the limits of dynamical systems

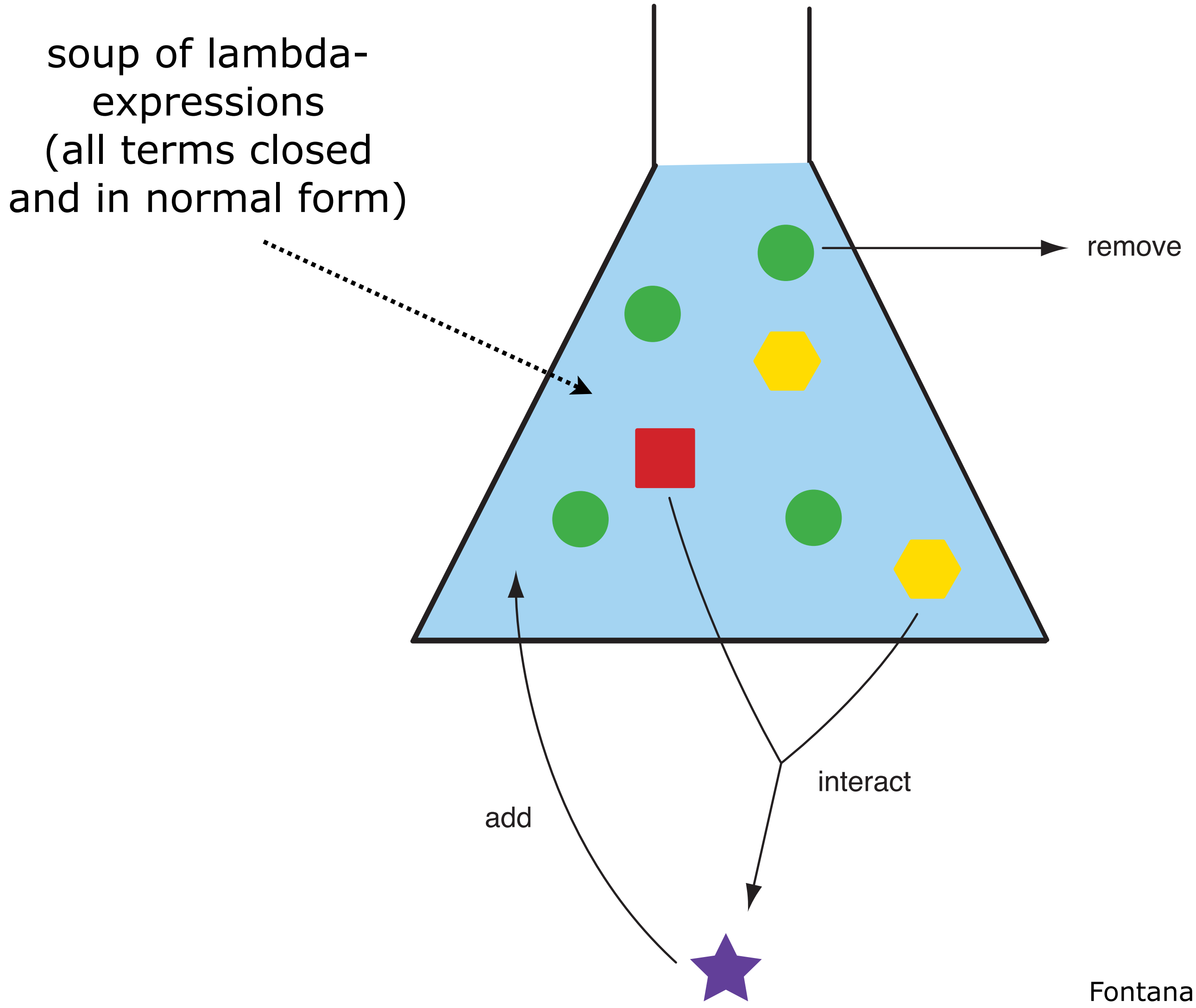
DS represent agents only in terms of the interactions that exist and are assumed relevant in a given context; they do *not* represent agents in terms of *potential* interactions that are not causally effective now, but would become so if context was changing.

To describe agents in these terms requires a representation of their structure, which holds the key to possible interactions that can become actualized in other contexts.

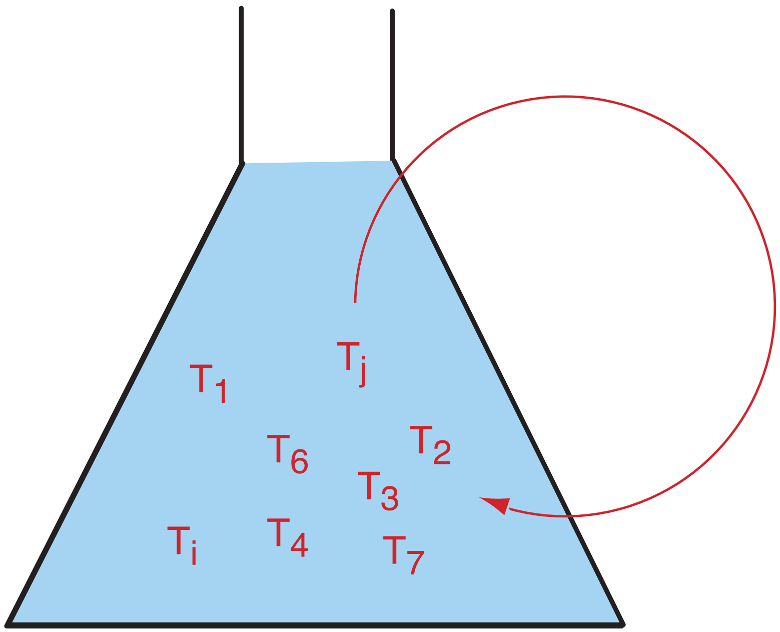
It is an open question to what extent *physical* structure and modes of interaction can be lifted into a formal logical representation that permits such reasoning in the molecular realm.

The bottleneck in biology is not quantification, but description. (ouch!)

Turing Gas or Church Soup or AlChemy



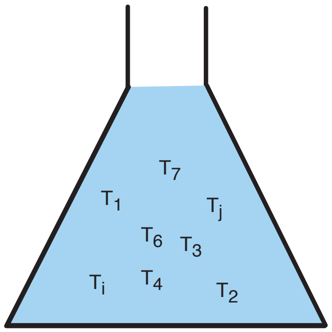
Fontana & Buss, 1994-1996



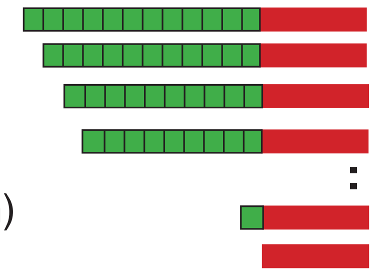
Self-maintenance is the consequence of a constructive feed-back loop: it occurs when the construction processses induced by the constituents of a system permit the continuous regeneration of these same constituents.

Immanuel Kant (Kritik der Urteilskraft, 1790): “[...] an organized product of nature is one in which all is end and, reciprocally, means too.”

independent level of description



characteristic grammar

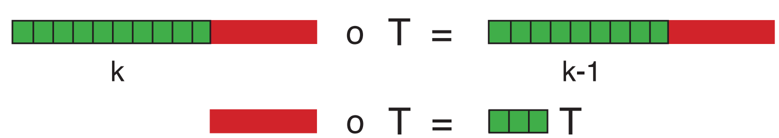


parse all terms into prefixes (not a λ-term)
and terminals (closed λ-term)

self-maintaining ensemble

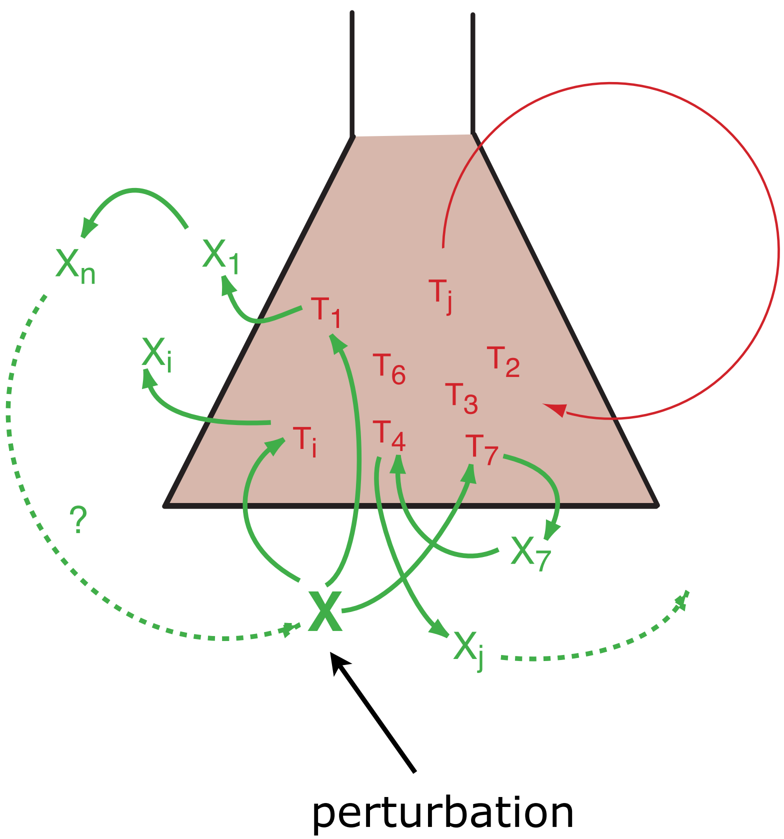
derive the transformational behavior of building blocks and describe all interactions in terms of a set of rewrite rules

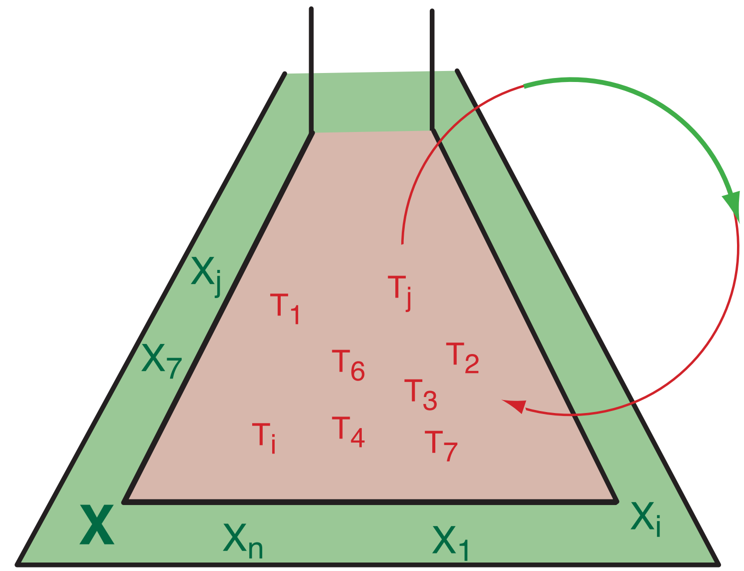
yields a specific algebraic structure



all reference to the underlying micro-mechanics (λ-calculus) has been removed

constrained extension





Applying a function to an argument in a typed calculus ...

$$\frac{A \longrightarrow B \qquad A}{B}$$

... corresponds to *modus ponens* in logic

This correspondence is known as the Curry-Howard isomorphism:

type σ $\longleftrightarrow$ logical formula (predicate) σ

λ-term of type σ $\longleftrightarrow$ proof of σ

so, our picture of chemistry becomes....

molecular shape	chemical predicate σ (statement about a chemical action)
molecule with that shape	proof of the validity of σ
chemical reaction	rule of inference
reactants / products	(proofs of) premises / conclusions

A more formal approach to agent-based systems is the π-calculus.
Its application to biology was pioneered by Shapiro, Regev, and Priami.
Its potential for biology was considerably deepened by Danos and Laneve.

The π-calculus
(Milner, Walker and Parrow 1989)

- a program specifies a network of interacting processes
- processes are defined by their potential communication activities
- communication occurs on complementary channels, identified by names
- message content: channel name

Processes and channels

	$P,\ Q,\ \cdots$	process names (2.1)
	$x,\ y,\ \cdots$	channel names (2.2)
	$\overline{x},\ \overline{y},\ \cdots$	channel co-names (2.3)

Events

$\pi ::=$	x	communication on channel name x (2.4)
	$\overline{x}$	communication on channel co-name x (2.5)
	$x(y)$	receive y along x (2.6)
	$\overline{x}\langle y\rangle$	send y along x (2.7)

Process syntax

$P ::=$	$P_1 \mid P_2$	parallel processes (2.8)
	$\pi\ .\ P_1$	sequential prefixing by communication (2.9)
	$\pi_1\ .\ P_1\ +\ \pi_2\ .\ P_2$	mutually exclusive communications (2.10)
	$(\mathsf{new}\ x)P$	new communication scope (2.11)
	0	inert process (2.12)

Structural congruence

$P \mid Q \equiv Q \mid P$	commutativity of PAR (2.13)
$(P \mid Q) \mid R \equiv P \mid (Q \mid R)$	associativity of PAR (2.14)
$P\ +\ Q \equiv Q\ +\ P$	commutativity of summation (2.15)
$(P\ +\ Q)\ +\ R \equiv P\ +\ (Q\ +\ R)$	associativity of summation (2.16)
$(\mathsf{new}\ x)0 \equiv 0$	scope of inert processes (2.17)
$(\mathsf{new}\ x)(\mathsf{new}\ y)P \equiv (\mathsf{new}\ y)(\mathsf{new}\ x)P$	multiple communication scopes (2.18)
$((\mathsf{new}\ x)P) \mid Q) \equiv (\mathsf{new}\ x)(P \mid Q)$ if $x \notin FN(Q)$	scope extrusion (2.19)
$A(\vec{y}) \equiv \{\vec{y}/\vec{x}\}Q_A$	recursive parametric definition (2.20)
$x(y).P = x(z).(\{z/y\}\ P)$ if $z \notin FN(P)$	renaming of input channel y (2.21)
$(\mathsf{new}\ y).P = (\mathsf{new}\ z).(\{z/y\}\ P)$ if $z \notin FN(P)$	renaming of restricted channel y (2.22)

Reaction rules

$(\cdots + \overline{x}\langle z\rangle.Q)\vert(\cdots + x(y).P) \to Q\vert P\,\{z/y\}$	communication (COMM)(2.23)
if $P \to P'$ then $P\vert Q \to P'\vert Q$	reaction under parallel composition (2.24)
if $P \to P'$ then $(\mathsf{new}\ x)P \to (\mathsf{new}\ x)P'$	reaction within restricted scope (2.25)
if $Q \equiv P, P \to P'$, and $P' \equiv Q'$ then $Q \to Q'$	reaction up to structural congruence (2.26)

$$E + S \rightleftarrows ES \longrightarrow E + P$$

- Says nothing about internal structure of E, S, P, ES
- We want to encode the reaction scheme… but according to certain principles

$$[\![\; E + S \rightleftarrows ES \longrightarrow E + P \;]\!]_{\pi}$$

- $[\![- \rightarrow_{CHEM} -]\!]_{\pi} = - \rightarrow_{\pi}^{*} -$
- $[\![- +_{CHEM} -]\!]_{\pi} = - \mid -$

$$E + S \rightleftarrows ES \longrightarrow E + P$$

from these we deduce

- $[\![E + S]\!]_\pi = [\![E]\!]_\pi \mid [\![S]\!]_\pi \rightarrow_\pi^* [\![ES]\!]_\pi$
- $[\![ES]\!]_\pi \rightarrow_\pi^* ([\![E]\!]_\pi \mid [\![S]\!]_\pi) + ([\![E]\!]_\pi \mid [\![P]\!]_\pi)$

from these we deduce

- $\exists x_0.([\![E]\!]_\pi \approx (\upsilon\ e)(x_0[e].[\![E]\!]_\pi' + X_E))\ \&\ ([\![S]\!]_\pi \approx x_0(y).[\![S]\!]_\pi' + X_S)$
- $[\![ES]\!]_\pi \approx (\upsilon\ e)([\![E]\!]_\pi' \mid [\![S]\!]_\pi'\{e/y\})$

therefore

- $(\upsilon\ e)([\![E]\!]_\pi' \mid [\![S]\!]_\pi'\{e/y\}) \rightarrow_\pi^* ([\![E]\!]_\pi \mid [\![S]\!]_\pi) + ([\![E]\!]_\pi \mid [\![P]\!]_\pi)$

$$E + S \rightleftharpoons ES \longrightarrow E + P$$

since E is an enzyme, $[\![E]\!]_\pi$ is the future of $[\![E]\!]_\pi{}'$,
and $[\![S]\!]_\pi$ and $[\![P]\!]_\pi$ are the futures of $[\![S]\!]_\pi{}'\{e/y\}$

- $(\upsilon\ e)([\![E]\!]_\pi{}' \mid [\![S]\!]_\pi{}'\{e/y\}) \rightarrow_\pi^* ([\![E]\!]_\pi \mid [\![S]\!]_\pi) + ([\![E]\!]_\pi \mid [\![P]\!]_\pi)$

implies

- $\exists x_1 x_2.([\![E]\!]_\pi{}' \approx x_1(y).[\![E]\!]_\pi + x_2(y).[\![E]\!]_\pi + X_{E'}) \& ([\![S]\!]_\pi{}' \approx x_1[e].[\![S]\!]_\pi + x_2[e].[\![P]\!]_\pi + X_{S'})$

setting ***X's*** to ***0*** and minimizing the number of $\rightarrow_\pi$ steps
we arrive at

- $[\![E]\!]_\pi = (\upsilon\ e)(x_0[e].(x_1(y).[\![E]\!]_\pi + x_2(y).[\![E]\!]_\pi))$
- $[\![S]\!]_\pi = x_0(y).(x_1[e].[\![S]\!]_\pi + x_2[e].[\![P]\!]_\pi)$

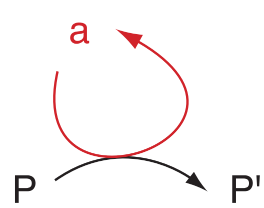
L.Greg Meredith (2005)

$$E + S \rightleftarrows ES \longrightarrow E + P$$

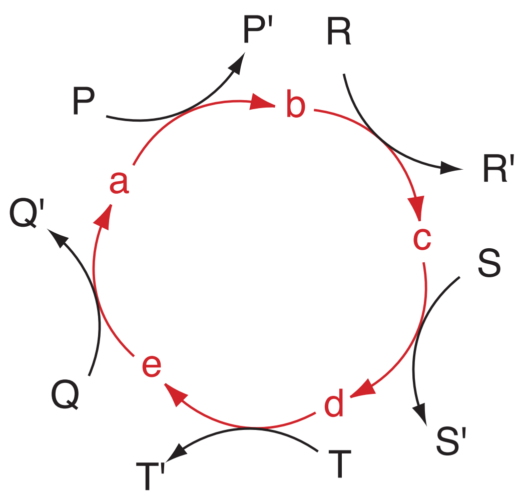
is really a reaction (network) type.

- use spatial logic (L.Caires) to capture the logical content (the characteristic formula F) of the process corresponding to this reaction
- translate biological networks into pi-processes x_i
- model-check F against the x_i
- thus identify networks with a (possibly dynamic) communication structure that behave like F (have that type)

The logic formula,
"the largest process X that behaves in some way and eventually becomes X",
describes the type "catalyst", which picks out the following red processes:

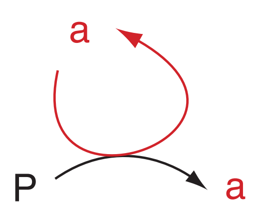


$$P \xrightarrow{a} P'$$

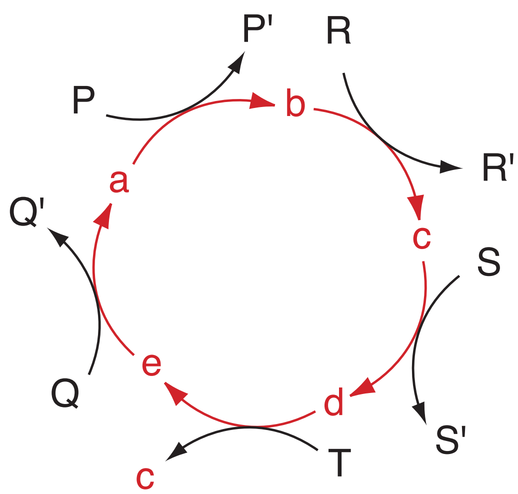


$$\{P, Q, R, S, T\} \xrightarrow{\{a, b, c, d, e\}} \{P', Q', R', S', T'\}$$

The spatial logic formula,
"the largest process X that behaves in some way and eventually becomes X|X",
describes the type "autocatalyst", which picks out the following red processes:

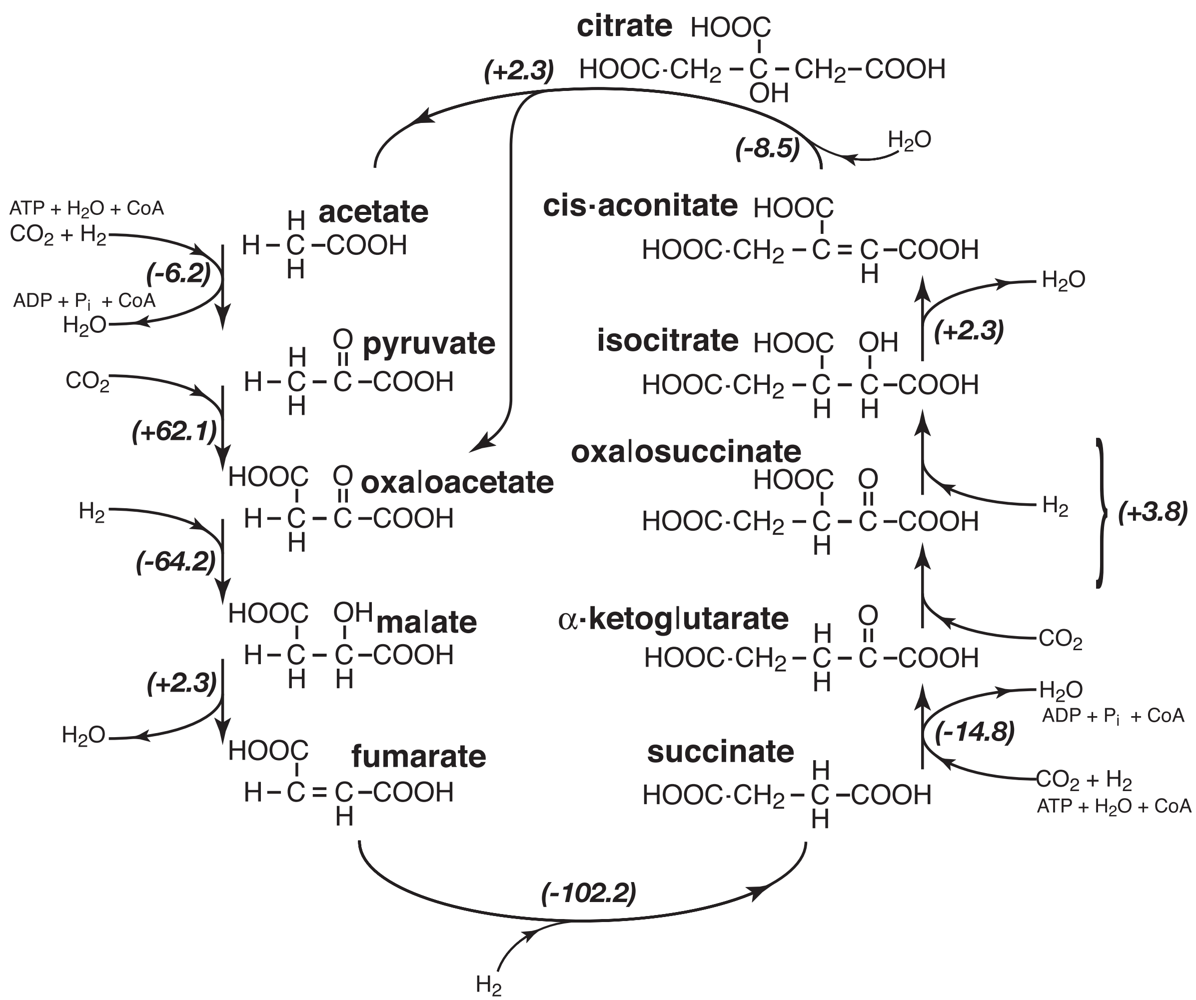


$$P \xrightarrow{a} a$$



$$\{P, Q, R, S, T\} \xrightarrow{\{a, b, c, d, e\}} \{P', Q', R', S', c\}$$

an autocatalytic network at the dawn of life ?

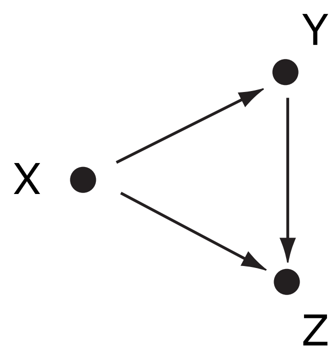


Eric Smith & Harold Morowitz, PNAS, 101, 13168-13173 (2004)

The search for networks that inhabit certain types is important, because it extends current efforts at detecting network motifs.

Such efforts focus on syntactical motifs, but network types are behavioral motifs!

- detect whether, in a network, certain subgraphs occur more frequently than expected (expectation means a suitably randomized control)
- those that do are presumably solutions to some problem(s)
- figure out the problem(s)

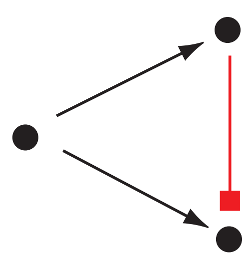


“coherent”

most abundant in
E.coli and yeast

example:
feed-forward loop

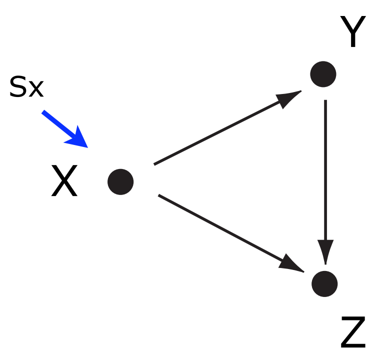
S. Shen-Orr, R. Milo, S. Mangan, U. Alon, *Nature Genetics*, **31**, 64 (2002)

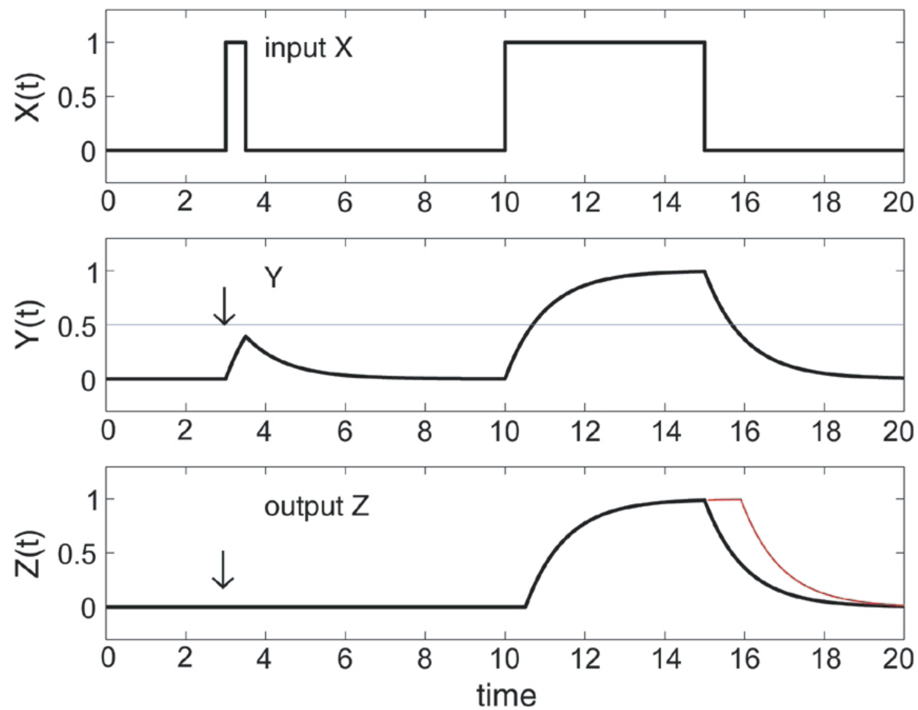


“incoherent”

fairly abundant in
yeast

a delay mechanism...

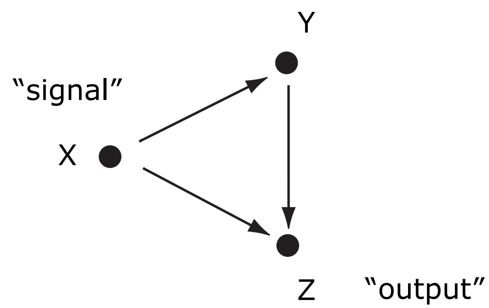




...implementing a pulse-filter

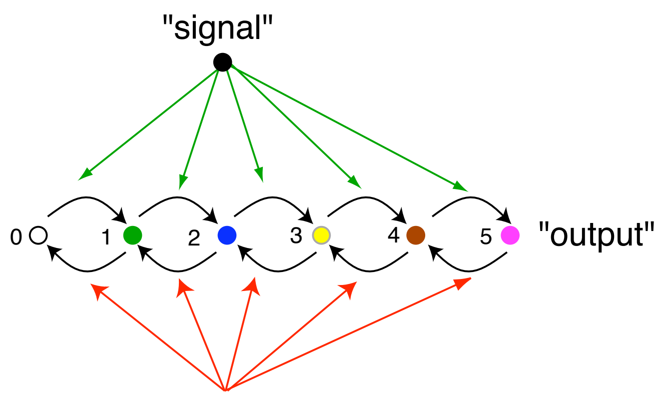
are these types expressible and checkable?

is “delay” a type?



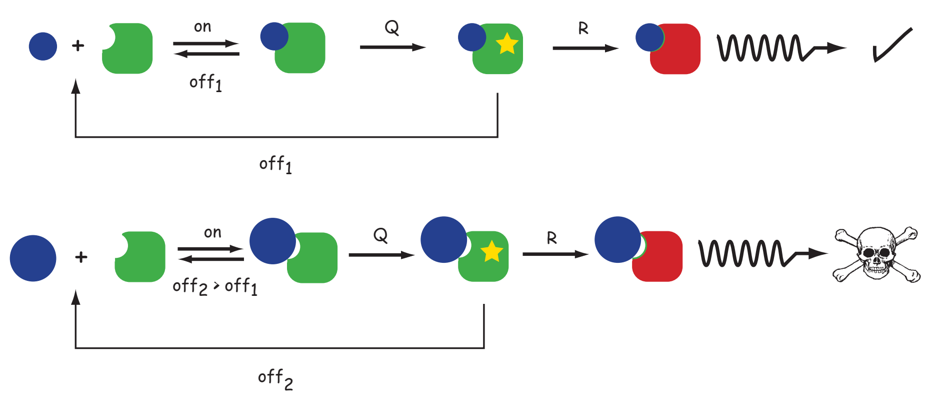
feed-forward

“delay” to filter



multisite phosphorylation

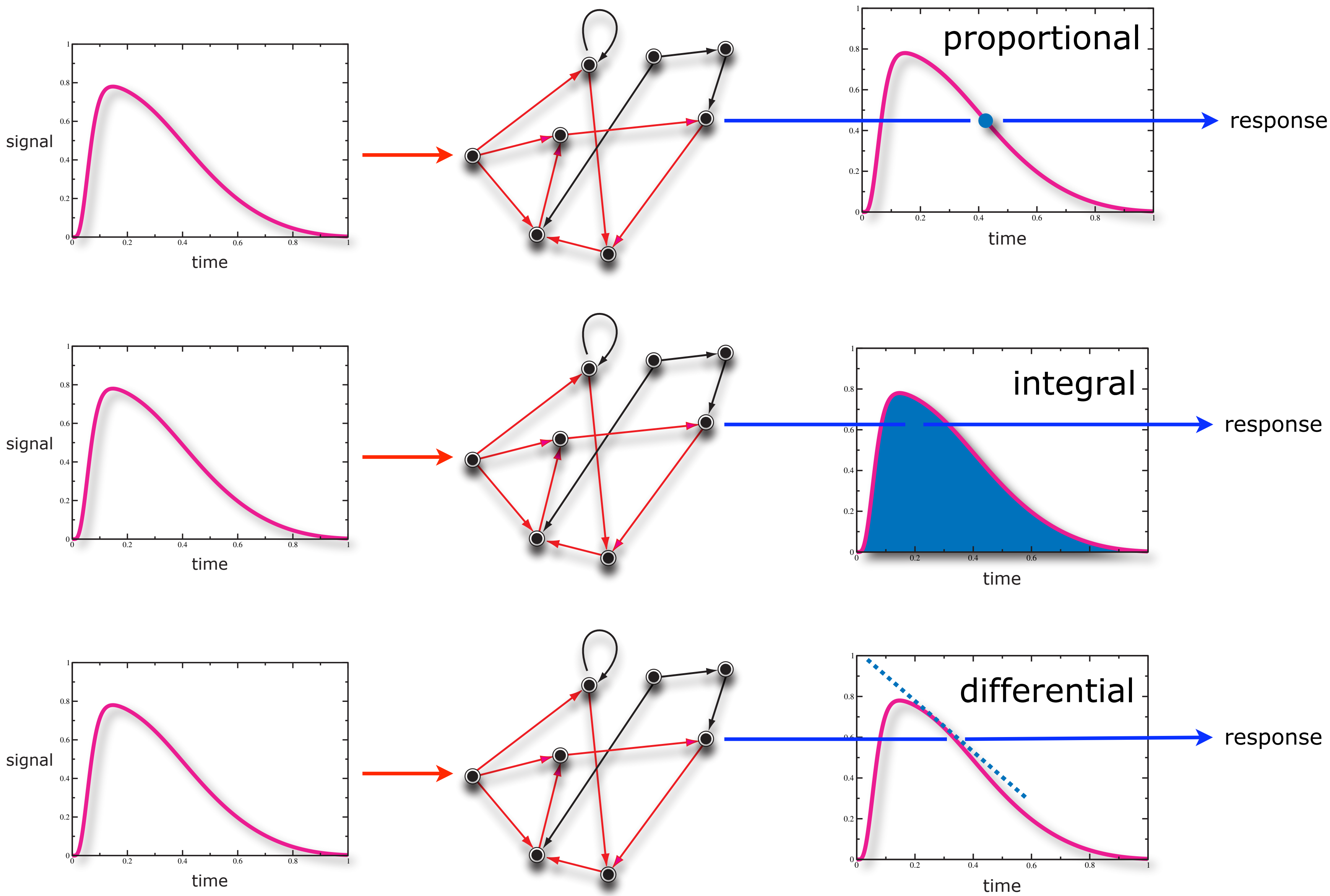
“delay” to postpone commitment



kinetic proofreading

“delay” to postpone commitment

are these types expressible and checkable?



from a physics of information to a biology of information

got guts?

i'm looking for a postdoc at the concurrency/biology interface of type:

must survive in a lab atmosphere & $\diamond$ talk to biologists & have some physics intuition.

(is this type inhabited?)