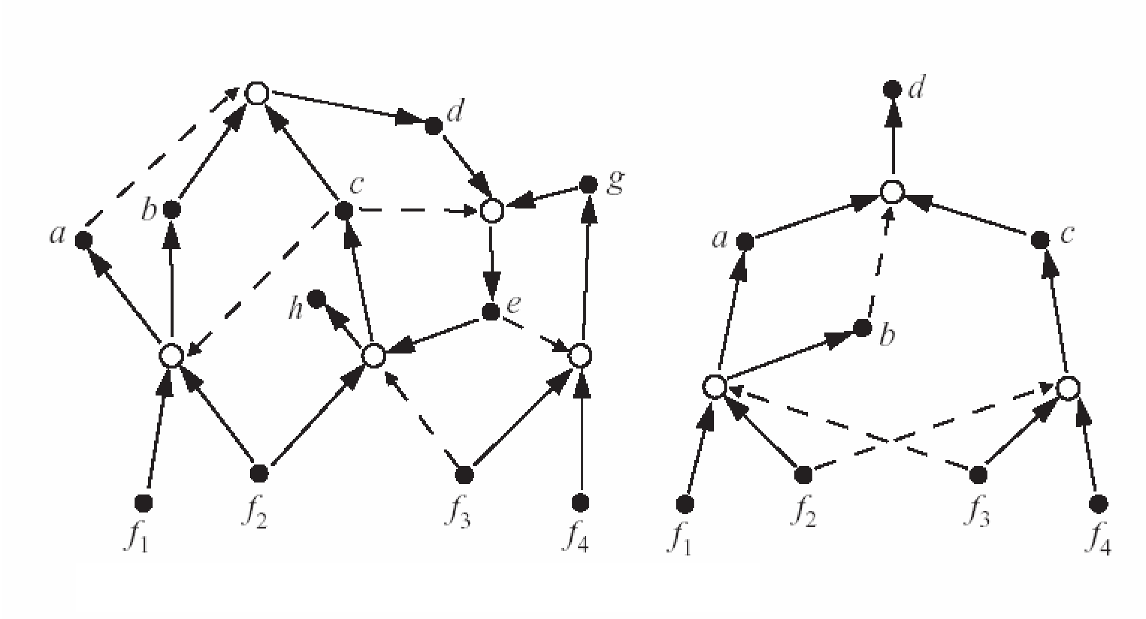
Random autocatalytic networks



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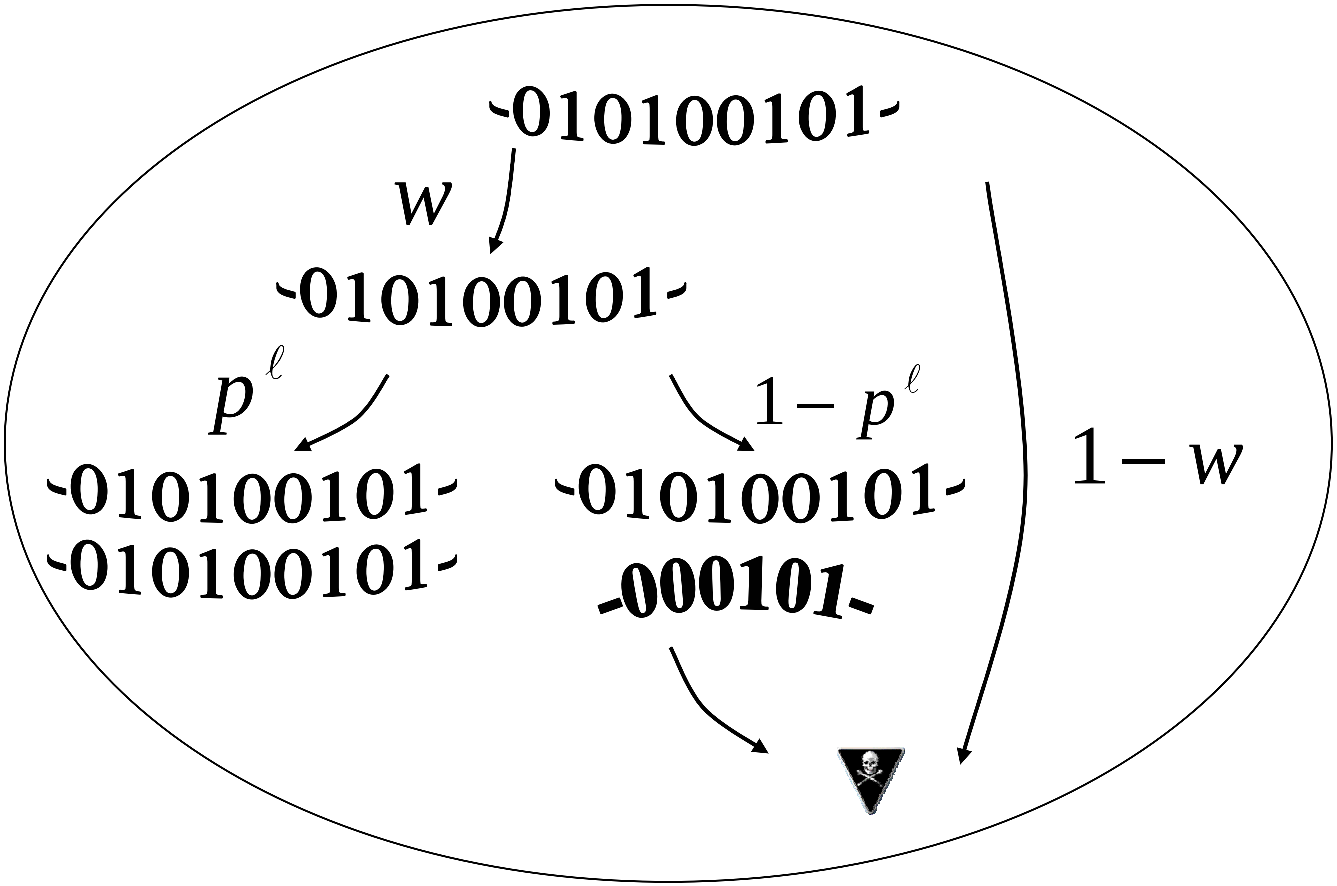
Random autocatalytic networks

•Origin of Life

many theories (Oparin, Haldane, Eigen, Schuster, Maynard-Smith, Dyson, Kauffman, du Duvre, Wachtershauser, Morowitz, Deamer, Lancet, Lindhal, Russel, Dyson, Kauffman, Lifson, Joyce, Scheuring, Szathmary, Poole, Penny …) – problems with most of them

•Metabolism-first (protein/enzyme) vs genetics-replication (RNA)-first

Sequence length vs error-correction



Demetrius, Schuster and Sigmund, 1985.

$$L \sim c/_{1-p}$$

Rates of spontaneous mutation in DNA-based microbes

			Mutation rate	
Organism	**Genome size (bp)**	**Target**	**Per bp (μ_{bp})**	**Per genome (μ_g)**
Bacteriophage M13	6.41×10^3	*lacZα*	7.2×10^{-7}	0.0046
Bacteriophage λ	4.85×10^4	*cI*	7.7×10^{-8}	0.0038
Bacteriophage T2	1.60×10^5	*rII*	2.7×10^{-8}	0.0043
Bacteriophage T4	1.66×10^5	*rII*	2.0×10^{-8}	0.0033
Escherichia coli	4.70×10^6	*lacI*	4.1×10^{-10}	0.0019
			6.9×10^{-10}	0.0033
		his GDCBHAFE	5.1×10^{-10}	0.0024
Saccharomyces cerevisiae	1.38×10^7	*URA3*	2.8×10^{-10}	0.0038
		SUP4	(7.9×10^{-9})	(0.11)
		CANI	1.7×10^{-10}	0.0024
Neurospora crassa	4.19×10^7	*ad-3AB*	4.5×10^{-11}	0.0019
		mtr	(4.6×10^{-10})	(0.019)
			1.0×10^{-10}	0.0042

From Maynard-Smith and Szathmary, 1997

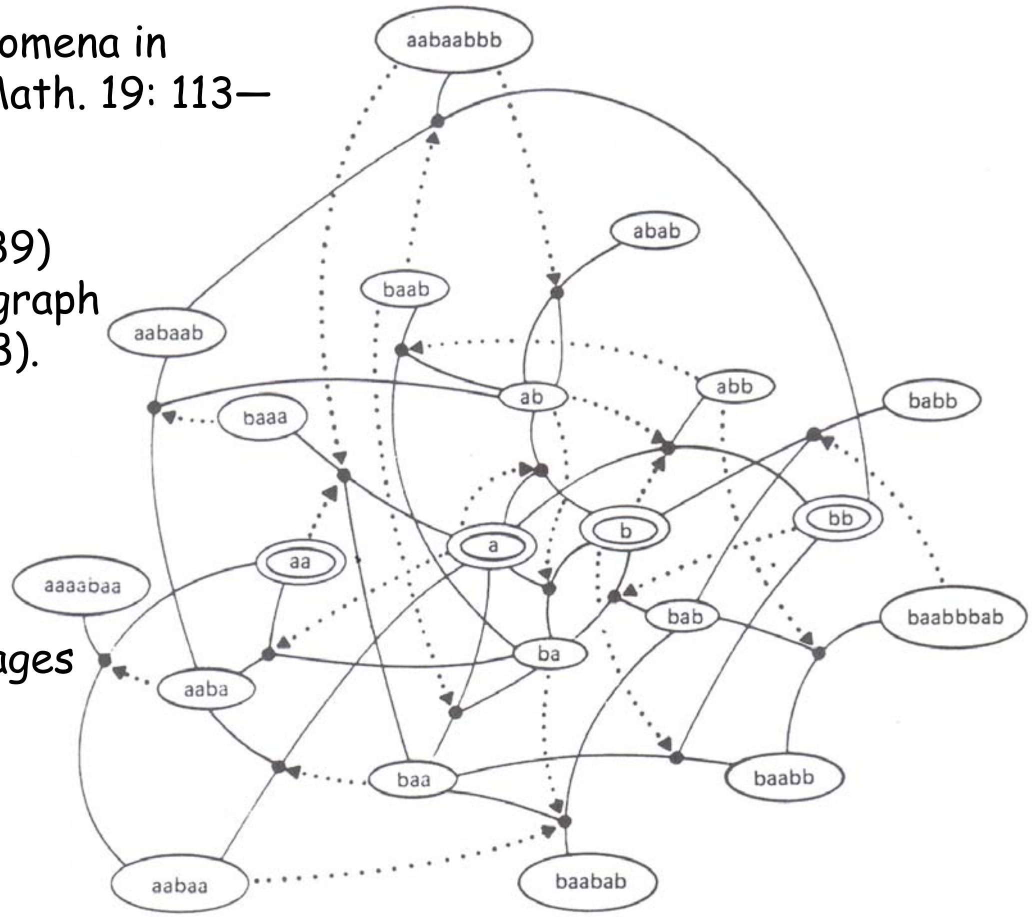
Random molecular networks

J.E. Cohen, 1988. Threshold phenomena in random structures. Discr. Appl. Math. 19: 113–128.

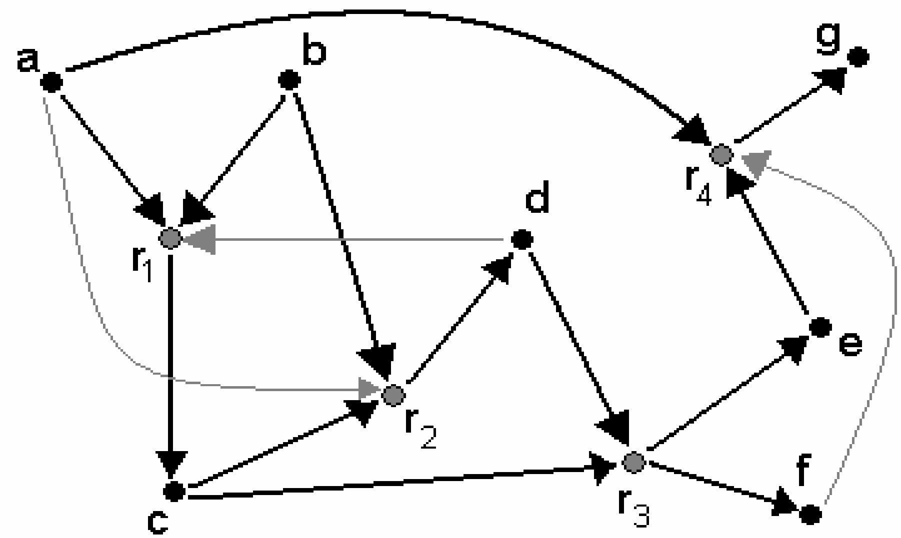
B. Bollobas and S. Rasmussen (1989) (First cycles in random directed graph processes, *Discr. Math.* **75**: 55-68).

S. Kauffman (1986, 1993) (Autocatalytic sets of proteins, *J. Theor. Biol.* **119**: 1-24).

Lifson (1997). "On the critical stages in the origin of animate matter. *J. Mol. Evol.* 44, 1-8.



Catalytic Reaction Graphs



$$X = \{a, b, c, d, e, f, g\}$$

$$R = \{r_1, r_2, r_3, r_4\}$$

$$C = \{(d, r_1), (a, r_2), (f, r_4)\}$$

$$F = \{a, b\}$$

$$r_1 : a + b \xrightarrow{d} c$$

$$r_2 : b + c \xrightarrow{a} d$$

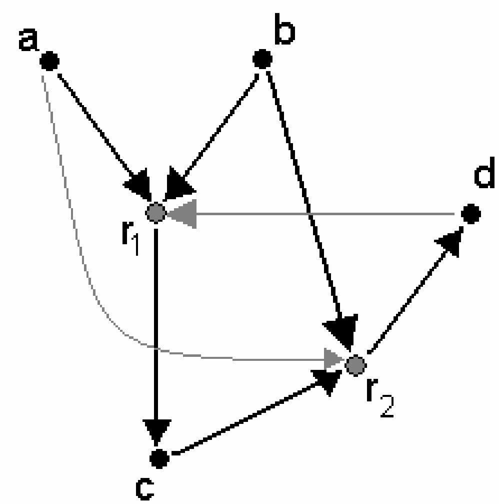
$$r_3 : c + d \rightarrow e + f$$

$$r_4 : a + e \xrightarrow{f} g$$

Definition of a RAF (semi-formal)

- Given a set of reactions R, a subset R′ is an RAF if
  - (*RA*) Each reaction in R′ is catalysed by at least one molecule that is involved in R′
  - (*F-connected*) Each molecule involved in R′ can be constructed from F by repeated application of reactions in R′

Example of RAF Set



F = {a,b}

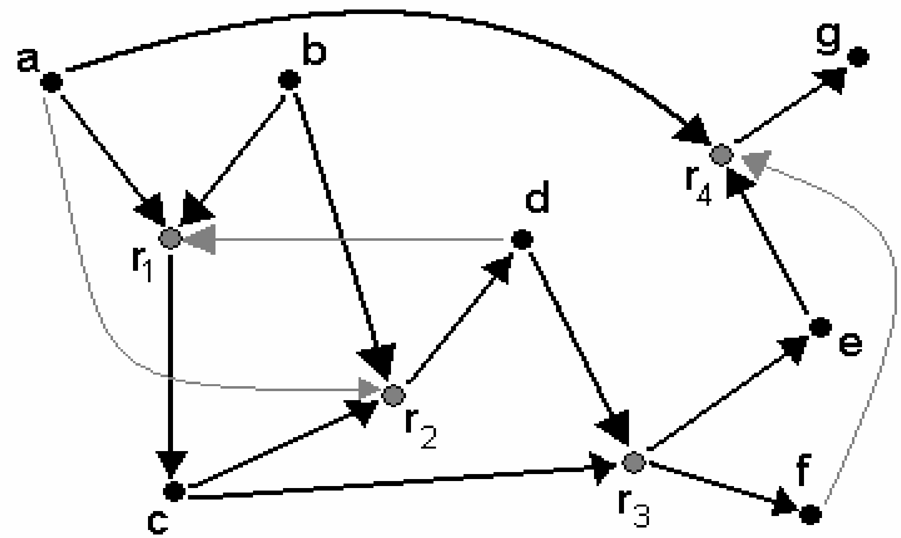
Observation and questions

- ‘Contain an RAF’ is a monotone property
- How much catalysis is needed? Without high catalysis is the existence of an RAF rare (require ‘fine tuning’) or expected?

Properties of RAF Sets

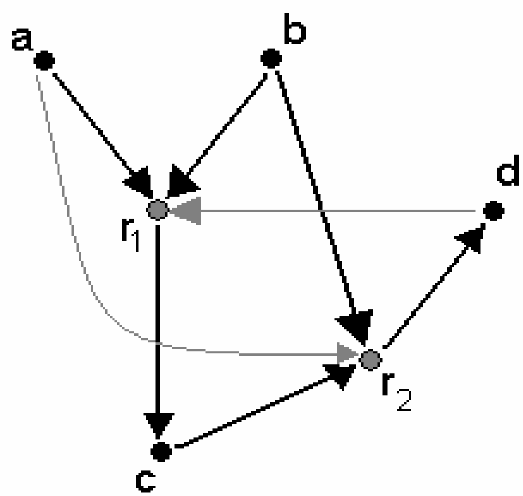
- Let $Q = (X, R, C)$ be a CRS
  - If $R_1, R_2 \subseteq R$ are RAF, then $R_1 \cup R_2$ is RAF
  - If Q has an RAF set, then it has a maximal RAF set:
    $\bigcup (R' : R' \subseteq R \text{ is RAF})$
  - "Irreducible RAF set": no proper subset is RAF

Finding an RAF set

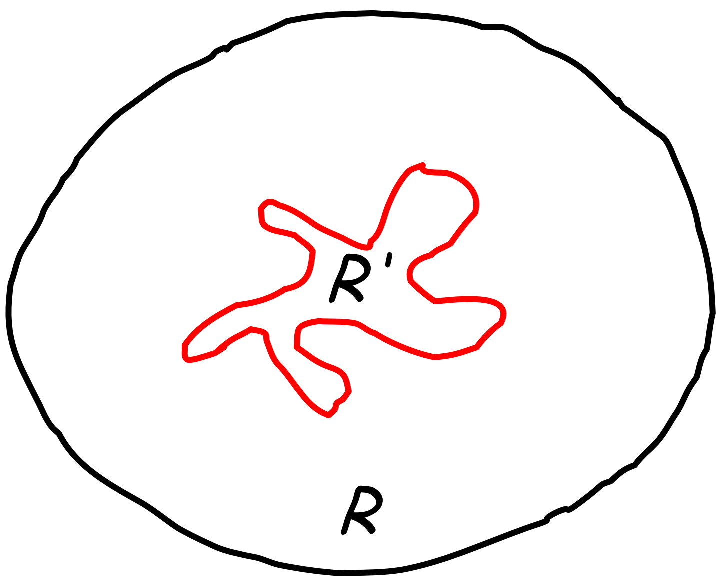


$$F = \{a, b\}$$

Unique irreducible RAF Set



Finding RAFs



Theorem (Hordijk and S, 2004):

There is an algorithm for determining if R contains a RAF and if so constructing an irreducible one in polynomial time in |R|, |X|.

Random catalytic sets of sequences

- Molecules: $X(n) = \{0,1,\ldots,\kappa-1\}^{\leq n}$
- Reactions: $R(n) = R_+(n) \cup R_-(n)$
  - $R_+(n)$ forward (ligation): $a + b \rightarrow ab$
  - $R_-(n)$ backward (cleavage): $ab \rightarrow a + b$

Example

$0 + 10 \rightarrow 010$

$100 \rightarrow 1 + 00$

- Food set $F = \{0,1,\ldots,\kappa\}^{\leq t}$
- Assumptions:
  - (R1)The events `x catalyses r' are independent
  - (R2) Pr[x catalyses r] depends only on x

- Note: R is given, the catalysis is random!

Quantities of interest:

$$P_n = \Pr[\text{system has a RAF}], \qquad P_\infty = \lim_{n\to\infty} P_n$$

$\mu_n(x)$:= average # (forward) reactions molecule *x* catalyses

$$\mu_n(x) = \Pr[x \text{ catalyses } r]\cdot|R_+(n)|$$

A criticism (?)

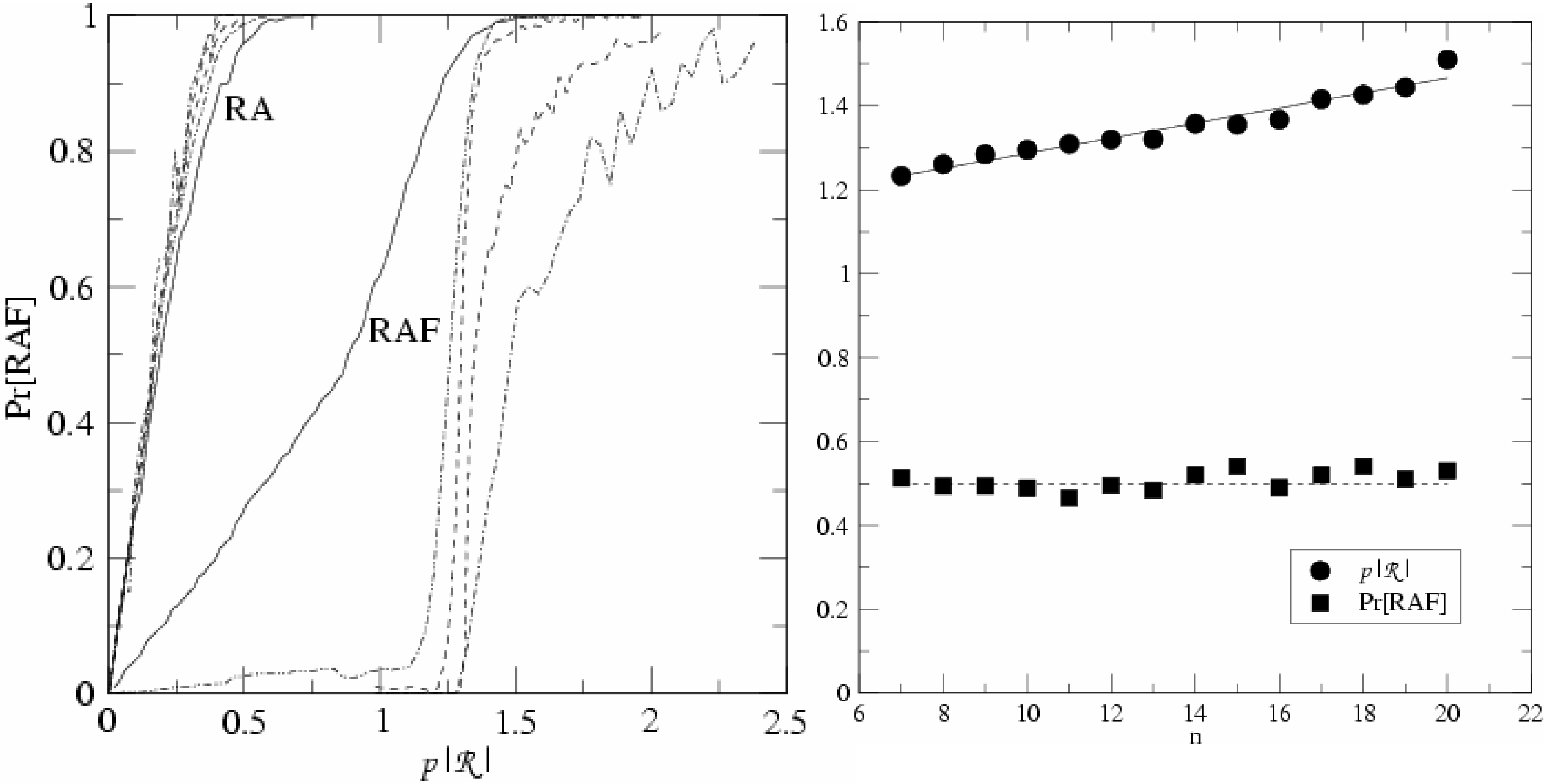
- Kauffman: $\mu_n(x) \propto 2^n \;\Rightarrow P_\infty = 1$
- Lifson: $\mu_n(x) = c \;\not\Rightarrow P_\infty = 1$

- **Theorem** (S, 2000):

$$\mu_n(x) < \tfrac{1}{3} e^{-1} \Rightarrow P_\infty = 0$$

$$\mu_n(x) \geq cn^2 \Rightarrow P_\infty = 1$$

Simulations



Proposition (2005, *Mossel + S, J. Theor. Biol.*)

$$\max_{x\in X(n)} \frac{\mu_n(x)}{n} \to 0 \Rightarrow P_\infty = 0$$

$$\min_{x\in X(n)} \frac{\mu_n(x)}{n} \to \infty \Rightarrow P_\infty = 1$$

Can replace $\frac{\mu_n(x)}{n}$ by $\frac{\mu_n(x)}{|x|}$

Two further conditions on an RAF R′

- Products of R′ are not all in F.

- Given $\Omega \subseteq 2^{X-F}$ possible minimal requirements for 'life'

  If $\Omega \neq \emptyset$ then there is some ω in Ω all of whose molecules is produced by R′.

Theorem (2005, Mossel + S, *J. Theor. Biol.*)

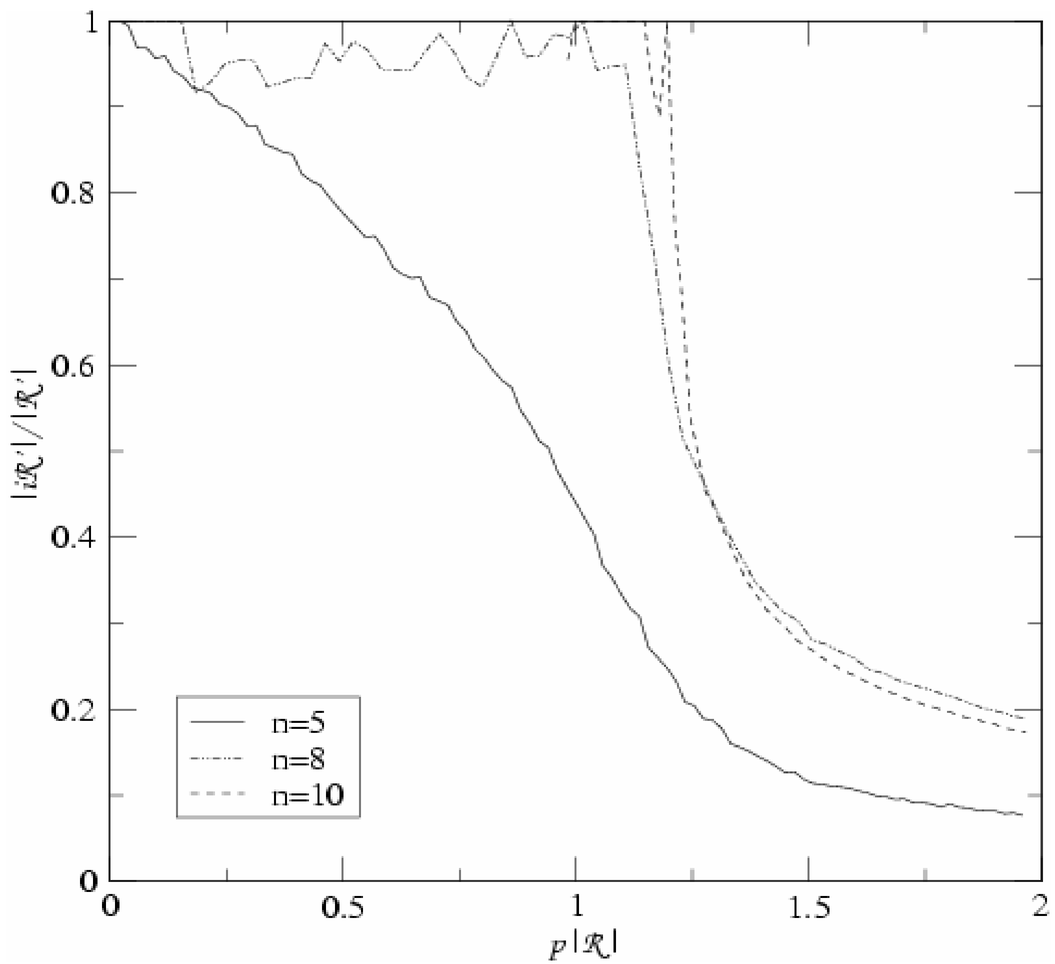
$$\mu_n(x) \le \lambda n \Rightarrow P_n(\Omega) \le 1 - \exp(-2\lambda c(t)^2 (1 + O(\frac{1}{n}))$$

$$\mu_n(x) \ge \lambda n \Rightarrow P_n(\Omega) \ge 1 - \frac{\kappa(\kappa e^{-\lambda c(t)})^t}{1 - \kappa e^{-\lambda c(t)}}$$

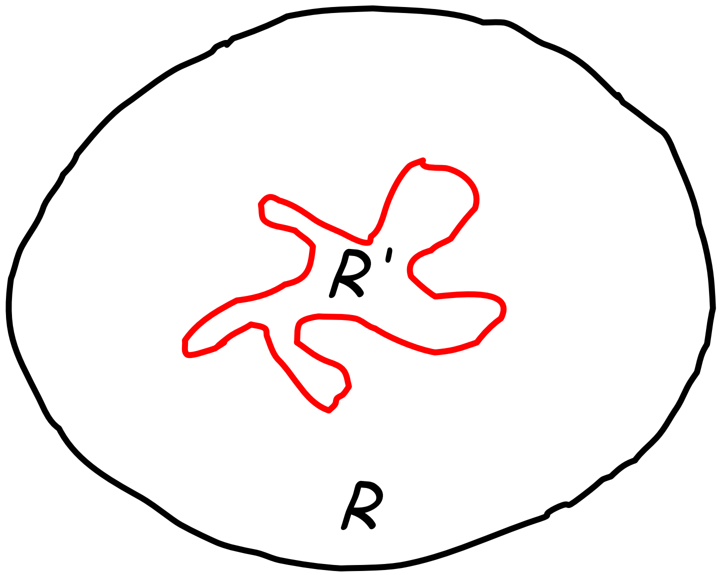
$c(t) = \kappa + \kappa^2 + \ldots + \kappa^t$

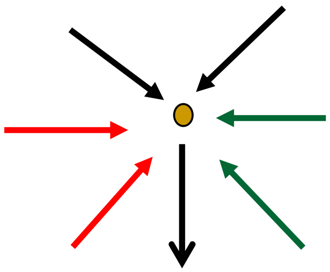
Example: $\kappa=2$, $t=2$, $\lambda = 4$, $P_n(\Omega)>0.99$

Irreducible RAF Sets



Extension (I) Inhibition

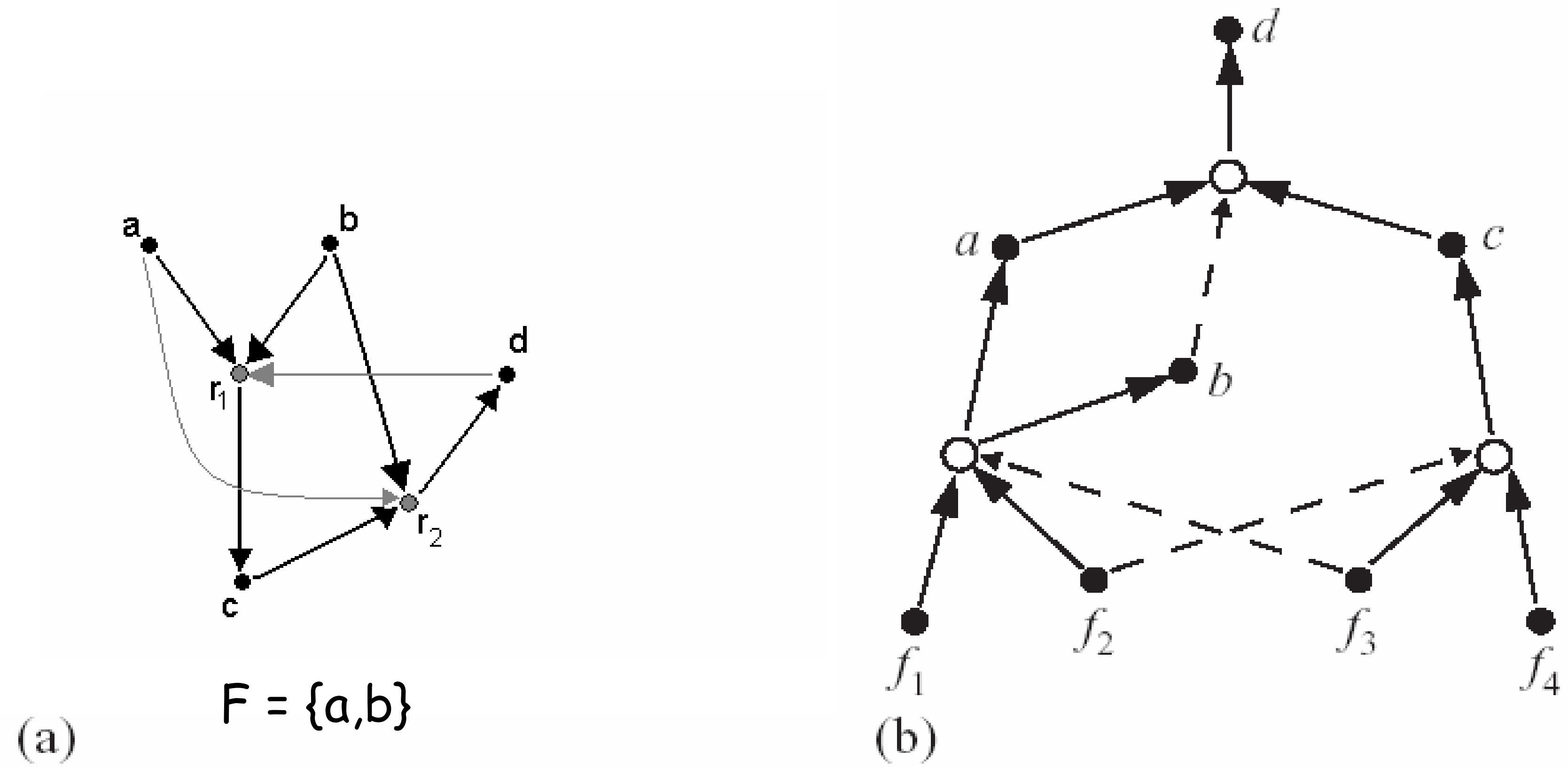




Theorem (Mossel and S, 2005):

Determining whether R contains an RAF is NP-complete

Extension (II): RAFs vs CAFs



Theorem (2005, Mossel + S, *J. Theor. Biol.*)

$$\mu_n(x) \leq \lambda \cdot r_n \Rightarrow P_n^{CAF}(\Omega) \leq 2\lambda c(t)^2$$

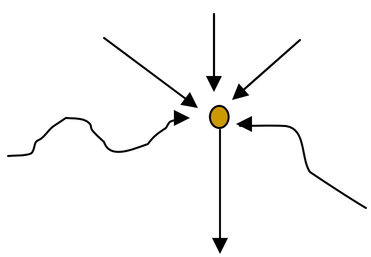
$$\mu_n(x) \geq \lambda \cdot r_n \Rightarrow P_n^{CAF}(\Omega) \geq 1 - \frac{\kappa(\kappa e^{-\lambda c(t)})^t}{1 - \kappa e^{-\lambda c(t)}}$$

Extensions

- Inhibition, concentration
- Other molecular networks

Other applications?

- Spontaneous combustion?
- Random neural networks?



Further details

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Steel, M. The emergence of a self-catalysing structure in abstract origin-of-life models, *Applied Mathematics Letters* 3: 91-95 (2000).