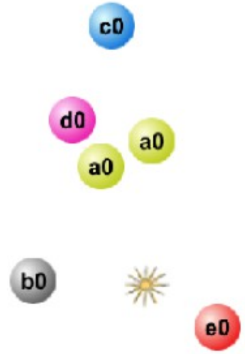
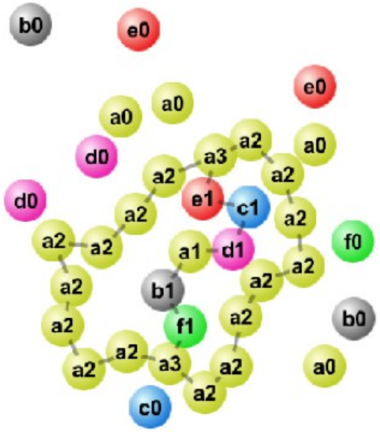


Emergence in Artificial Chemistries

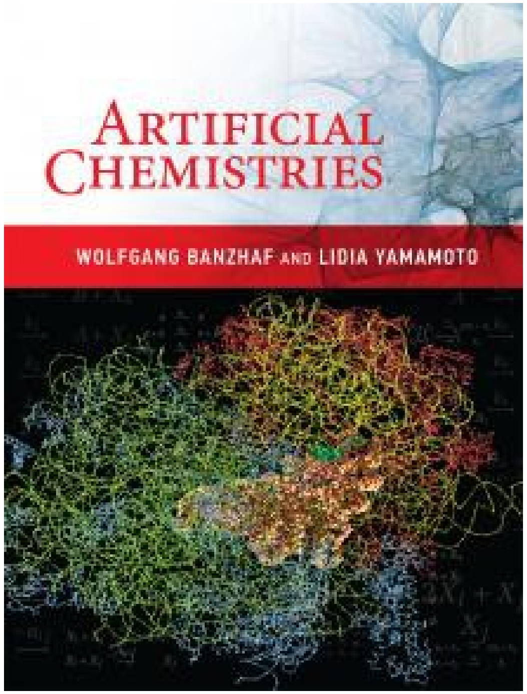


Lidia Yamamoto
(KULeuven, Belgium)
and
Wolfgang Banzhaf
(Memorial University of Newfoundland, Canada)

Emergence in Chemical Systems, Anchorage, Alaska, June 2015

Contents

- Artificial Chemistries (ACs) in a Nutshell
  - Wet (“*in vitro*”, “*in vivo*”) vs. virtual (“*in silico*”) ACs
  - Constructive vs. nonconstructive ACs
- Emergent phenomena in ACs
  - Computational studies on the origin of life
  - Computation with ACs: role of emergence
- PyCellChemistry software package
  - `www.artificial-chemistries.org`
  - Nonconstructive AC example
  - Constructive AC example
- Summary and Outlook



MIT Press, Summer/Fall 2015 (571 pages)
`https://mitpress.mit.edu/books/artificial-chemistries`

Artificial Chemistries (ACs)

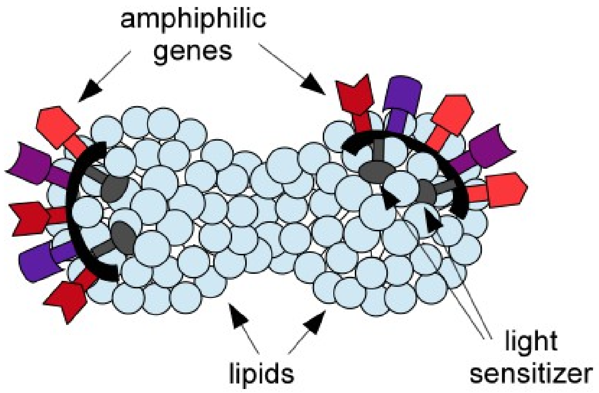
- Man-made virtual or physical systems where objects are transformed in interactions, like molecules in chemical reactions

  $abc + d \to abcd \quad , \quad 0101100 \to 01 + 1100 \quad , \quad 40 + 10 \to 10 + 4$

- Spin-off of Artificial Life:
  - from *"life as it could be"* to *"chemistry as it could be (imagined)?"*
- Goals:
  - understand phenomena leading to the emergence of life
  - create new forms of synthetic life from the bottom up
    - *"in vitro", "in vivo"*: "Wet" ACs in the laboratory
    - *"in silico"*: computational systems
      - high-level modelling and simulation of (real) chemistry and biology
      - chemistry as a metaphor for distributed and parallel computer algorithms
      - chemistry as a general model for interacting systems of objects: nuclear physics, language, music, economies

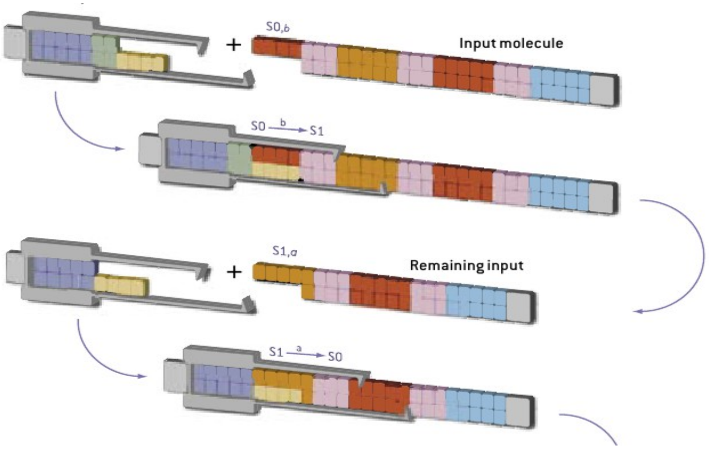
Wet ACs

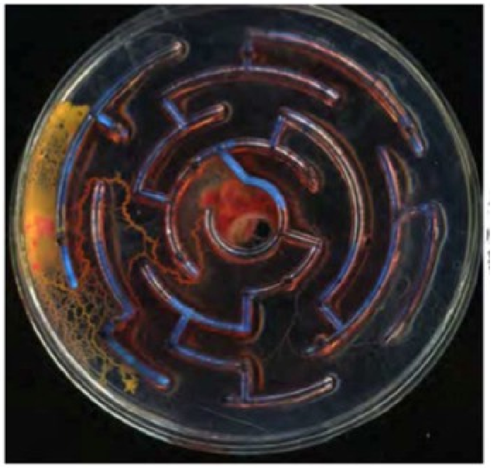
- DNA computing
- Reaction-diffusion computers
- Synthetic life and protocells
- Computing with bacteria, slime mold, ...



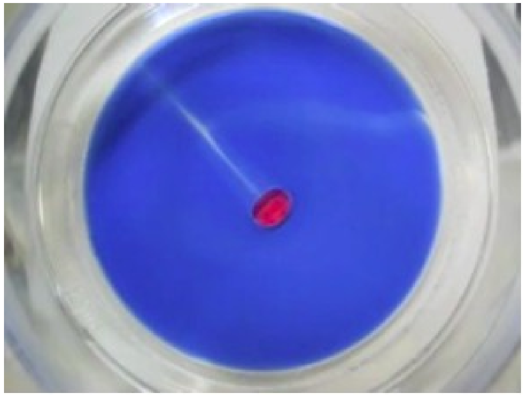
Los Alamos Bug
Rasmussen et al.

Molecular Automaton
Shapiro & Benenson





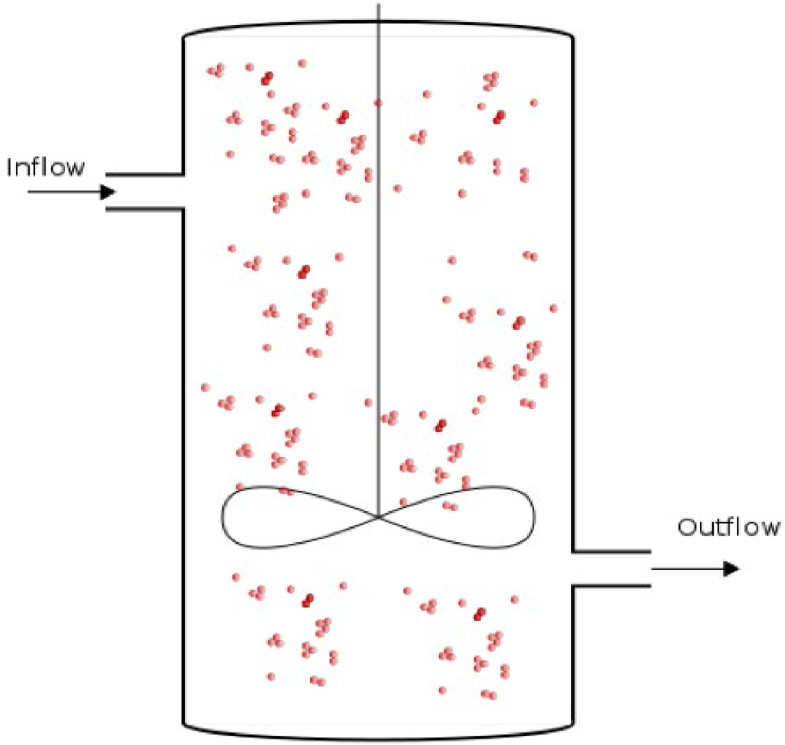
slime mold maze solver
A. Adamatzky et al.



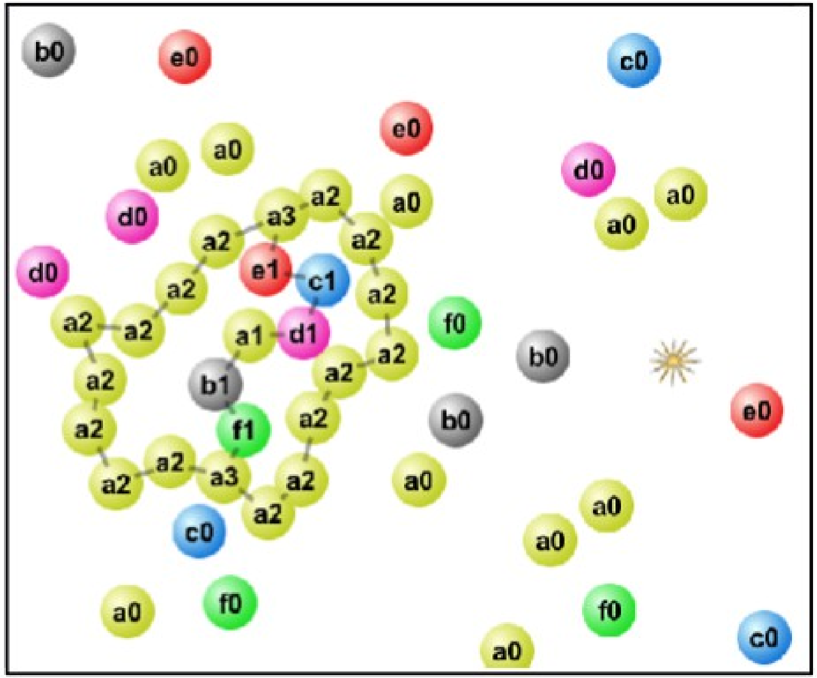
self-propelled oil droplet
Hanczyc et al.

Artificial Chemistries "in silico"

- Virtual, abstract ACs:
  - well-stirred: molecules as a "gas" or dissolved in well-mixed reactor
  - spatially-resolved: molecules move in 2D or 3D space
  - compartmentalized: molecules inside various (nested) containers



well-stirred AC



example of spatial AC:
Tim Hutton's Organic Builder

Components of an Artificial Chemistry

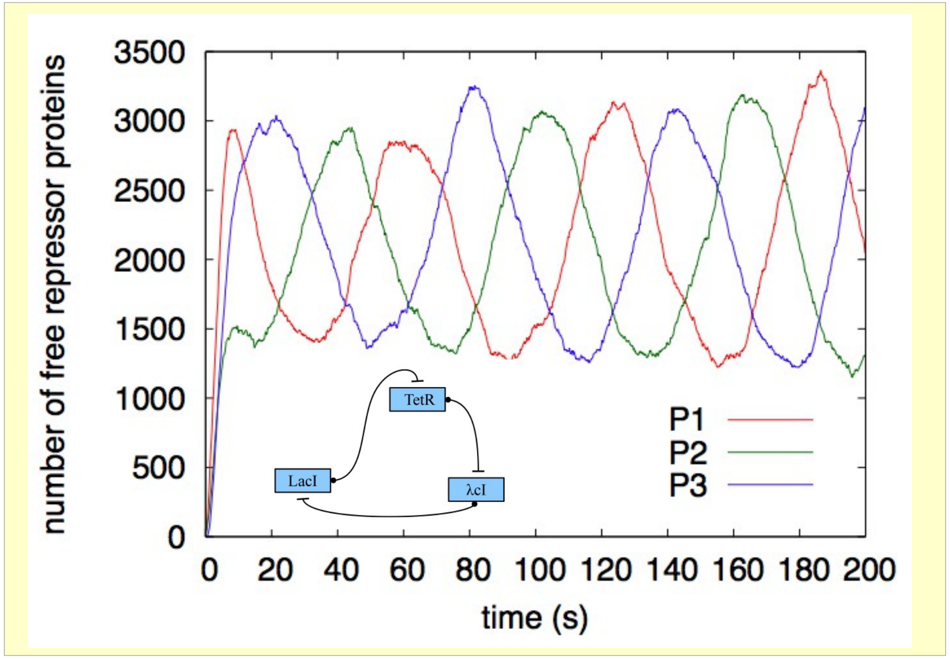
- Triple (S,R,A)
  - S = set of molecules
  - R = set of reaction rules
  - A = algorithm that applies rules to molecules
- Some algorithms:

granularity	well mixed	spatial, compartmental
individual molecules, single reactions	random molecular collisions: effective or elastic	move, collide, react (gas vs. fluid dynamics, lattice systems, crowding)
molecular species, effective reactions	reaction probability proportional to propensity (Gillespie SSA, next reaction method)	next subvolume method, multicompartment Gillespie
groups of molecules and reactions	fire groups of reactions together within interval tau (tau leaping)	spatial tau-leaping
concentration changes	numerical ODE integration	PDE integration

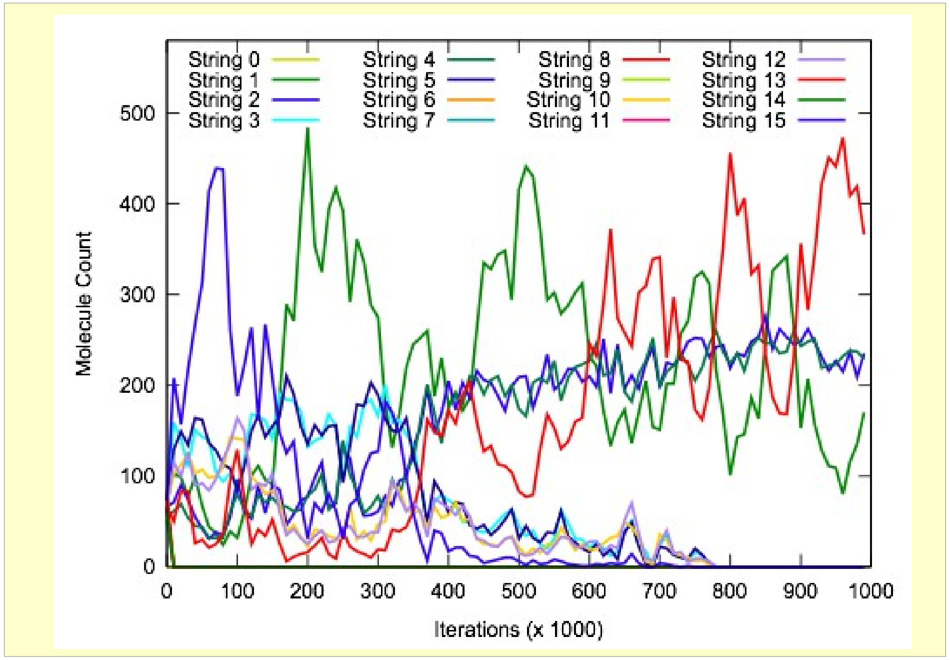
Constructive vs. Nonconstructive ACs

- N = total number of possible molecular species
- M = number of species present in the reactor at a given moment
- Nonconstructive: M = N or close: fixed set of molecules
- Constructive: M << N
  - new molecules may be created, with potentially new interactions

nonconstructive AC: repressilator



constructive AC: matrix chemistry



Emergent Phenomena in ACs

- Studying the origins of life "in silico":
  - Emergence of organizations
  - Emergence of autocatalytic sets
  - Emergence of evolution
  - Emergence of protocell-like structures
  - Emergence of cell differentiation and multicellularity
  - Emergence of ecology-like or other higher-level interactions

Emergence of Organizations in ACs

- **Autopoeisis** [Maturana, Varela 1973]: self-maintainance, system continuously regenerates itself
- **Organization** [Fontana1991,94]: closed and self-maintaining set of molecular species
  - AlChemy: an artificial chemistry in lambda-calculus
  - Matrix Chemistry [Banzhaf 1993]: binary strings "fold" into matrices that are multiplied
- **Chemical Organization Theory** [Dittrich2007]:
  - formal theory of organizations
  - algorithms to compute and analyze organizations
  - structuring computer programs as organizations [Matsumaru 2011]
- From organizations to **evolution**:
  - emergence of recombination in a binary string automata reaction chemistry [Dittrich1998]
  - evolution as a movement in the space of organizations [Matsumaru 2006]

AlChemy

- **AlChemy** [Fontana1991,94]: AC created to investigate how novelty arises and is maintained in a system able to produce a combinatorial variety of structures: constructive dynamical systems
- molecules are *functions* expressed in *lambda-calculus*
  - capture object/function duality in chemistry
  - (loose) analogy to *functional groups* in chemistry:

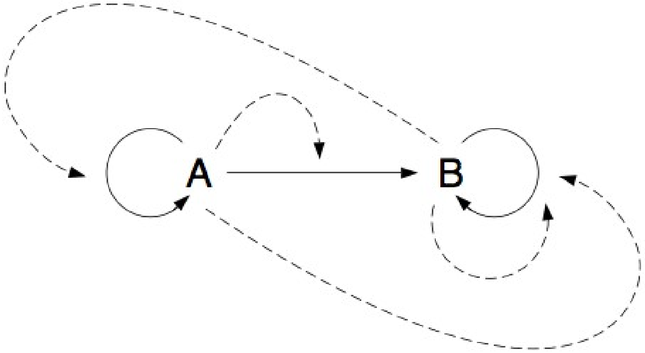
    Hydroxyl group $(-OH)$ *Carboxyl group* $(-COOH)$
- reactions apply function *f* to function *g* to produce function *h*:

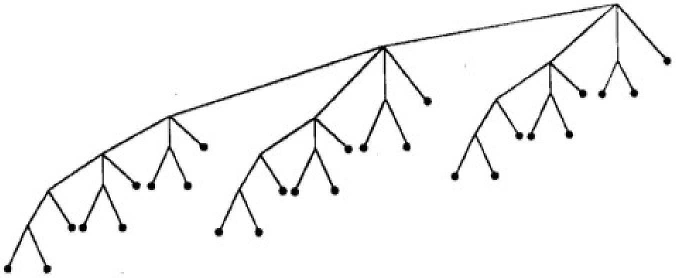
$$f(x) + g(x) \longrightarrow f + g + f(g(x)) \longrightarrow f + g + h(x)$$

- if successful (effective reaction) another random molecule is destroyed

AlChemy Experiments

- Starting from a population of random molecules:
  - diversity decreases
  - system converges to small set of self-copying molecules
  - n-membered elementary hypercycles, but brittle, easily collapse
- When self-copying is disabled:
  - “polymerization”: formation of long “polymers” by concatenating “monomers”
  - formation of large organizations that are stable and resilient to perturbations
  - more rarely, formation of interacting, inter-dependent organizations

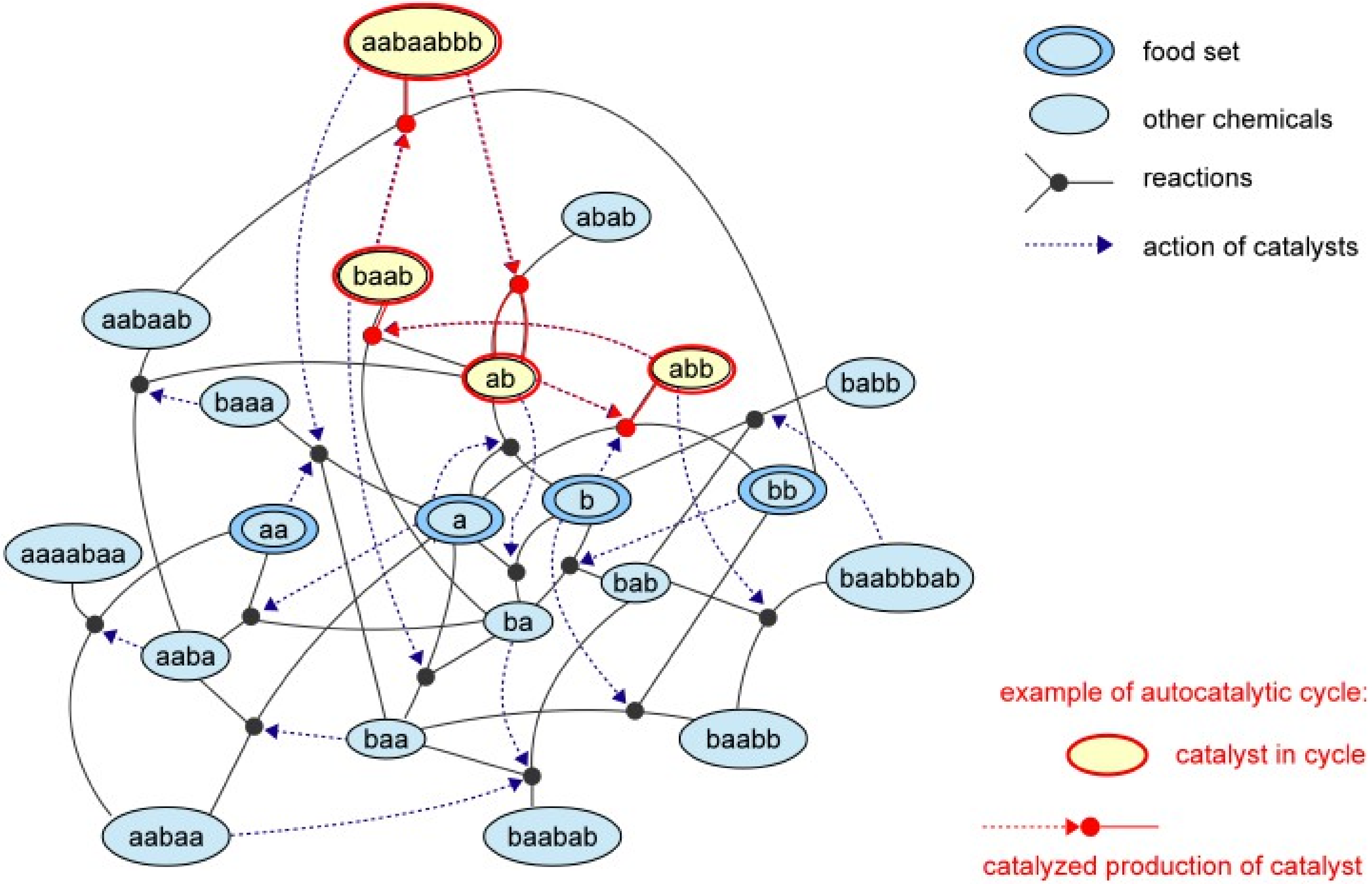




Emergence of Autocatalytic Sets

- Autocatalytic set: every molecule in the set is produced in reactions catalyzed by members of the set
- **Kauffman (1986)**: could life have originated from an autocatalytic set of proteins?
  - do autocatalytic sets inevitably form if the number of catalytic reactions is large enough?
  - model: strings (polymer sequences) with maximum length L, from an alphabet of size B
    - condensation/cleavage reactions: $ba + aabb \overset{ab}{\leftrightharpoons} baaabb + H_2O$
    - graph-theoretical analysis: minimum probability of catalysis (P) that would favor the formation of autocatalytic sets: $P_{crit} \approx B^{-2L}$
    - autocatalytic sets would form for P > Pcrit
    - for a given L: proteins (B=20) need lower P than RNA or DNA (B=4)

Emergence of Autocatalytic Sets

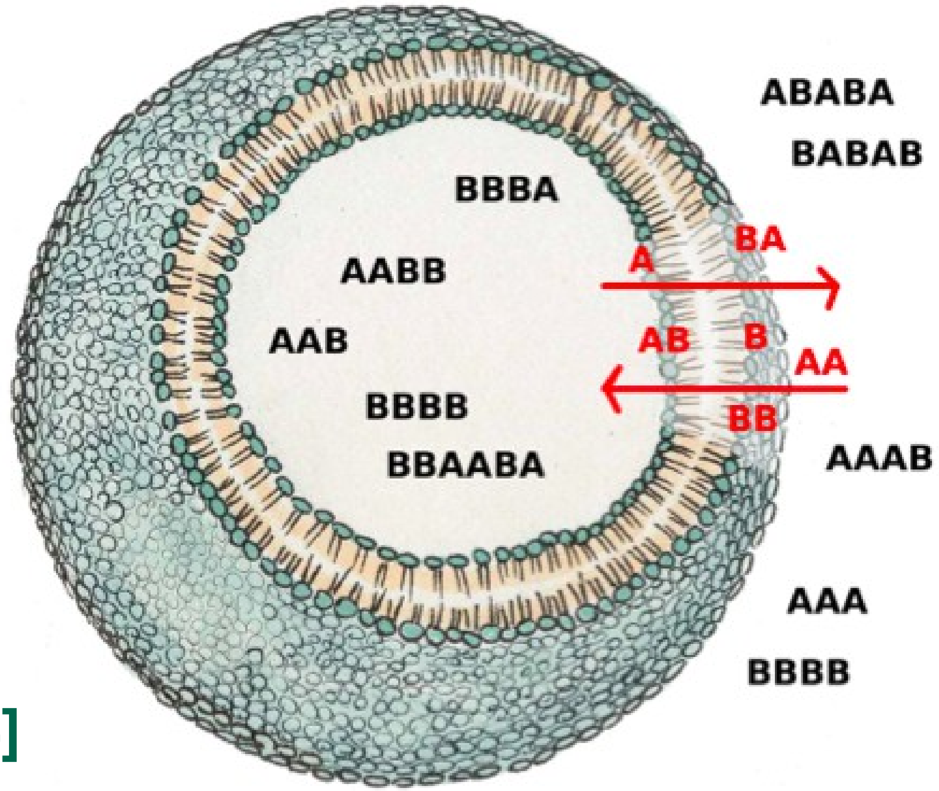


Autocatalytic Metabolisms

- **Kauffman (1986)**: from autocatalytic sets of proteins to the emergence of metabolisms
  - proteins catalyze formation & breakdown of organic compounds
- **Bagley & Farmer (1992)**: dynamical system model of **autocatalytic metabolisms**
  - **catalytic focusing**: when the system is kept out of equilibrium, catalysis focuses the mass of the system into a core of few species
  - computer simulations:
    - emergence of autocatalytic networks able to take up food and turn it into a stable core: autocatalytic metabolism (fixpoint)
    - when subject to mutations: autocatalytic metabolisms "evolve" by jumping from one fixpoint to a different one

Autocatalytic Sets: Challenges and Progress

- Realistic conditions hamper the system's capacity to survive and evolve:
  - dynamic and stochastic effects
  - leaks and errors caused by side reactions
  - autocatalysis compensates for losses and errors but not fully
- Emergence of autocatalytic sets under stochastic fluctuations **[Filisetti 2010]:**
  - autocatalytic sets emerge more rarely
  - sets are less stable, may be wiped out by stochastic fluctuations
  - more recently: autocatalytic sets within lipid vesicles **[Serra 2014]**

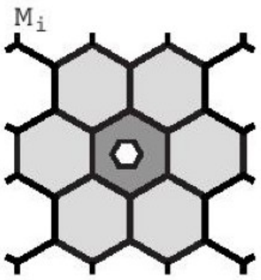


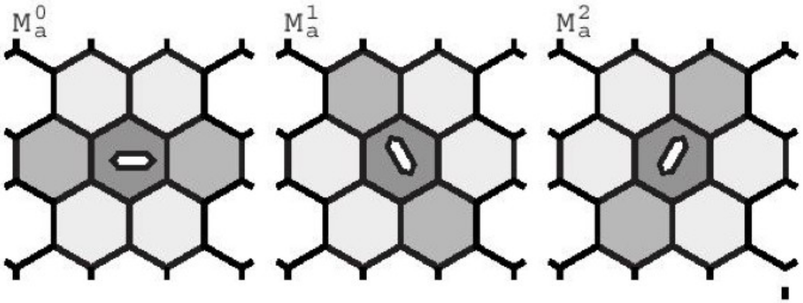
Emergence of Protocell-like Structures

- **Ono & Ikegami (2001)**: self-replicating autopoietic protocells
  - 5 types of particles move, rotate, and interact on a hexagonal grid
    - hydrophobic vs. hydrophilic: isotropic vs. anisotropic repulsion
    - neutral vs. others: weak interaction

particle	role	property	reactions
A	autocatalyst	hydrophilic	$A + X \xrightarrow{A} 2A$: autocatalytic production of A
W	water	hydrophilic	
M	membrane	hydrophobic	$X \xrightarrow{A} M$: catalytic production of M
X	food	neutral	$Y + e \longrightarrow X$: recycle using energy
Y	waste	neutral	$A \longrightarrow Y$, $M \longrightarrow Y$, $X \longrightarrow Y$: decay

isotropic repulsion

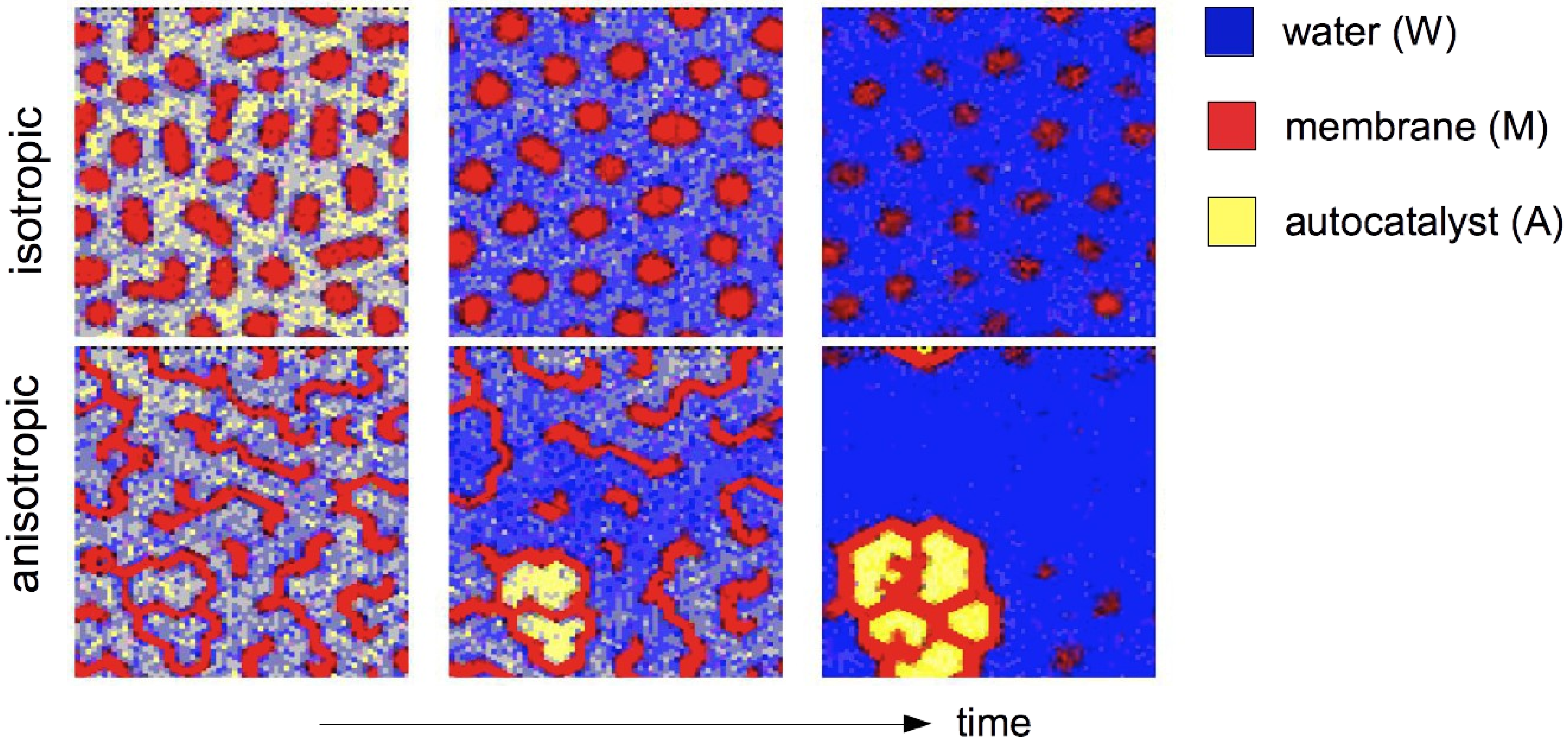




anisotropic repulsion

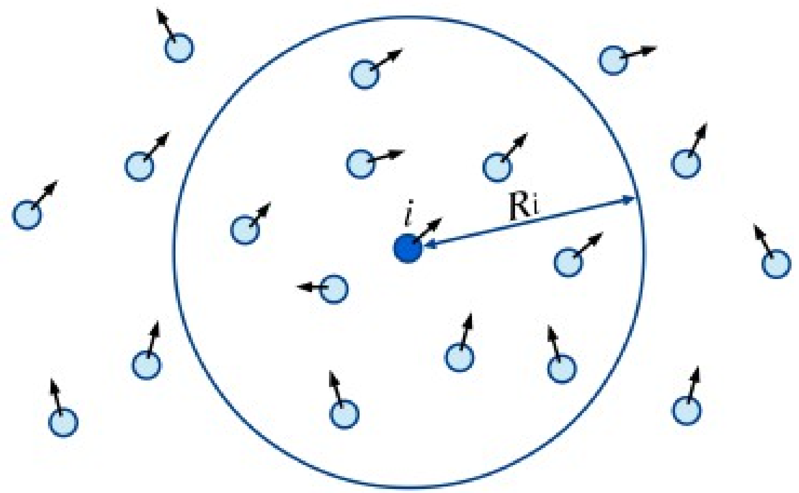
Autopoietic Protocells

- isotropic M molecules cluster together but soon die out
- anisotropic M molecules: protocell-like structures form under low supply of food molecules

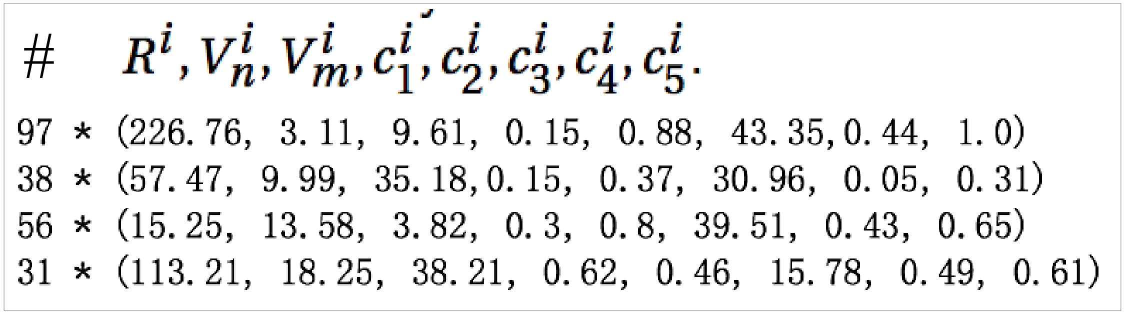


Emergence of Higher Level Interactions

- **Swarm Chemistry** [Sayama 2009-]
  - particles of several types move in 3D space:
    - move towards nearby particles
    - adjust speed to average speed of neighbors
    - avoid collision
  - behavior governed by "recipe" of parameters:



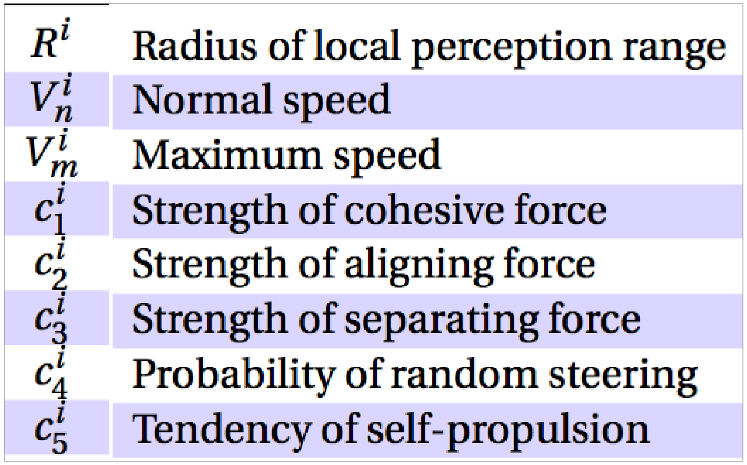
Recipe:



# $R^i, V^i_n, V^i_m, c^i_1, c^i_2, c^i_3, c^i_4, c^i_5$.

```
97 * (226.76, 3.11, 9.61, 0.15, 0.88, 43.35, 0.44, 1.0)
38 * (57.47, 9.99, 35.18, 0.15, 0.37, 30.96, 0.05, 0.31)
56 * (15.25, 13.58, 3.82, 0.3, 0.8, 39.51, 0.43, 0.65)
31 * (113.21, 18.25, 38.21, 0.62, 0.46, 15.78, 0.49, 0.61)
```

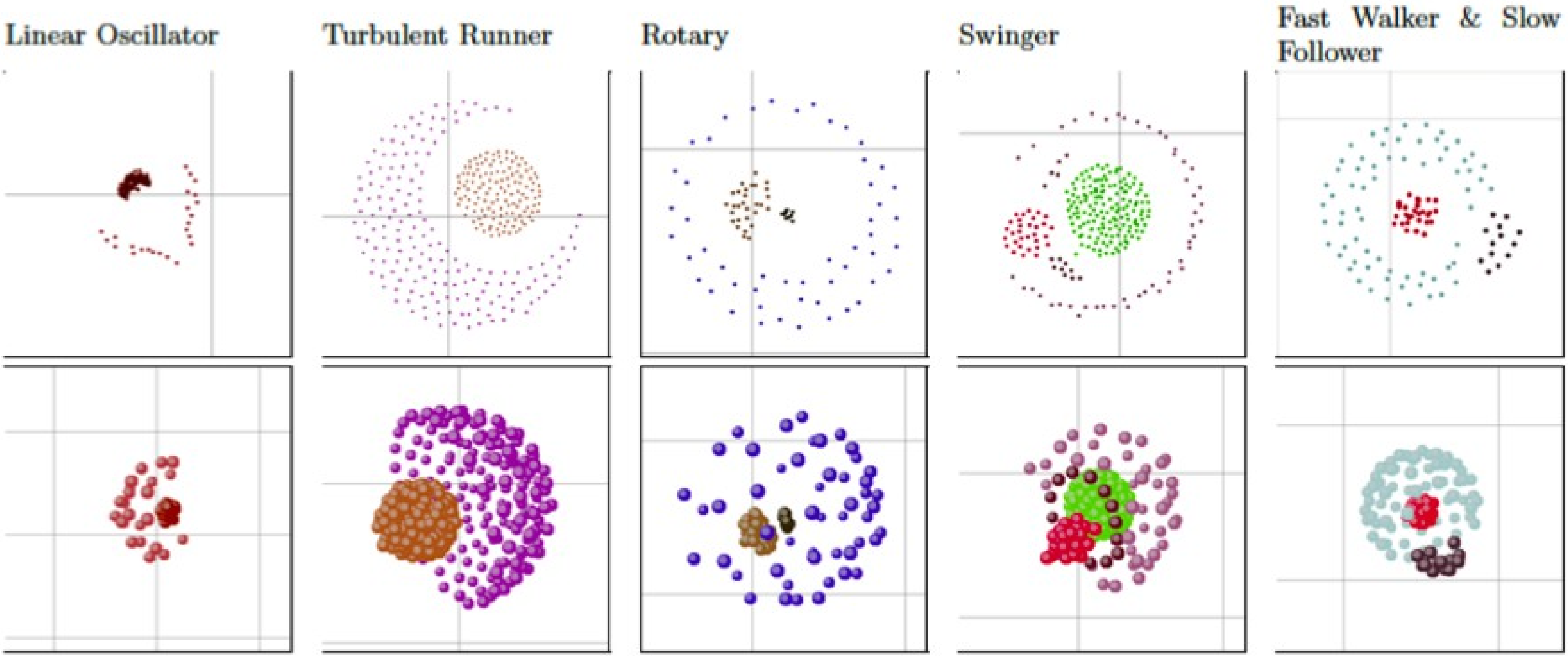
Parameters:



R^i	Radius of local perception range
V^i_n	Normal speed
V^i_m	Maximum speed
c^i_1	Strength of cohesive force
c^i_2	Strength of aligning force
c^i_3	Strength of separating force
c^i_4	Probability of random steering
c^i_5	Tendency of self-propulsion

Swarm Chemistry

- Behaviors (with underlying recipe) evolved by interactive evolution
- Java demo:
  `http://bingweb.binghamton.edu/~sayama/SwarmChemistry`
- Some behaviors displayed:



An Artificial Chemistry in Python

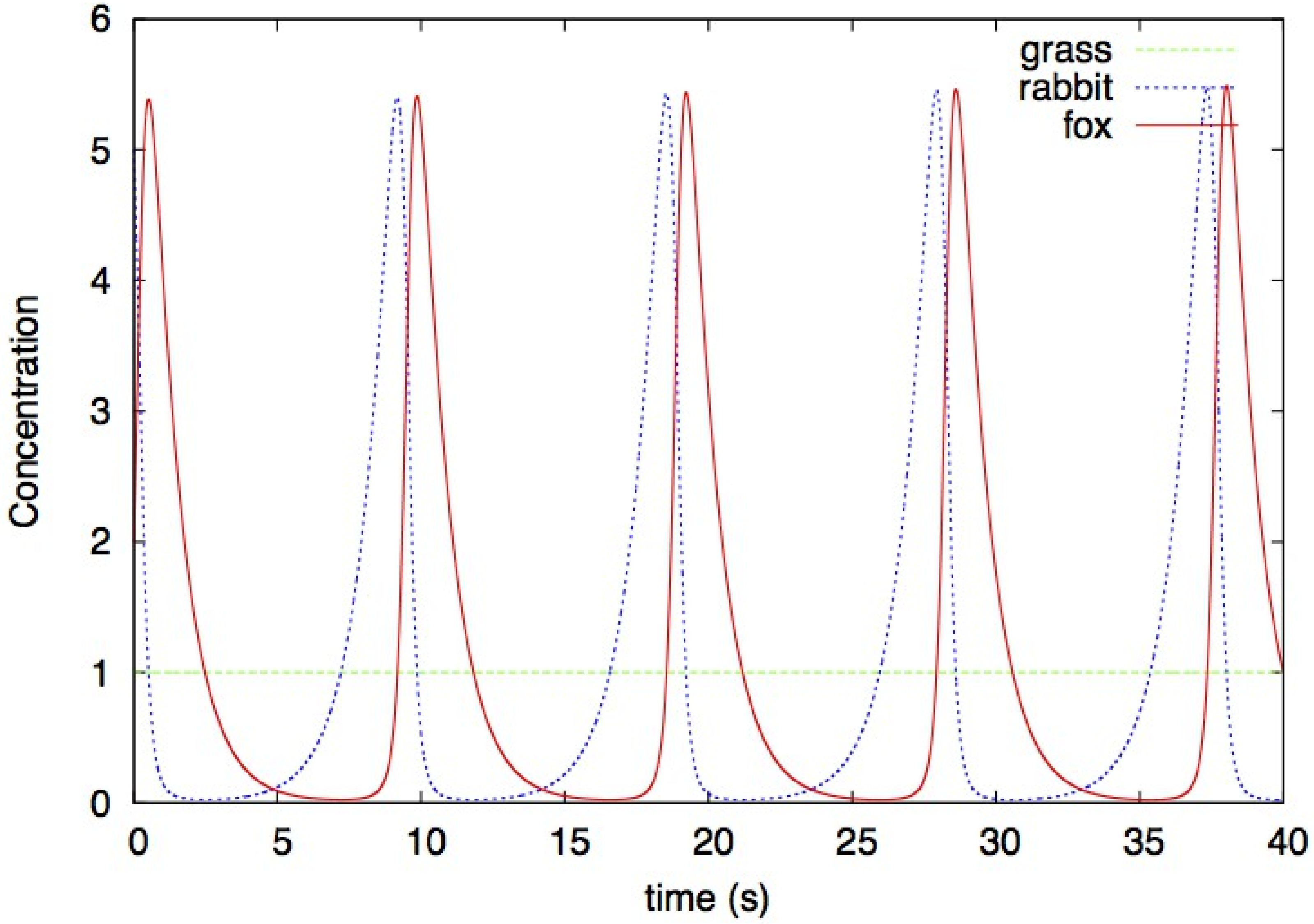
- **PyCellChemistry**: python package to let users program their own ACs (to be released this summer)
  - `www.artificial-chemistries.org`
- Basic system:
  - multisets (bags) of molecules
  - chemical reactions
  - conversion from chemical reactions to ODE and Gillespie SSA
  - hierarchical cell compartments
- Example ACs:
  - basic: chameleons, prime number chemistry, matrix chemistry
  - biochemical circuits: dimerization, logistic growth, repressilator
  - ecology and evolution: Lotka-Volterra, quasispecies, NK landscapes
  - distributed & parallel computing: molecular TSP, fraglets, disperser

A Non-Constructive AC: Lotka-Volterra

```
class LotkaVolterra:
    def __init__( self, usestoch ):
        reactionstrs = [
            "rabbit + grass --> 2 rabbit + grass , k=1",
            "fox + rabbit   --> 2 fox            , k=1",
            "fox            -->                  , k=1" ]
        if usestoch:
            self.reactor = GillespieVessel(nav=40)
        else:
            self.reactor = WellStirredVessel()
        self.reactor.parse(reactionstrs)
        self.reactor.deposit('rabbit', 5.0)
    ...
    def run( self ):
        while (not self.extinct() and not self.exploded() and \
               self.reactor.vtime() <= 40.0):
            self.reactor.integrate(dt=0.001)
```

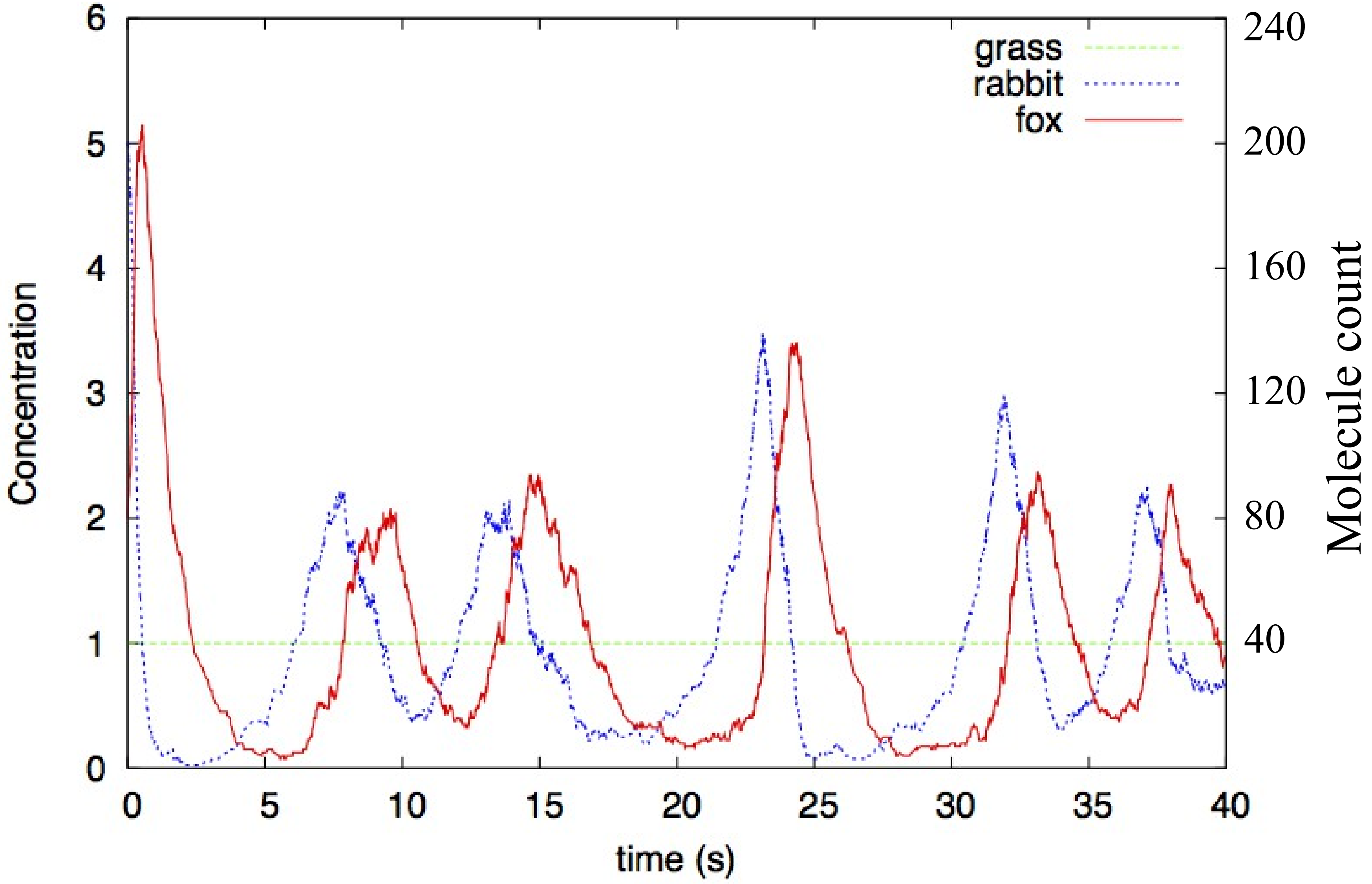
Lotka-Volterra: Deterministic vs. Stochastic

- Deterministic simulation via ODE integration:



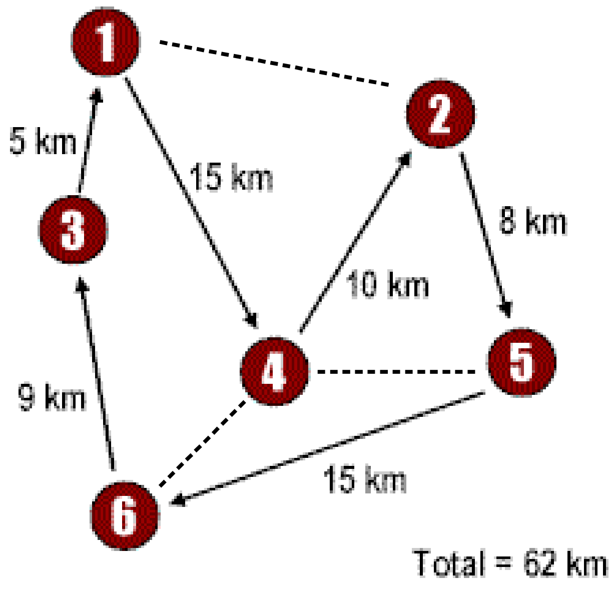
Lotka-Volterra: Deterministic vs. Stochastic

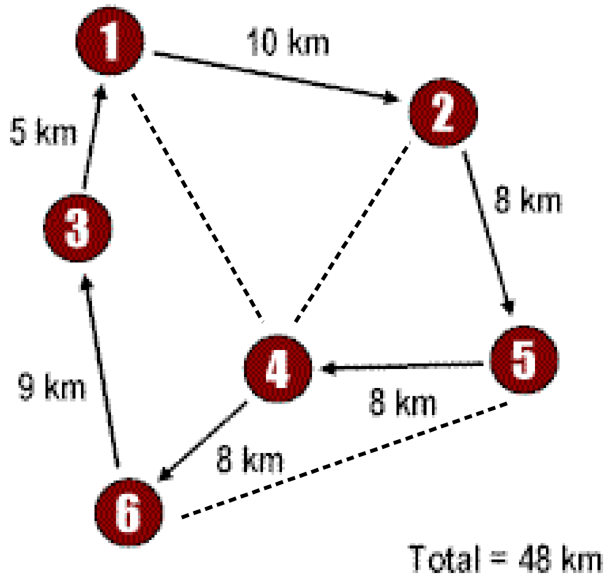
- Stochastic simulation via Gillespie SSA for V = 40 / N_A:



A Constructive AC: The Molecular TSP

- Traveling Salesman Problem (TSP):
  - find the tour of minimum cost that visits all the cities on a map
  - use only the available roads
  - visit each city only once
  - known to be NP-hard:
    - cannot be solved in general within a polynomial number of operations
    - typically heuristic algorithms are used: find approximate solutions





A Constructive AC: The Molecular TSP

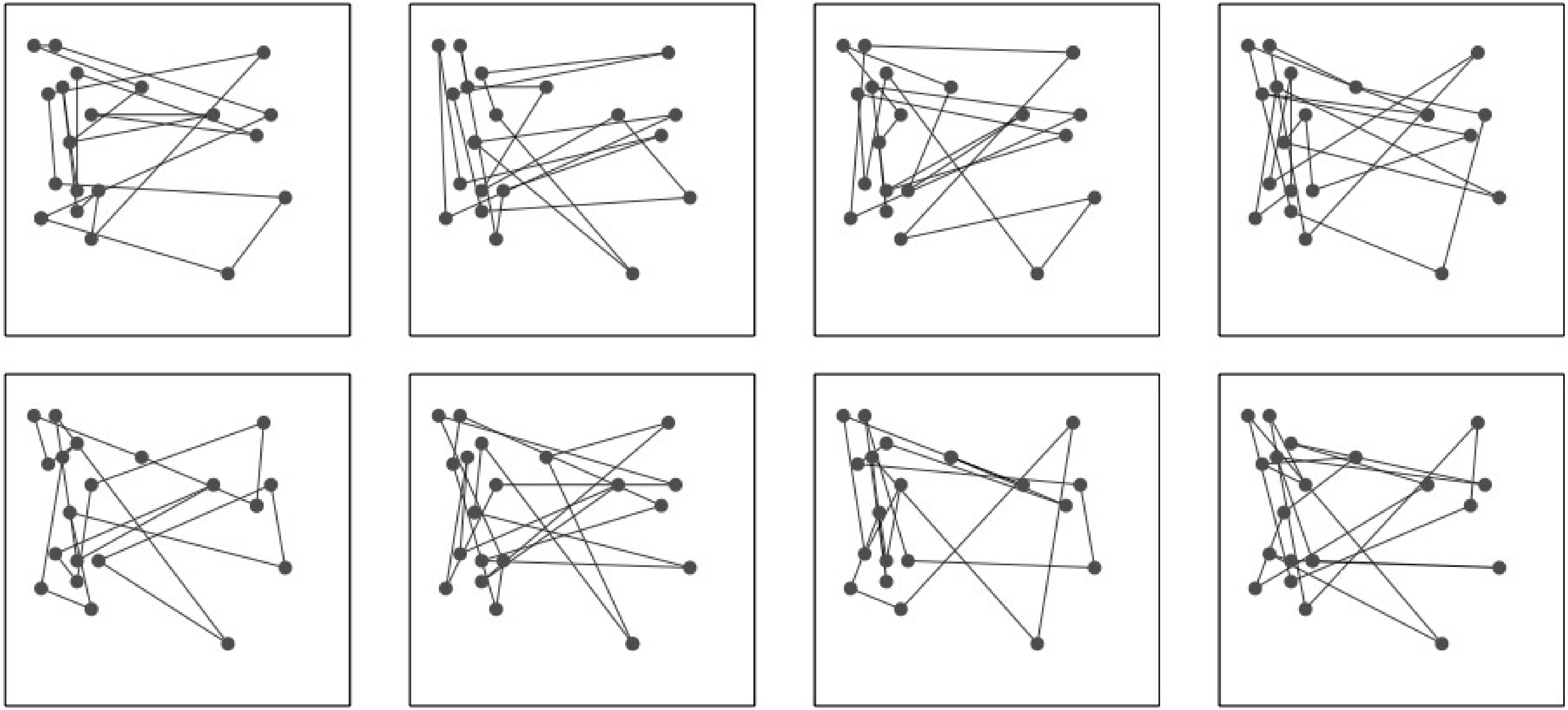
- **Molecular TSP** [Banzhaf 1990]: TSP heuristic inspired by chemistry
  - 2 types of molecules: machines and tours
    - tour: list of cities in the order they are visited, e.g. [1 2 5 4 6 3 1]
  - Machines (“enzymes”) operate on tours (“substrates”)
    - E-machine: swaps two random cities in a tour
    - C-machine: cuts a tour segment and pastes it elsewhere in tour
    - I-machine: cuts and inverts the segment before pasting it
    - R-machine: recombination (crossover) between 2 tours
  - Start with a “chemical soup” of random tours
  - Machines operate on tours independently (potentially in parallel)
    - draw 1 random molecule (2 for R-machine), perform operation
    - evaluate cost of each tour (educts and products)
    - inject best tour (2 best for R-machine) into soup, discard rest
  - Result: progressive selection of best tours

Molecular TSP in PyCellChemistry

```
class MolecularTSP( HighOrderChem ):
    def __init__( self, ncities ): ...
        tsp = TSPgraph(ncities, ...) # create road map
        for i in range(popsize):  # produce random tours
            mol = self.randomMolecule()
            self.mset.inject(mol)
        rule = 'self.exchangeMachine(%s)'
        self.rset.inject(rule, count)
        rule = 'self.cutMachine(%s)'
        self.rset.inject(rule, count)
    ...
    def run( self ): ...
        while gen <= self.maxgen:
            for j in range(genops):
                self.iterate() # pick rules and tours for reaction
            (bfit, bmol) = self.bestMolecule()
            gen += 1
```

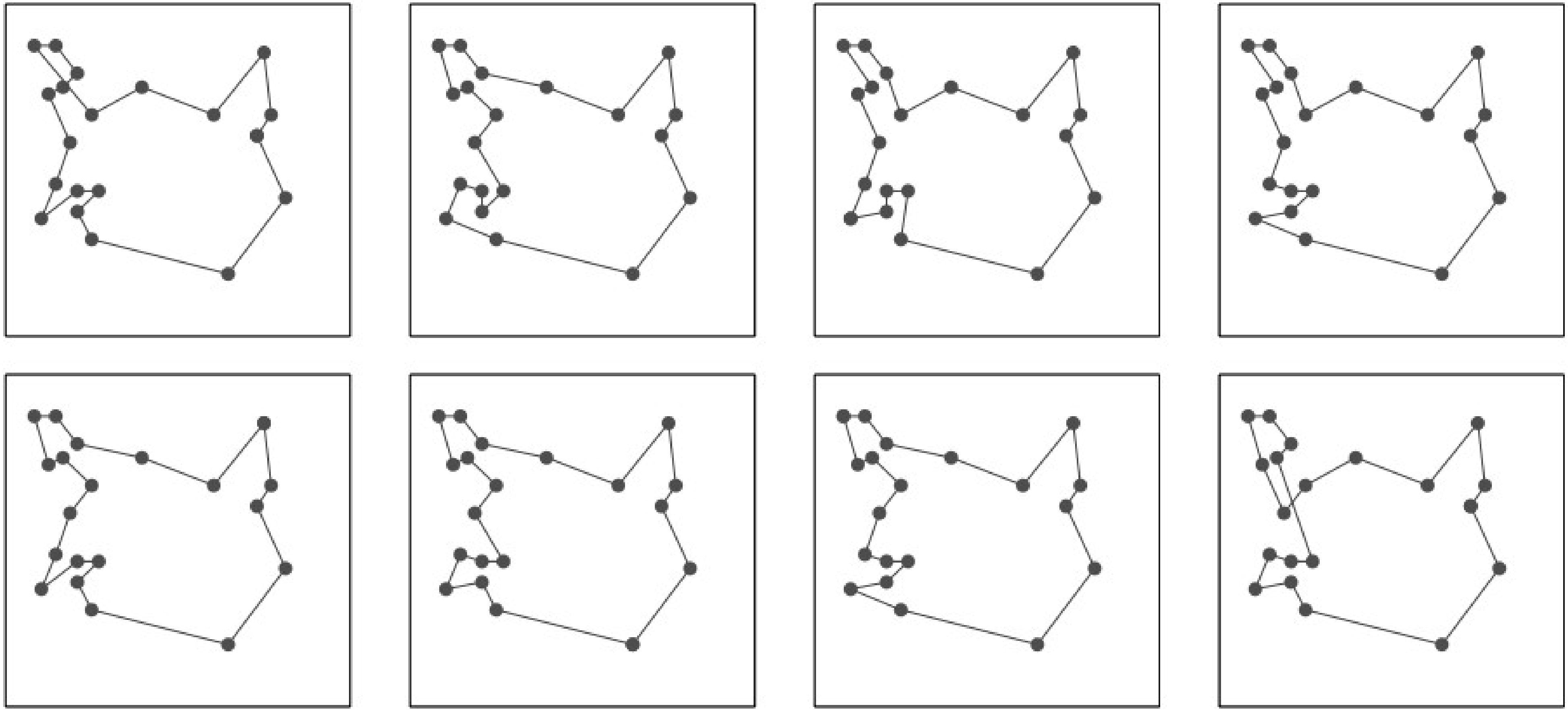
Molecular TSP: Initial Population

- Some random tours selected out of a population of 100 molecules:



Molecular TSP: After 4000 Generations

- Random tours selected out of the final population of 100 molecules:



Summary and Outlook

- What can we learn from ACs? Are they just toy chemistries?
  - Learn how things work by building them:
    build complexity starting from the bottom up
  - Natural computing and emergent computation:
    computation is embedded in the chemical system
    - ACs make such tight association more clear
  - Understand emergent phenomena through mathematical analysis:
    - formalizing ACs: Chemical Organization Theory, RAF theory (reflexively autocatalytic sets), Chemical Reaction Automata (DNA computing), P systems, Brane calculi, ...

Summary and Outlook

- Towards a discipline of AC: challenges
  - AC field not mature yet: scattered attempts, no coherent big picture
  - Barely scratching the surface of commonality between emergent phenomena (shared challenge with complex systems research)
  - Move upwards in complexity:
    - existing systems still take too much for granted (autocatalysis, container, replication mechanism...)
    - once something emerges, difficult to move beyond it, to reach the next level of complexity: need automatic encapsulation of the acquired emergent properties
- Future:
  - Tigher interdisciplinarity and integration between wet and virtual
  - Fuzzy line between virtual and real, more and more hybrid systems
  - Seamless programming: compile chemistry? chemical computers?

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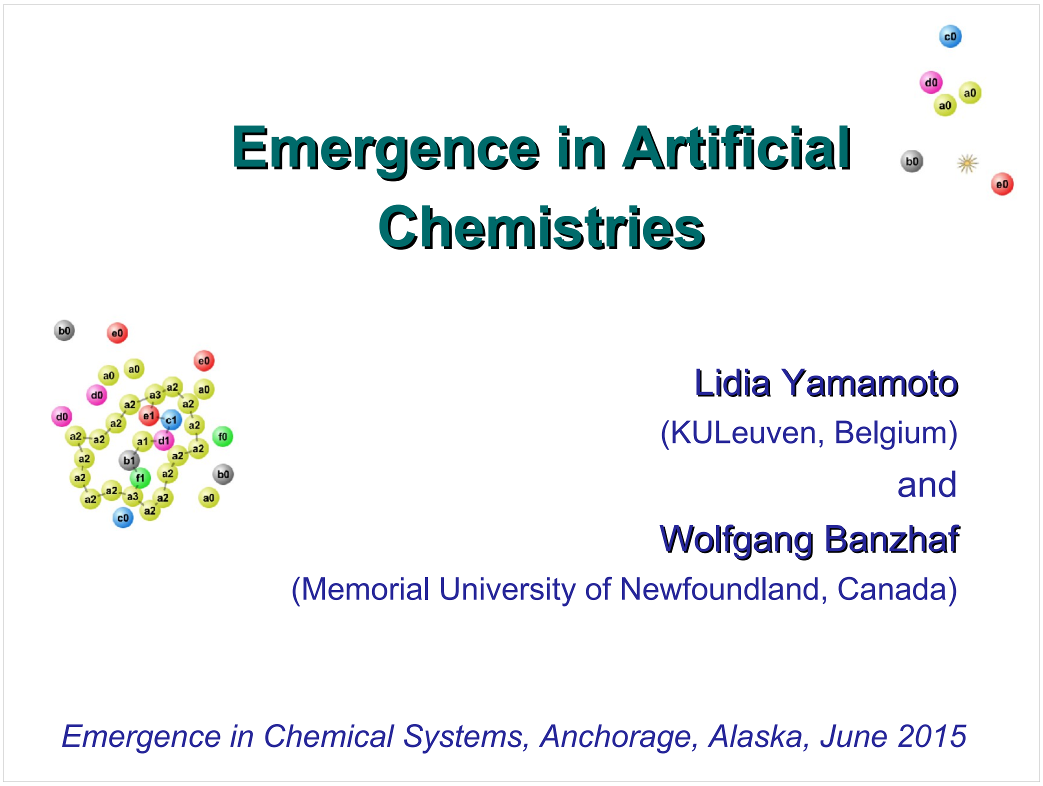


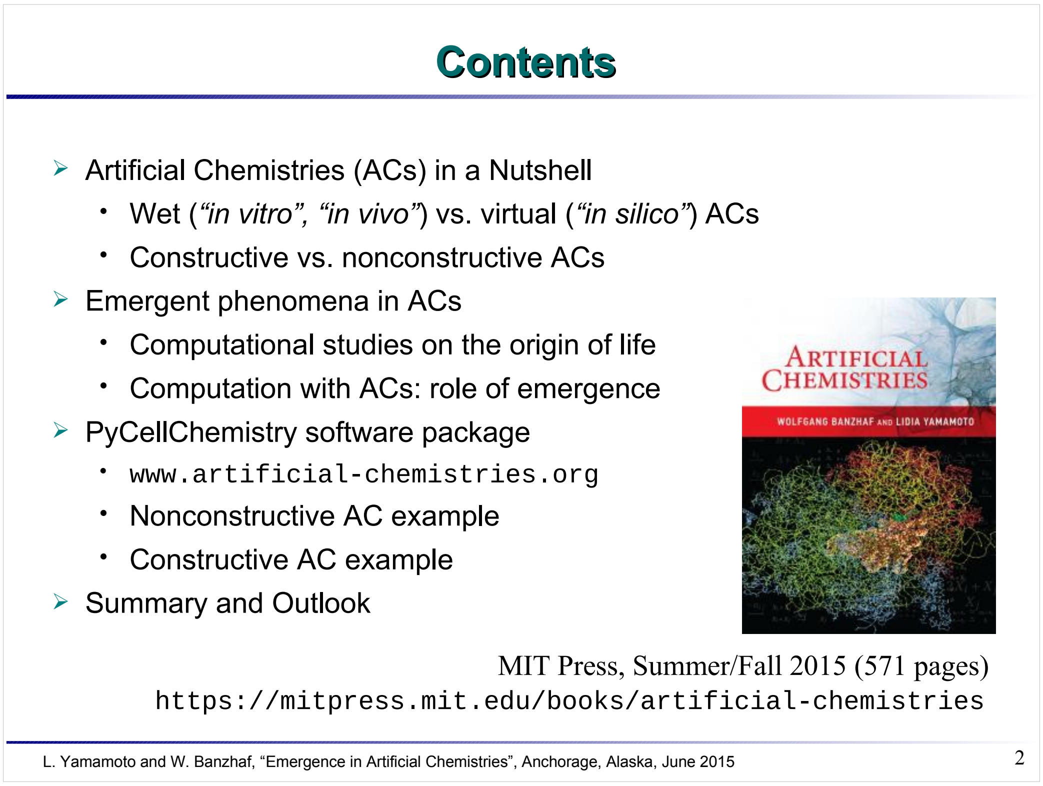
Emergence in Artificial Chemistries

Lidia Yamamoto
(KULeuven, Belgium)
and
Wolfgang Banzhaf
(Memorial University of Newfoundland, Canada)

Emergence in Chemical Systems, Anchorage, Alaska, June 2015

I'm going to talk about artificial chemistries and emergent phenomena occuring in artificial chemistries.

This work is a result of a collaboration with Prof.Banzhaf on our upcoming book about artificial chemistries. <next slide>



ARTIFICIAL CHEMISTRIES
WOLFGANG BANZHAF AND LIDIA YAMAMOTO

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- Artificial Chemistries (ACs) in a Nutshell
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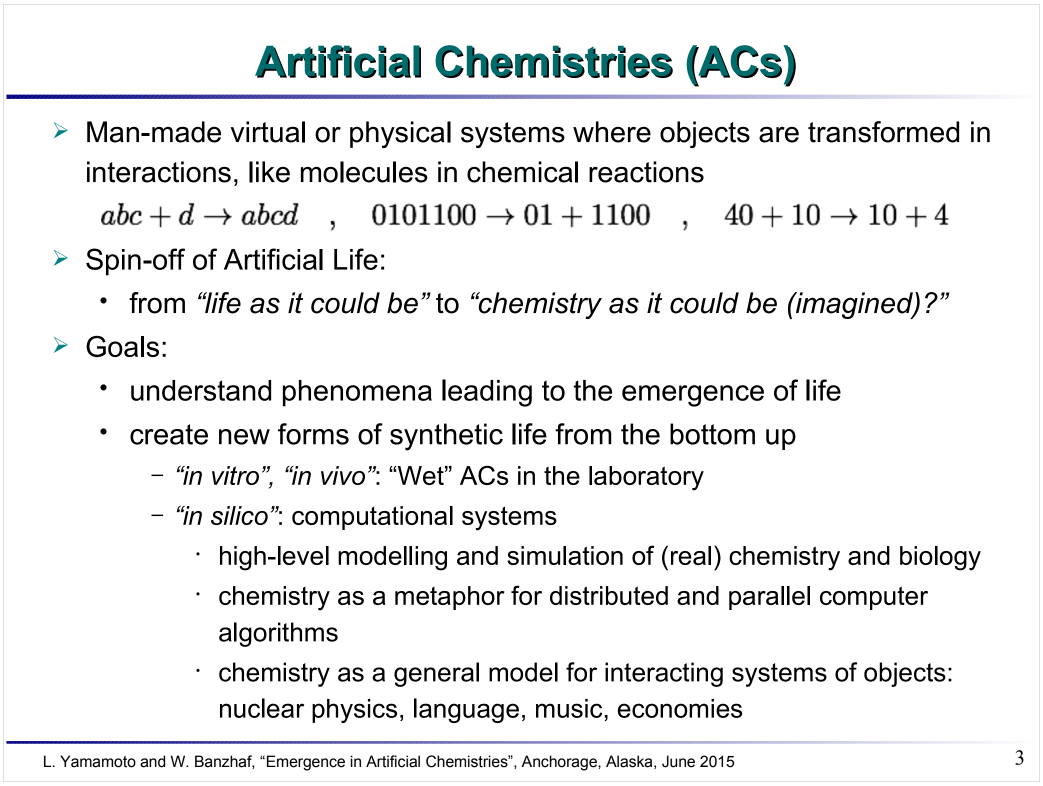
  - Nonconstructive AC example
  - Constructive AC example
- Summary and Outlook

MIT Press, Summer/Fall 2015 (571 pages)
`https://mitpress.mit.edu/books/artificial-chemistries`

Together with the book there will be a software package in python that we hope will be useful for people to get a quick start in the field and learn how to program their own artificial chemistries in a very simple and intuitive way.

So during this talk I'll introduce ACs and discuss some emergent phenomena within ACs, and will also introduce our software package that will be released in the next couple of weeks.



Artificial Chemistries (ACs)

- Man-made virtual or physical systems where objects are transformed in interactions, like molecules in chemical reactions

  $abc + d \rightarrow abcd \quad , \quad 0101100 \rightarrow 01 + 1100 \quad , \quad 40 + 10 \rightarrow 10 + 4$
- Spin-off of Artificial Life:
  - from *“life as it could be”* to *“chemistry as it could be (imagined)?”*
- Goals:
  - understand phenomena leading to the emergence of life
  - create new forms of synthetic life from the bottom up
    - *“in vitro”, “in vivo”*: “Wet” ACs in the laboratory
    - *“in silico”*: computational systems
      - high-level modelling and simulation of (real) chemistry and biology
      - chemistry as a metaphor for distributed and parallel computer algorithms
      - chemistry as a general model for interacting systems of objects: nuclear physics, language, music, economies

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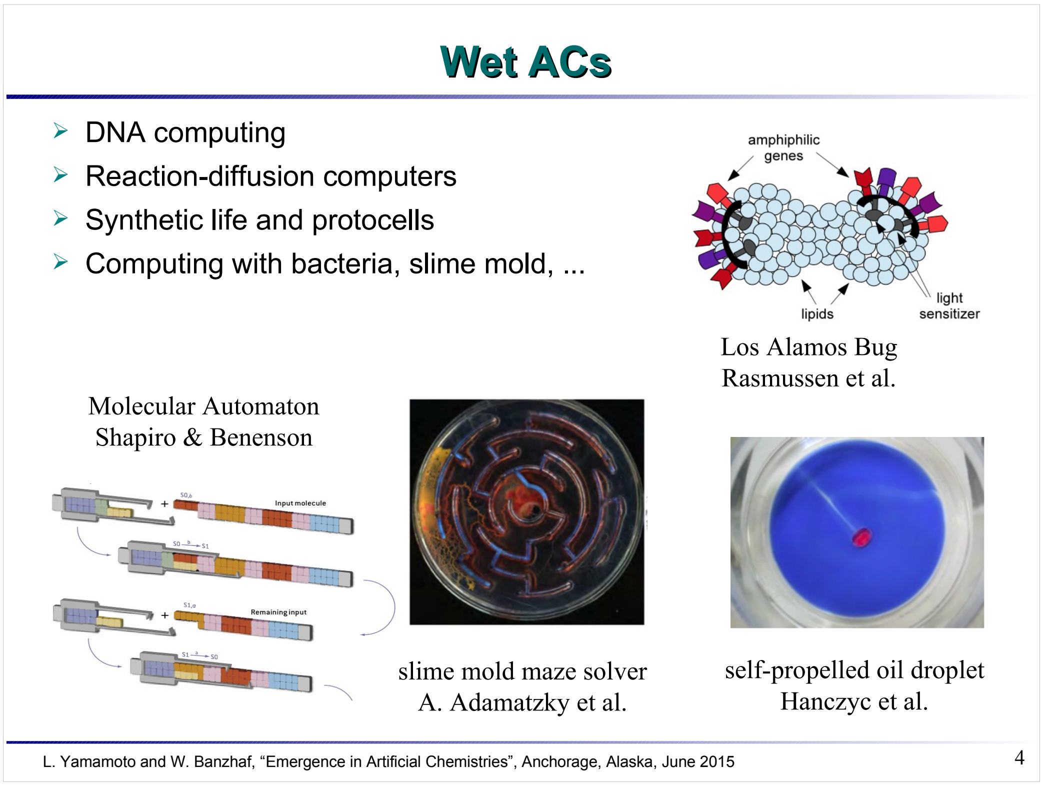
Artificial chemistries can refer to experiments in the web lab trying to understand the emergence of life or to create new building blocks for life

- but mostly they refer to computational systems where people try to study some phenomena related to the origins of life out of some chemicals,
- or (as it was my case when I started in this field) as inspiration for new algorithms for distributed and parallel computation. In my case, I was working in computer networks, like algorithms for the internet for instance, and we had a programming language inspired by chemistry in which fragments of computer programs could react and modify themselves like in a chemical reaction.
- and you'll also be surprised to see that artificial chemistries can also be applied to very distinct fields such as the modelling of human language, like the emergence of a shared vocabulary and grammar in a group of individuals, and even to compose music or to model the way goods are transformed and sold in economies.

Today I'll be focusing on these in silico systems, because I'm a computer scientist, so I only have a vague abstract idea about the real wet lab stuff.



Wet ACs

- DNA computing
- Reaction-diffusion computers
- Synthetic life and protocells
- Computing with bacteria, slime mold, ...

Los Alamos Bug
Rasmussen et al.

Molecular Automaton
Shapiro & Benenson

slime mold maze solver
A. Adamatzky et al.

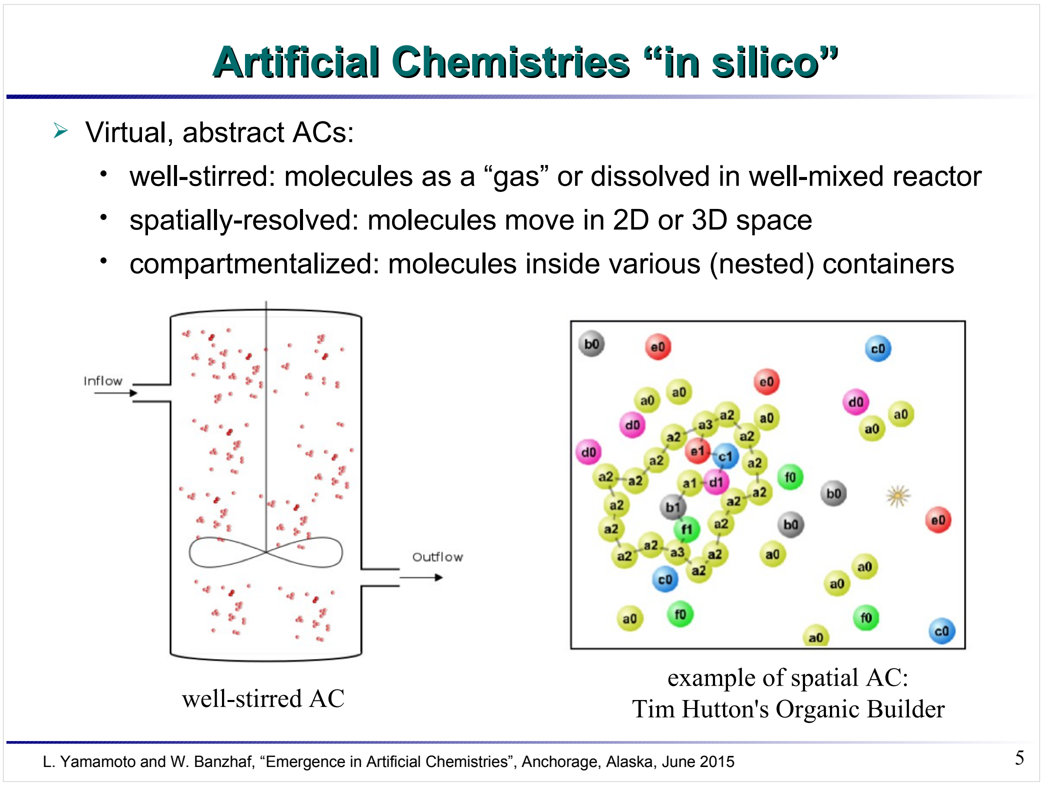
self-propelled oil droplet
Hanczyc et al.

so I only have this one slide on the wet systems, just to give you a flavor of the extent of the sytems covered:

- from molecular computing as in the DNA automaton, which is a finite state machine built with DNA and enzymes,
- to crazy micelles with non-biological nucleic acids sticking out of them
- and oil droplets that move and dance and even start talking to each other
- and slime molds that find their way out of a labyrinth using a form of chemotaxis following gradients of chemicals, which can be seen as a form of biological computer on a petri dish.

these are only a few examples.

most of these wet systems actually have corresponding computer simulations, so I think one of the most interesting and promising applications of artificial chemistries is in the computational modelling of these wet systems, which have mainly 2 purposes: to understand how life can originate and as a consequence how to construct life, and to apply this knowledge to “programmable life” and “programmable chemistries”



Artificial Chemistries “in silico”

- Virtual, abstract ACs:
  - well-stirred: molecules as a “gas” or dissolved in well-mixed reactor
  - spatially-resolved: molecules move in 2D or 3D space
  - compartmentalized: molecules inside various (nested) containers

well-stirred AC

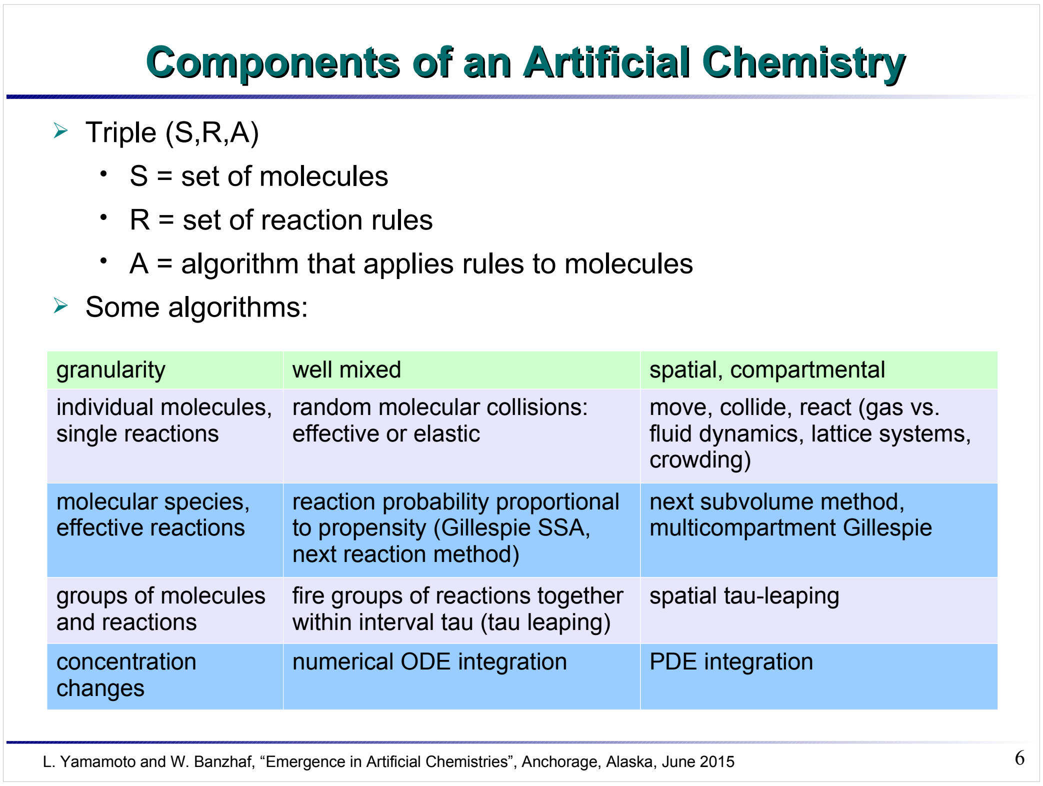
example of spatial AC:
Tim Hutton's Organic Builder

now turning to the computational systems, we can distinguish mainly between two types of artificial chemistries:

- well mixed in which any molecule has the same probabability of encountering any other molecule in the system (no explicit notion of space)

- and chemistries where space is explicitly represented, for instance the molecules move in a 2D or 3D space, where they may form some closed compartments

- or the compartments can be taken for grated with some molecules being exchanged between compartments, and inside every compartment we mainly have a well mixed system



Components of an Artificial Chemistry

- Triple (S,R,A)
  - S = set of molecules
  - R = set of reaction rules
  - A = algorithm that applies rules to molecules
- Some algorithms:

granularity	well mixed	spatial, compartmental
individual molecules, single reactions	random molecular collisions: effective or elastic	move, collide, react (gas vs. fluid dynamics, lattice systems, crowding)
molecular species, effective reactions	reaction probability proportional to propensity (Gillespie SSA, next reaction method)	next subvolume method, multicompartment Gillespie
groups of molecules and reactions	fire groups of reactions together within interval tau (tau leaping)	spatial tau-leaping
concentration changes	numerical ODE integration	PDE integration

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When designing an artificial chemistry we must specify 3 elements:

- the set of possible molecules in the system and their shapes,

- the way they react,

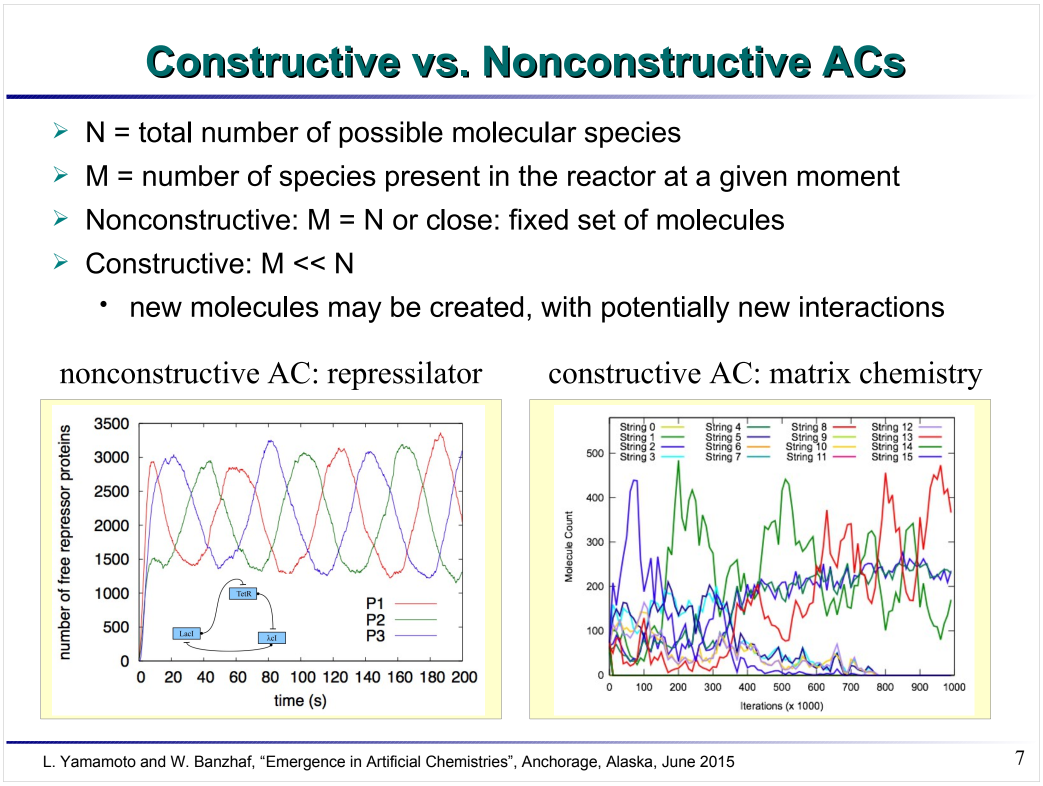
- and the algorithm that chooses which molecules collide and when, and apply the reaction rules from R to them

some of the algorithms are mentioned in this table:

depending on the granularity we're looking at, we can look at the system at the level of individual molecules, or sets of molecules reacting in a similar way, or a more coarse-grain level

as we move towards more coarse grain levels, the stochastic effects due to random molecule collisions get smaller until they disappear and the system can be treated with ordinary differential equations which is still a very common approach in the modelling of real chemical and biological systems.

the same happens also in systems with spatial considerations, where the algorithms also model the physics of the motion, diffusion or transport of particles from one position in space to another, or between compartments.



Constructive vs. Nonconstructive ACs

- N = total number of possible molecular species
- M = number of species present in the reactor at a given moment
- Nonconstructive: M = N or close: fixed set of molecules
- Constructive: M << N
  - new molecules may be created, with potentially new interactions

nonconstructive AC: repressilator

number of free repressor proteins
3500
3000
2500
2000
1500
1000
500
0
0 20 40 60 80 100 120 140 160 180 200
time (s)
TetR
LacI
λcI
P1
P2
P3

constructive AC: matrix chemistry

Molecule Count
500
400
300
200
100
0
0 100 200 300 400 500 600 700 800 900 1000
Iterations (x 1000)
String 0
String 1
String 2
String 3
String 4
String 5
String 6
String 7
String 8
String 9
String 10
String 11
String 12
String 13
String 14
String 15

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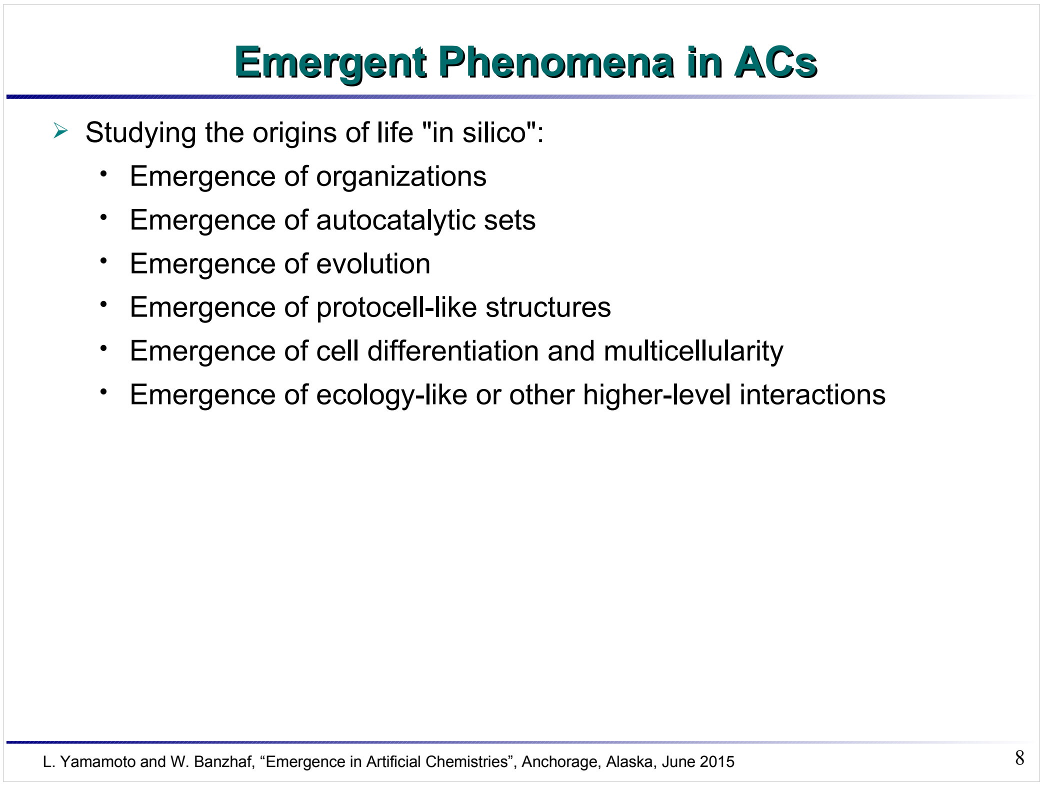
another important distinction is between constructive and non-constructive chemistries: basically constructive chemistries are those where new molecules may be produced all the time, with potentially new chemical reactions happening between them

talk by Yuagsheng Cao yesterday: repressilator



Emergent Phenomena in ACs

- Studying the origins of life "in silico":
  - Emergence of organizations
  - Emergence of autocatalytic sets
  - Emergence of evolution
  - Emergence of protocell-like structures
  - Emergence of cell differentiation and multicellularity
  - Emergence of ecology-like or other higher-level interactions

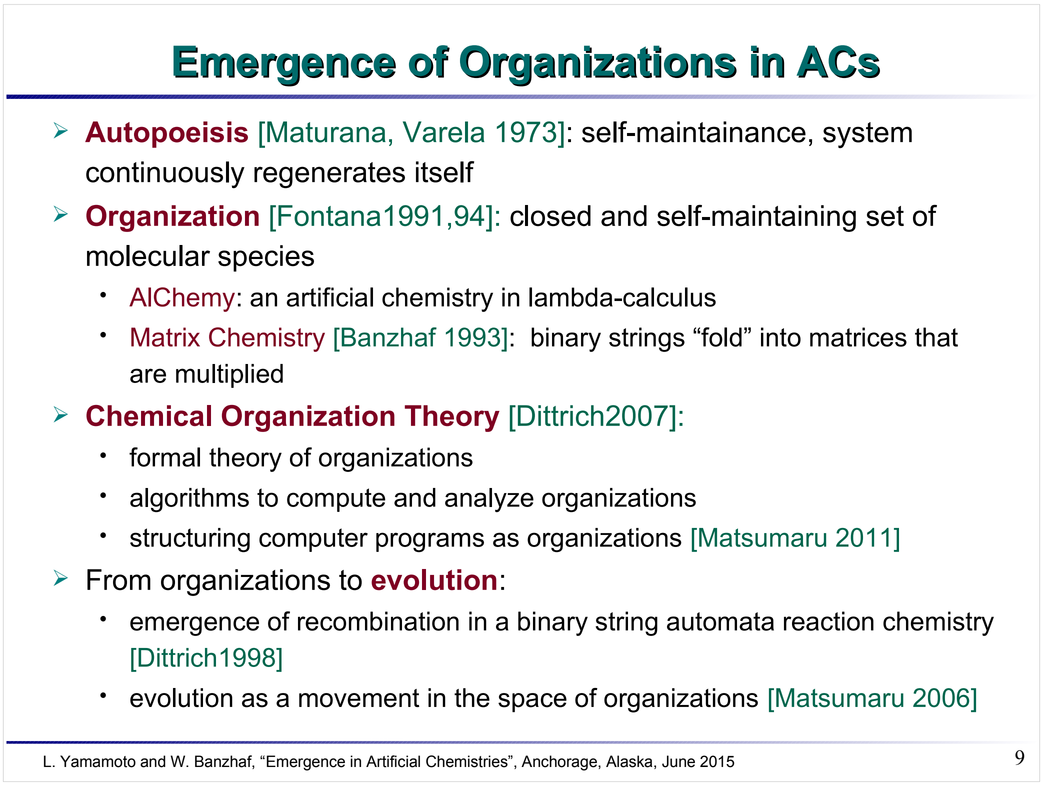
Emergence of organizations, autocatalytic sets: random catalytic reaction nets, Kauffman, recent work by Filisetti & al.

Emergence of evolution: automata reaction chemistry (Dittrich), Bagley&Farmer

Emergence of protocell-like structures: Hutton's chemistry, Ono's protocells

Emergence of cell differentiation and multicellularity

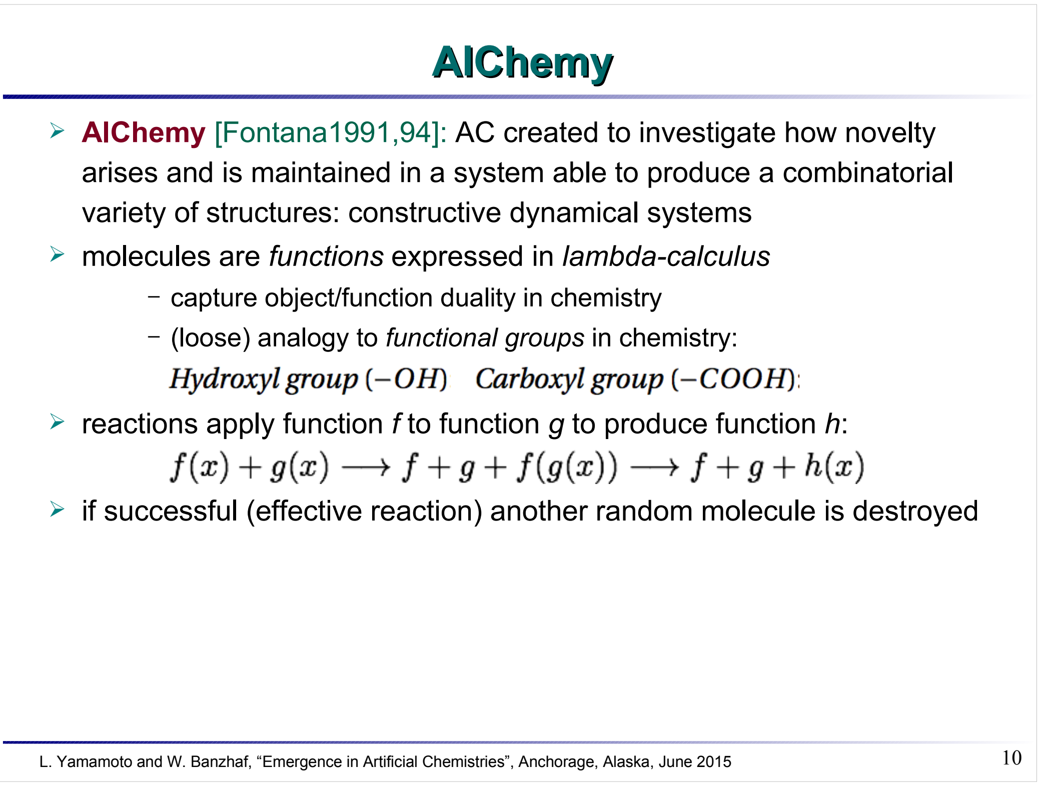
Emergence of ecology-like or other higher-level interactions: Tangled nature, Avida, Swarm Chemistry



Emergence of Organizations in ACs

- **Autopoeisis** [Maturana, Varela 1973]: self-maintainance, system continuously regenerates itself
- **Organization** [Fontana1991,94]: closed and self-maintaining set of molecular species
  - AlChemy: an artificial chemistry in lambda-calculus
  - Matrix Chemistry [Banzhaf 1993]: binary strings “fold” into matrices that are multiplied
- **Chemical Organization Theory** [Dittrich2007]:
  - formal theory of organizations
  - algorithms to compute and analyze organizations
  - structuring computer programs as organizations [Matsumaru 2011]
- From organizations to **evolution**:
  - emergence of recombination in a binary string automata reaction chemistry [Dittrich1998]
  - evolution as a movement in the space of organizations [Matsumaru 2006]

the notion of organization is related to the notion of autopoeisis where a (living) system must maintain itself



AlChemy

- **AlChemy** [Fontana1991,94]: AC created to investigate how novelty arises and is maintained in a system able to produce a combinatorial variety of structures: constructive dynamical systems
- molecules are *functions* expressed in *lambda-calculus*
  - capture object/function duality in chemistry
  - (loose) analogy to *functional groups* in chemistry:

    $\mathit{Hydroxyl\ group}\ (-OH)\quad \mathit{Carboxyl\ group}\ (-COOH)$:
- reactions apply function *f* to function *g* to produce function *h*:

$$f(x) + g(x) \longrightarrow f + g + f(g(x)) \longrightarrow f + g + h(x)$$

- if successful (effective reaction) another random molecule is destroyed

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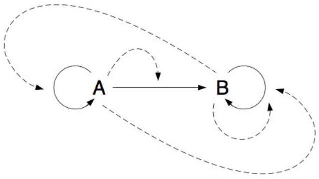
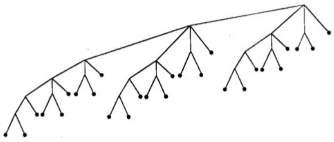
hydroxyl broup, carbonyl group

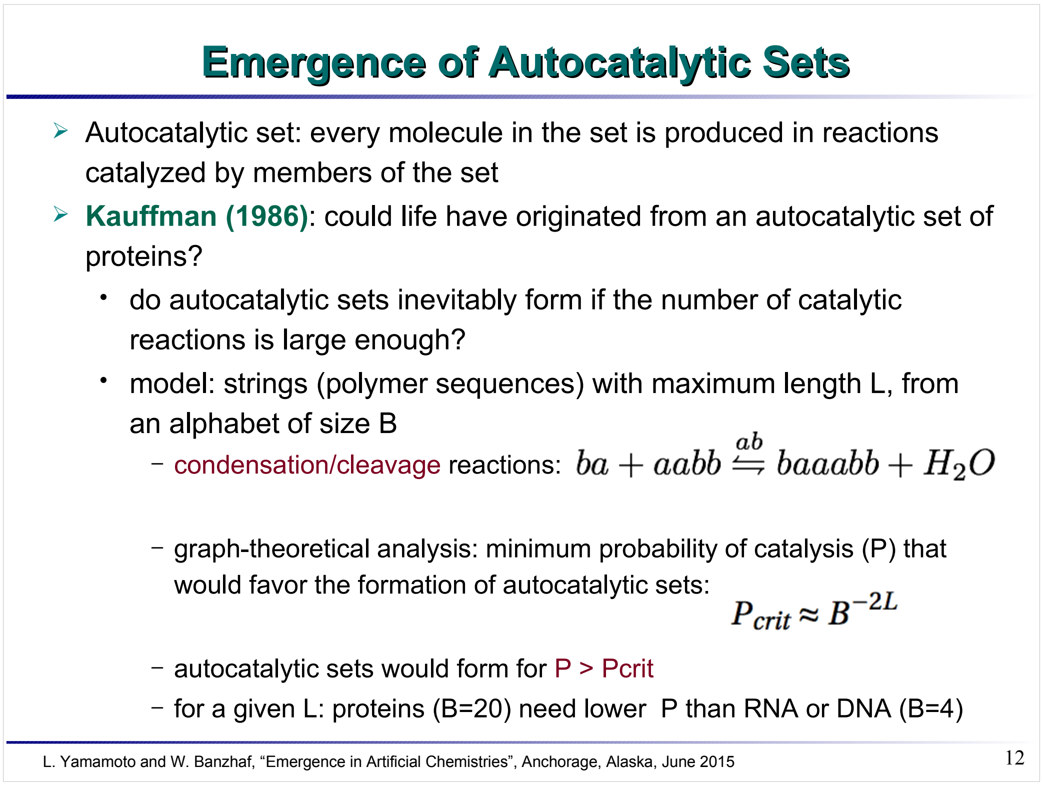
reduced form of the composition of the two functions: called the normal form h(x)

AlChemy Experiments

- Starting from a population of random molecules:
  - diversity decreases
  - system converges to small set of self-copying molecules
  - n-membered elementary hypercycles, but brittle, easily collapse
- When self-copying is disabled:
  - "polymerization": formation of long "polymers" by concatenating "monomers"
  - formation of large organizations that are stable and resilient to perturbations
  - more rarely, formation of interacting, inter-dependent organizations







Emergence of Autocatalytic Sets

- Autocatalytic set: every molecule in the set is produced in reactions catalyzed by members of the set
- **Kauffman (1986)**: could life have originated from an autocatalytic set of proteins?
  - do autocatalytic sets inevitably form if the number of catalytic reactions is large enough?
  - model: strings (polymer sequences) with maximum length L, from an alphabet of size B
    - condensation/cleavage reactions: $ba + aabb \overset{ab}{\rightleftharpoons} baaabb + H_2O$
    - graph-theoretical analysis: minimum probability of catalysis (P) that would favor the formation of autocatalytic sets: $P_{crit} \approx B^{-2L}$
    - autocatalytic sets would form for P > Pcrit
    - for a given L: proteins (B=20) need lower P than RNA or DNA (B=4)

starting from reactions that look like the formation of peptide bonds, in a reversible way such that these bonds can also be broken up

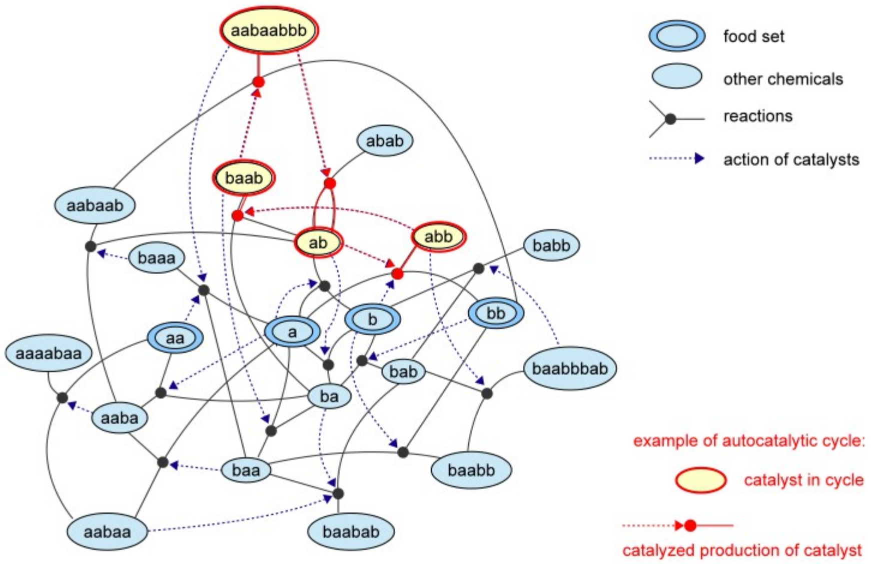
P: prob of catalysis = prob that a prot catalysis the formation of another

the lower Pcritical, the easier it is for autocatalytic sets to form

Pcrit decreases with B and with L, hence high B and high L favor autocat sets

even if catalysis is very improbable, still autocatalytic sets would emerge

Emergence of Autocatalytic Sets



food set

other chemicals

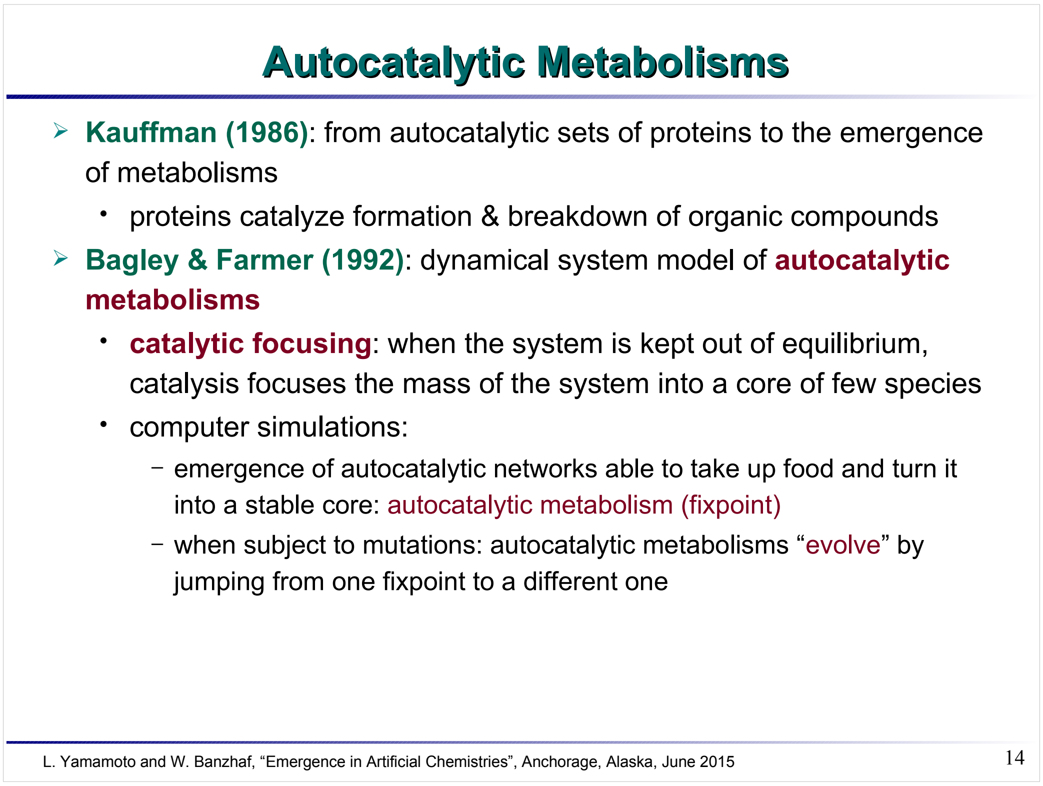
reactions

action of catalysts

example of autocatalytic cycle:

catalyst in cycle

catalyzed production of catalyst



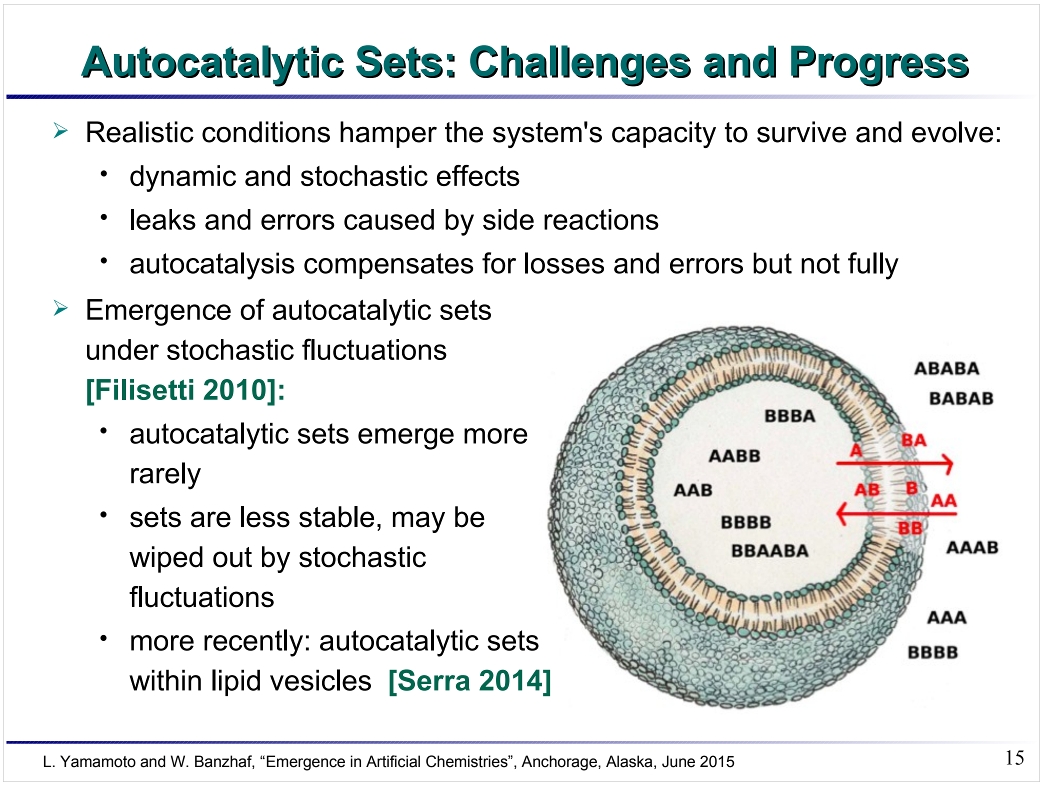
Autocatalytic Metabolisms

- **Kauffman (1986)**: from autocatalytic sets of proteins to the emergence of metabolisms
  - proteins catalyze formation & breakdown of organic compounds
- **Bagley & Farmer (1992)**: dynamical system model of **autocatalytic metabolisms**
  - **catalytic focusing**: when the system is kept out of equilibrium, catalysis focuses the mass of the system into a core of few species
  - computer simulations:
    - emergence of autocatalytic networks able to take up food and turn it into a stable core: autocatalytic metabolism (fixpoint)
    - when subject to mutations: autocatalytic metabolisms “evolve” by jumping from one fixpoint to a different one

autocatalytic metabolism: autocatalytic set in which the species concentrations are significantly different from those expected without catalysis

only by a steady inflow of food molecules (because catalysis accelerates reaction in both directions, equilibrium does not change)

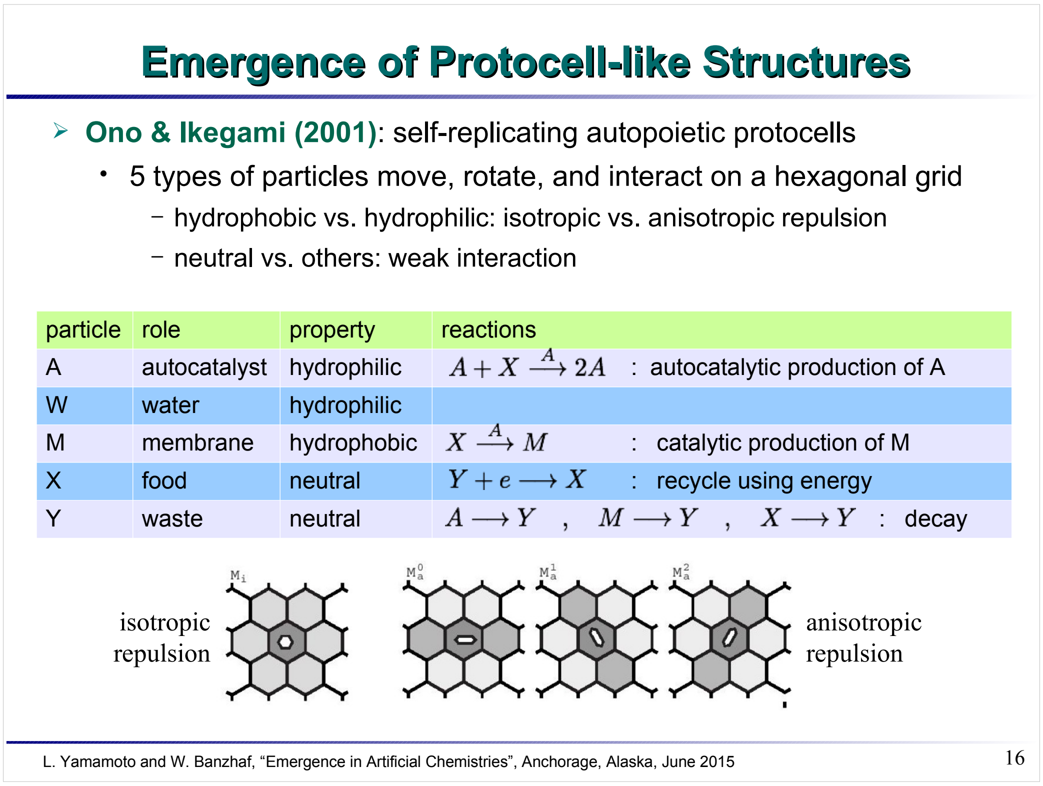
mutations (production of new catalysts in spontaneous reactions):



Autocatalytic Sets: Challenges and Progress

- Realistic conditions hamper the system's capacity to survive and evolve:
  - dynamic and stochastic effects
  - leaks and errors caused by side reactions
  - autocatalysis compensates for losses and errors but not fully
- Emergence of autocatalytic sets under stochastic fluctuations **[Filisetti 2010]:**
  - autocatalytic sets emerge more rarely
  - sets are less stable, may be wiped out by stochastic fluctuations
  - more recently: autocatalytic sets within lipid vesicles **[Serra 2014]**

Serra: only species shorter than 3 letters can cross the membrane



Emergence of Protocell-like Structures

- **Ono & Ikegami (2001)**: self-replicating autopoietic protocells
  - 5 types of particles move, rotate, and interact on a hexagonal grid
    - hydrophobic vs. hydrophilic: isotropic vs. anisotropic repulsion
    - neutral vs. others: weak interaction

particle	role	property	reactions
A	autocatalyst	hydrophilic	$A + X \xrightarrow{A} 2A$: autocatalytic production of A
W	water	hydrophilic	
M	membrane	hydrophobic	$X \xrightarrow{A} M$: catalytic production of M
X	food	neutral	$Y + e \longrightarrow X$: recycle using energy
Y	waste	neutral	$A \longrightarrow Y$, $M \longrightarrow Y$, $X \longrightarrow Y$: decay

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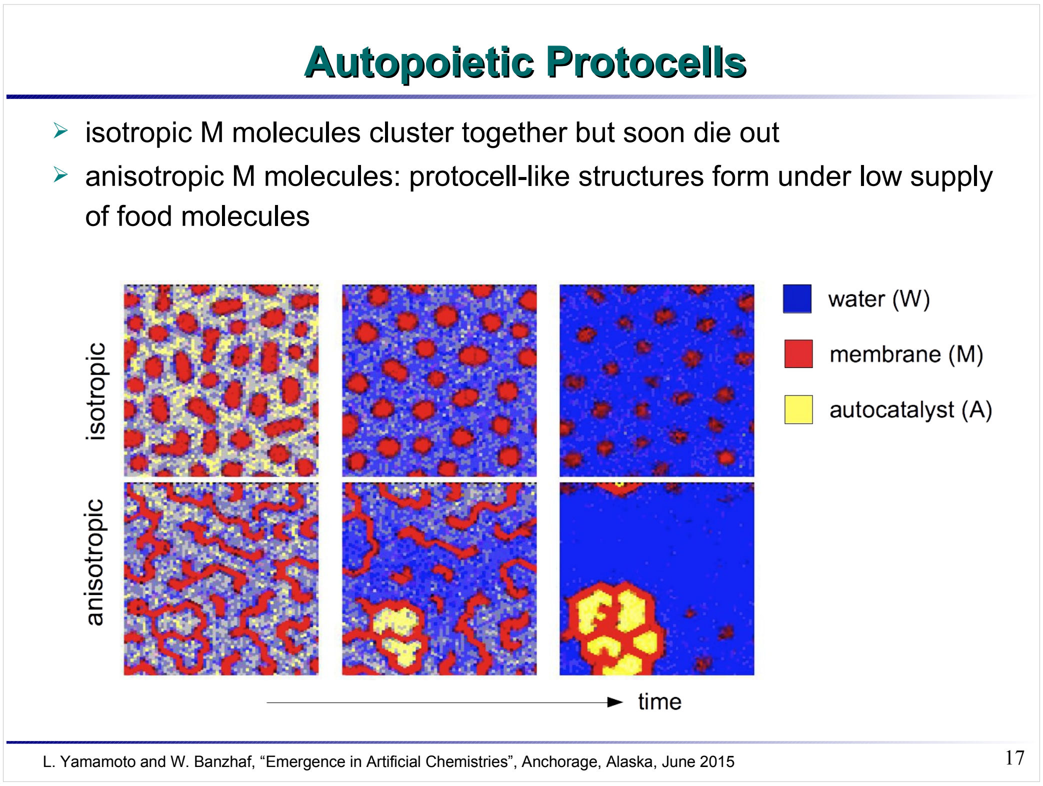
Hydrophilic and hydrophobic particles repel each other

neutral particle may establish weak interactions with the other two types

Hydrophobic particles: isotropic or anisotropic.

Isotropic hydrophobic particles repel hydrophilic particles with equal strength in all directions

Anisotropic particles: stronger repulsion in one direction



Autopoietic Protocells

- isotropic M molecules cluster together but soon die out
- anisotropic M molecules: protocell-like structures form under low supply of food molecules

anisotropic case:

- osmosis of resource particles across membranes

- as a result of competition, some closed cells survive and begin to grow

under low supply of X food molecules, protocell-like structures form:

- top: M particles are isotropic, clusters resembling cells form, but are unable to sustain themselves and end up dying out

- bottom: M particles are anisotropic, irregular membrane filaments form initially, and some of them form closed protocells able to grow, divide and sustain their internal metabolism.

emergence of a protocell structure after membrane formation

cells grow and divide

stick together because of clustering of hydrophobic membrane particles

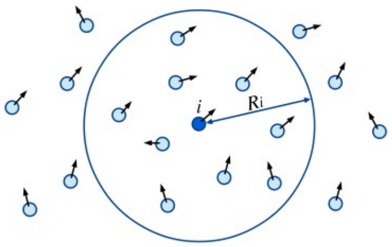
Blue: Water (W) particles

red: membrane (M) particles

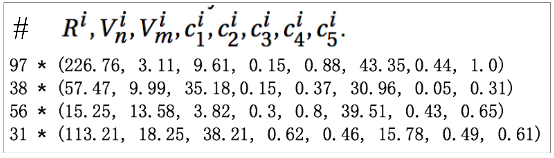
yellow: autocatalysts (A).

Emergence of Higher Level Interactions

- **Swarm Chemistry** [Sayama 2009-]
  - particles of several types move in 3D space:
    - move towards nearby particles
    - adjust speed to average speed of neighbors
    - avoid collision
  - behavior governed by "recipe" of parameters:

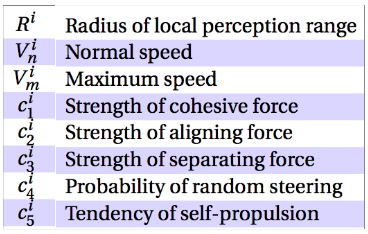


Recipe:



```
#    R^i, V_n^i, V_m^i, c_1^i, c_2^i, c_3^i, c_4^i, c_5^i.
97 * (226.76,  3.11,  9.61,  0.15,  0.88,  43.35, 0.44,  1.0)
38 * (57.47,  9.99,  35.18, 0.15,  0.37,  30.96,  0.05,  0.31)
56 * (15.25,  13.58,  3.82,  0.3,  0.8,  39.51,  0.43,  0.65)
31 * (113.21,  18.25,  38.21,  0.62,  0.46,  15.78,  0.49,  0.61)
```

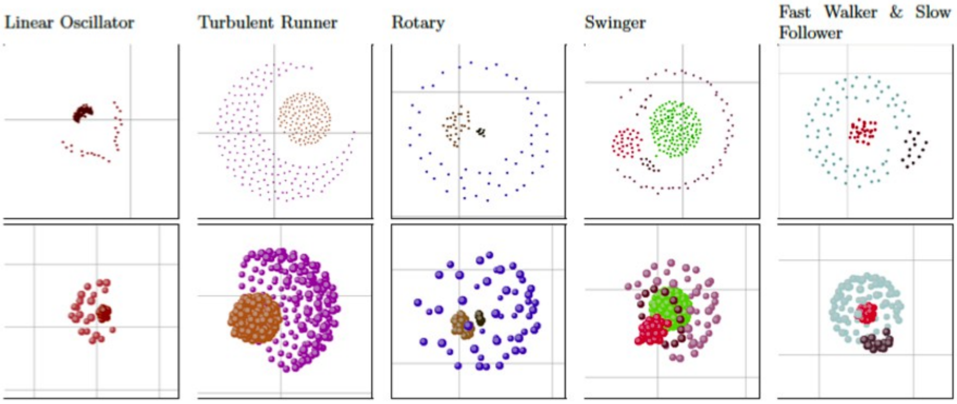
Parameters:



R^i	Radius of local perception range
V_n^i	Normal speed
V_m^i	Maximum speed
c_1^i	Strength of cohesive force
c_2^i	Strength of aligning force
c_3^i	Strength of separating force
c_4^i	Probability of random steering
c_5^i	Tendency of self-propulsion

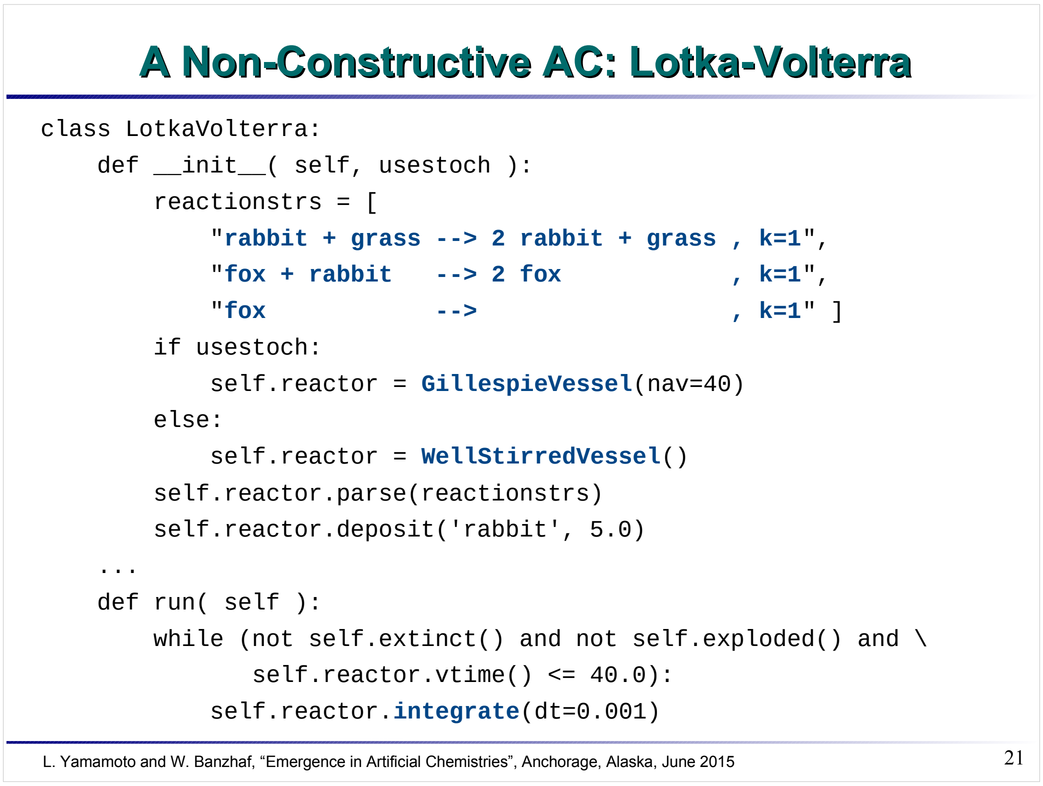
Swarm Chemistry

- Behaviors (with underlying recipe) evolved by interactive evolution
- Java demo: `http://bingweb.binghamton.edu/~sayama/SwarmChemistry`
- Some behaviors displayed:



An Artificial Chemistry in Python

- **PyCellChemistry**: python package to let users program their own ACs (to be released this summer)
  - `www.artificial-chemistries.org`
- Basic system:
  - multisets (bags) of molecules
  - chemical reactions
  - conversion from chemical reactions to ODE and Gillespie SSA
  - hierarchical cell compartments
- Example ACs:
  - basic: chameleons, prime number chemistry, matrix chemistry
  - biochemical circuits: dimerization, logistic growth, repressilator
  - ecology and evolution: Lotka-Volterra, quasispecies, NK landscapes
  - distributed & parallel computing: molecular TSP, fraglets, disperser

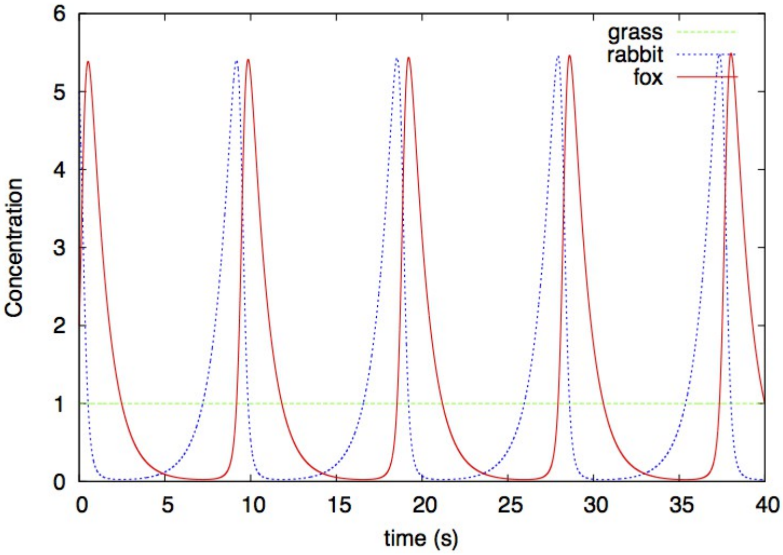


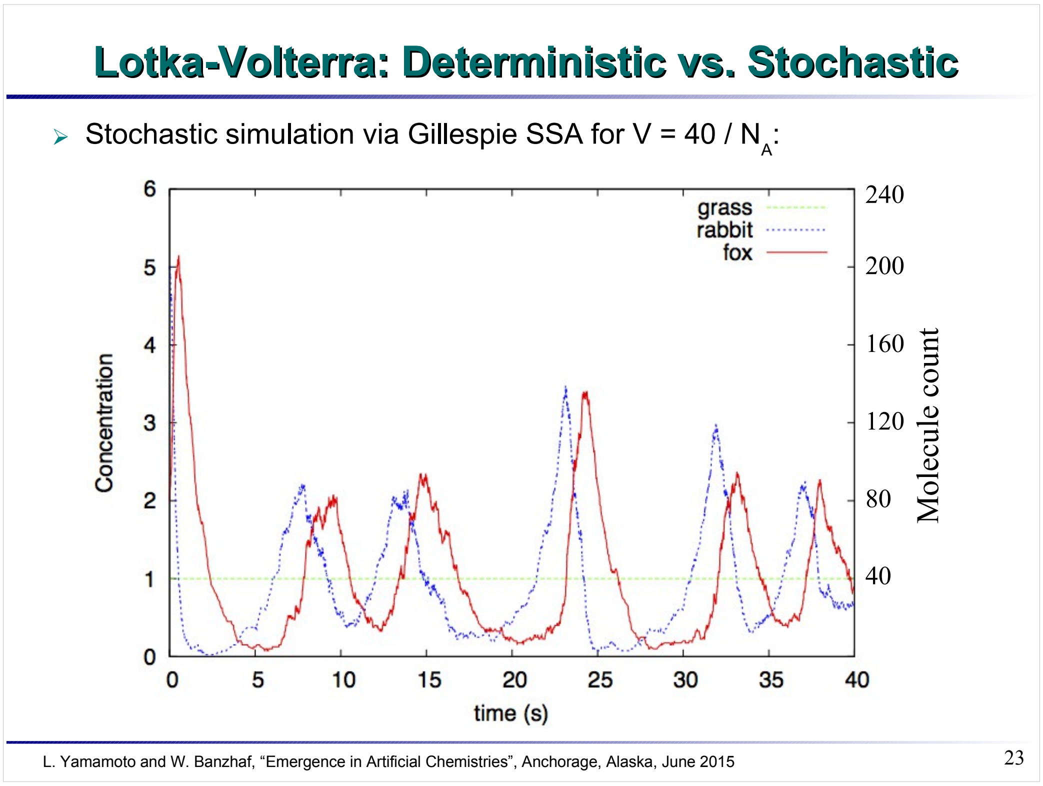
A Non-Constructive AC: Lotka-Volterra

```
class LotkaVolterra:
    def __init__( self, usestoch ):
        reactionstrs = [
            "rabbit + grass --> 2 rabbit + grass , k=1",
            "fox + rabbit   --> 2 fox            , k=1",
            "fox            -->                  , k=1" ]
        if usestoch:
            self.reactor = GillespieVessel(nav=40)
        else:
            self.reactor = WellStirredVessel()
        self.reactor.parse(reactionstrs)
        self.reactor.deposit('rabbit', 5.0)
    ...
    def run( self ):
        while (not self.extinct() and not self.exploded() and \
               self.reactor.vtime() <= 40.0):
            self.reactor.integrate(dt=0.001)
```

Lotka-Volterra: Deterministic vs. Stochastic

- Deterministic simulation via ODE integration:





Lotka-Volterra: Deterministic vs. Stochastic

- Stochastic simulation via Gillespie SSA for V = 40 / N_A:

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Many systems do not survive to the end of the simulation (typically because one of the species goes extinct)

This is a well selected case where they survived long enough to compare with the previous simulation

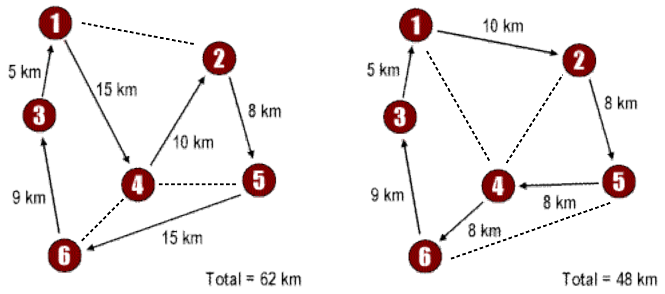
NAV=40

c0(rabbit) = 5 = n0(rabbit) / NAV => n0(rabbit) = 5 * 40 = 200

c0(fox) = 2 = n0(fox) / NAV => n0(fox) = 2 * 40 =80

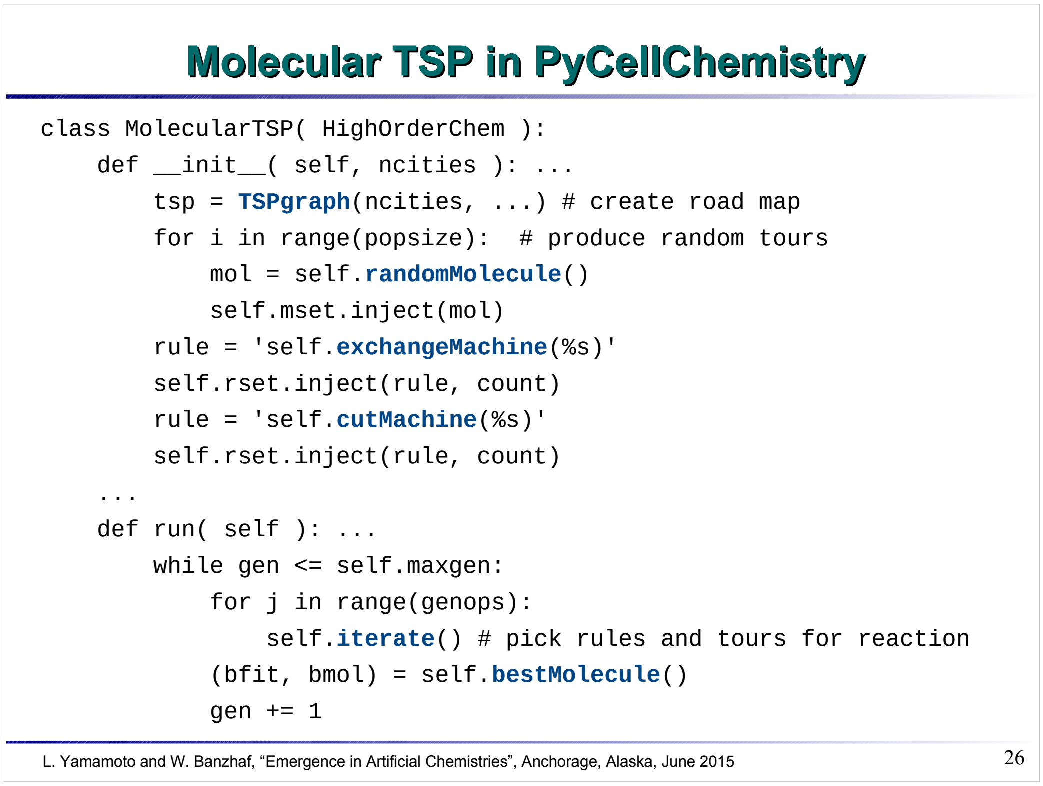
A Constructive AC: The Molecular TSP

- Traveling Salesman Problem (TSP):
  - find the tour of minimum cost that visits all the cities on a map
  - use only the available roads
  - visit each city only once
  - known to be NP-hard:
    - cannot be solved in general within a polynomial number of operations
    - typically heuristic algorithms are used: find approximate solutions



A Constructive AC: The Molecular TSP

- **Molecular TSP** [Banzhaf 1990]: TSP heuristic inspired by chemistry
  - 2 types of molecules: machines and tours
    - tour: list of cities in the order they are visited, e.g. [1 2 5 4 6 3 1]
  - Machines (“enzymes”) operate on tours (“substrates”)
    - E-machine: swaps two random cities in a tour
    - C-machine: cuts a tour segment and pastes it elsewhere in tour
    - I-machine: cuts and inverts the segment before pasting it
    - R-machine: recombination (crossover) between 2 tours
  - Start with a “chemical soup” of random tours
  - Machines operate on tours independently (potentially in parallel)
    - draw 1 random molecule (2 for R-machine), perform operation
    - evaluate cost of each tour (educts and products)
    - inject best tour (2 best for R-machine) into soup, discard rest
  - Result: progressive selection of best tours



Molecular TSP in PyCellChemistry

```
class MolecularTSP( HighOrderChem ):
    def __init__( self, ncities ): ...
        tsp = TSPgraph(ncities, ...) # create road map
        for i in range(popsize):  # produce random tours
            mol = self.randomMolecule()
            self.mset.inject(mol)
        rule = 'self.exchangeMachine(%s)'
        self.rset.inject(rule, count)
        rule = 'self.cutMachine(%s)'
        self.rset.inject(rule, count)
    ...
    def run( self ): ...
        while gen <= self.maxgen:
            for j in range(genops):
                self.iterate() # pick rules and tours for reaction
            (bfit, bmol) = self.bestMolecule()
            gen += 1
```

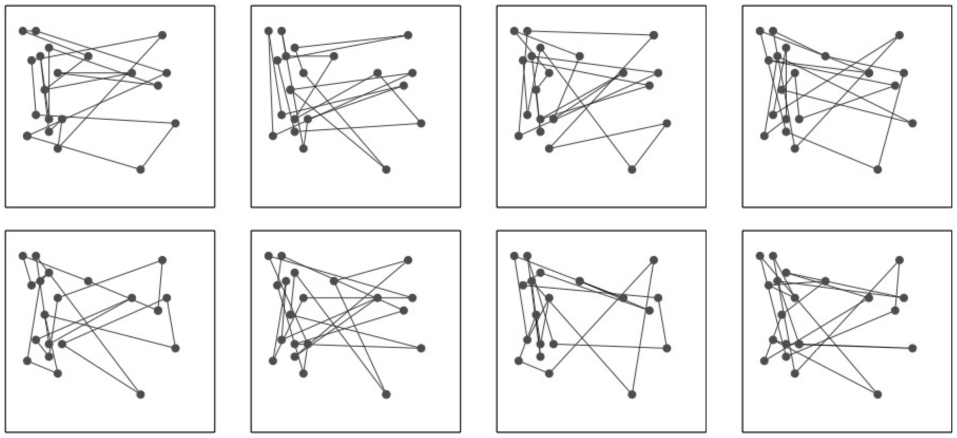
L. Yamamoto and W. Banzhaf, “Emergence in Artificial Chemistries”, Anchorage, Alaska, June 2015

with this it is easy to program a chemistry, say, if you're familiar with python, which can be learned very quickly, then depending on the complexity of the chemistry it can be programmed in a couple of hours or a couple of days.

of course the performance of such system cannot be compared with more powerful systems, for instance a couple of years ago I worked with GPU programming for parallelizing artificial chemistry algorithms, where you can get orders of magnitude better performance but also the learning curve is much more difficult.

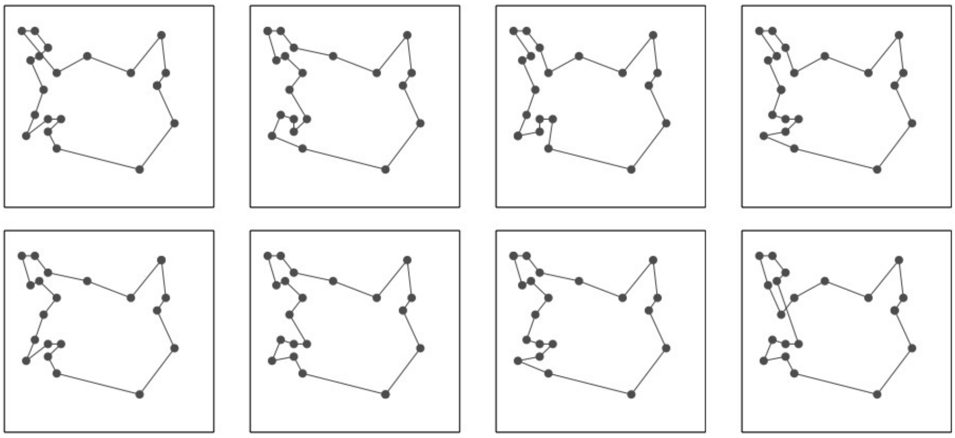
Molecular TSP: Initial Population

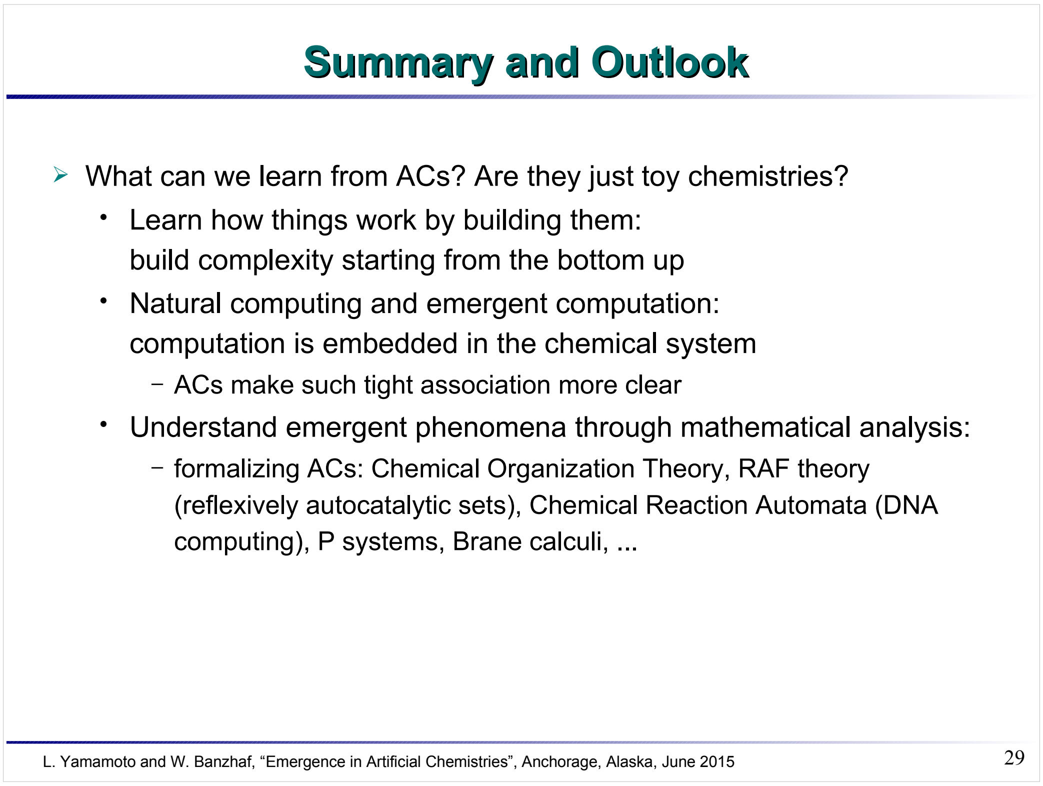
- Some random tours selected out of a population of 100 molecules:



Molecular TSP: After 4000 Generations

- Random tours selected out of the final population of 100 molecules:





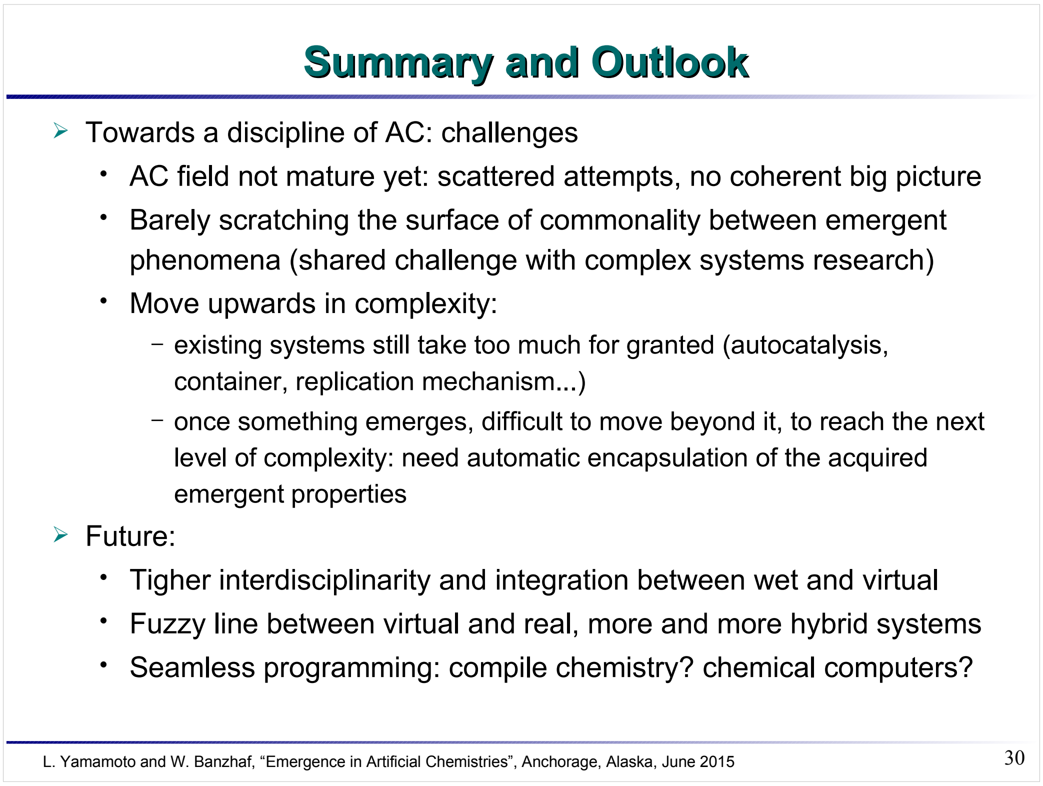
Summary and Outlook

- What can we learn from ACs? Are they just toy chemistries?
  - Learn how things work by building them:
    build complexity starting from the bottom up
  - Natural computing and emergent computation:
    computation is embedded in the chemical system
    - ACs make such tight association more clear
  - Understand emergent phenomena through mathematical analysis:
    - formalizing ACs: Chemical Organization Theory, RAF theory (reflexively autocatalytic sets), Chemical Reaction Automata (DNA computing), P systems, Brane calculi, ...

understand theoretical boundaries, limitations and potential

either the container is predesigned, or replication is predesigned, or the way the molecules interact is carefully designed in order to reach the desired effect.

once something emerges, cannot move beyond it, to the next level: no automatic encapsulation of the acquired emergent properties



Summary and Outlook

- Towards a discipline of AC: challenges
  - AC field not mature yet: scattered attempts, no coherent big picture
  - Barely scratching the surface of commonality between emergent phenomena (shared challenge with complex systems research)
  - Move upwards in complexity:
    - existing systems still take too much for granted (autocatalysis, container, replication mechanism...)
    - once something emerges, difficult to move beyond it, to reach the next level of complexity: need automatic encapsulation of the acquired emergent properties
- Future:
  - Tigher interdisciplinarity and integration between wet and virtual
  - Fuzzy line between virtual and real, more and more hybrid systems
  - Seamless programming: compile chemistry? chemical computers?

2 examples: reversibility & logic gates (binary)

feedback loop from experiments to simulation and so on:
cannot make progress unless we join forces

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