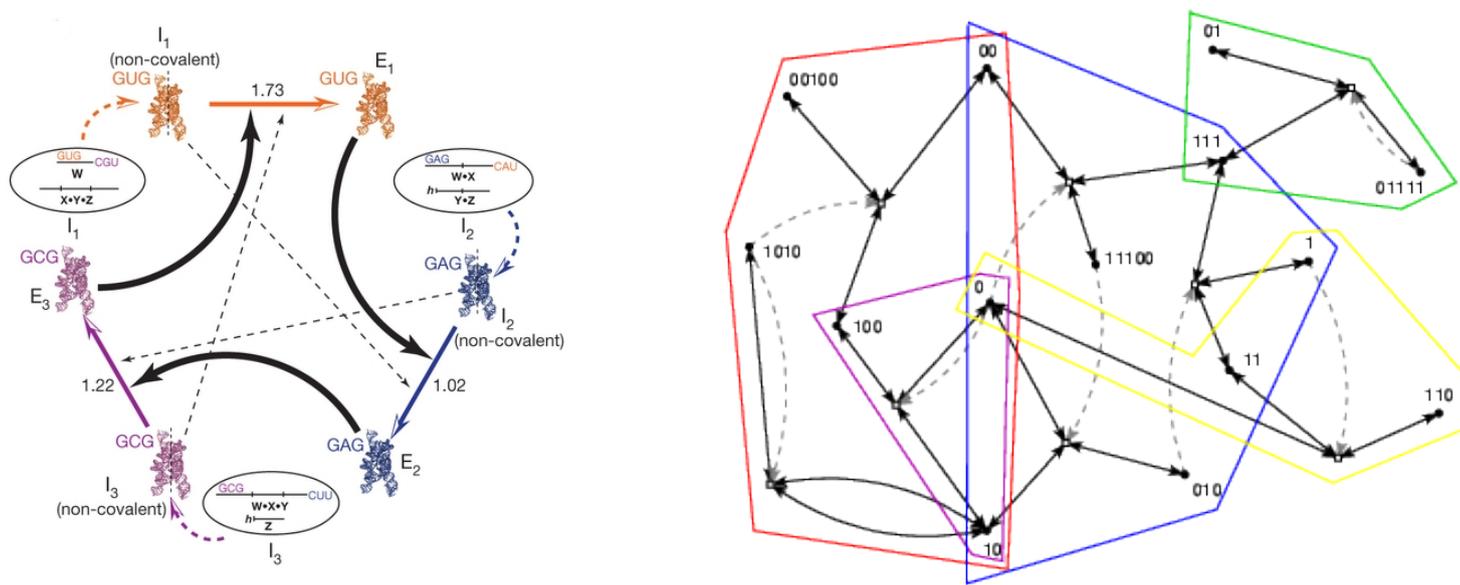


# Autocatalytic Sets and the Origin of Life



**Wim Hordijk**



**SmartAnalytiX.com**  
 BUSINESS ANALYTICS USING "SMART" COMPUTING

An Institute for the Advanced Study  
 of Natural Complex Systems



# A 17<sup>th</sup> Century Recipe for Life



*“If you press a piece of underwear soiled with sweat together with some wheat in an open mouth jar, after about 21 days the odor changes and the ferment coming out of the underwear and penetrating through the husks of the wheat, **changes the wheat into mice.**”*

Jan Baptist van Helmont, ~1620



## Spontaneous generation



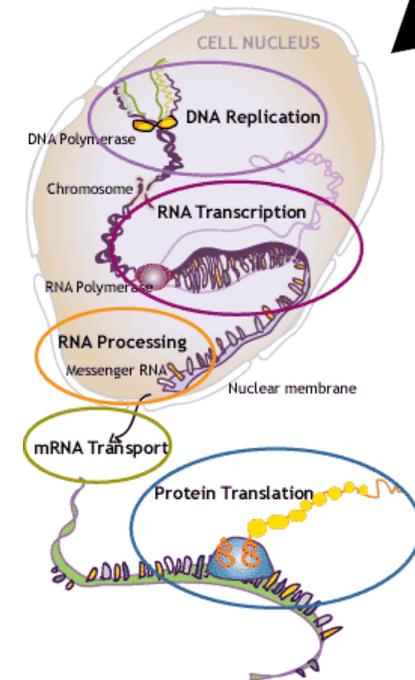
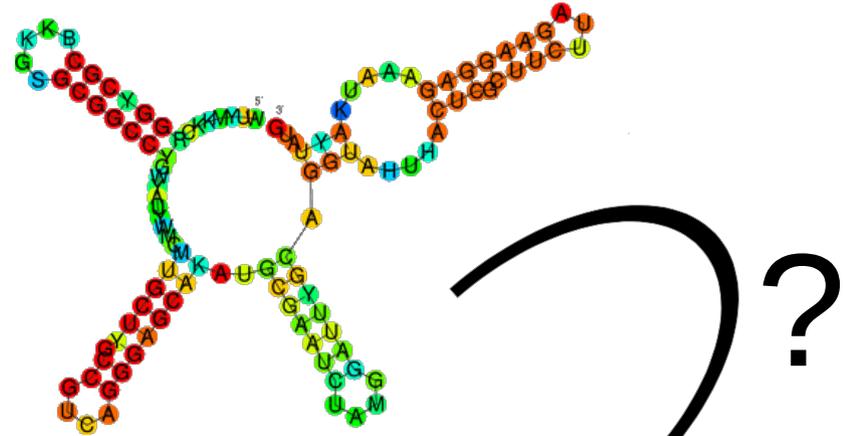
# The Origin of Life

- **Main paradigm:**

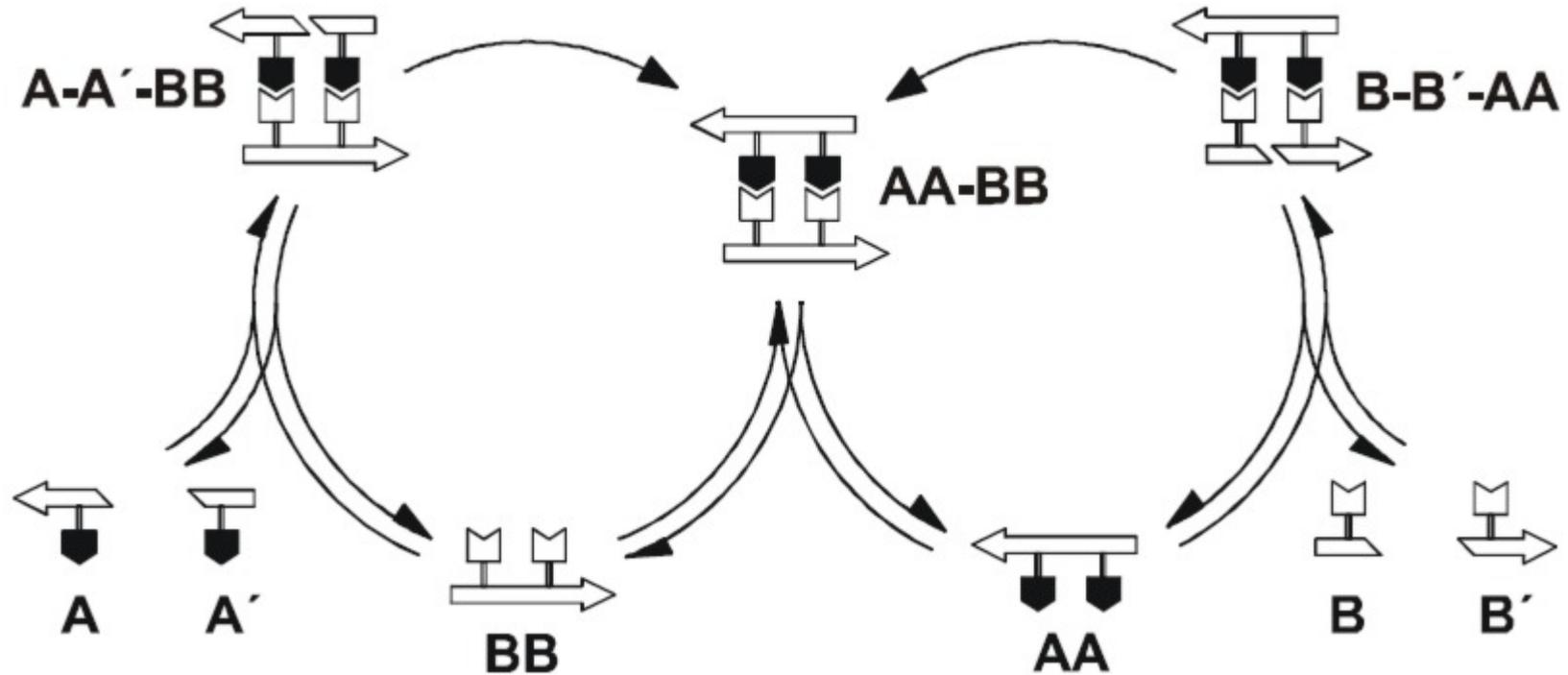
- The RNA world.
- Life started with one or more self-replicating RNA molecules.

- **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

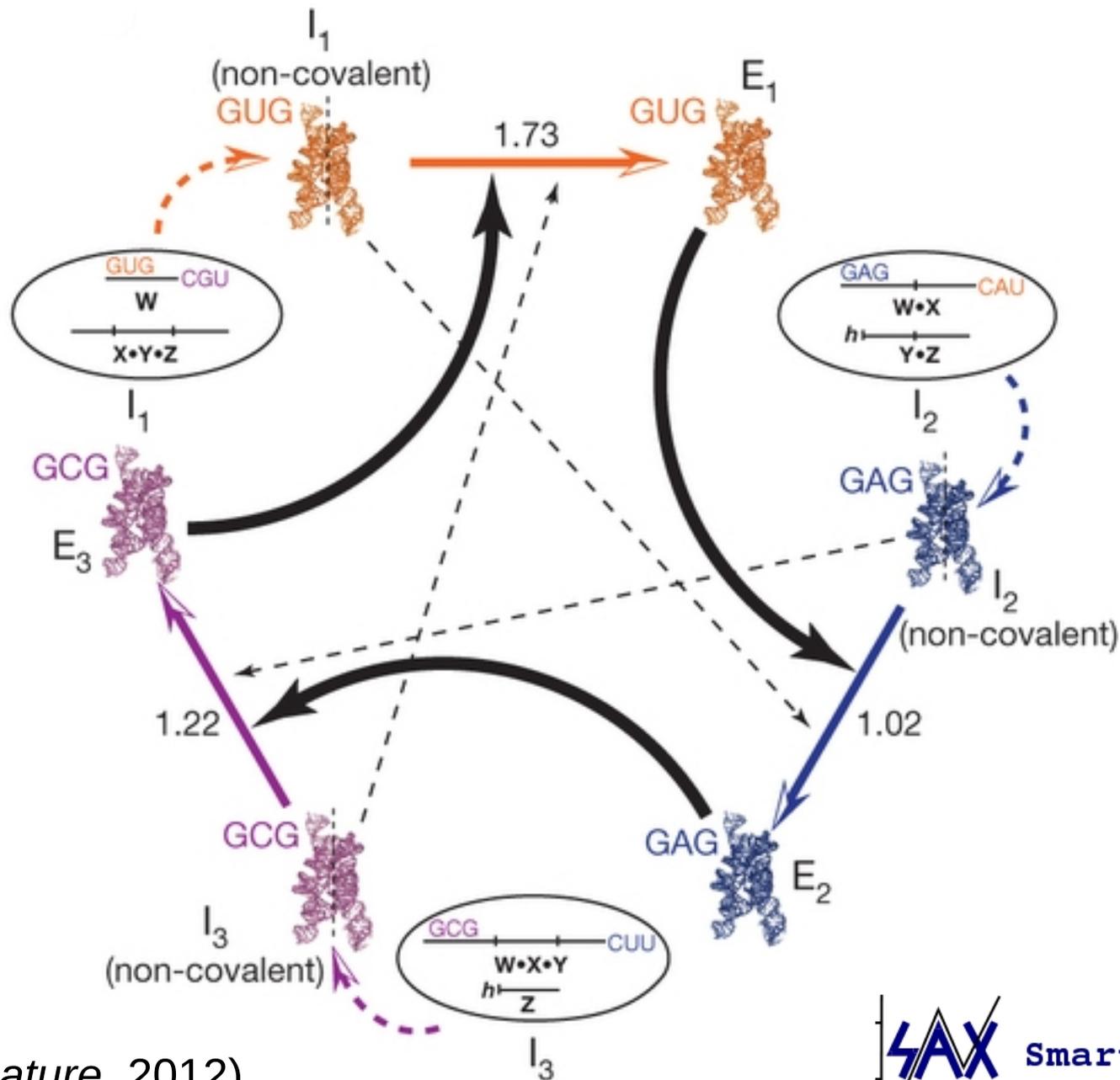


$A = CCG$      $B = CGG$

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



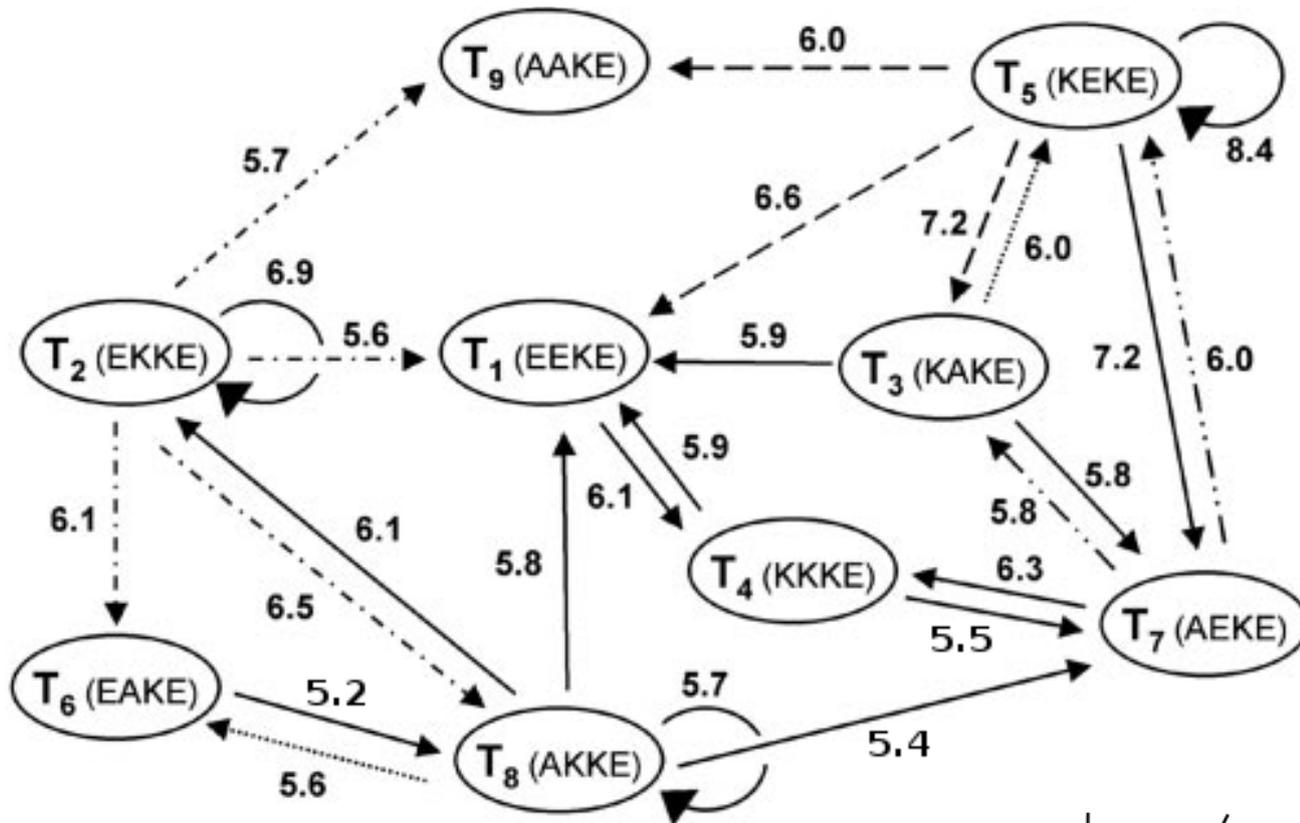
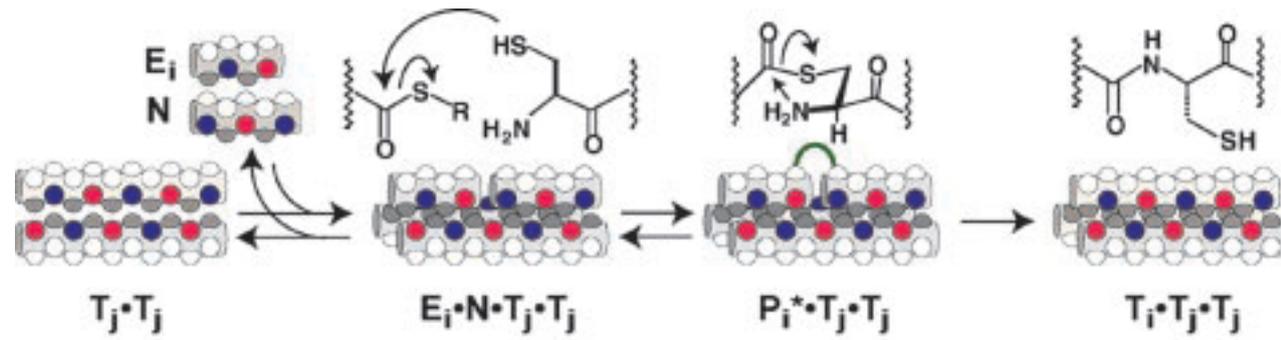
# Mutual Catalysis with RNA



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



# Mutual Catalysis with Peptides

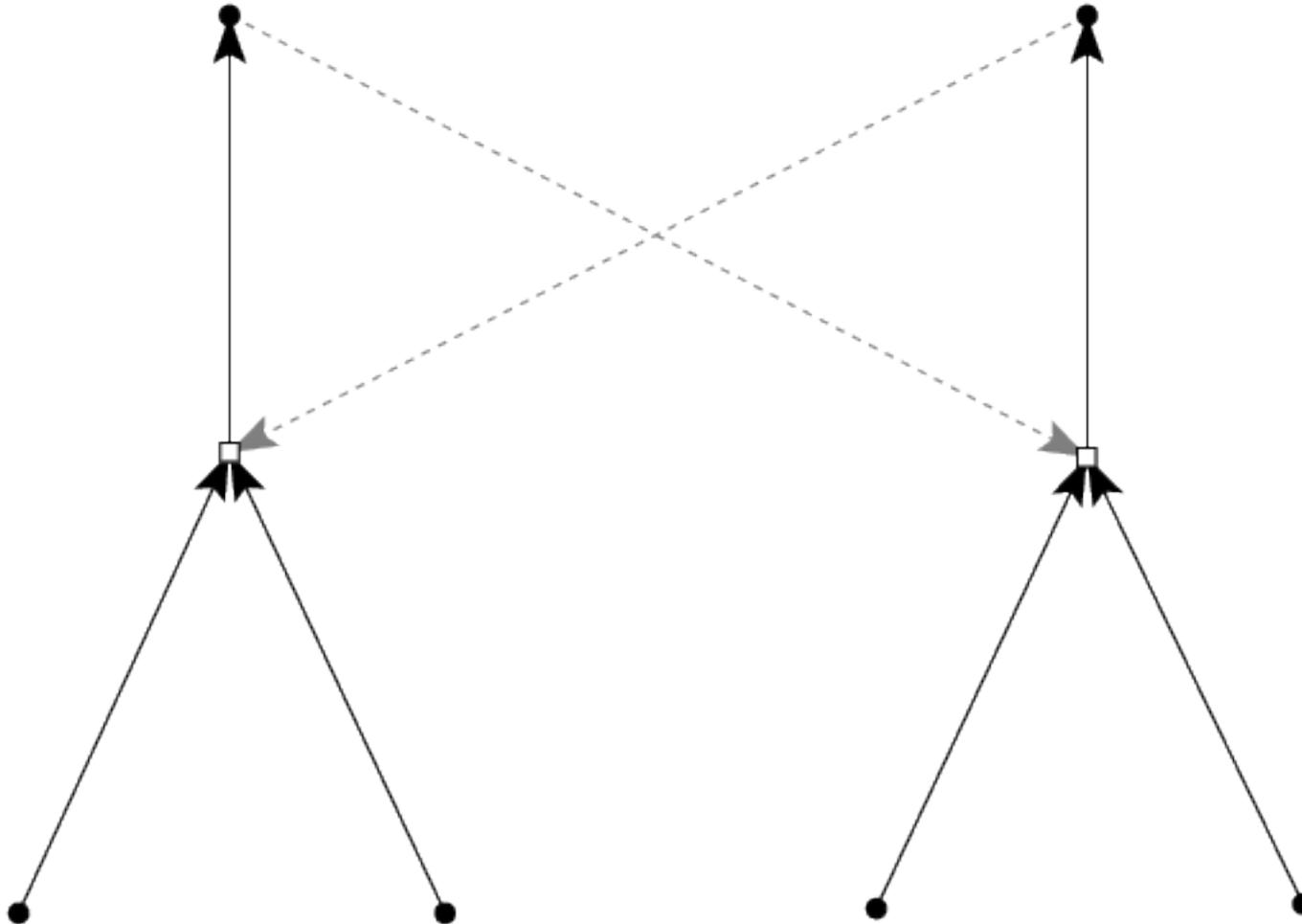


(Ashkenasy et al., *PNAS*, 2004)



# Autocatalytic Set

---



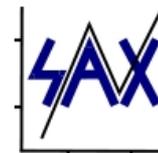
# Autocatalytic Set

---

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

- 1. Reflexively Autocatalytic (RA)*: all reactions are catalyzed by at least one molecule from the set.
- 2. Food-generated (F)*: all molecules can be produced from a “food set” using only reactions from the set.

→ 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)



# The Binary Polymer Model

---

The binary polymer model consists of:

1. **Molecules** ( $X$ ): bit strings up to length  $n$   
(with food up to length  $t$ ).

$\{0, 1, 00, 01, 10, 11, 000, 001, \dots, 111111111111\}$

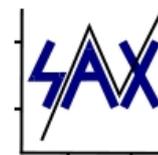
2. **Reactions** ( $R$ ):

• **Ligation**:  $000 + 111 \rightarrow 000111$

• **Cleavage**:  $0101010 \rightarrow 0101 + 010$

3. **Catalysis** ( $C$ ):

•  $\Pr[m \text{ catalyzes } r] = p$





# Earlier Criticisms

---

Autocatalytic sets capture the **functionally closed and self-sustaining** properties of life, and they are **highly likely** to arise spontaneously. *But:*

- Kauffman's argument requires an **exponential growth rate** in level of catalysis. (Lifson, 1996)
- Autocatalytic sets **lack evolvability**.  
(Vasas, Szathmáry & Santos, 2010)
- Binary polymer model is **not realistic** enough.



# Maths & Computers to the Rescue!

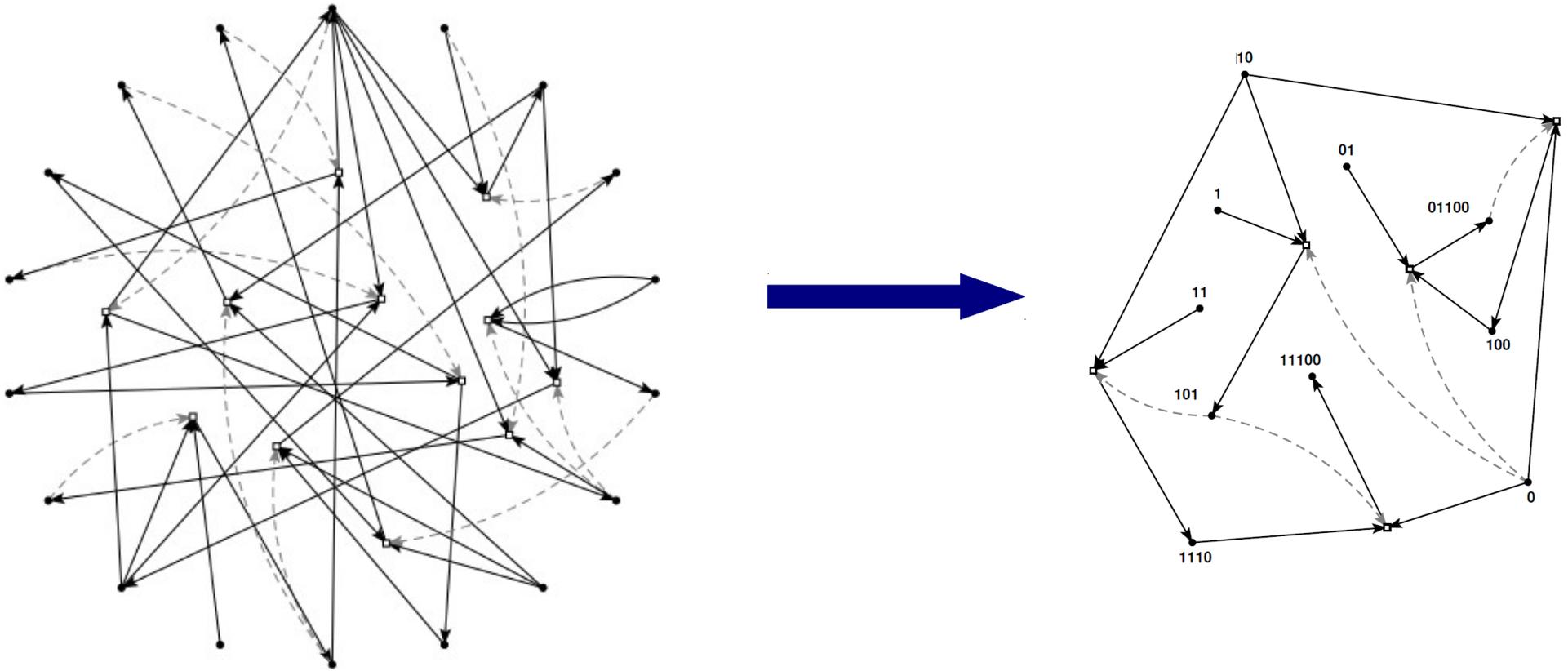
---

- **Mathematical formalization** of autocatalytic sets (RAF theory).
- **Efficient algorithm** for finding autocatalytic sets in chemical reaction systems.
- Using maths & computers to study the **likelihood and structure** of autocatalytic sets.

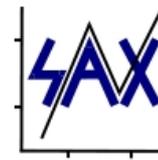
(Hordijk & Steel, 2004-2017)



# RAF Algorithm

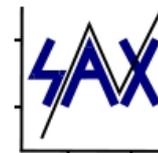
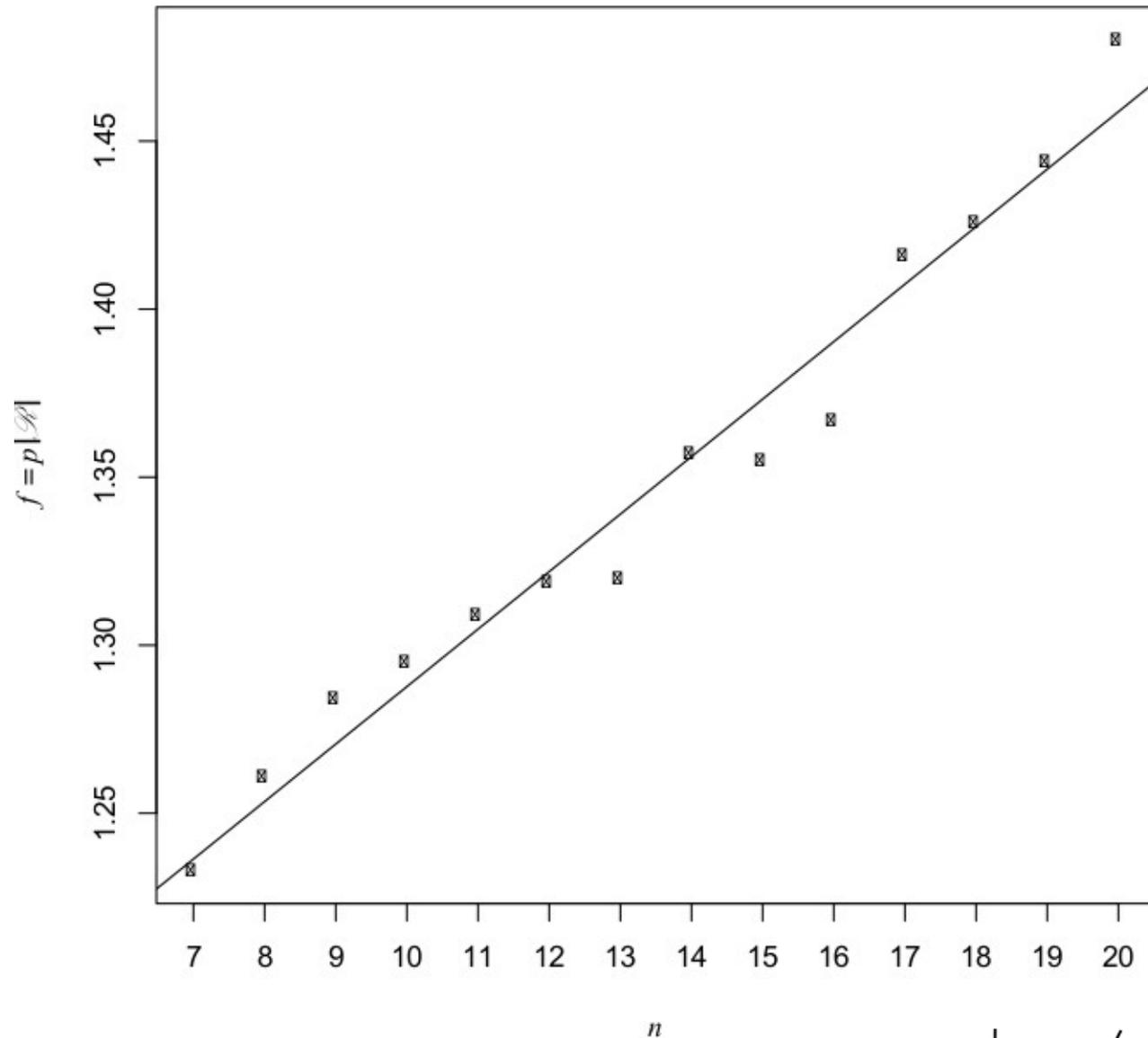


Worst-case run-time:  $O(|R|^2 \log |R|)$

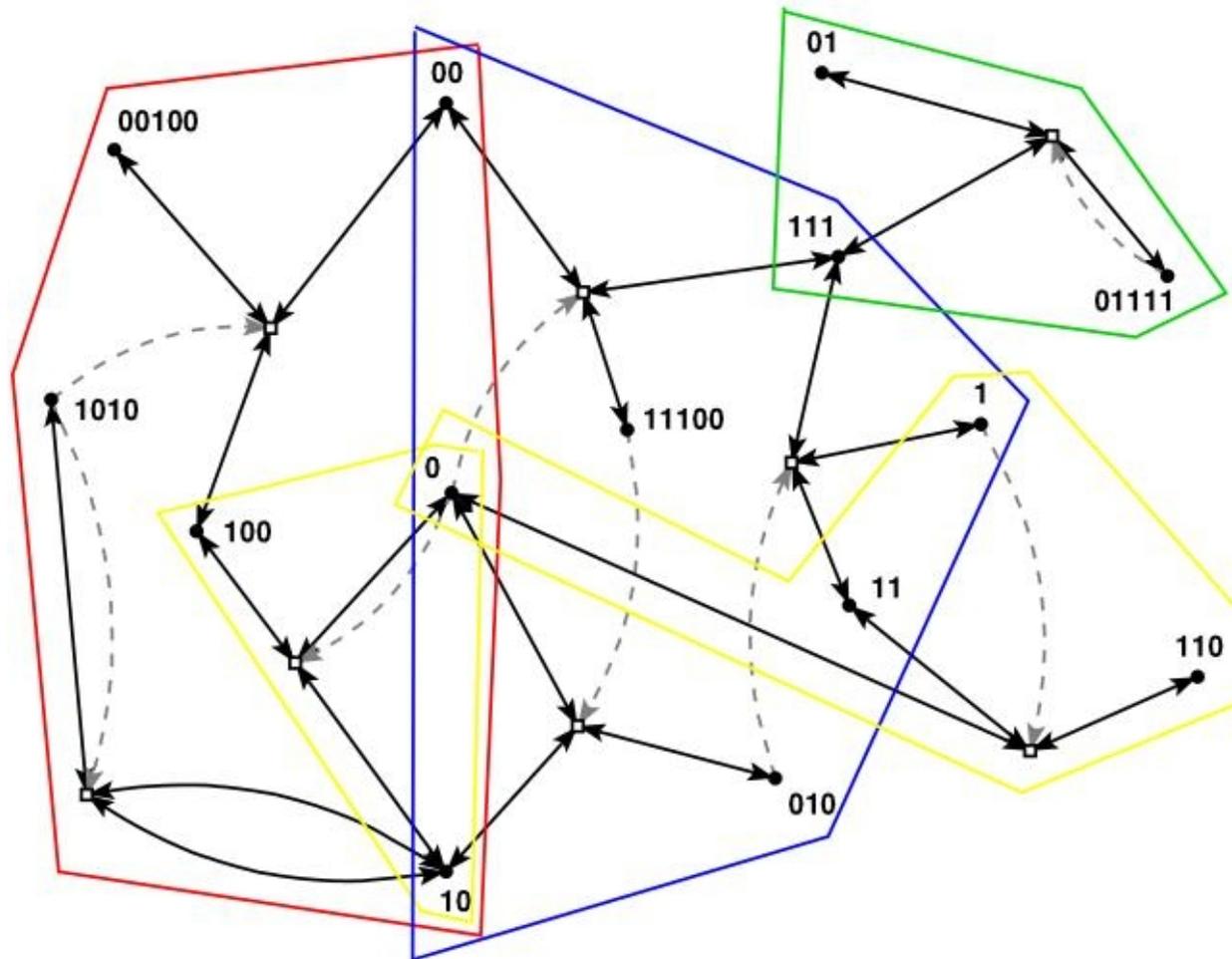


# Growth Rate in Level of Catalysis

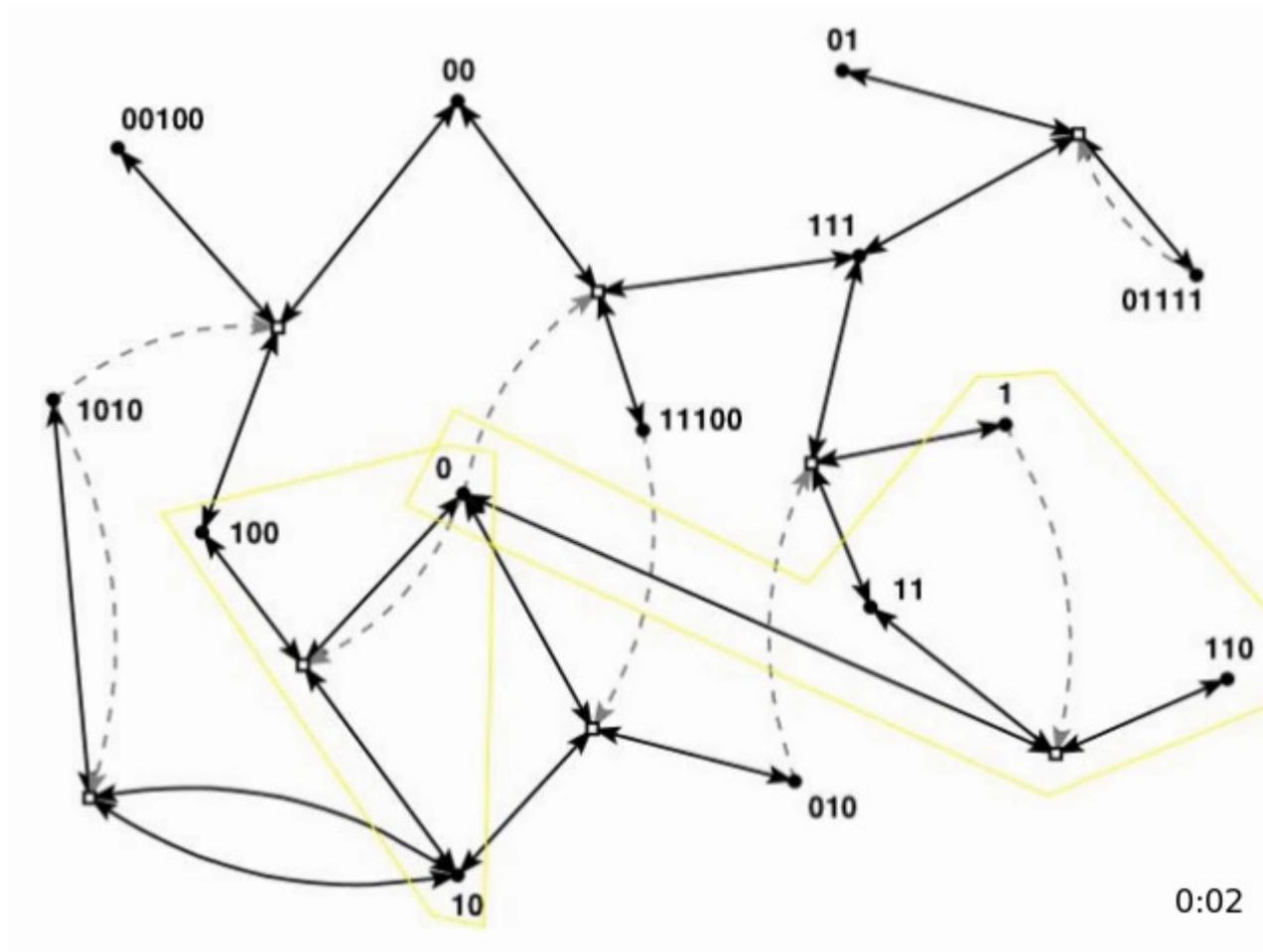
---



# Hierarchy of subRAFs

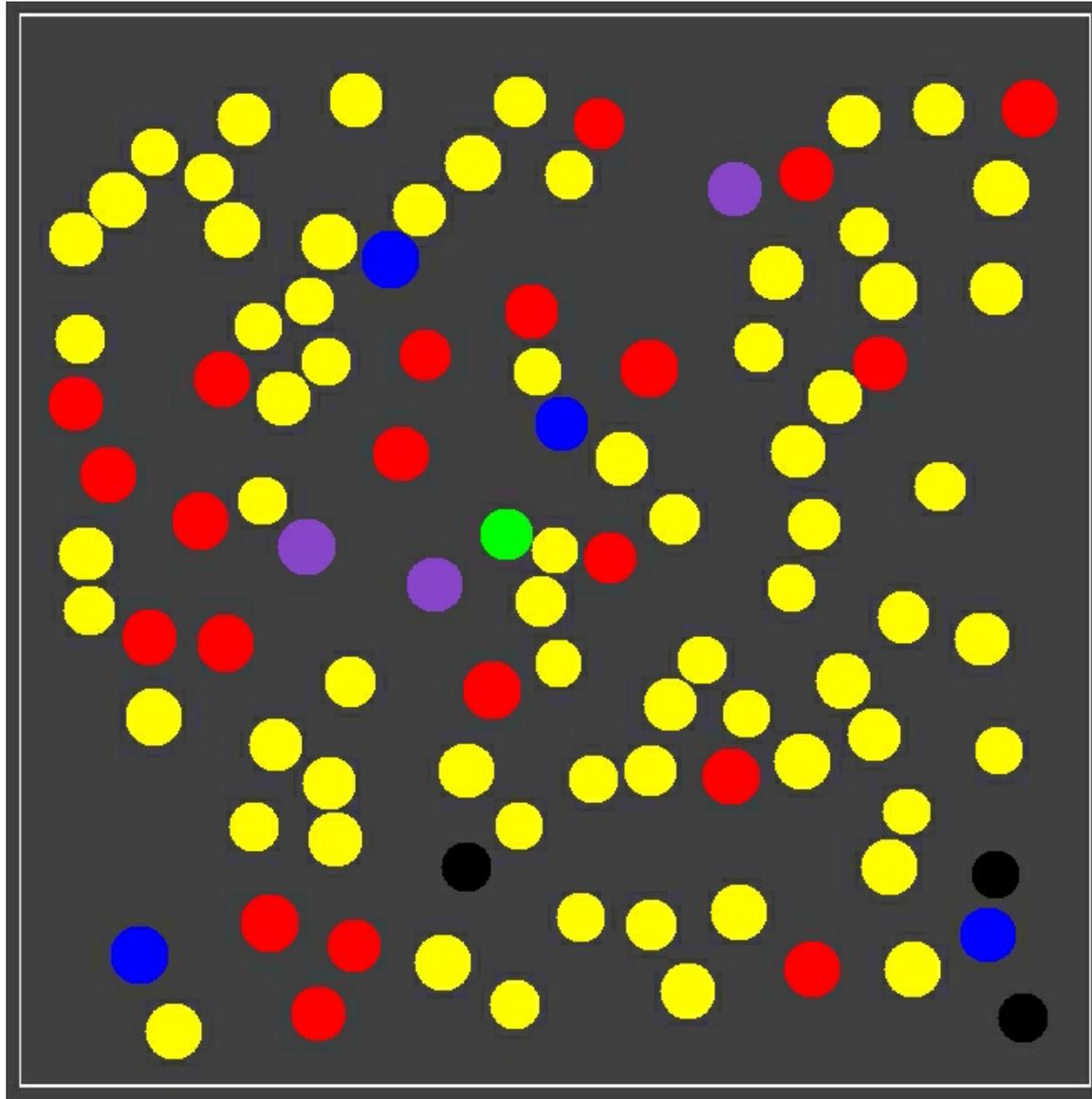


# Dynamics of subRAFs



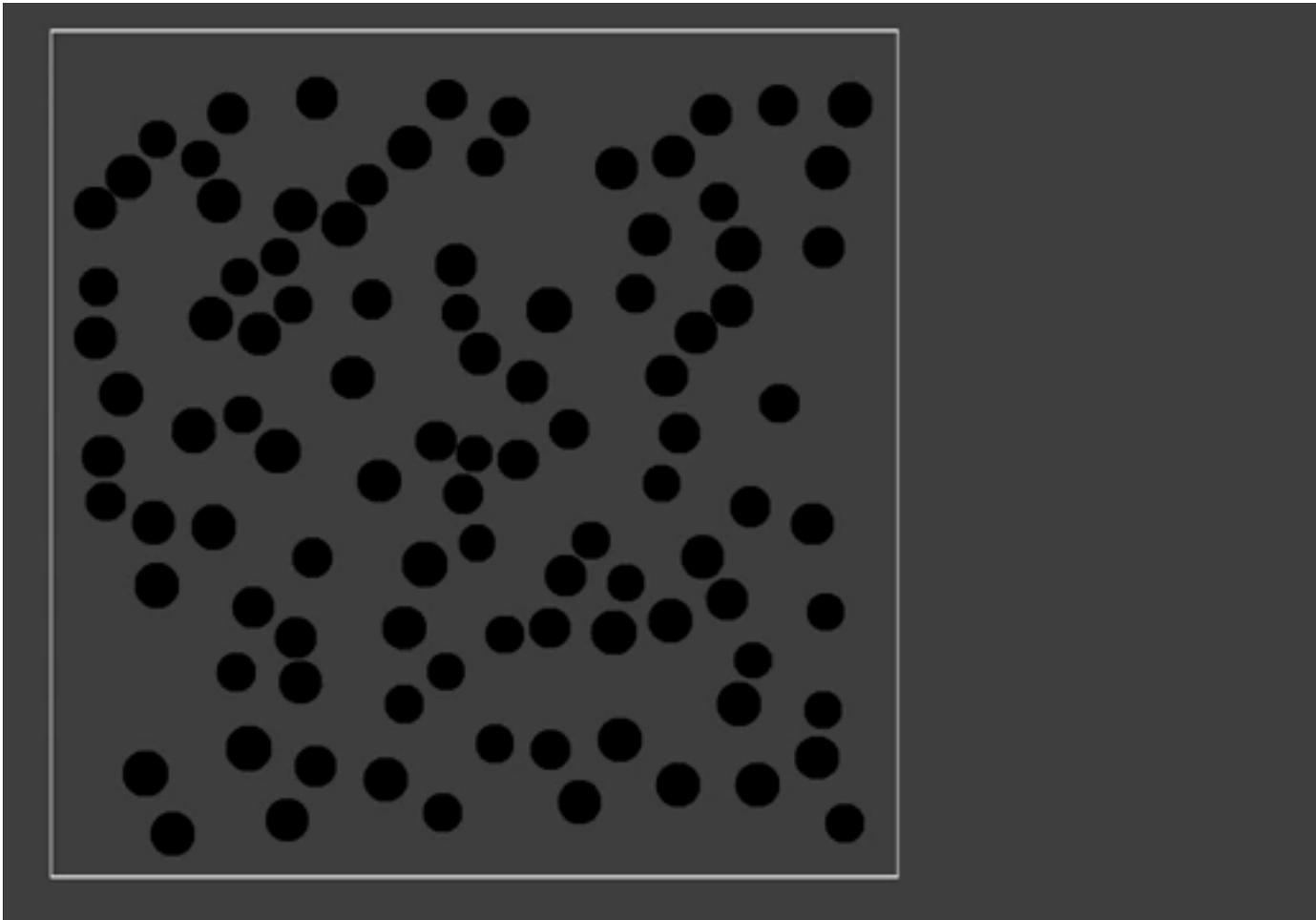
# RAFs in Compartments

---

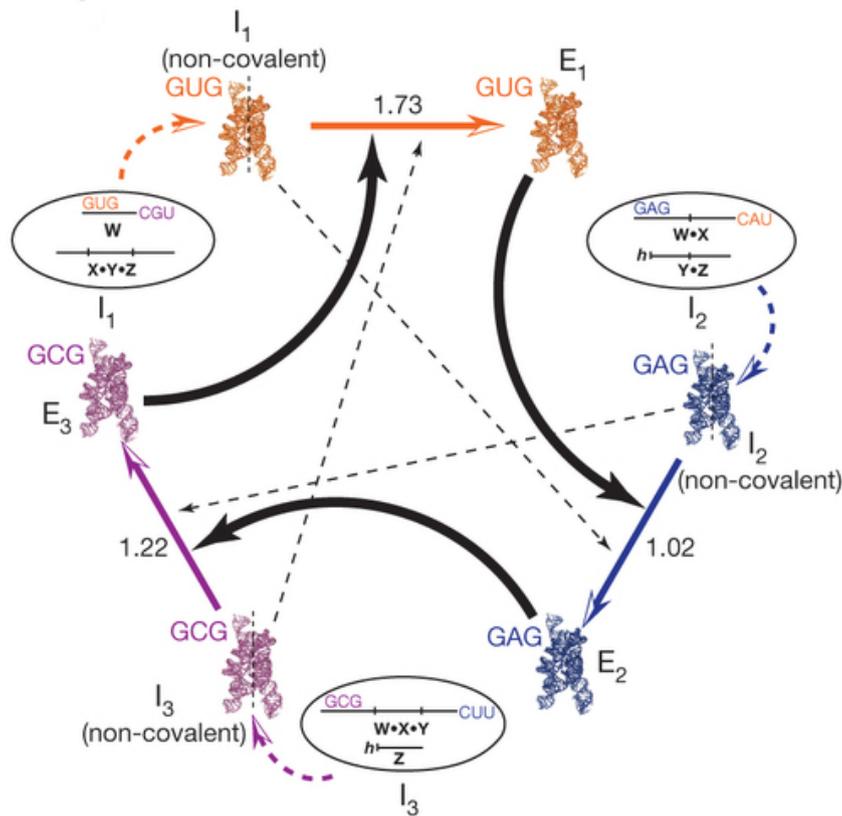


# RAFs in Compartments

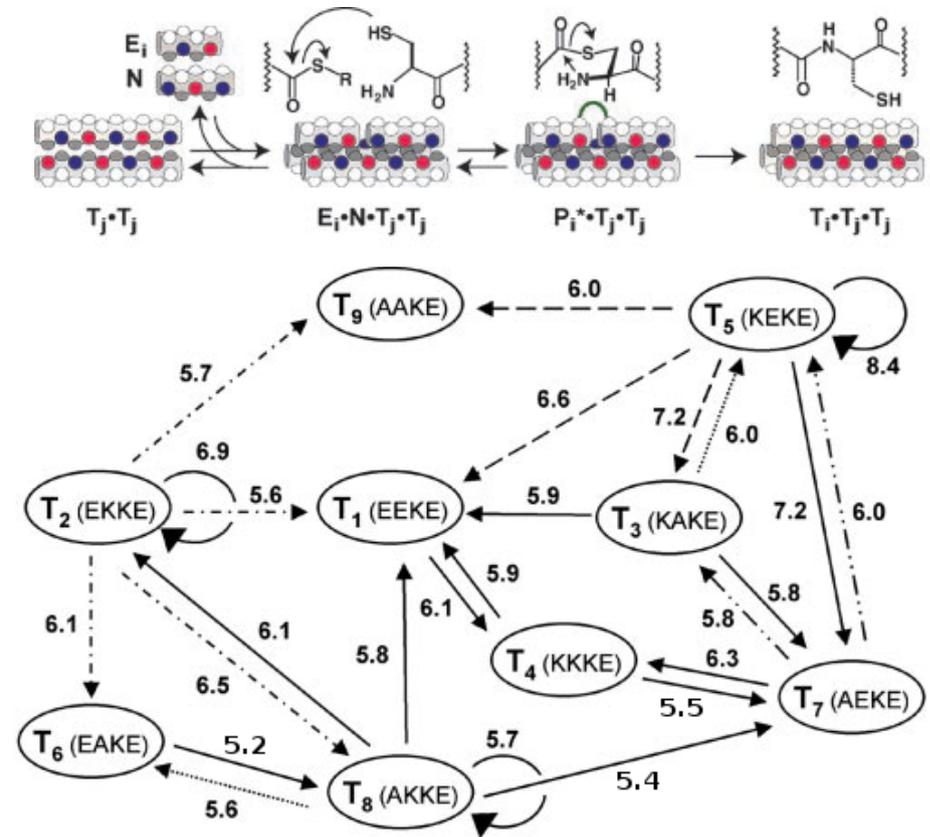
---



# Modeling Experimental Systems

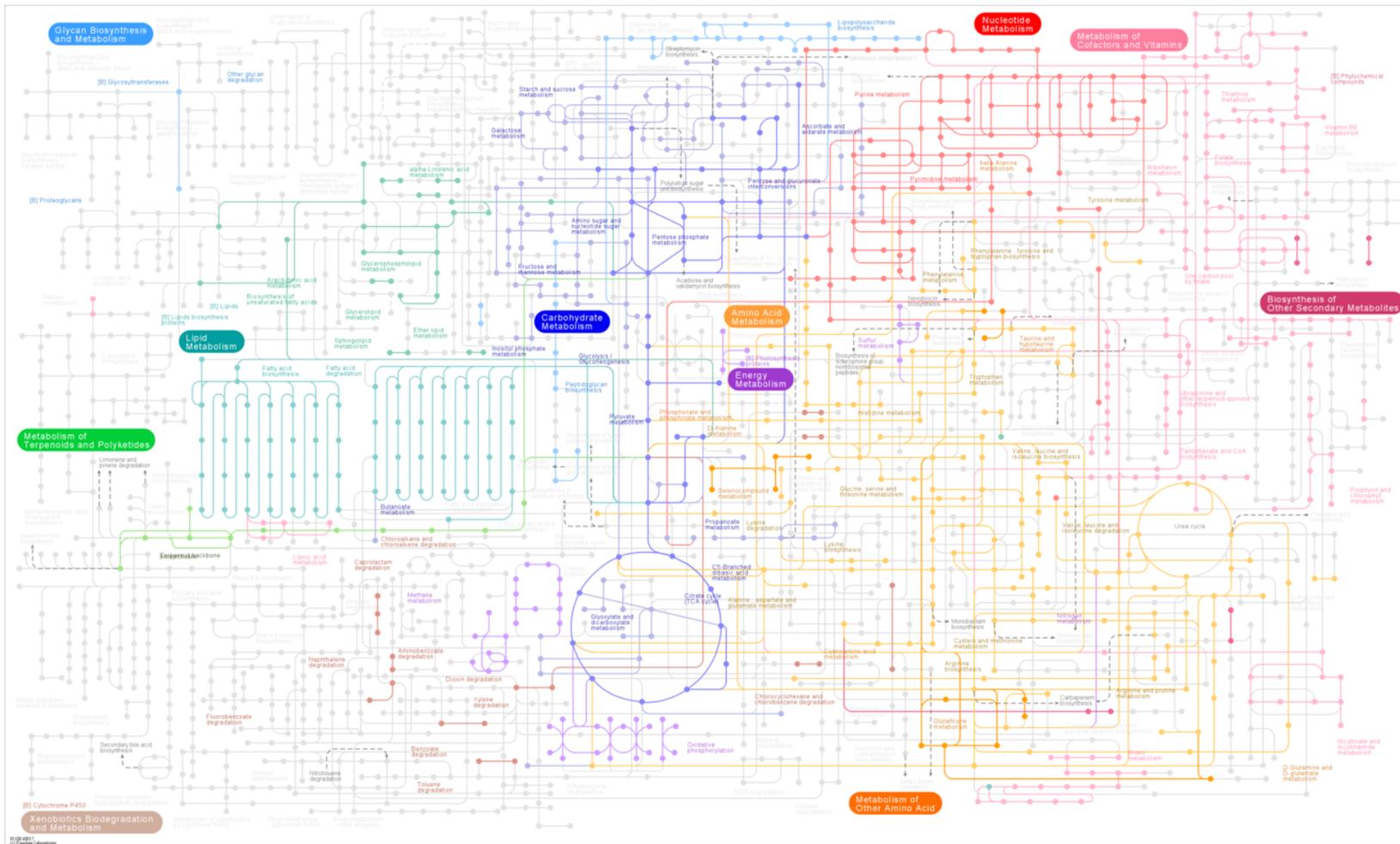


(Vaidya et al., *Nature*, 2012)



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

# Metabolic Network of *E. coli*



RAF set:

$|R| \approx 1800$

$|X| \approx 1200$

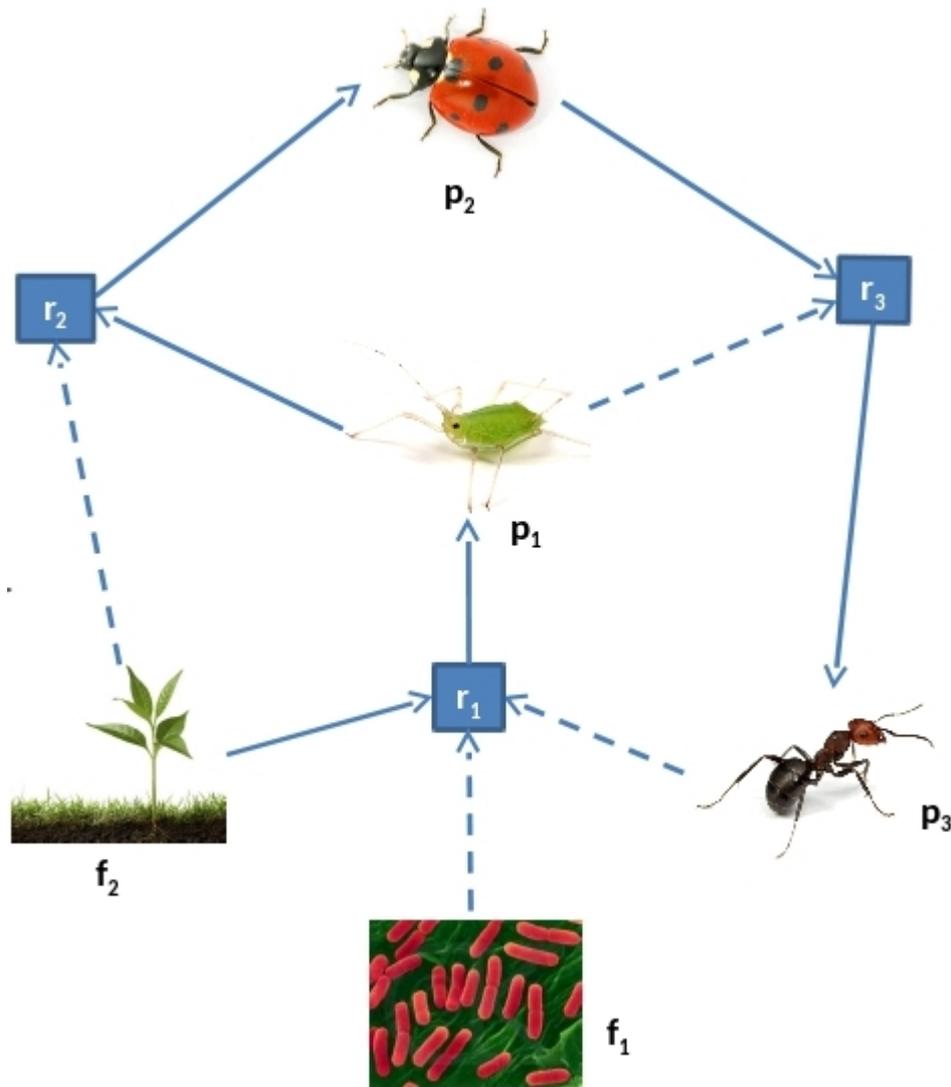


(Sousa et al., *J. Syst. Chem.*, 2015)

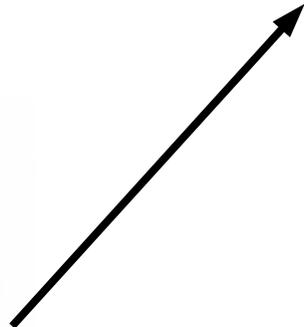
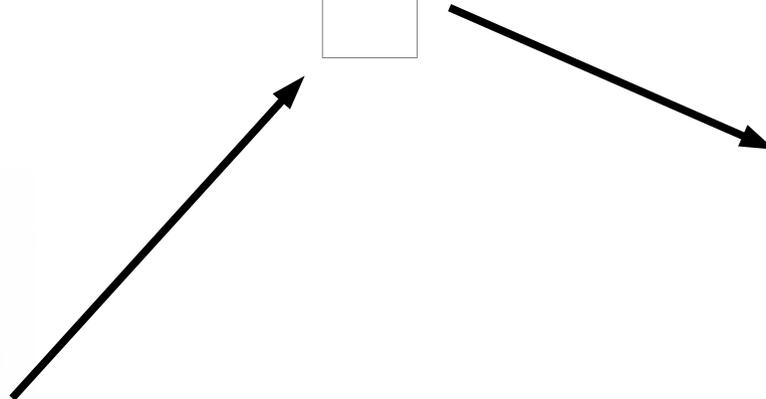
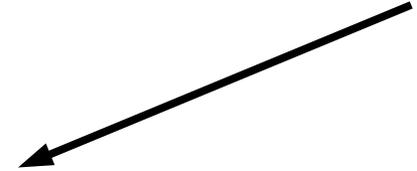
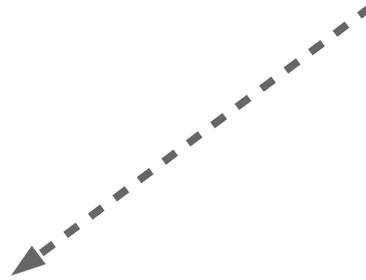
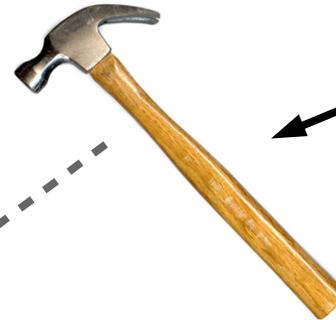
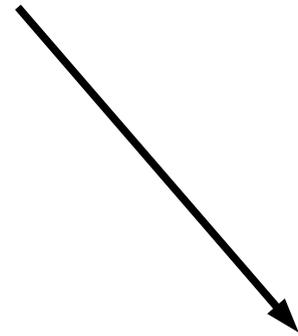


SmartAnalytiX.com  
BUSINESS ANALYTICS USING "SMART" COMPUTING

# Beyond Chemistry: Ecosystems

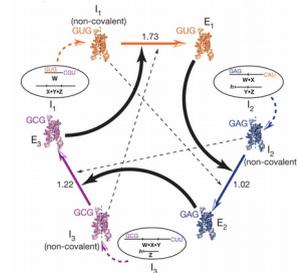
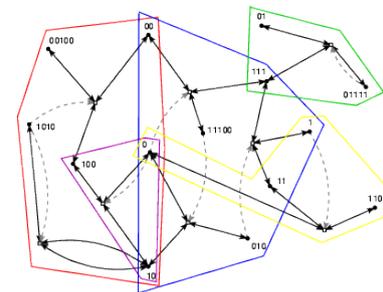
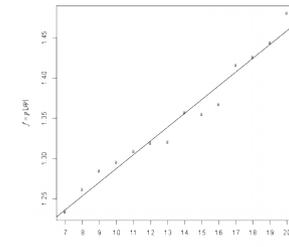
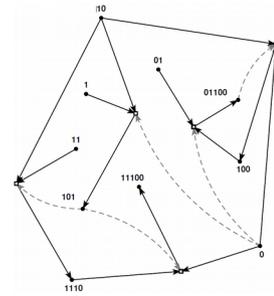


# Beyond Chemistry: The Economy



# Summary

- Autocatalytic sets capture the catalytically closed, self-sustaining organization of life.
- They are highly likely to exist, also for realistic catalysis levels: origin of life?
- They can be evolvable due to existence of multiple autocatalytic subsets.
- The formal framework can be applied to real chemical and biological networks.
- Applications beyond chemistry?



# Autocatalytic Set of Collaborators

---



Stuart Kauffman



Mike Steel



Niles Lehman



Bill Martin



Filipa Sousa

Peter Wills  
Josh Smith  
Jotun Hein  
Peter Dittrich  
Roberto Cazzolla Gatti  
Philippe Nghe  
Roberto Serra  
Gonen Ashkenasy



# Further Reading

---

- **W. Hordijk.** The Living Set. *The Scientist*, June 2015.

**TheScientist**  
EXPLORING LIFE, INSPIRING INNOVATION



- **COOLscience.club**
- **WorldWideWanderings.net**



**SmartAnalytiX.com**  
BUSINESS ANALYTICS USING "SMART" COMPUTING