Stochastic Collectives
Stochastic Collectives

- "Collective":
  - A large set of interacting finite state automata:
    - Not quite language automata ("large set")
    - Not quite cellular automata ("interacting" but not on a grid)
    - Not quite process algebra ("finite state" and "collective")
    - Not quite calculus (rate of change of "automata"?)
    - Cf. "multi-agent systems" and "swarm intelligence"

- "Stochastic":
  - Interactions have rates

- Very much like biochemistry
  - Which is a large set of stochastically interacting molecules/proteins
  - Are proteins finite state and subject to automata-like transitions?
    - Let's say they are, at least because:
    - Much of the knowledge being accumulated in Systems Biology
      is described as state transition diagrams [Kitano].
State Transitions
Reverse Engineering Nature

- That's what Systems Biology is up against
  - Exemplified by a technological analogy:

- Tamagotchi: a technological organism
  - Has inputs (buttons) and outputs (screen/sound)
  - It has state: happy or needy (or hungry, sick, dead...)
  - Has to be petted at a certain rate (or gets needy)
  - Each one has a slightly different behavior

- Reverse Engineering Tamagotchi
  - Running experiments that elucidate their behavior
  - Building models that explain the experiments

- Applications
  - Engineering: Can we build our own Tamagotchi? (Sadly, no longer made.)
  - Maintenance: Can we fix a broken Tamagotchi?
Understanding T. Nipponensis

- **Tamagotchi Nipponensis**: a stochastic interactive automata
  - 40 million sold worldwide; discontinued in 1998
  - Still found “in the wild” in Akihabara

- **Traditional scientific investigations fail**
  - Design-driven understanding fails
    - We cannot read the manual (Japanese)
    - What does a Tamagotchi “compute”? What is its “purpose”?
    - Why does it have 3 buttons?
  - Mechanistic understanding fails
    - Few moving parts. Removing components mostly ineffective or “lethal”
    - The “tamagotchi folding problem” (sequence of manufacturing steps) is too hard and gives little insight on function
  - Behavioral understanding fails
    - Subjecting to extreme conditions reveals little and may void warranty
    - Does not answer consistently to individual stimuli, nor to sequences of stimuli
    - There are stochastic variations between individuals
  - Ecological understanding fails
    - Difficult to observe in its native environment (kids’ hands)
    - Mass produced in little-understood automated factories
    - It evolved by competing with other products in the baffling Japanese market
  - Mathematical understanding fails
    - What differential equations does it obey? (Uh?)
A New Approach

● “Systems Technology” of T. Nipponensis
  - High-throughput experiments (get all the information you possibly can)
    • Decode the entire software and hardware
    • Take sequences of tamagotchi screen dumps under different conditions
    • Put 300 in a basket and shake them; make statistics of final state
  - Modeling (organize all the information you got)
    • Ignore the “folding” (manufacturing) problem
    • Ignore materials (it’s just something with buttons, display, and a program.)
    • Abstract until you find a conceptual model (ah-ha: it’s a stochastic automata).

● Do we understand what stochastic automata collectives can do?

Communicating Tamagotchi
Automata Collectives
Communicating automata: a graphical FSA-like notation for “finite state restriction-free π-calculus processes”. Interacting automata do not even exchange values on communication.

The stochastic version has rates on communications, and delays.

“Finite state” means: no composition or restriction inside recursion.
Analyzable by standard Markovian techniques, by first computing the “product automata” to obtain the underlying finite Markov transition system. [Buchholz]
Interacting Automata Transition Rules

@r !a

Interaction

a@r ?a !a

Delay

r

Current State

Delay

Transition
Groupies and Celebrities

Groupie (wants to be like somebody different)

- !a
- ?b
- !b

Celebrity (does not want to be like somebody else)

- !a
- ?b
- ?a

A stochastic collective of celebrities:

Unstable because within an A majority, an A has difficulty finding a B to emulate, but the few B's have plenty of A's to emulate, so the majority may switch to B. Leads to deadlock when everybody is in the same state and there is nobody different to emulate.

A stochastic collective of groupies:

Stable because as soon as an A finds itself in the majority, it is more likely to find somebody in the same state, and hence change, so the majority is weakened.

```
#A
#B
always equilibrium

#A
always eventually deadlock
```

```
directive sample 0.1 1000
directive plot A(); B()
new a@1.0:chan()
new b@1.0:chan()
let A() = do !a; A() or ?a; B()
and B() = do !b; B() or ?b; A()
run 100 of (A() | B())
```
A way to break the deadlocks: Groupies with just a few Celebrities

A tiny bit of “noise” can make a huge difference

Many Groupies

A few Celebrities

never deadlock
**Doped Groupies**

A similar way to break the deadlocks: destabilize the groupies by a small perturbation.

```plaintext
A technical term in microelectronics
```

---

```plaintext
(1) A technical term in microelectronics
```
**Hysteric Groupies**

We can get more regular behavior from groupies if they “need more convincing”, or “hysteresis” (history-dependence), to switch states.

```
directive sample 10.0 1000
directive plot Ga(); Gb()
new a@1.0:chan()
new b@1.0:chan()
let Ga() = do !a; Ga() or ?b; ?b; ?b;
Gb() = do !b; Gb() or ?a; ?a; ?a;
let Da() = !a; Da() and Db() = !b; Db()
run 100 of (Ga() | Gb())
run 1 of (Da() | Db())
```

A “solid threshold” to observe switching

(Still with doping)
Hysteric 3-Way Groupies

directive sample 3.0 1000
directive plot A(); B(); C()

new a@1.0:chan()
new b@1.0:chan()
new c@1.0:chan()

let A() = do !a; A() or ?c; ?c; C()
and B() = do !b; B() or ?a; ?a; A()
and C() = do !c; C() or ?b; ?b; B()

let Da() = !a; Da()
and Db() = !b; Db()
and Dc() = !c; Dc()

run 100 of (A() | B() | C())
run 1 of (Da() | Db() | Dc())
The Strength of Populations

At size 2N, on a shared channel, μ is N times stronger than λ: interaction easily wins over delay.

```
val lam = 1000.0
val mu = 1.0
new a@mu:chan
let A() = !a; A()
and B() = ?a; C()
and C() = delay@lam; B()
run 1000 of (A() | B())
```

Equilibrium
**Boolean Inverter Collectives**

- **b = not a**  
  - ![b = not a](image)
  - "signal"
  - in presence of a, b goes low
  - the high b state reinforces itself (as a population)

- **!b**  
  - ![!b](image)
  - "no signal"
  - in absence of a, b goes high

- **!a**
  - ![!a](image)
  - resistant

- **?a**
  - ![?a](image)
  - hysteresis

- **?b**
  - ![?b](image)
  - zero-point noise resistant

- **!c**
  - ![!c](image)
  - perfect rectifier

- **c = not b**
  - ![c = not b](image)
  - stimulus

- **?c**
  - ![?c](image)

**Examples and Code Snippets**

```plaintext
let SN(n:int, t:float, a:chan, tick:chan, tock:chan) = if n=0 then clock(t, tock) else ?tick; (S1(a, tock) | SN(n-1, t, a, tick, tock))

let raisingfalling(a:chan, n:int, t:float) = run (clock(t, tick) | SN(n, t, a, tick, tock))

let step(n:int) = if n<=0 then !tick; clock(t, tick) else delay@d; step(n-1)

let S1(a:chan, tock:chan) = do !a; S1(a, tock) or ?tock; ()
```
new $c@\mu$ new $\text{stop}@1.0$

$A_{\text{free}} =$
(new $\text{rht}@\lambda; !c(\text{rht}); A_{\text{brht}}(\text{rht}))
+ ?c(\text{lft}); A_{\text{blft}}(\text{lft})

$A_{\text{blft}}(\text{lft}) =$
(new $\text{rht}@\lambda; !c(\text{rht}); A_{\text{bound}}(\text{lft},\text{rht}))

$A_{\text{brht}}(\text{rht}) =$
?c(\text{lft}); $A_{\text{bound}}(\text{lft},\text{rht})$

$A_{\text{bound}}(\text{lft},\text{rht}) = ?\text{stop}$

**Communicating Automata**
Bound output $!c(^r)$ and input $?c(l)$ on automata transitions to model complexation
Bidirectional Polymerization

Circular Polymer Lengths

Scanning and counting the size of the circular polymers (by a cheap trick).
Polymer formation is complete within 10t; then a different polymer is scanned every 100t.

100x$A_{\text{free}}$, initially.
The height of each rising step is the size of a separate circular polymer
(Unbiased sample of nine consecutive runs.)
new $c@\mu$

$$A_{\text{free}} = (\text{new } lft@\lambda; lft; A_{\text{blft}}(lft)) + \text{?c(rht); } A_{\text{brht}}(rht)$$

$$A_{\text{blft}}(lft) = lft; A_{\text{free}} + \text{?c(rht); } A_{\text{bound}}(lft, rht)$$

$$A_{\text{brht}}(rht) = \text{?rht; } A_{\text{free}}$$

$$A_{\text{bound}}(lft, rht) = lft; A_{\text{brht}}(rht)$$
The Law of Mass Interaction
The speed of interaction\(^\dagger\) is proportional to the number of possible interactions.

\[
[D]' = -\lambda [D]
\]
\[
[E]' = \lambda [D]
\]

Decay

Exponential Decay law
Rate of change proportional to number of possible decays.

Mass interaction

Interaction Law generalizes Decay Law

Mass Interaction law
Rate of change proportional to number of possible interactions

\[
[A]' = -\lambda [A] [B]
\]
\[
[B]' = -\lambda [A] [B]
\]
\[
[AB]' = \lambda [A] [B]
\]

\(\dagger\) speed of interaction (formally definable) = number of interactions over time
not proportional to the number of interacting processes!

\([P]\) is the number of processes \(P\) (this is informal; it is only meaningful for a set of processes offering a given action, but a set of such processes can be counted and plotted)

Chemical Law of Mass Action
http://en.wikipedia.org/wiki/Chemical_kinetics

The speed of a chemical reaction is proportional to the activity of the reacting substances.
(Activity = concentration, for well-stirred aqueous medium)
(Concentration = number of moles per liter of solution)
(Mole = 6.022141×10\(^{23}\) particles)
Activity and Speed
stochastic algebras disagree!

The speed of interaction is proportional to the number of possible interactions.

The activity (= “concentration”) on a channel is the number of possible interactions on that channel.

The speed of interaction on a channel, is the activity multiplied by the base rate of the channel.

The activity on a channel is the number of possible interactions on that channel.

The speed of interaction on a channel, is the activity multiplied by the base rate of the channel.

[c activity: 1
  speed: \( \lambda \)]

[c activity: 2
  speed: \( 2\lambda \)]

[c activity: 4
  speed: \( 4\lambda \)]

The mass interaction law [Buchholz] [Priami-Regev-Shapiro-Silverman] is compatible with chemistry [Gillespie] and incompatible with any other stochastic algebra in the literature! (including [Priami]; see [Hermanns])

Other algebras assign rates to actions, not channels, with speed laws:

\[ 2\lambda \times 2\lambda = 4\lambda^2 \]

\[ \max(2\lambda, 2\lambda) = 2\lambda \] [Goetz]

\[ \min(2\lambda, 2\lambda) = 2\lambda \] [Priami]

\[ 1/(1/(2\lambda) + 1/(2\lambda)) = \lambda \] [PEPA]

\[ 2\lambda \times 1 = 2\lambda \] (passive inputs)
Forbidden (Mix) interactions

Assume each process $P$ is in restricted-sum-normal-form. For each channel $x$:

- $\text{In}(x,P) = \text{Num of active } ?x \text{ in } P$
- $\text{Out}(x,P) = \text{Num of active } !x \text{ in } P$
- $\text{Mix}(x,P) = \text{In}(x,P) \times \text{Out}(x,P)$
  - #interactions that cannot happen in a given summation $P$
- $\text{In}(x) = \text{Sum } P \text{ of } \text{In}(x,P)$
- $\text{Out}(x) = \text{Sum } P \text{ of } \text{Out}(x,P)$
- $\text{Mix}(x) = \text{Sum } P \text{ of } \text{Mix}(x,P)$
  - total #interactions that cannot happen

The global **Activity** on channel $x$:

$$\text{Act}(x) = (\text{In}(x) \times \text{Out}(x)) - \text{Mix}(x)$$
- total cross product of inputs and outputs minus total #interactions that cannot happen

The global **speed** of interaction on a channel $x$:

$$\text{speed}(x) = \text{Act}(x) \times \text{rate}(x)$$

The speed of interaction is proportional to the number of possible interactions.

But a process cannot interact with itself.

Possible Interactions

![Diagram showing possible interactions and calculations for two processes A and B.](image-url)
Deriving Back Interaction Laws

The mass action law:

\[ [A]' = -\text{speed}(c) = -\lambda \text{Act}(c) \]
\[ \text{Act}(c) = (\text{In}(c)\times \text{Out}(c)) - \text{Mix}(c) \]
\[ = ([A]\times [B]) - 0 \]

hence \[ [A]' = -\lambda [A][B] \]

The mixed interaction law:

\[ [A]' = -\text{speed}(c) = -\lambda \text{Act}(c) \]
\[ \text{Act}(c) = (\text{In}(c)\times \text{Out}(c)) - \text{Mix}(c) \]
\[ = ([A]\times [A]) - [A] = [A]\times([A]-1) \]

hence \[ [A]' = -\lambda [A][A]-1 \]

The decay law:

\[ [A]' = \sum(c_i) -\text{speed}(c_i) \]
\[ = \sum(c_i) - \lambda \text{Act}(c_i) \]
\[ \text{Act}(c_i) = (\text{In}(c_i)\times \text{Out}(c_i)) - \text{Mix}(c_i) \]
\[ = (1\times1) - 0 = 1 \]

hence \[ [A]' = -\lambda [A] \]

\[ \text{Act}(x) = (\text{In}(x)\times \text{Out}(x)) - \text{Mix}(x) \]
Conclusions
Conclusions

• **Stochastic Collectives**
  - Complex global behavior from simple components
  - Emergence of collective functionality from “non-functional” components
  - (C.f. “swarm intelligence”: simple global behavior from complex components)

• **Artificial Biochemistry**
  - Stochastic collectives with Law of Mass Interaction kinetics
  - Connections to classical Markov theory, chemical Master Equation, and Rate Equation

• **The agent/automata/process point of view**
  - “Individuals” that transition between states
    (vs. transmutation between “unrelated” chemical species)
  - More appropriate for Systems Biology
  - Stochastic $\pi$-calculus (SPiM) for investigating stochastic collectives
    • Restriction+Communication $\Rightarrow$ Polymerization: FSA that “stick together”