), 5276.

The process of providing the pieces (pyruvate polymers)



Network model for the pyruvate reaction network (PRN).



Andro Rios



George Cooper

Explain what is observed in meteorites and predict how this can lead to metabolism

Interesting insights from in vitro evolution



In vitro evolution can be used to ask...

What RNA can do?

How can RNA evolve new functions?

How common are functional RNAs in sequence space?

How complex do functional RNAs need to be?

What were the roles of chance and necessity in the evolution biological RNA structures?

Initial DNA template library ($\sim 10^{15}$ unique sequences)

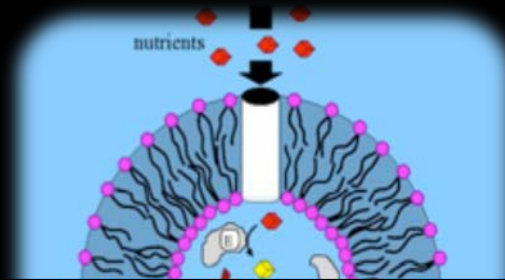
Geochemical, cellular, and genomic context of early evolutionary processes



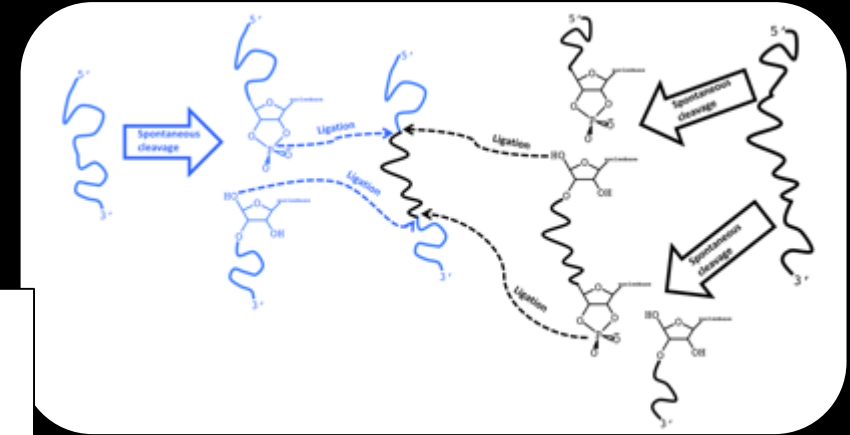
The early geochemical environment



The emerging cellular environment



Early and dynamic genomic environment



7070–7082 *Nucleic Acids Research*, 2015, Vol. 43, No. 14
doi: 10.1093/nar/gkv648

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***In vitro* evolution of distinct self-cleaving ribozymes in diverse environments**

Milena Popović^{1,2,3}, Palmer S. Fliss³ and Mark A. Ditzler^{2,*}

¹NASA Postdoctoral Program, NASA Ames Research Center, Moffett Field, CA 94035, USA, ²Space Science and Astrobiology Division, Exobiology Branch, NASA Ames Research Center, Moffett Field, CA 94035, USA, ³Marble Space Institute of Science, Seattle, WA 98145, USA

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Evolution of ribozymes in the presence of a mineral surface

JAMES D. STEPHENSON,^{1,2} MILENA POPOVIĆ,^{2,3} THOMAS F. BRISTOW,² and MARK A. DITZLER²

¹NASA Postdoctoral Program, NASA Ames Research Center, Moffett Field, California 94035, USA

²Space Science and Astrobiology Division, Exobiology Branch, NASA Ames Research Center, Moffett Field, California 94035, USA

³Blue Marble Space Institute of Science, Seattle, Washington 98145, USA

Journal of Molecular Evolution (2019) 87:240–253
<https://doi.org/10.1007/s00239-019-09906-3>

ORIGINAL ARTICLE

Big on Change, Small on Innovation: Evolutionary Consequences of RNA Sequence Duplication

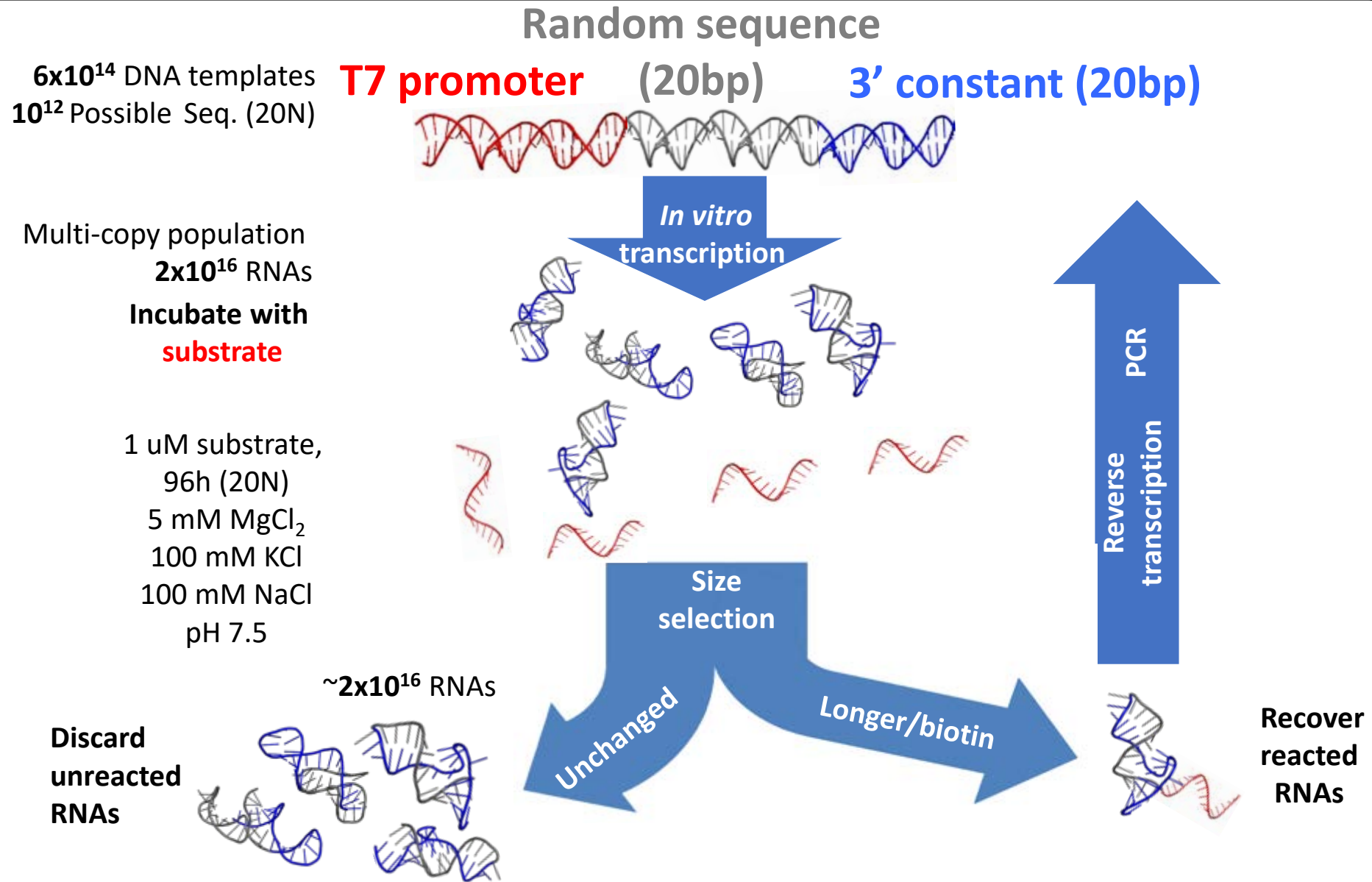
Andrew Plebanek^{1,2} · Caleb Larned³ · Milena Popović^{1,4,5} · Chenyu Wei^{1,2,4} · Andrew Pohorille^{1,2,4} · Mark A. Ditzler^{1,4}

Early and dynamic genomic environment

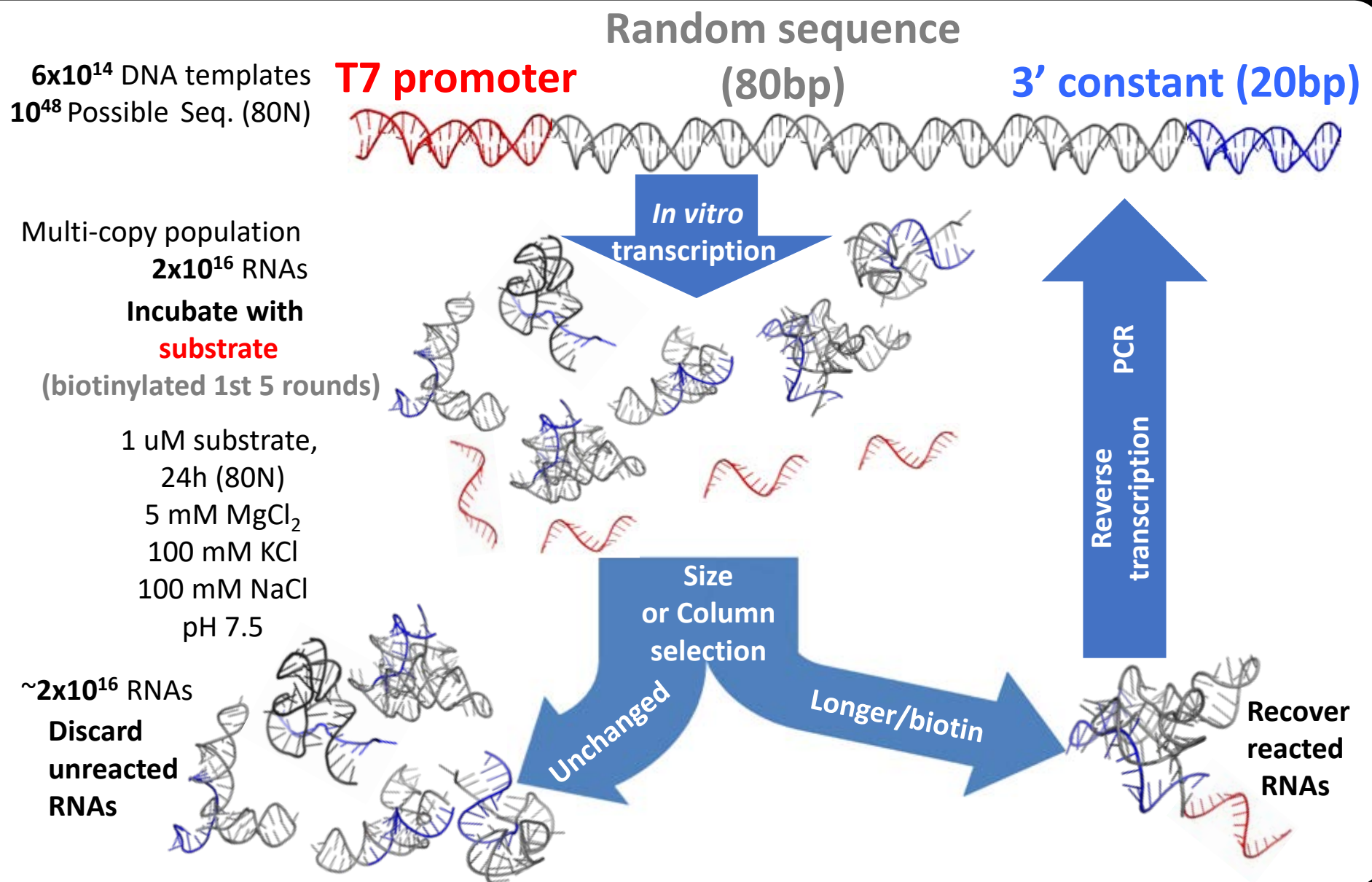


**What is the role of polymer length in
RNA evolution?**

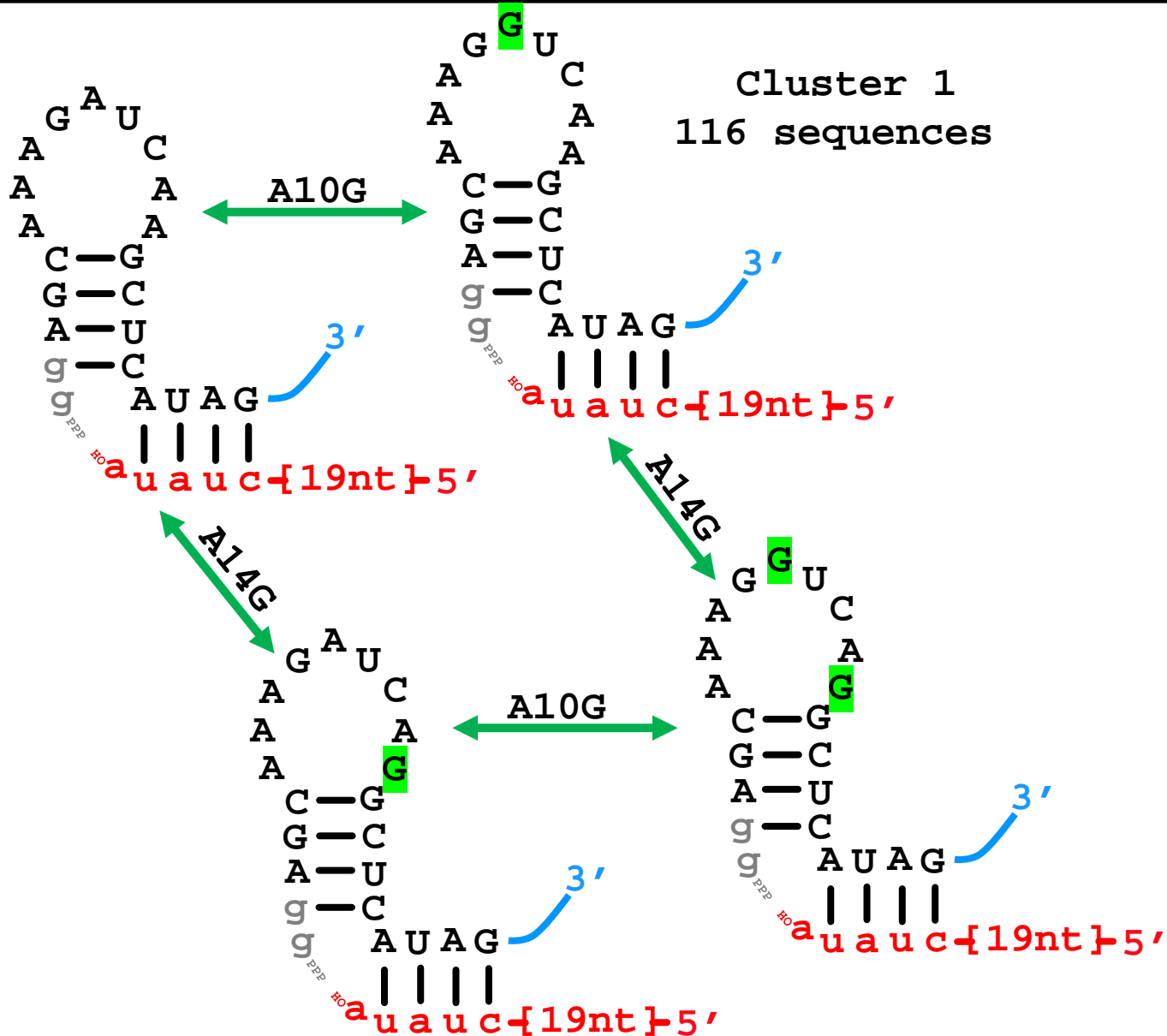
In vitro evolution of ligase ribozymes (20N)



In vitro evolution of ligase ribozymes (80N)



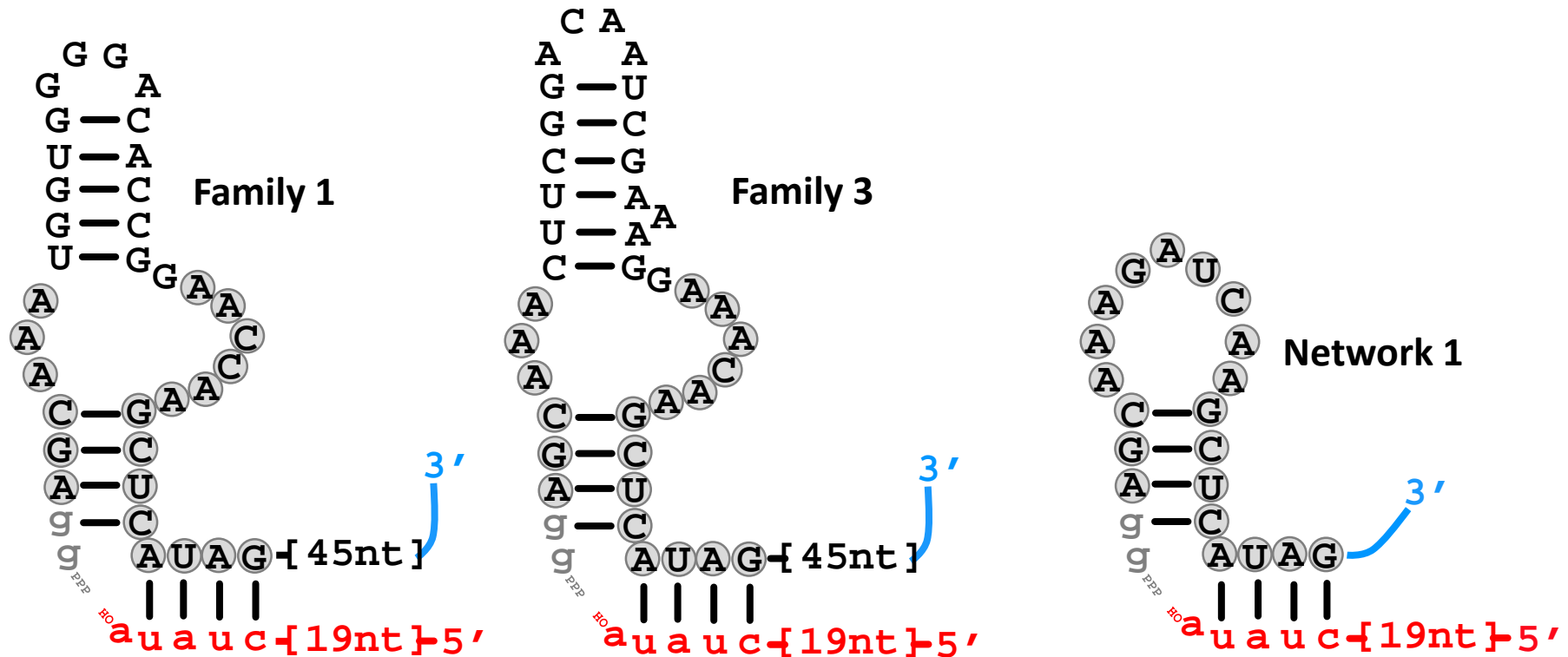
20N ligases: isolated networks for small RNAs



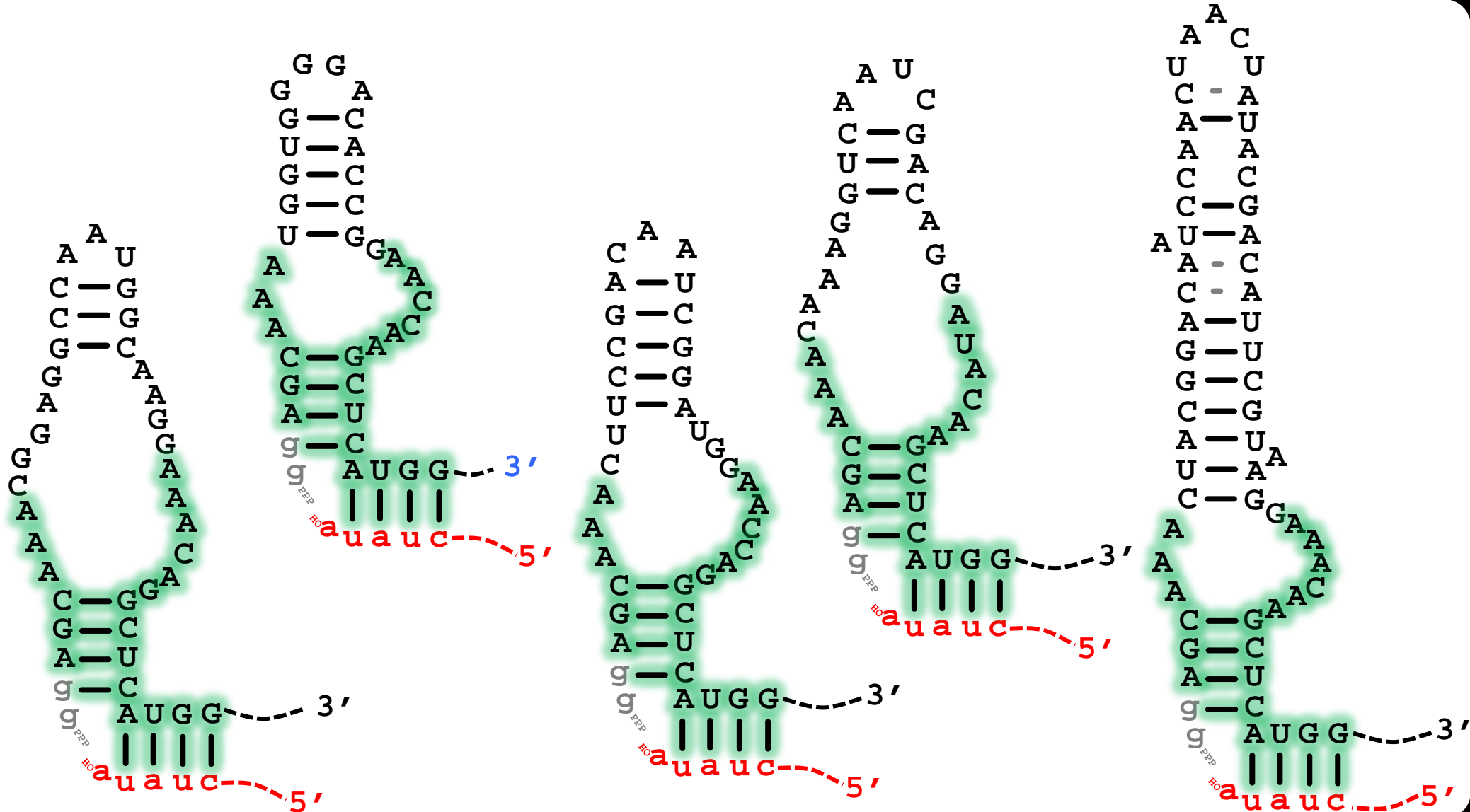
Milena Popović

Small networks
of rare
sequences are
the most active

80N ligase: Independent lineages converge on the an internal loop motif with a terminal loop core



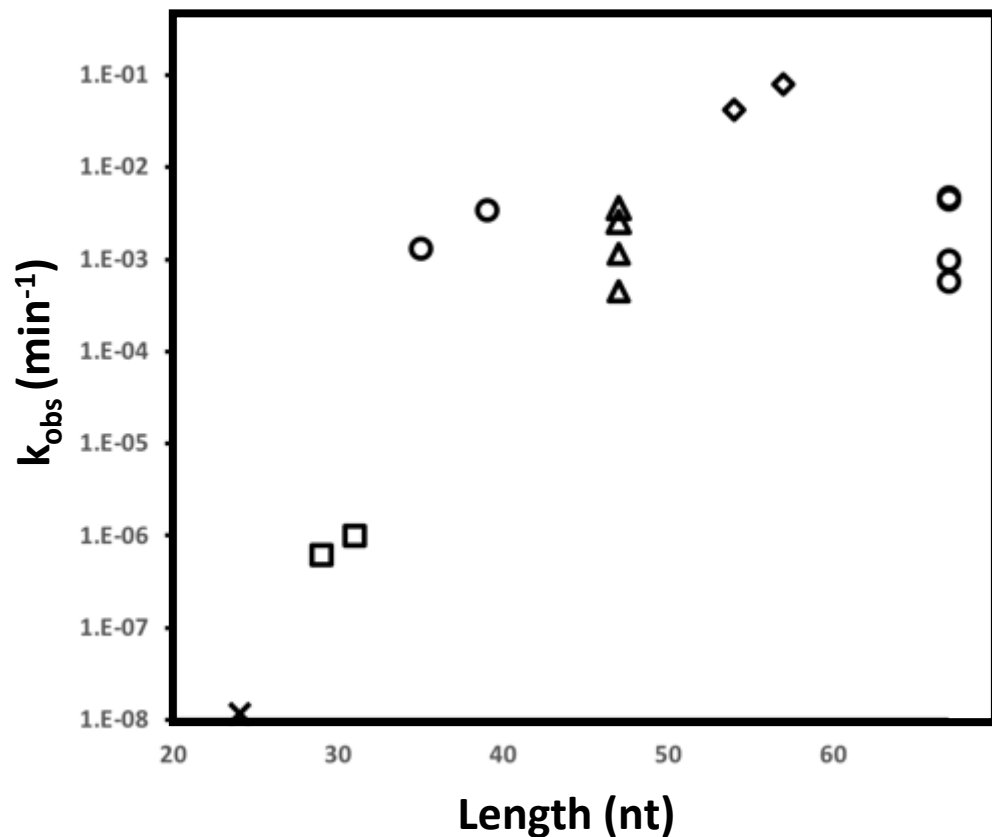
Reselection: Evidence for isolated network for long RNAs



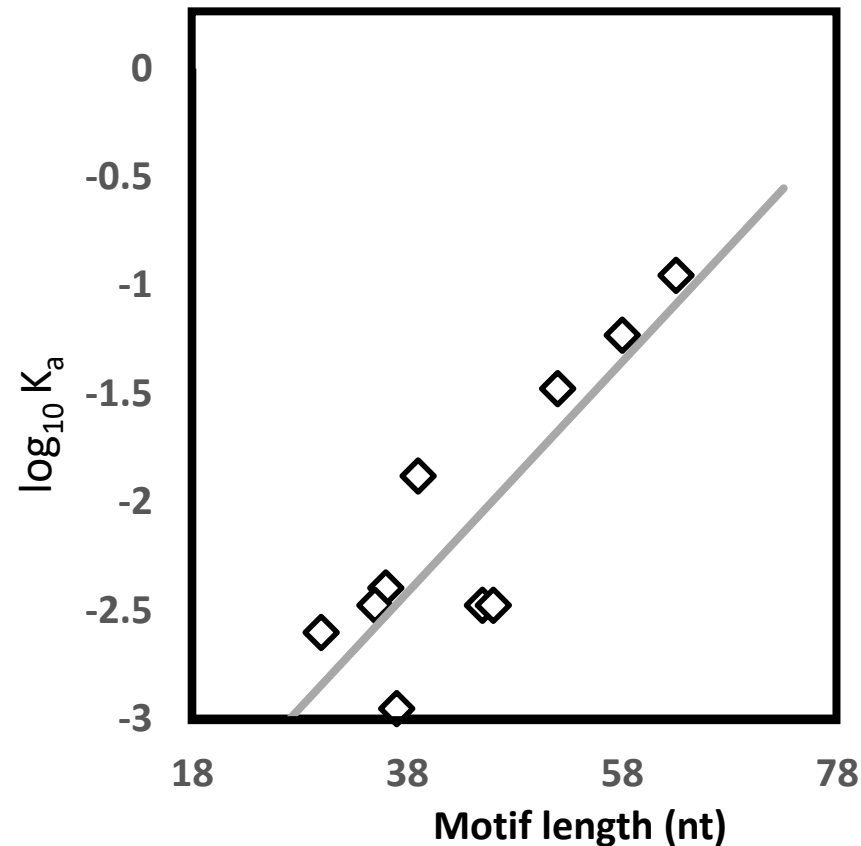
Sequences expansion offers a tremendous selective advantage



RNA Ligase Ribozyme Activity



GTP aptamer affinity



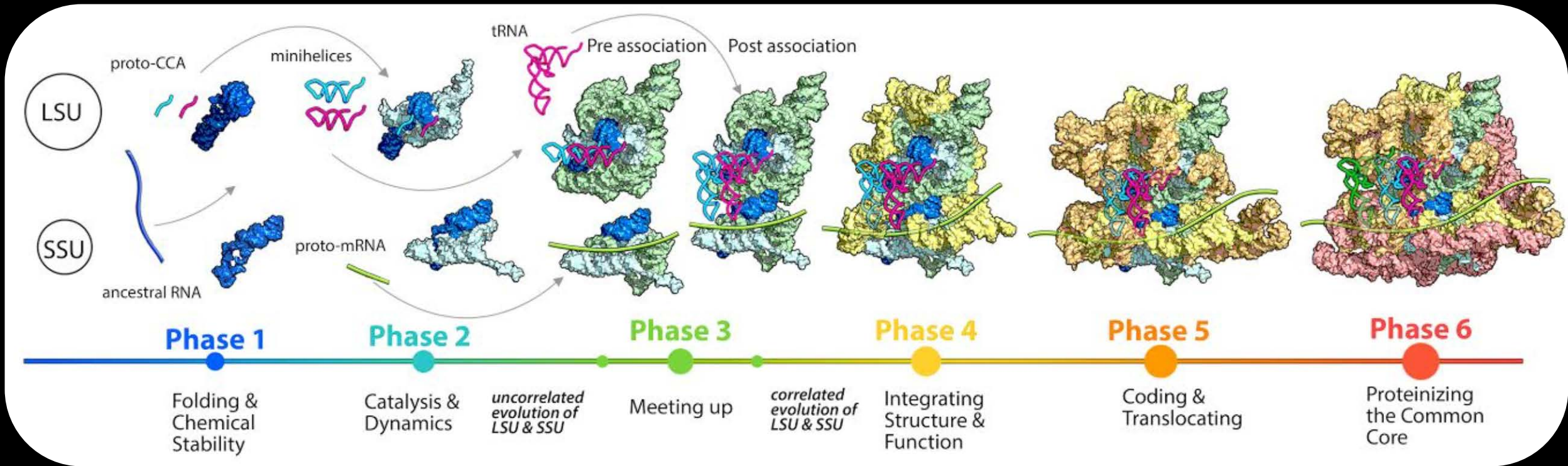
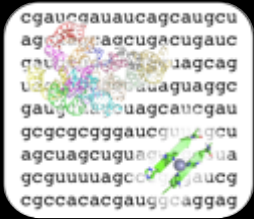
Carothers JM, et al. JACS. 2004 Apr 28;126(16):5130-7.

What about actual biological systems?



By examining the diversity of modern biological structures we infer features of ancient biochemistry.

The Accretion Model of ribosome evolution



Petrov, A. S., Gulen, B., Norris, A. M., Kovacs, N. A., Bernier, C. R., Lanier, K. A., ... & Williams, L. D.

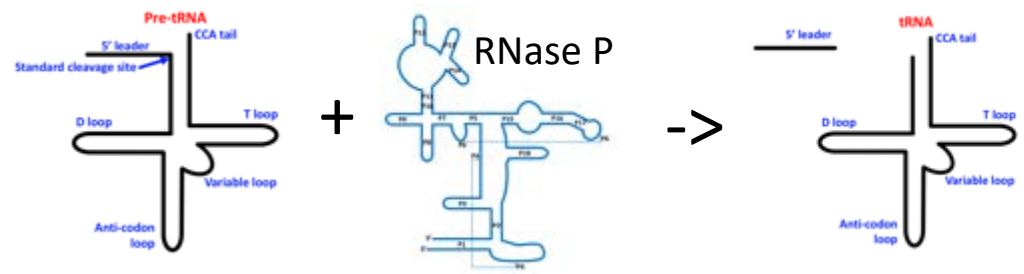
"History of the ribosome and the origin of translation."

Proceedings of the National Academy of Sciences 112, no. 50 (2015): 15396-15401

Ribonuclease P (RNase P): a near universal ribozyme with a deep evolutionary history

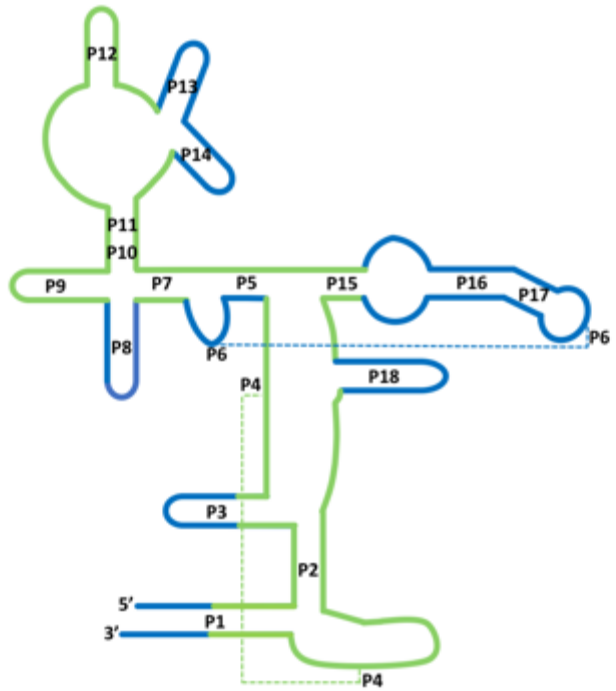


tRNA maturation in all three domains of life by a conserved RNA structure

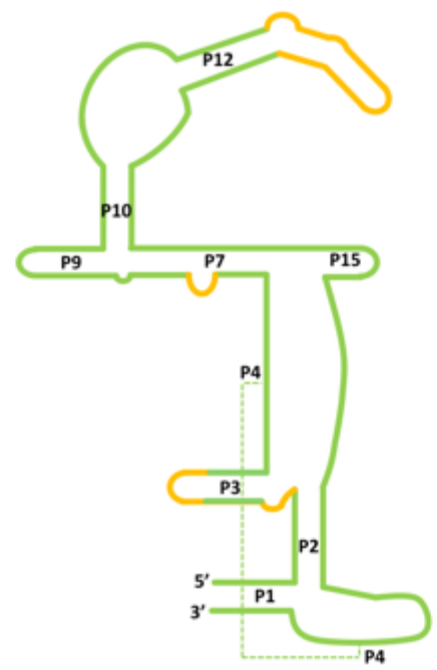


Conserved elements (structure and sequence)

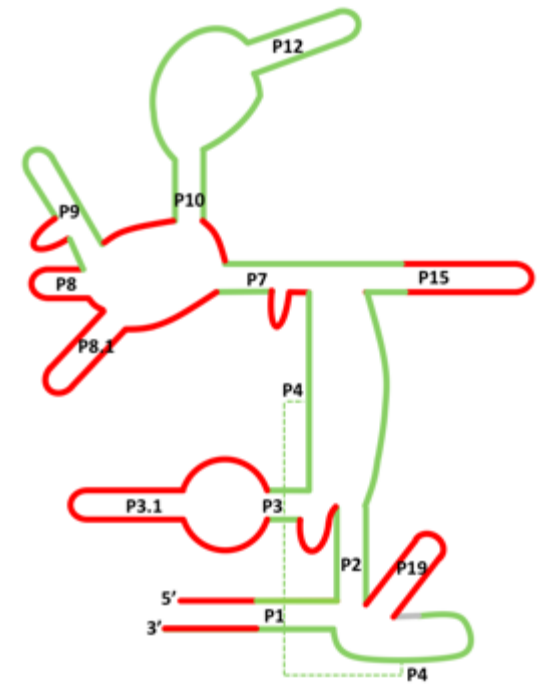
Thermotoga maritima



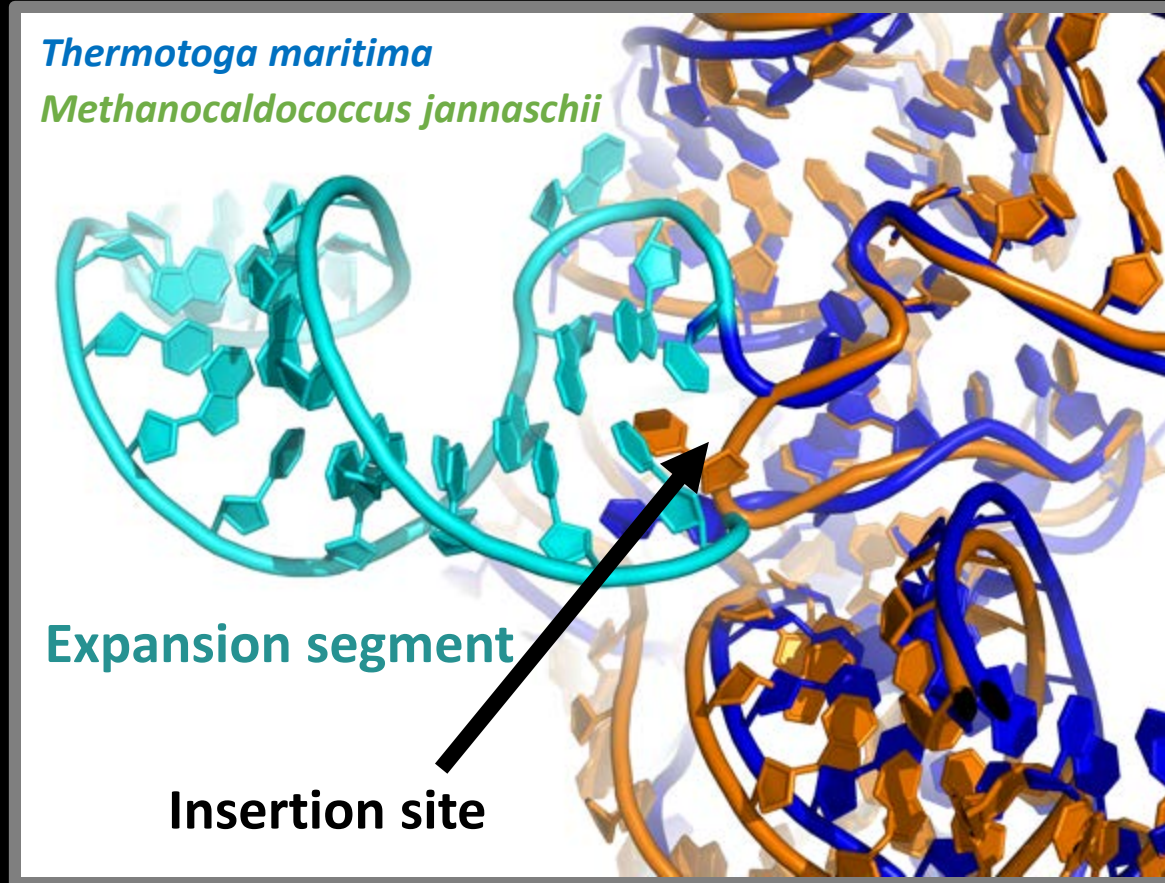
Methanocaldococcus jannaschii



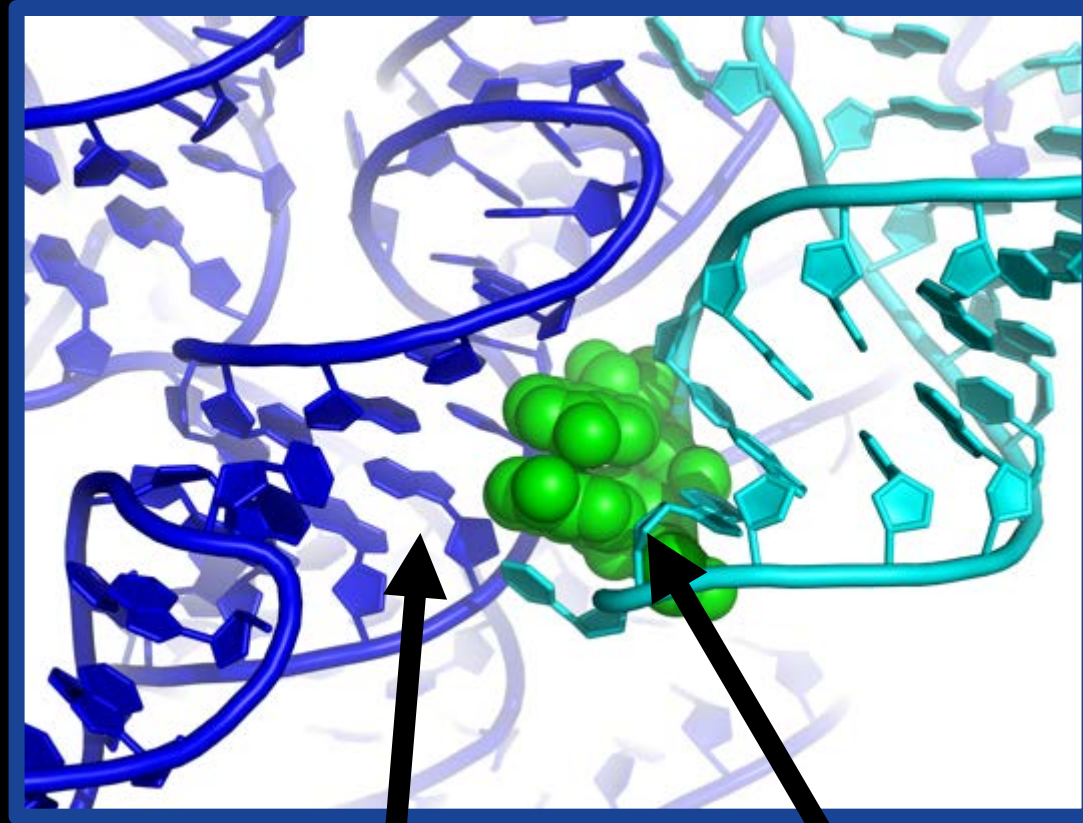
Saccharomyces cerevisiae



Insertion finger-prints in RNase P RNA



Chronology recorded in tertiary structures of RNase P

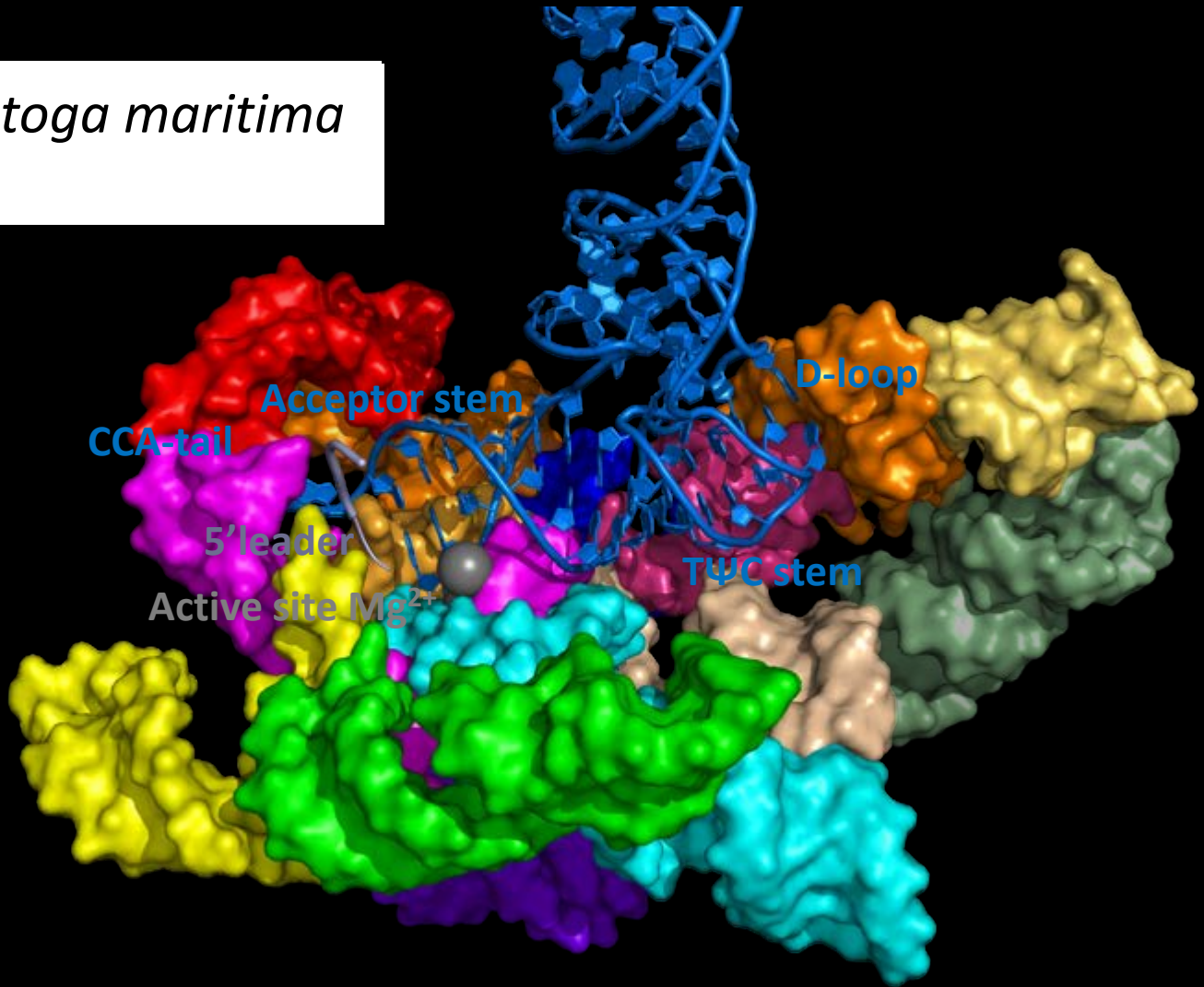


Independent structure
Older

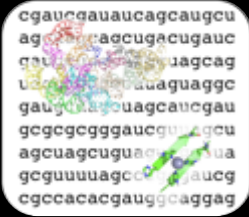
Dependent structure
Younger

Thermotoga maritima

```
cgaucgauaucagcaugcu  
agc...aacugacugauc  
gauc...uaagcag  
uauc...uaaguaggc  
gau...uaagcaucgau  
gcgcgcgggaucgu...gcu  
agcuagcuguac...ua  
gcguuuuagcc...gaucg  
cgccacacgauggcaggag
```



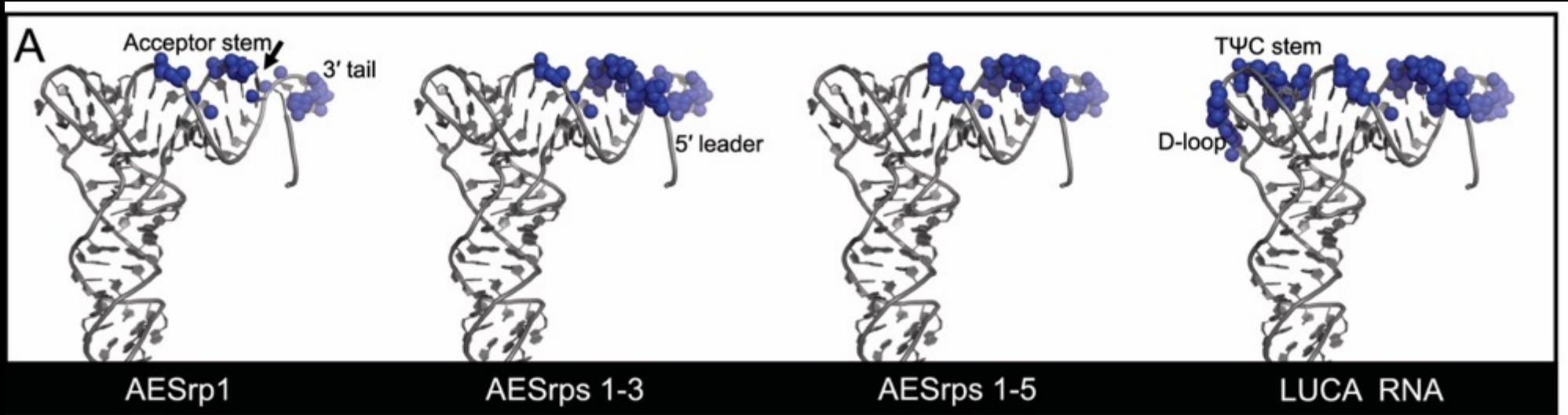
Can we synchronize timelines?



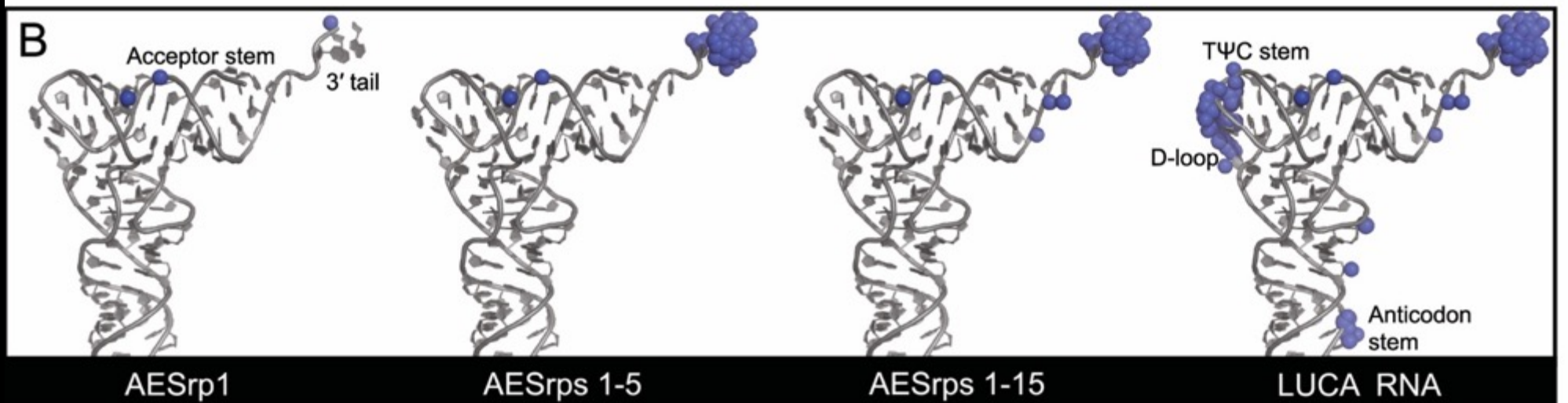
Linking time-lines through a shared substrate

```
cgauccgauaucagcaugcu  
agcuaacacugacugauc  
gcuuaacacagcagcag  
uuaacacagcagcagcag  
gauuaacacagcagcagc  
gcgcgcgggaucgucgcu  
agcuagcugaucgucgcu  
gcguuuuagccgucgucg  
cgccacacgauggcaggag
```

RNase P

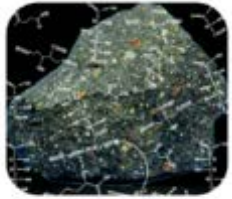


Ribosome
(A-site)

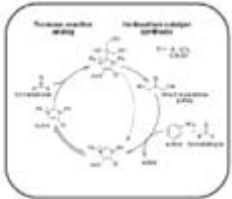


Systems protobiology: the future of studying the past

What evolves is a system, which in early evolution we identify as a protocell



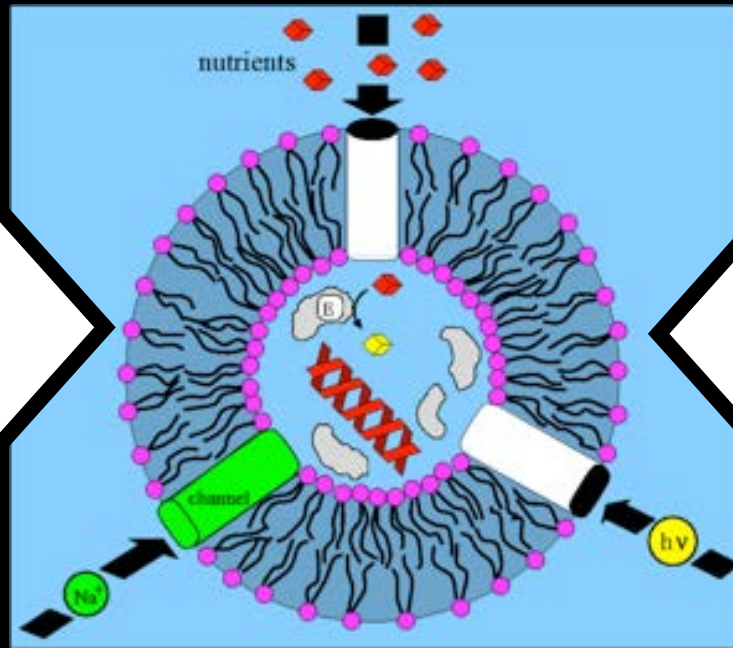
Cosmochemistry



Systems chemistry



Molecular modeling



In vitro evolution



Bioinformatics



Synthetic biology

To support stability, growth, replication, and evolution, all components must work in concert.

Acknowledgments

People at Ames

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Chenyu Wei (UCSF)
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The institutions

