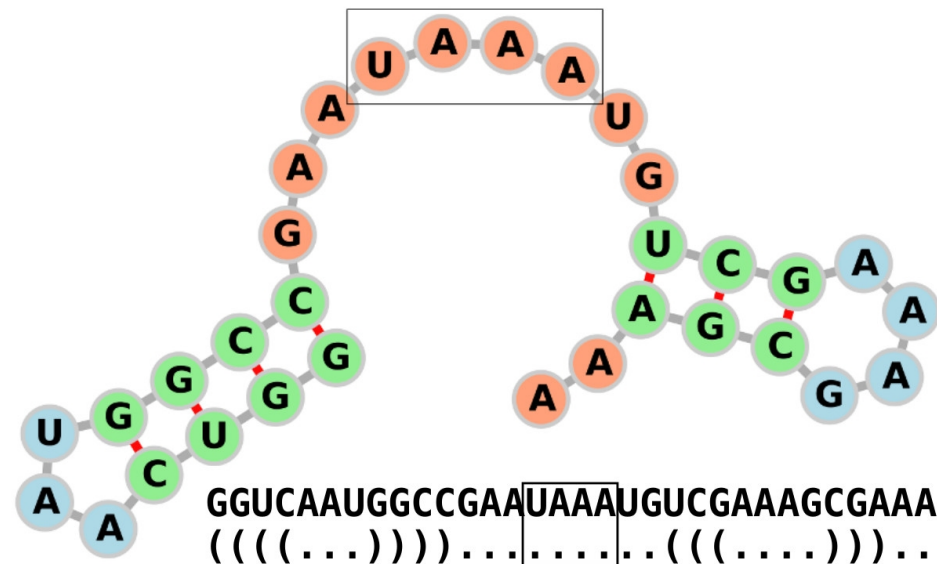
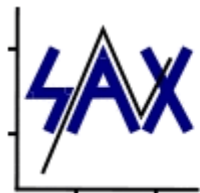


Autocatalytic Sets and RNA Secondary Structure



Wim Hordijk



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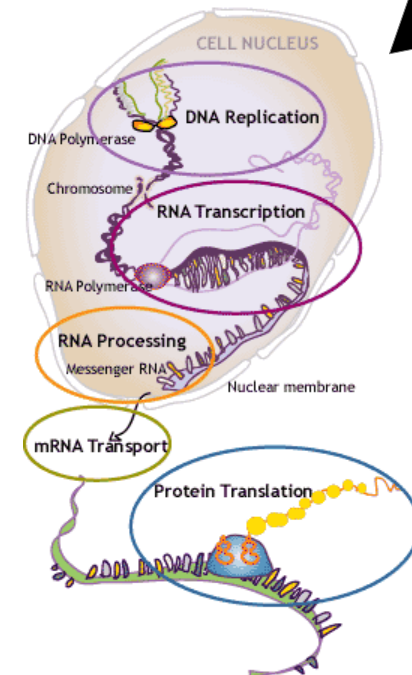
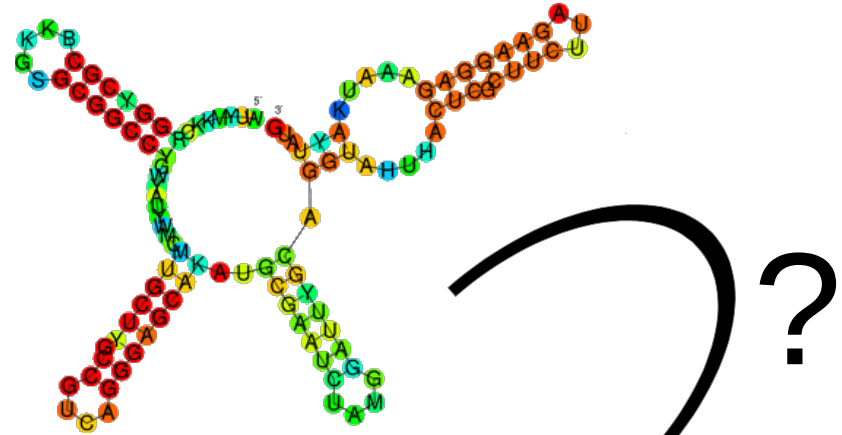
The Origin of Life

- **Main paradigm:**

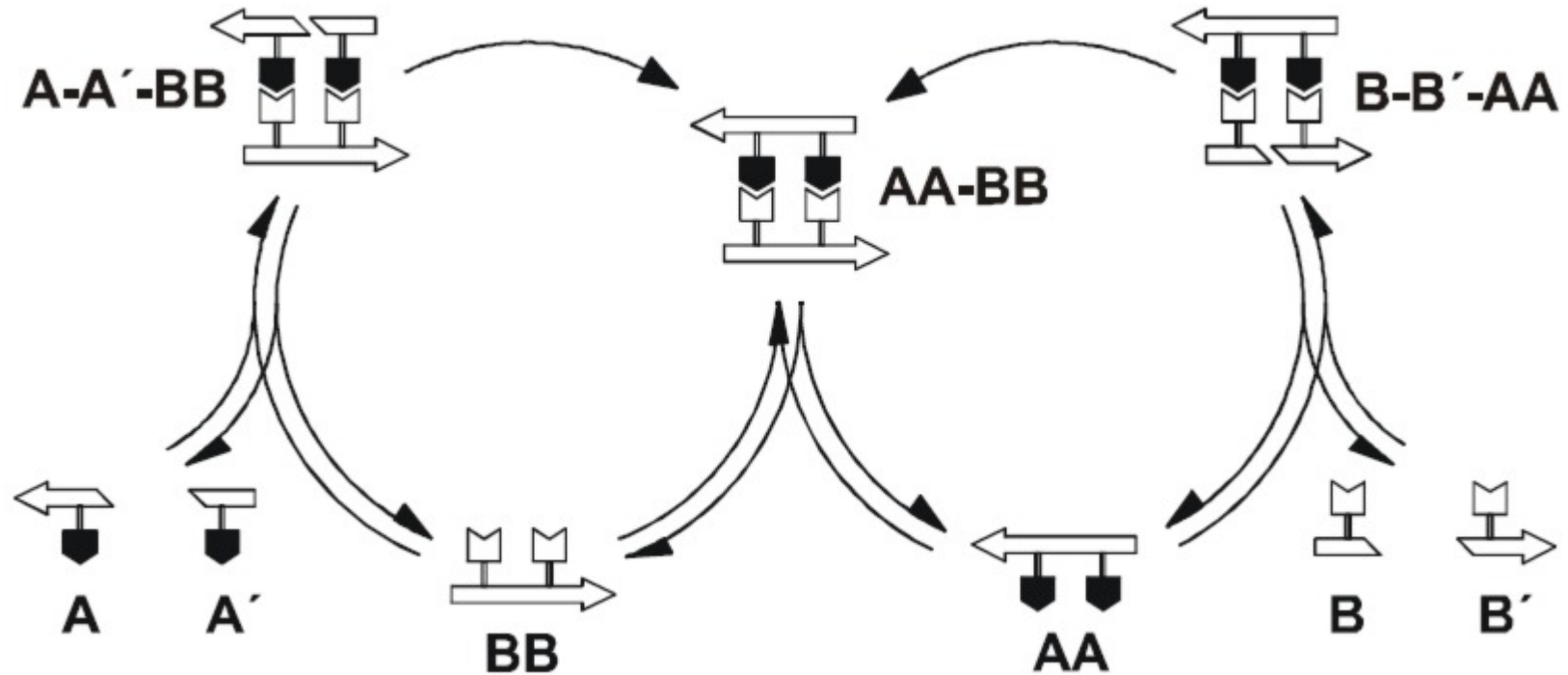
- The RNA world.
- Life started with one or more self-replicating RNA molecules.

- **Problems:**

- No experimental evidence that RNA can catalyze its own template-directed replication.
- How did cellular life (genetic code, metabolism, membrane) evolve from this?

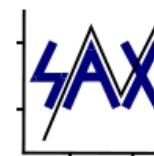


Mutual Catalysis

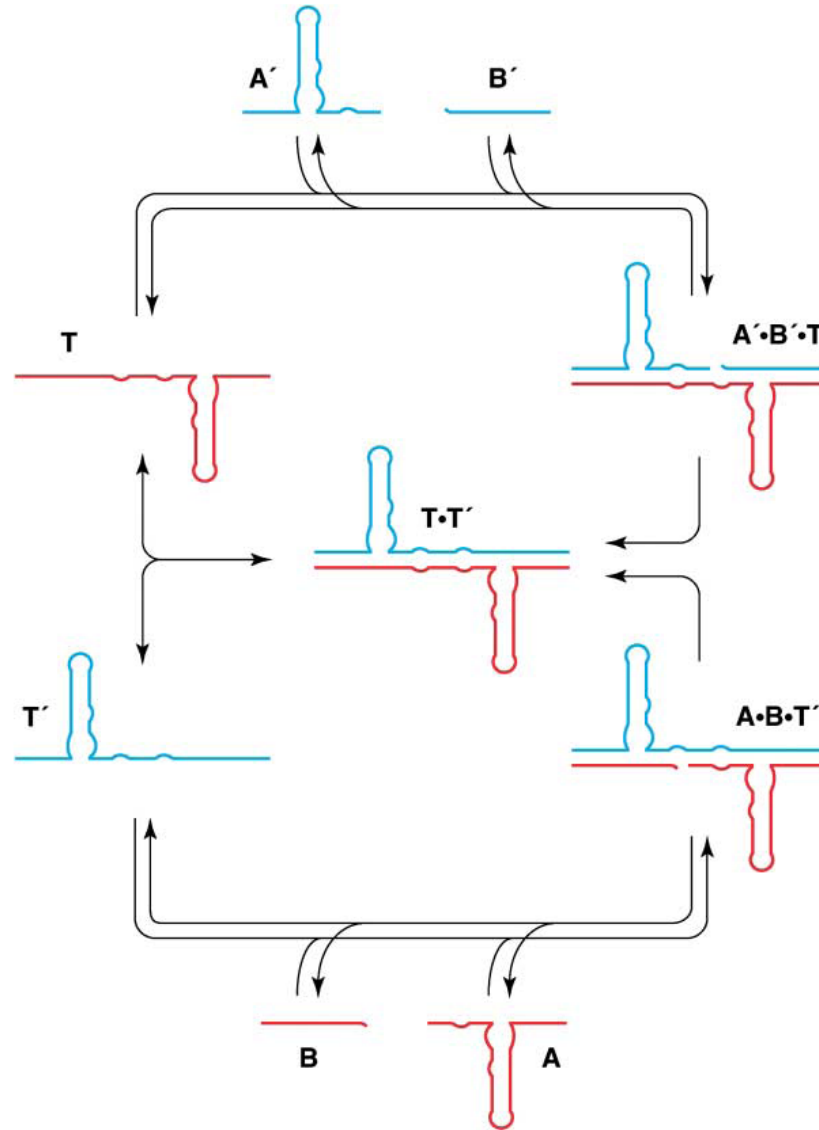


$A = CCG$ $B = CGG$

(Sievers & von Kiedrowski, *Nature*, 1994)



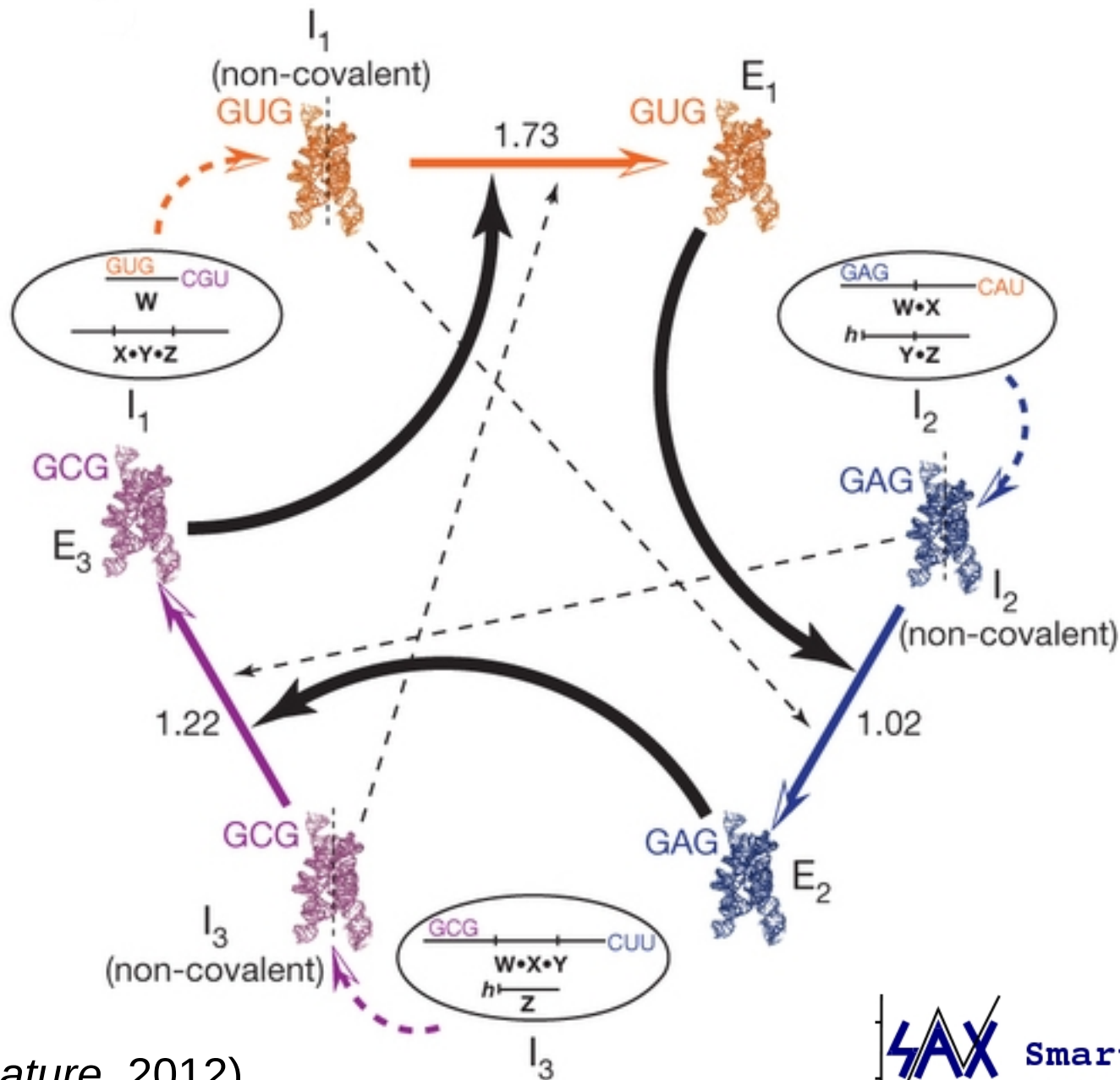
Mutual Catalysis



(Kim & Joyce, *Chemistry & Biology*, 2004)



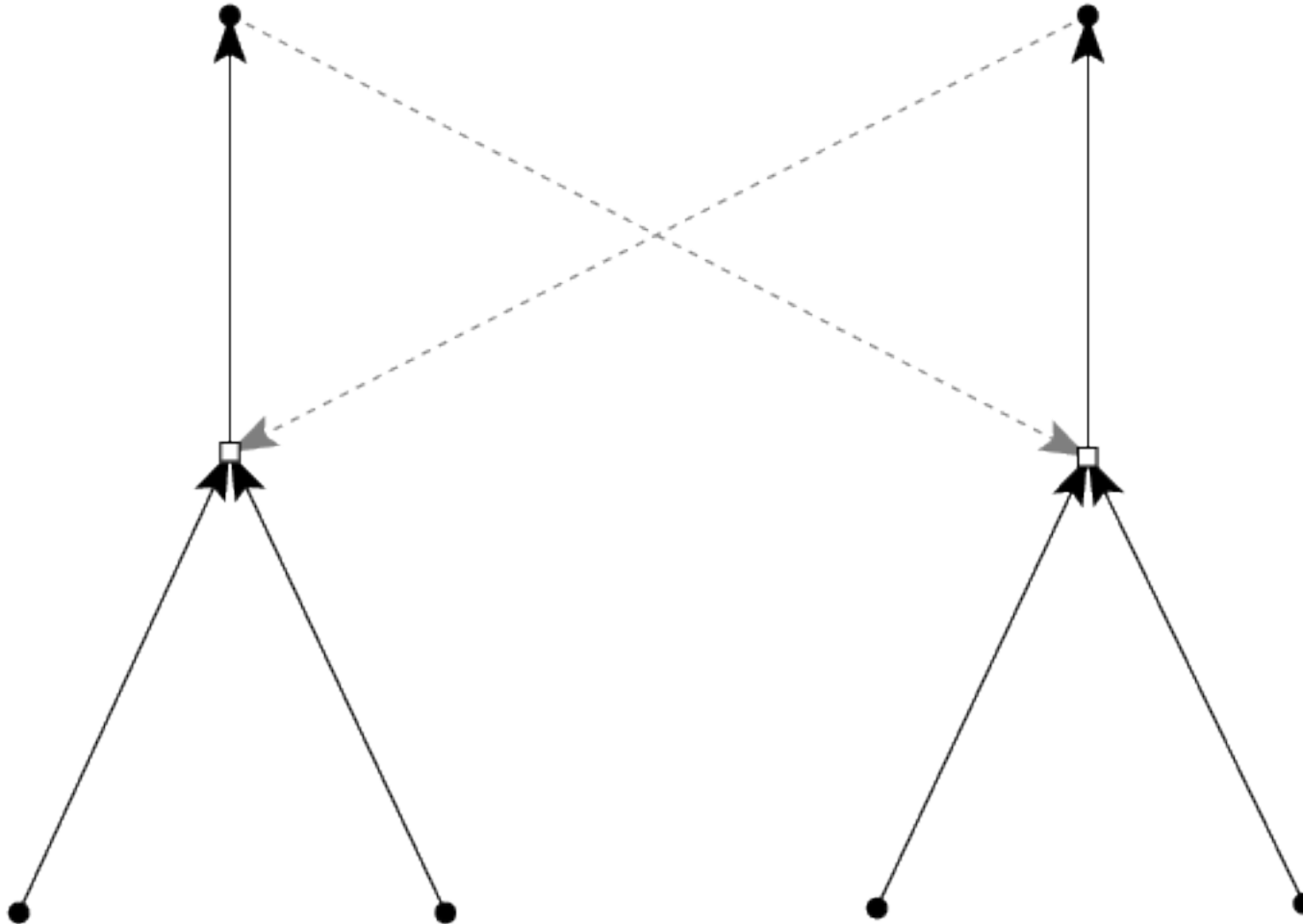
Mutual Catalysis



(Vaidya et al., *Nature*, 2012)



Autocatalytic Set



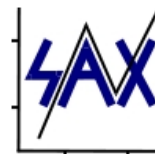
Autocatalytic Set

An autocatalytic (RAF) set is a set of chemical reactions and associated molecules which is:

1. *Reflexively Autocatalytic (RA)*: all reactions in the set are catalyzed by at least one molecule from the set itself.

2. *Food-generated (F)*: all molecules in the set can be produced from a “food set” using only reactions from the set itself.

→ A chemical reaction network that has catalytic closure (1) and is self-sustaining (2).



Original Claim

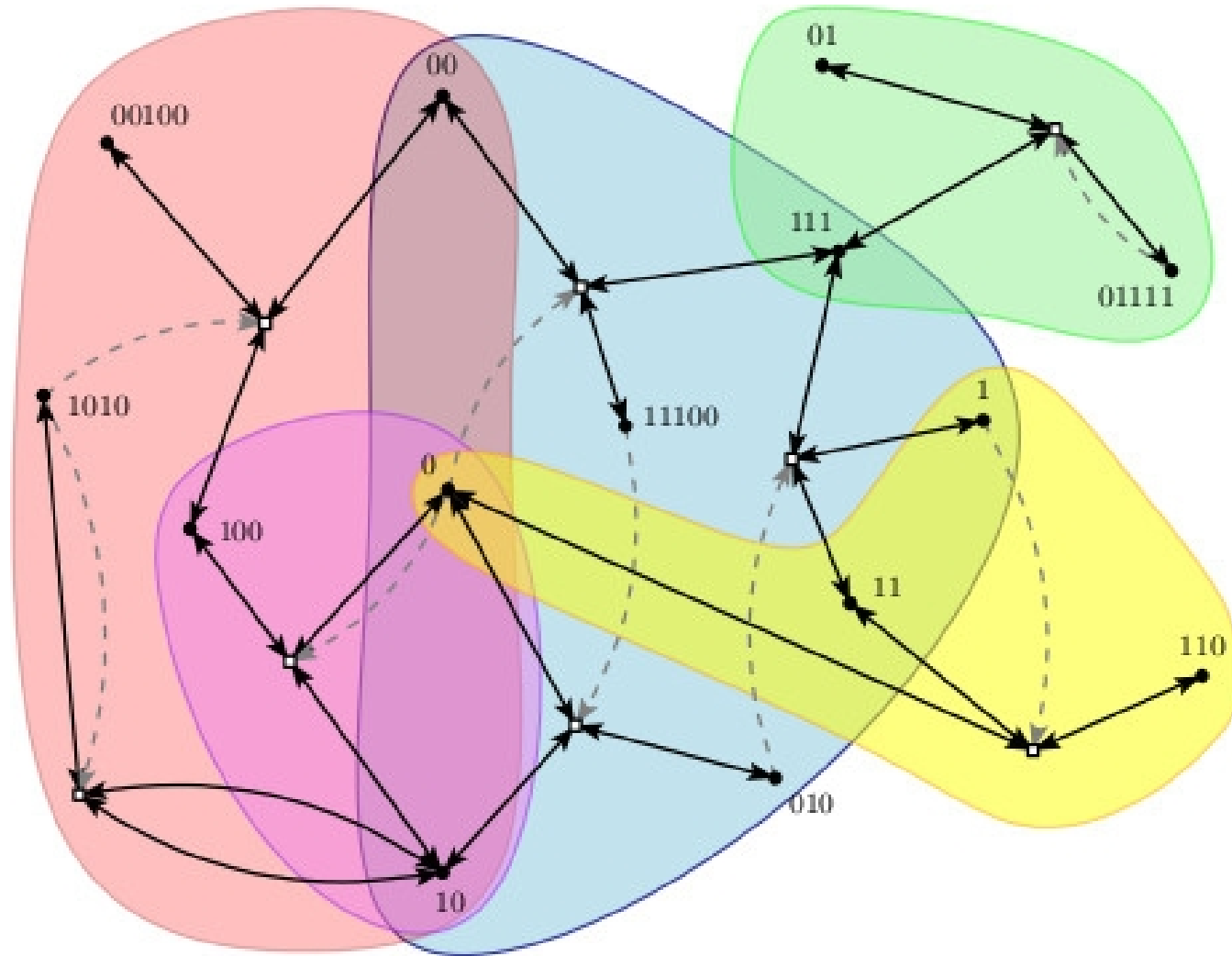


*“The formation of autocatalytic sets of polypeptide catalysts is an **expected emergent collective property of sufficiently complex sets of polypeptides, amino acids, and other small molecules.**”*

(Kauffman, 1986)

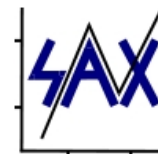


Binary Polymer Model Example



Computational Studies

- Hordijk & Steel (2004-2017)
- Farmer et al. (1986, 1991)
- Wills & Henderson (2000)
- Jain & Krishna (2001, 2002)
- Filisetti et al. (2011)
- Vasas et al. (2012)
- Tanaka et al. (2014)



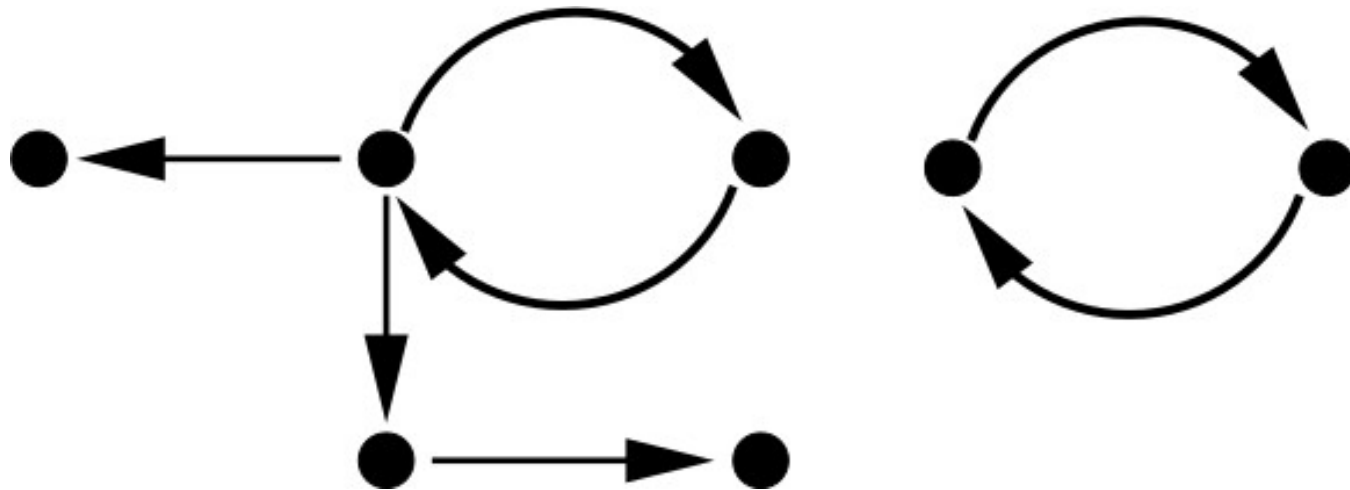
Computational Model

- Generate N random RNA sequences of length L .
- Fold each sequence into its MFE structure.
- For each RNA secondary structure:
 - Get all hairpin loops of length ≥ 4 .
 - Find “ligation template” of length 4.
- For each pair (\mathbf{A}, \mathbf{B}) of RNA secondary structures:
 - If $hairpin-loop(\mathbf{A})$ is the base-pair complement of $ligation-template(\mathbf{B}) \Rightarrow \mathbf{A}$ catalyzes ligation of \mathbf{B} .
- Use the RAF algorithm to find autocatalytic sets.

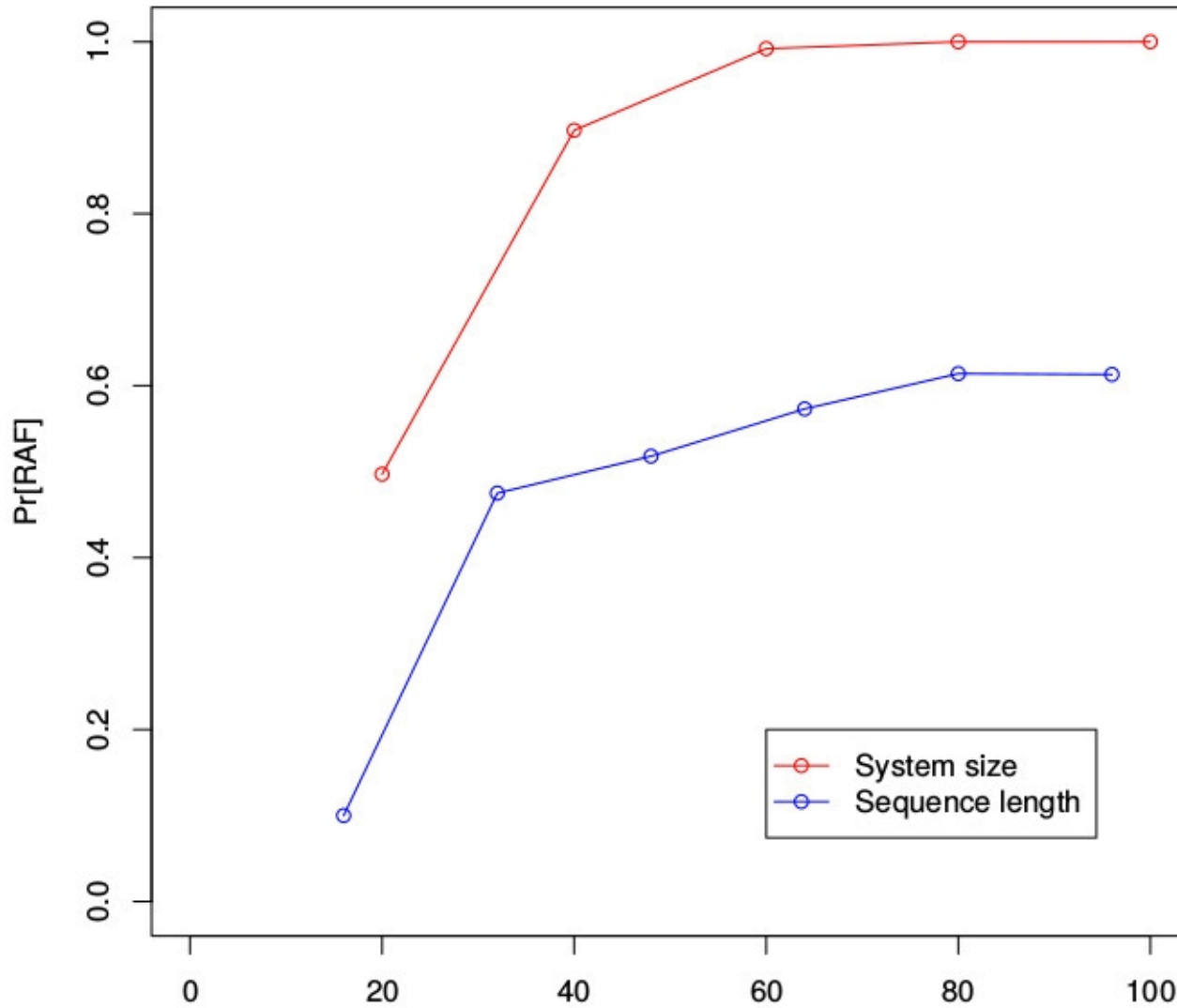


Existence of Autocatalytic Sets

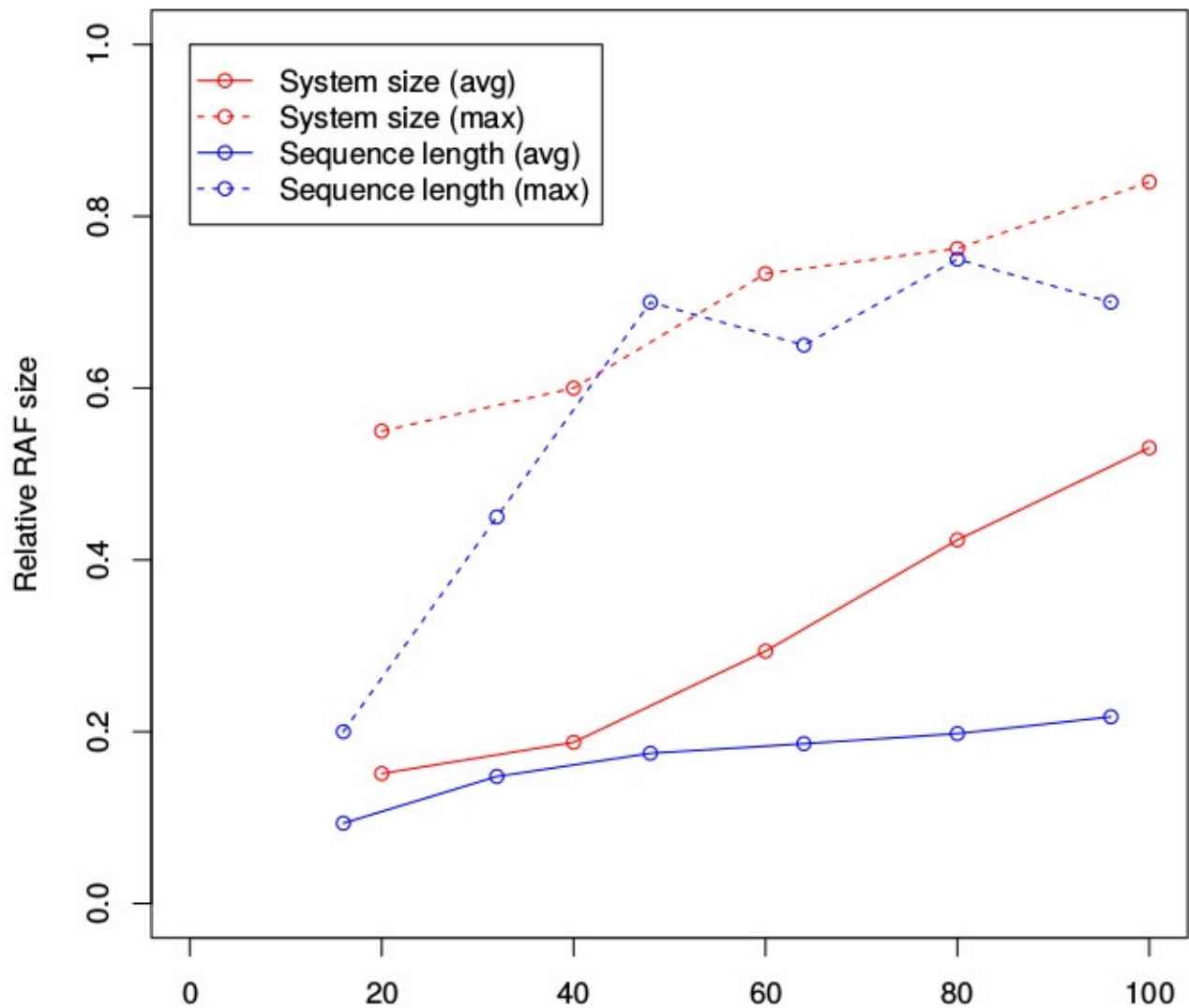
- $N = 20$, $L = 32$, 1000 random instances.
- $\Pr[\text{RAF}] = 0.50$



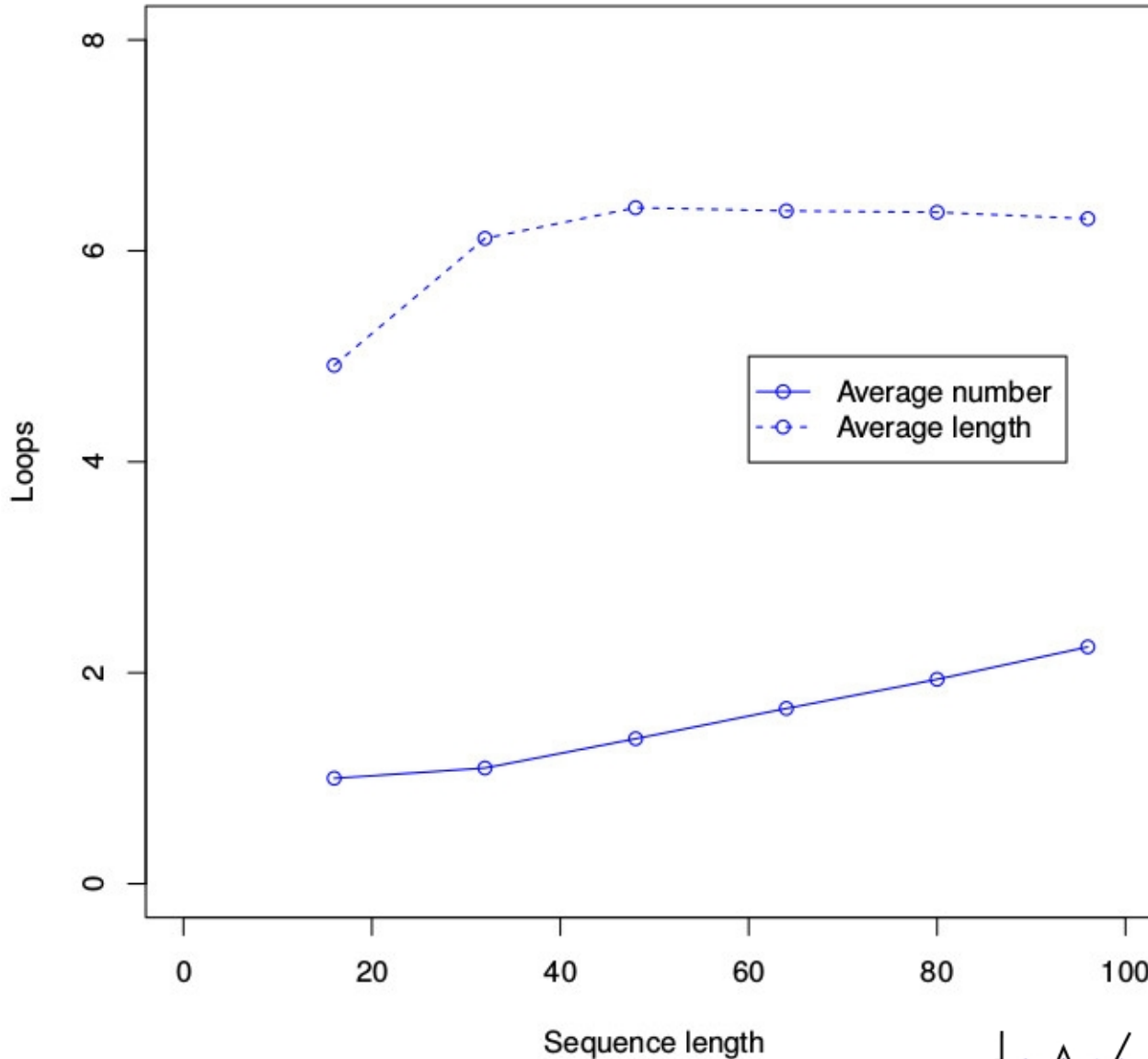
Dependence on N and L



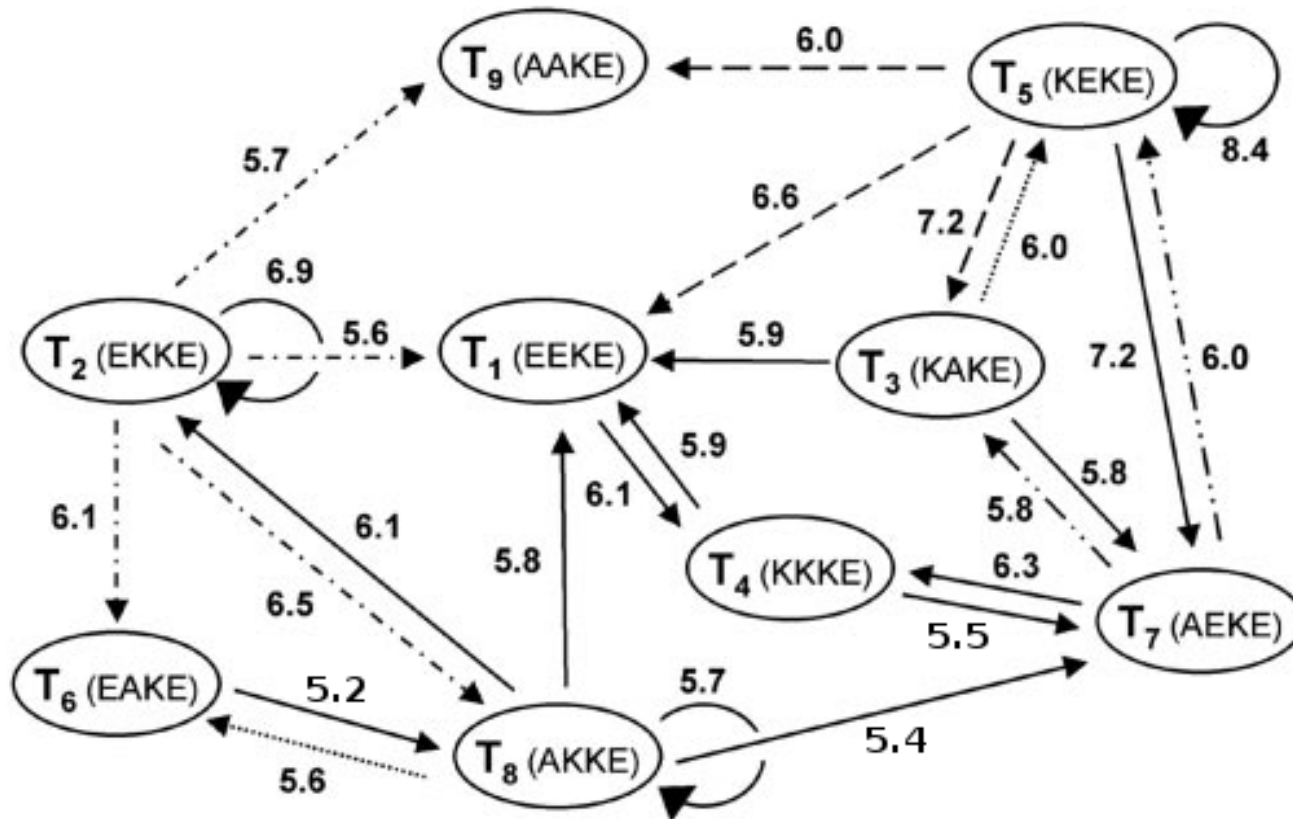
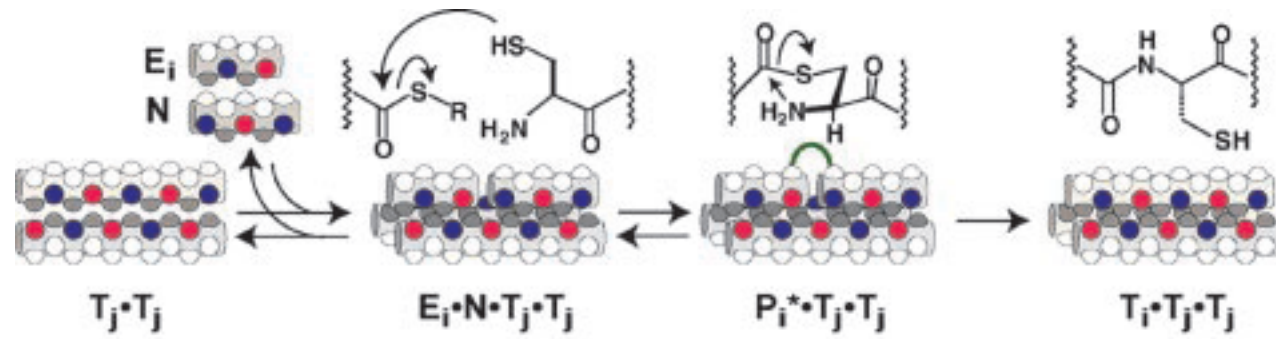
Relative Size of Autocatalytic Sets



Number and Size of Hairpin Loops



Peptide Autocatalytic Sets

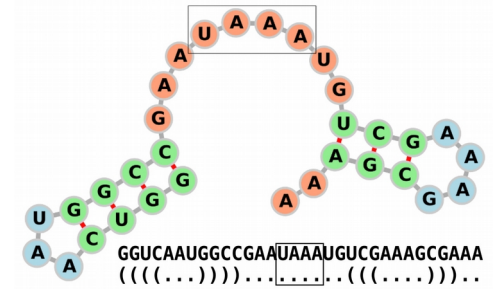


(Ashkenasy et al., *PNAS*, 2004)



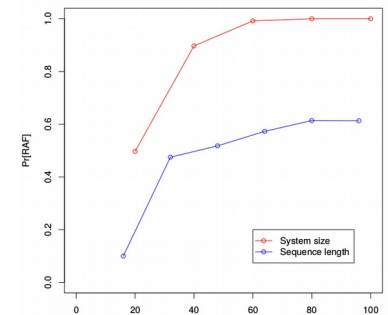
Conclusions

- New computational model taking molecular (RNA) structure into account.

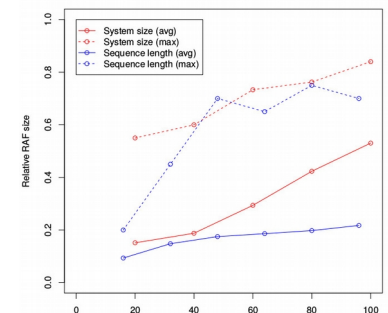


- Autocatalytic sets are likely to exist, even for small networks of short sequences.

- Probability increases with increasing network size and sequence length...



- ...but is mostly driven by sequence diversity rather than sequence length.



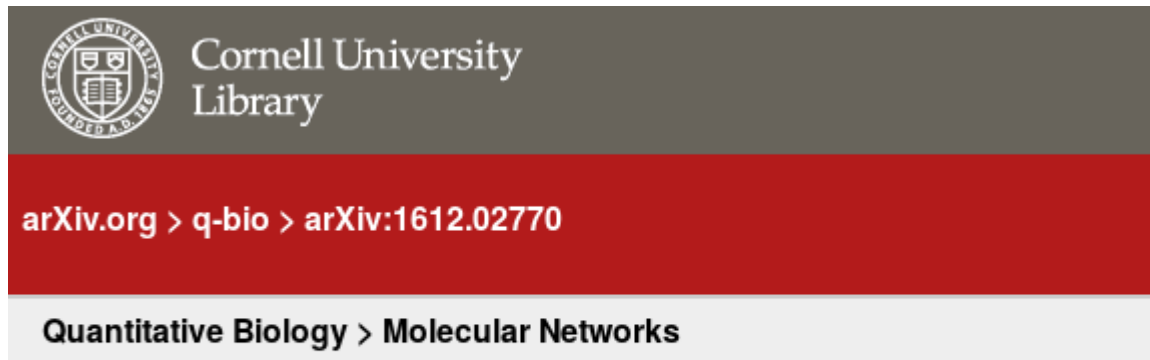
- Consequences for the origin and evolution of life?



Further Reading

W. Hordijk

Autocatalytic Sets and RNA Secondary Structure
Journal of Molecular Evolution (in press), 2017



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