Systems Biology and Category Theory

SUMS MATHEMATICS SOCIETY

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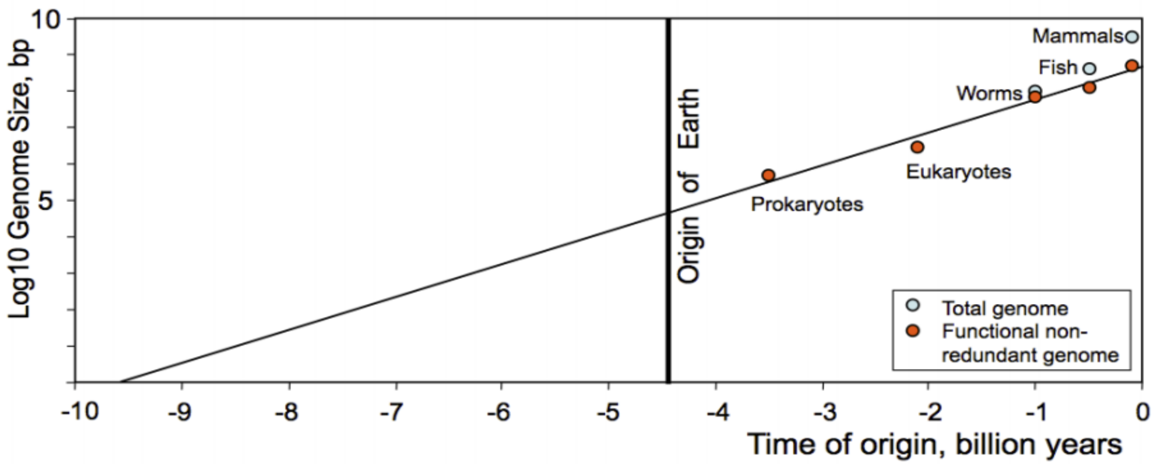
What is Life?

- Self-Propagating
- Obeys a form of natural selection

→ Emergent Qualities

→ Exponential increases in complexity



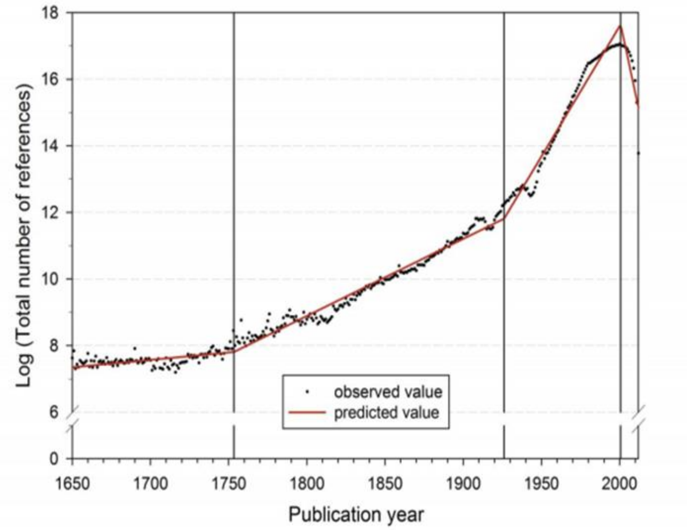


Figure 2. Segmented growth of the annual number of cited references from 1650 to 2012 (citing publications from 1980 to 2012)

Standard Definition of Life

1. **Homeostasis:** Regulation of the internal environment to maintain a constant state; for example, electrolyte concentration or sweating to reduce temperature.
2. **Organization:** Being structurally composed of one or more cells — the basic units of life.
3. **Metabolism:** Transformation of energy by converting chemicals and energy into cellular components (anabolism) and decomposing organic matter (catabolism). Living things require energy to maintain internal organization (homeostasis) and to produce the other phenomena associated with life.
4. **Growth:** Maintenance of a higher rate of anabolism than catabolism. A growing organism increases in size in all of its parts, rather than simply accumulating matter.
5. **Adaptation:** The ability to change over time in response to the environment. This ability is fundamental to the process of evolution and is determined by the organism's heredity, diet, and external factors.
6. **Response to stimuli:** A response can take many forms, from the contraction of a unicellular organism to external chemicals, to complex reactions involving all the senses of multicellular organisms. A response is often expressed by motion; for example, the leaves of a plant turning toward the sun..
7. **Reproduction:** The ability to produce new individual organisms, either asexually from a single parent organism, or sexually from two parent organisms or "with an error rate below the sustainability threshold."

Drawbacks:

- Too many axioms!

→ Not very generalizable

- Ex:
  - Viruses
  - Ant colonies
  - Gaia hypothesis
  - Cities, companies, governments, etc.

A Different Approach

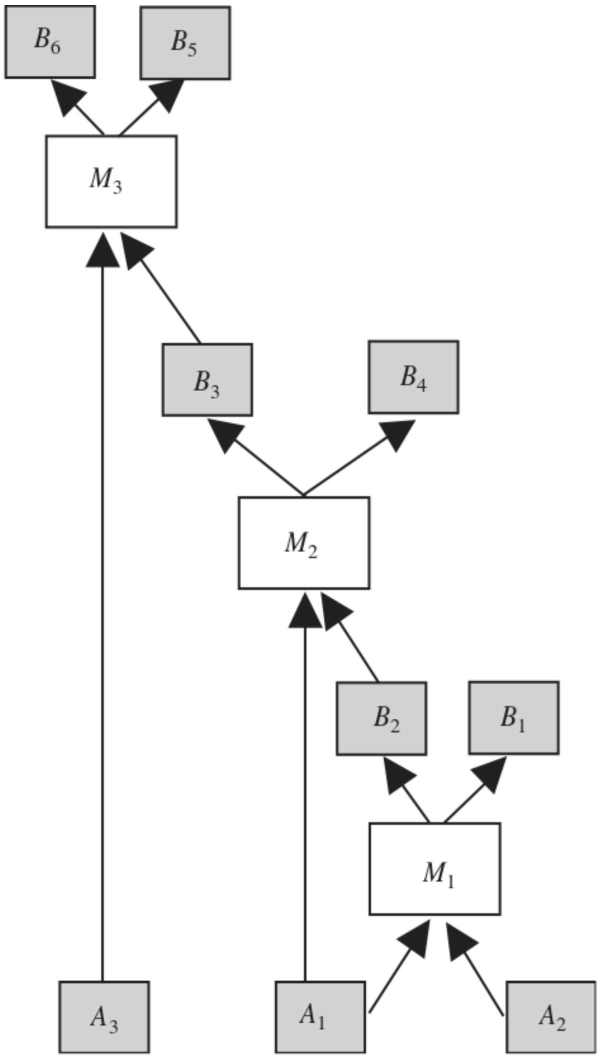
- Living Systems Biology:
  - "attempts to map general principles for how all living systems work"
  - "explores phenomena in terms of dynamic patterns of the relationships of organisms with their environment."
  - "life is a property of an ecological system rather than a single organism or species"
- Relational Biology → Categorical biology
- Stochastic Petri Nets

“Relational Theory of Systems”

- Developed by Robert Rosen in 1958
- Motivation: Many organisms have proteins which perform the same function but are chemically different:
  - beef insulin vs human insulin
  - Hemoglobin vs Hemocyanin
- Suggests a need to divorce physical substrate “fine structure” from relational structure “coarse structure”

Basic Terminology of the Theory

- A <u>system</u> **M** has <u>components</u> M_1, M_2..M_n
- These components take in <u>inputs</u> (chemicals) and produce <u>outputs</u>
- A <u>subsystem</u> **M'** is a subset of components of **M** such that **M'** receives no inputs from a component that is not in M' (Its closed)
- The <u>dependent set</u> S_i is the set of environmental outputs that are not produced when M_i is inhibite
- If M_i is a <u>terminal</u>, then the <u>terminal set</u> T_i is the se of environmental outputs produced by a given M_i
- The <u>inputs</u> of a given component are represented $I(M_i)$



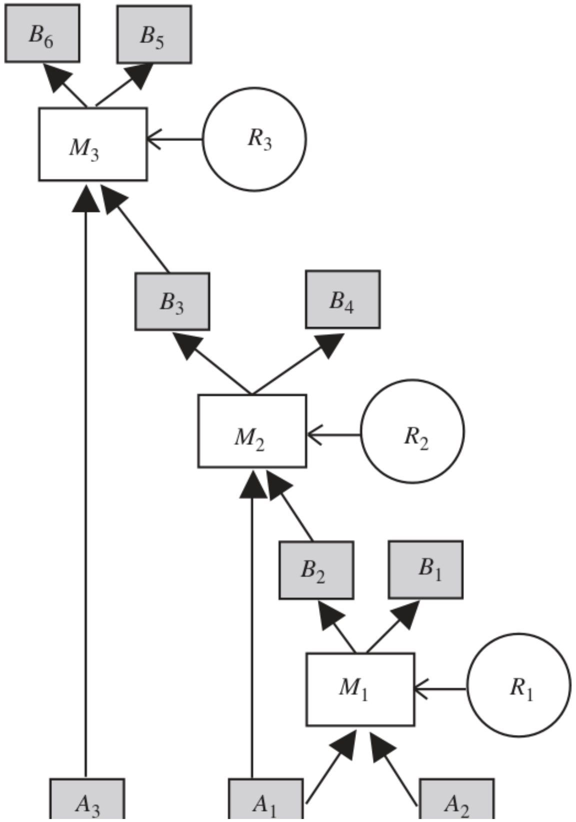
The (M,R) system

- Lets apply some assumptions to make this more applicable:
- M is connected
- Non-Contractibility: Each M_i does not produce its outputs unless all inputs are present
- Each component M_i has a finite lifetime until the component breaks
- For each M_i there exists a repair system R_i which will repair M_i from inputs $I(R_i)$, also R_i is non-contractible
- $T_i \cap (\cup I(R_j))$ is nonempty
  - Every terminal component outputs an input of some R_i
  - What I call the "Relevancy Assumption"

(M,R) systems Theorem 1

- If a component M_i is inhibited either:
  - The whole system fails (central component)
  - There exists a unique maximal subsystem that is unaffected

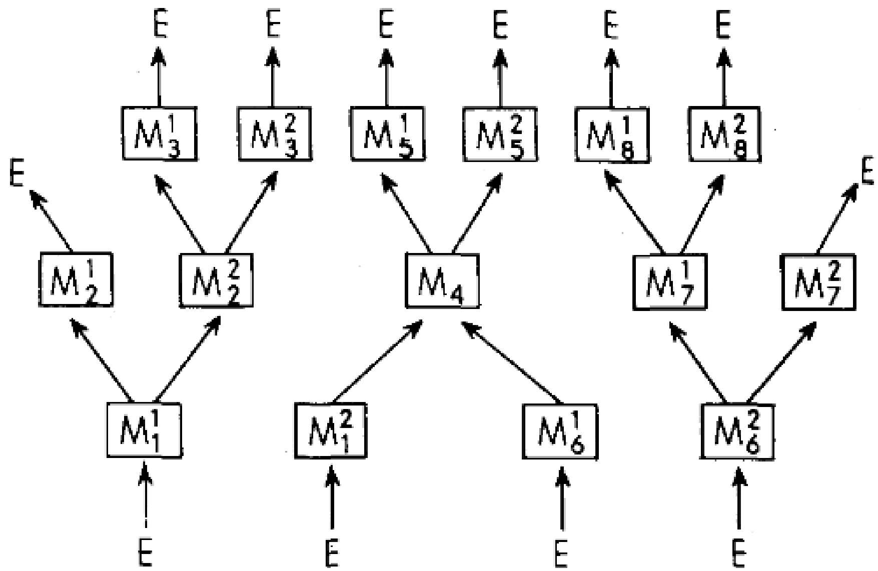
- Proof Sketch:
  - If M_j not inhibited →
  - R_j not inhibited →
  - Terminals producing inputs to R_j not inhibited
  - Consider the set of all such non inhibited terminals, Rj and Mj.
    - There are no inputs from outside the set because everything else is inhibited, and every component is non-contractible

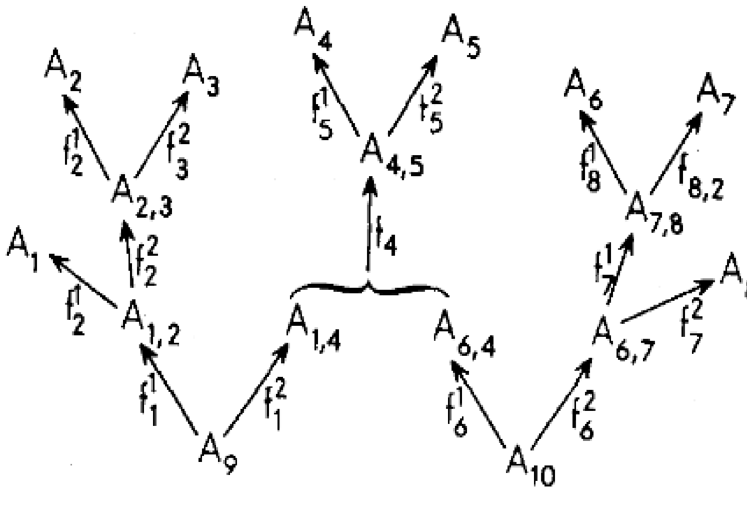


Theorem 2

- A component M_i is <u>re-establishable</u> iff
  $I(R_i) \cap S_i$ is empty
- In a (M,R) it is impossible for every component to be re-establishable
- Corollary:
  - There always exists a central set
  - Nucleus of the (M,R) system

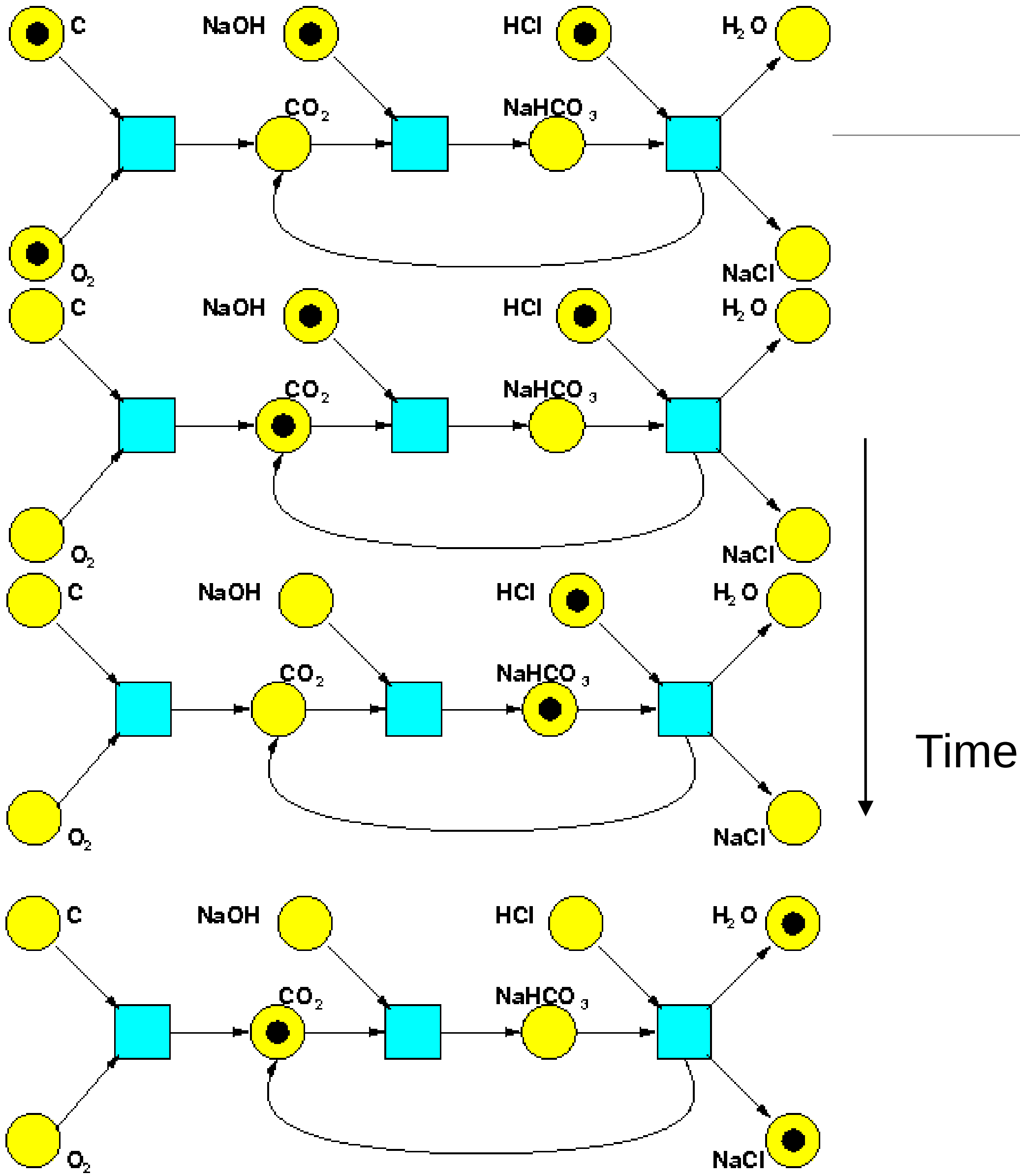
Translating to Category Theory

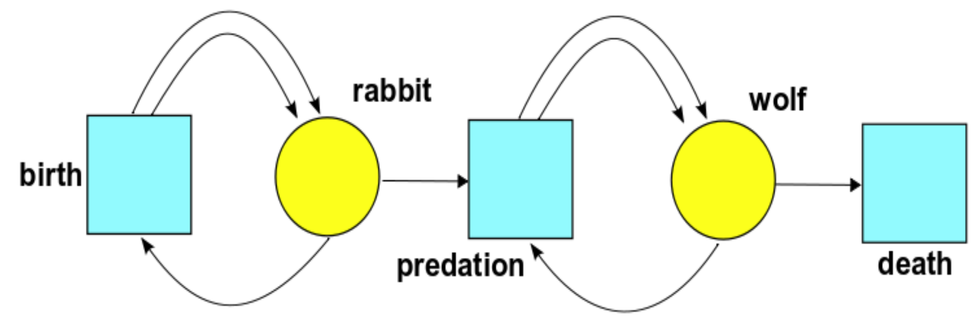




- Each input/output is an object in sets A, B respectively
- Each component is a mapping between inputs and outputs: M_i is an element of Hom(A,B)
- Each repair component is an element of Hom(B,Hom(AB))

Petri Nets


C
NaOH
HCl
H_2O
CO_2
$NaHCO_3$
O_2
NaCl
Time

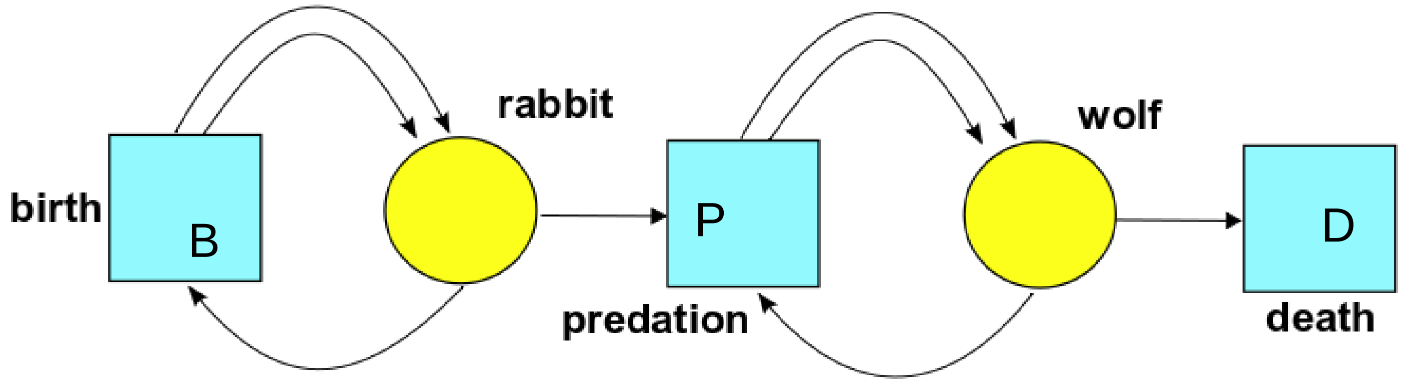

birth
rabbit
predation
wolf
death

More Formally

- Petri Net: A set of states S, and Transitions T, and an input and output function which gives the amount of inputs needed and the amount of outputs produced
  - $I: S \times T \rightarrow \mathbf{N}$, $O: S \times T \rightarrow \mathbf{N}$
- Stochastic Petri Nets also have a function
  - $R: T \rightarrow (0,\infty)$
- Which serves as a rate constant

Rate Equations: An example

- The Rate Equation says how the expected number of things in each state changes with time



- Let r(t) number of rabbits, w(t) be the number of wolves

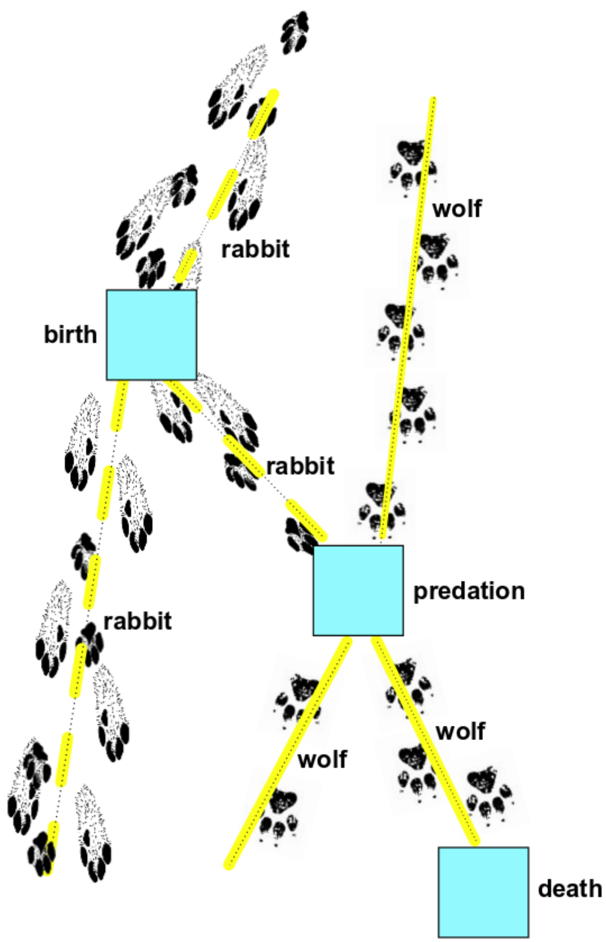
$$\frac{\partial r(t)}{\partial t} = B\, r(t) - P\, r(t)\, w(t)$$

$$\frac{\partial w(t)}{\partial t} = P\, r(t)\, w(t) - D\, w(t)$$

Master Equation in Brief

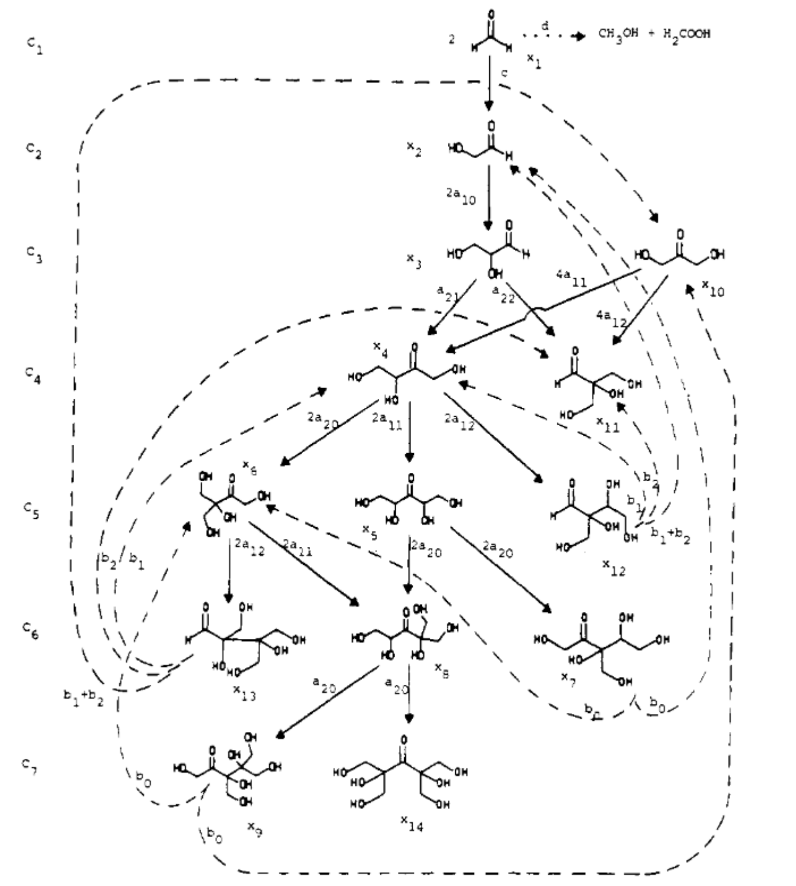
$$\frac{d}{dt}\psi_{\ell'}(t) = \sum_{\ell} H_{\ell'\ell}\psi_{\ell}(t)$$

- The master equation says how the probability that we have a given number of things in each state changes with time.
- The probability that a given transition occurs in a short time t is approximately the product of:
  - the rate constant for that transition
  - the time t
  - the number of ways the transition can occur.



Relation to life systems

- A system is self-reproducing if there is a finite sequence of transitions (i.e., reactions) that results in the increase of the numbers of all components within the system.
- These reactions propagate until all available resources are consumed
- Petri Nets can compete for resources



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