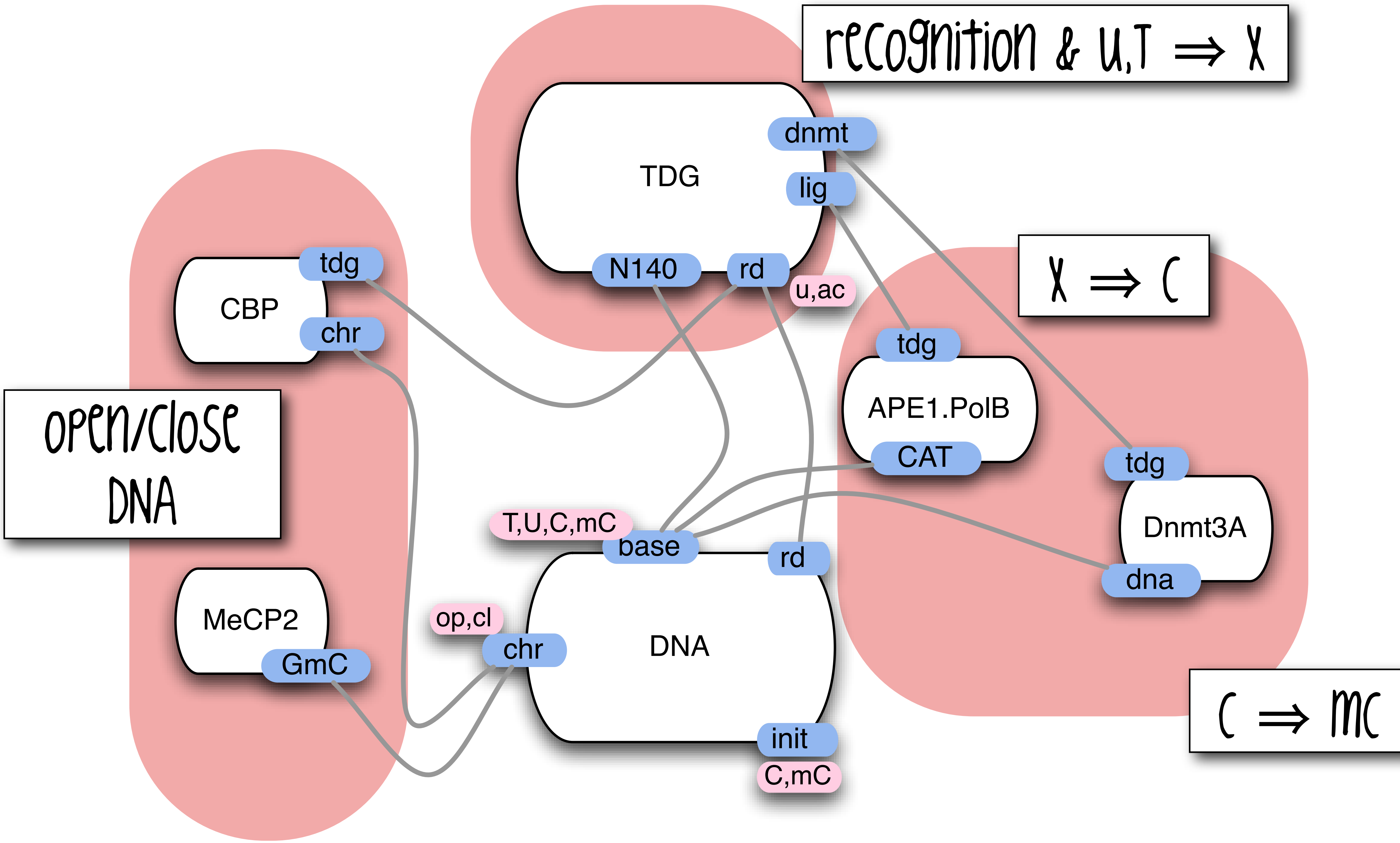
rule-based/energy-based

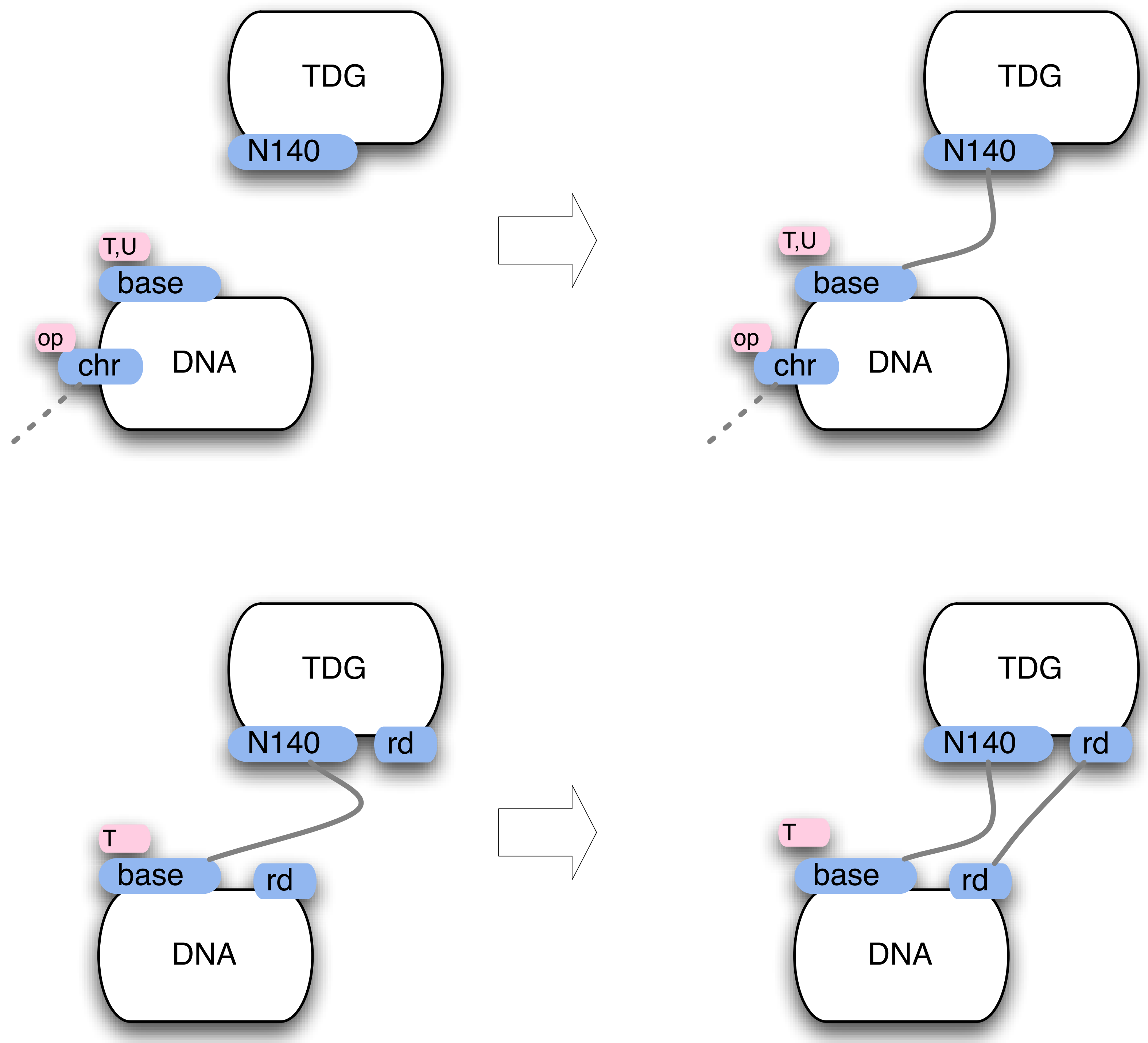
WCSB, June 2011

The Kappa language

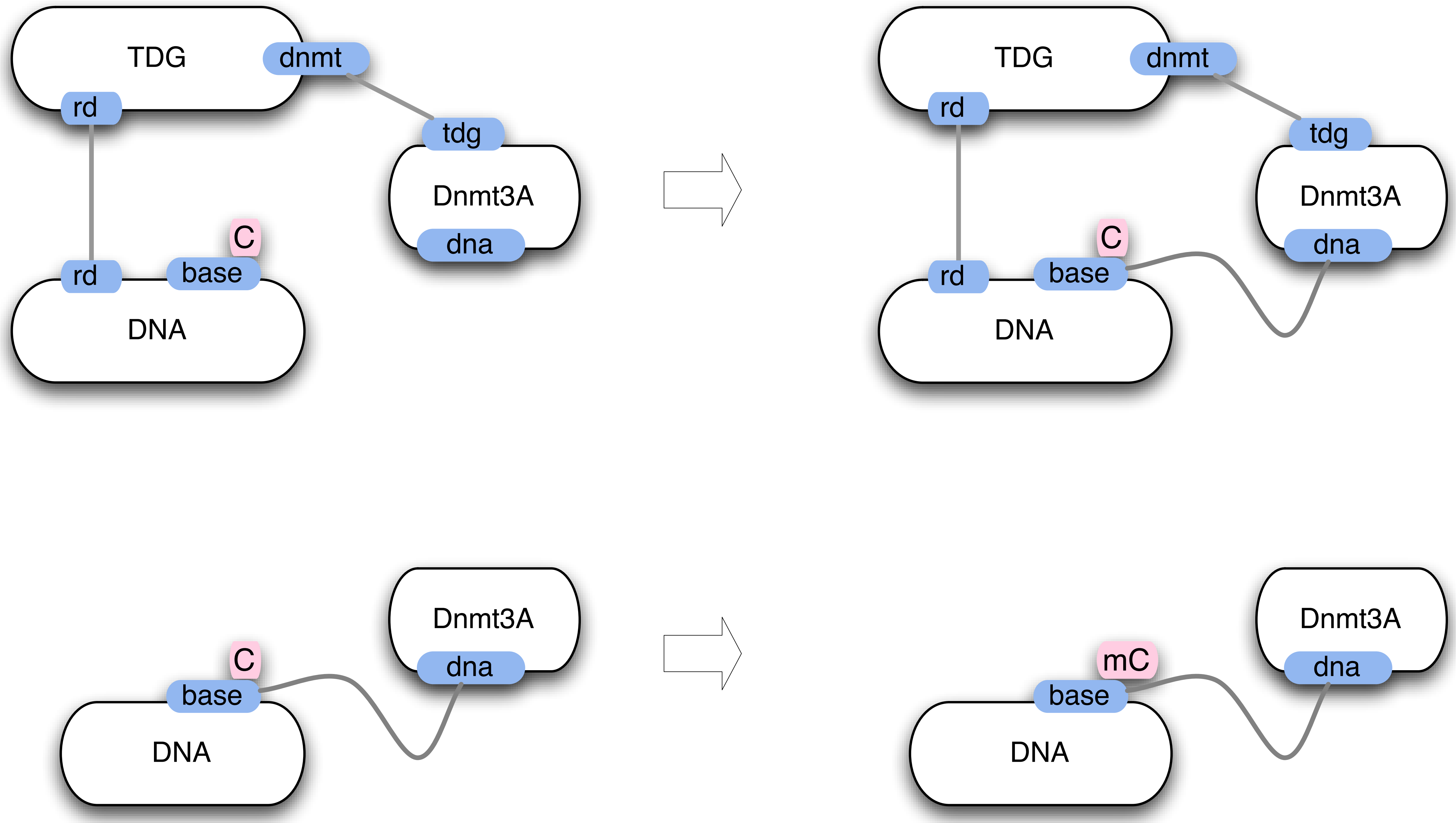
Combinatorial dynamics



TDG-DNA: mismatch recognition



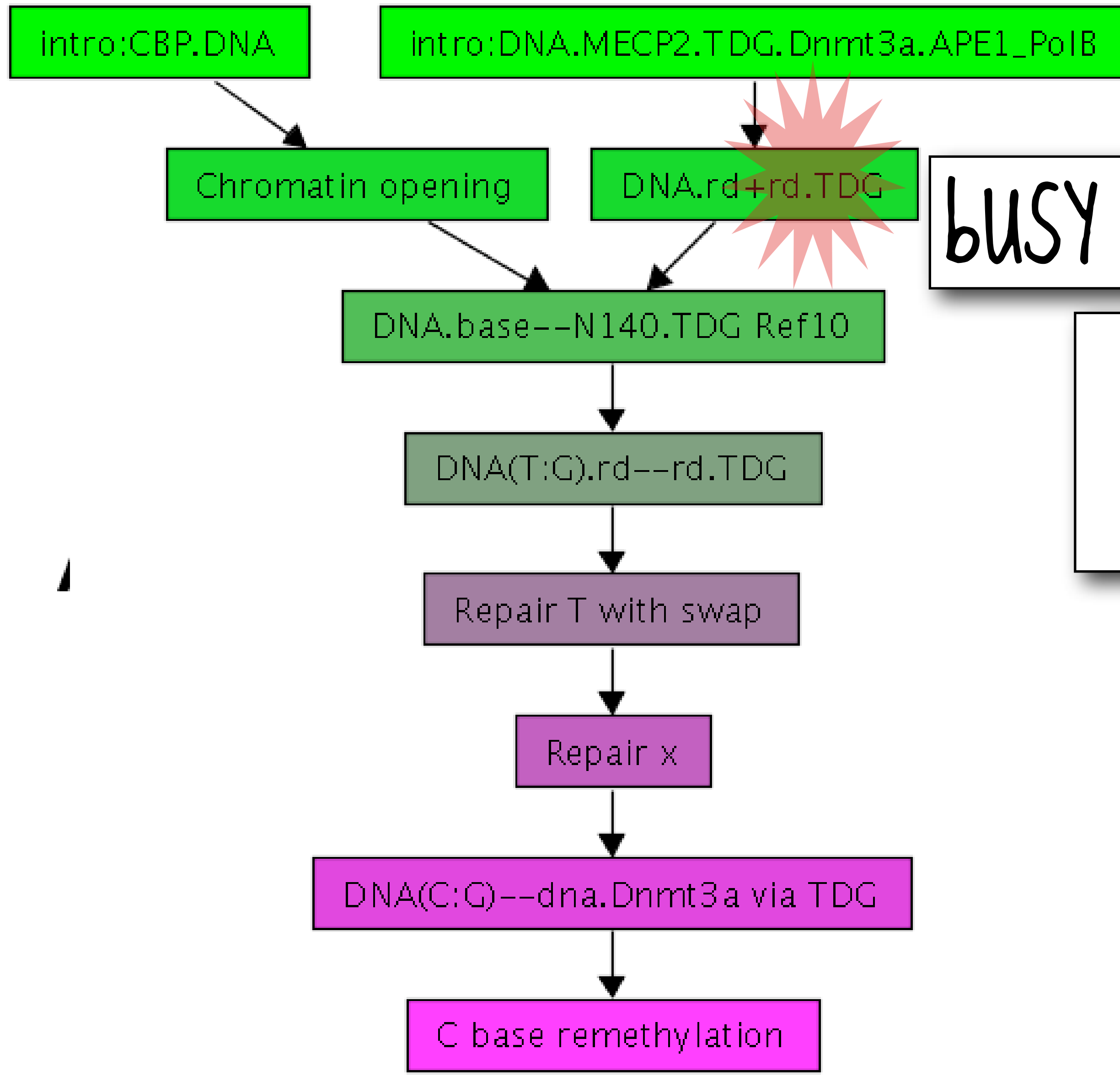
TDG:DNA-Dnmt3A C to mC



memory in transient assembly !

causal summaries

story := incompressible causal trace
-
"everything matters"
-
causal debugging of the model

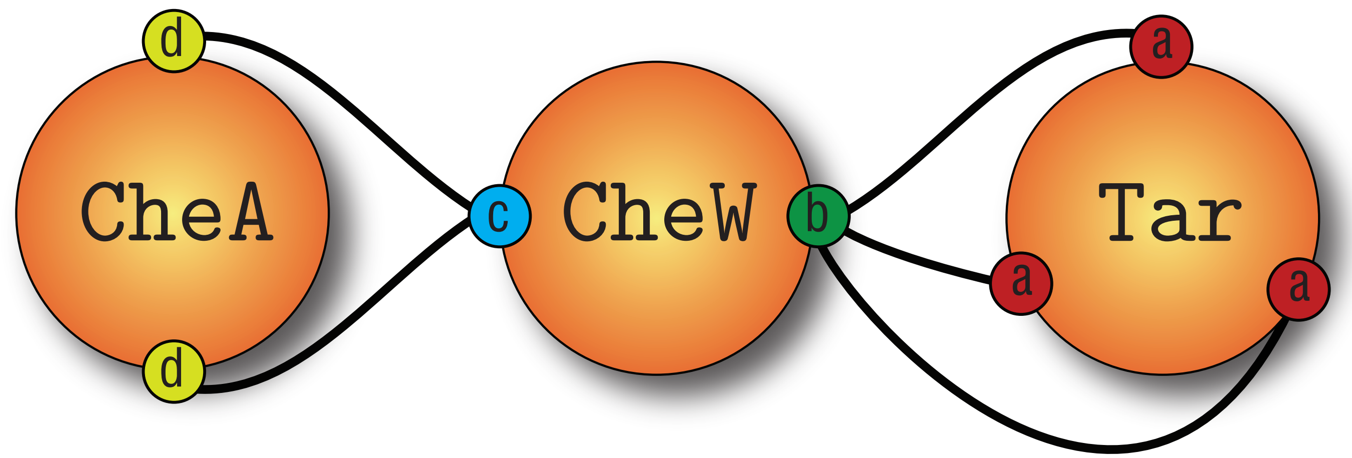


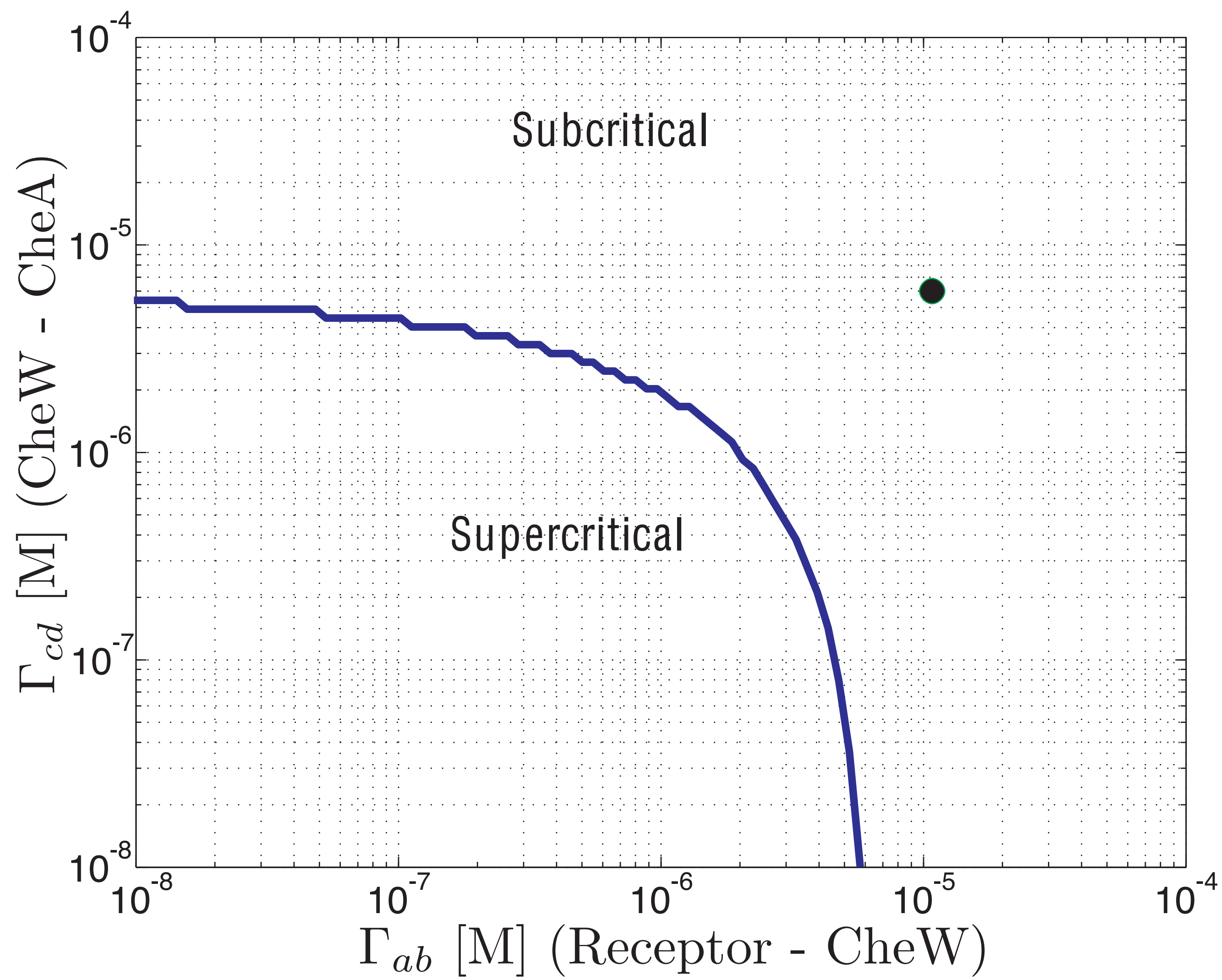
busy TDG

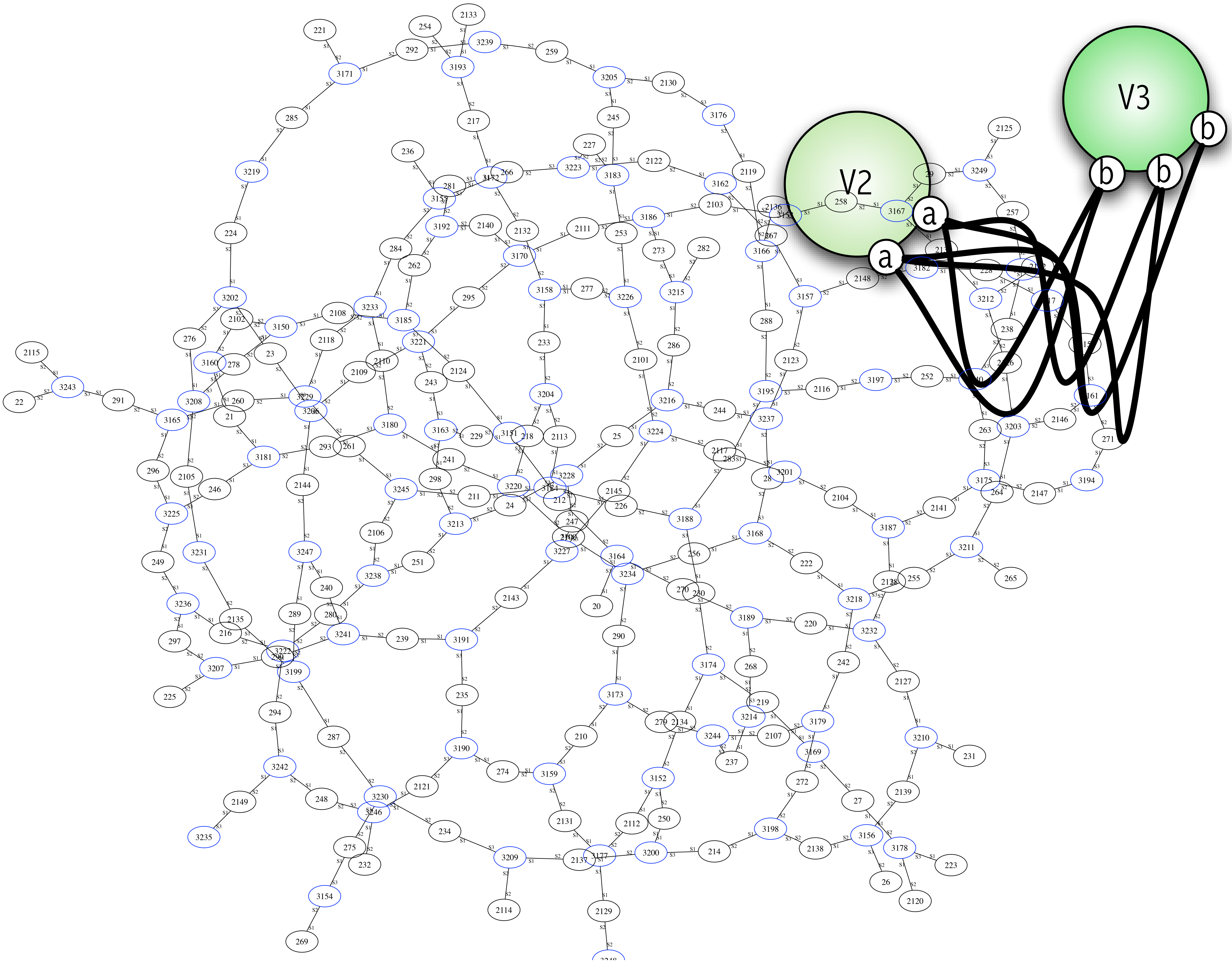
about 10% indirect repair

energy 1

percolation control


CheA
CheW
Tar
d
d
c
b
a
a
a

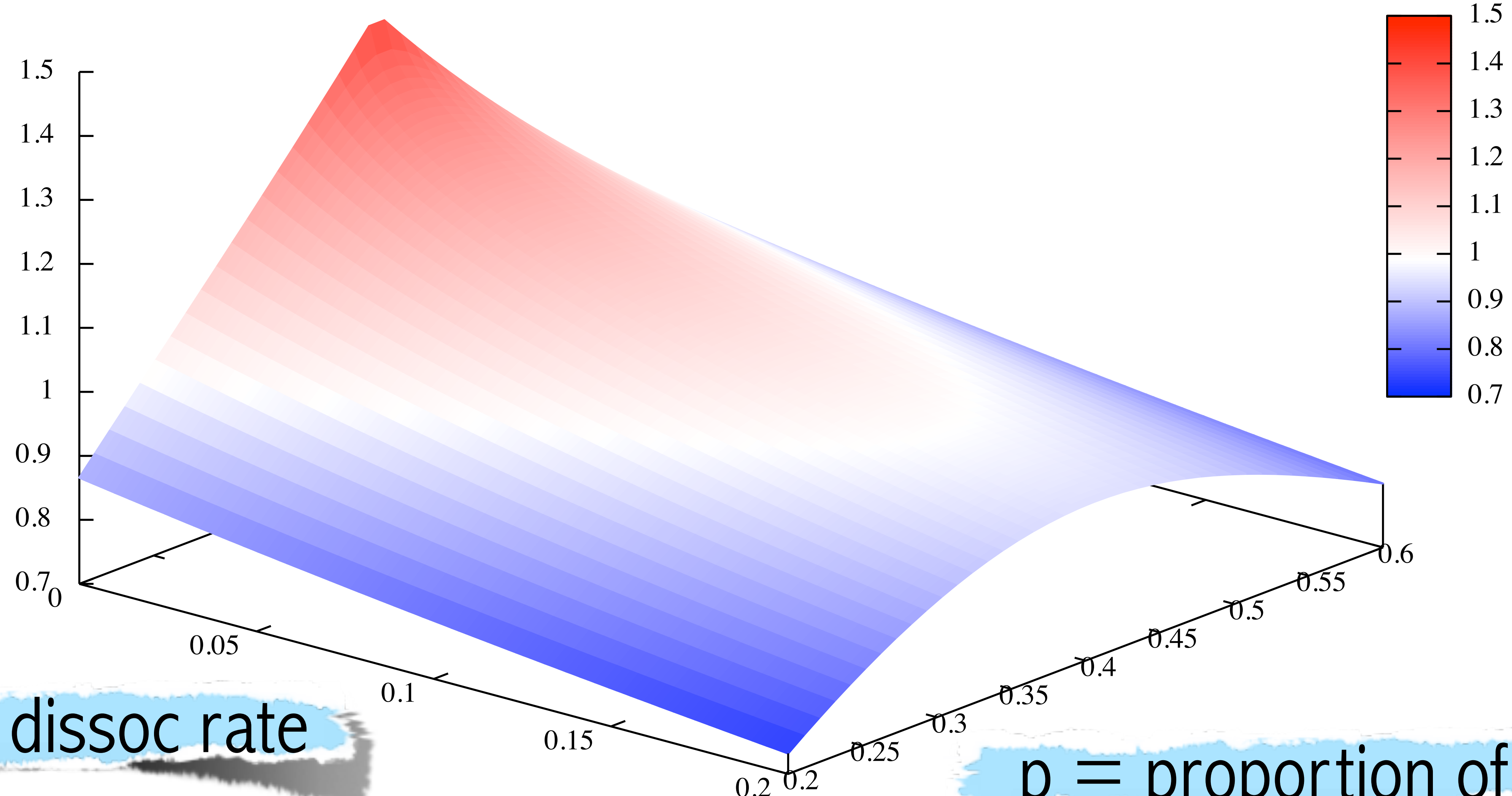

Subcritical
Supercritical
Γ_{cd} [M] (CheW - CheA)
Γ_{ab} [M] (Receptor - CheW)
10^{-4}
10^{-5}
10^{-6}
10^{-7}
10^{-8}



Monday, 6 June 2011

Control?

$$\lambda(p, K) := \frac{2 + p + K - \sqrt{(2 + p + K)^2 - 24p(1-p)}}{2\sqrt{3p(1-p)}}$$



K = ab dissoc rate

p = proportion of 3b

Equilibrium/Cooperative case

$$\rho(x, y) \quad = \quad \frac{\Gamma_{i,j}}{(v_A - i)(v_B - j)}$$

$$\Gamma \text{ has an equilibrium iff } \Gamma = \Gamma_A \Gamma_B^t \text{ for some } \Gamma_A \in \mathbb{R}_+^{v(A)},\ \Gamma_B \in \mathbb{R}_+^{v(B)}$$

$$V(x) \quad = \quad \sum_{u \in x} \ln \frac{\prod_{0 \leq i < o(u)} \Gamma_{\tau(u)}(i)}{[o(u); v_{\tau(u)}]}$$

deterministic approx.

$$A'_i = -\mathbf{1}_{i<v_A} \sum_{0\le j<v_B} \gamma^+_{i,j}(v_A - i)(v_B - j)A_i B_j$$
$$- \mathbf{1}_{i>0} \sum_{0<j\le v_B} \gamma^-_{i-1,j-1} A_i : B_j$$
$$+ \mathbf{1}_{i>0} \sum_{0<j\le v_B} \gamma^+_{i-1,j-1}(v_A - i + 1)(v_B - j + 1)A_{i-1}B_{j-1}$$
$$+ \mathbf{1}_{i<v_A} \sum_{0\le j<v_B} \gamma^-_{i,j} A_{i+1} : B_{j+1}$$

$$A_i' = \mathbf{1}_{\{i<v_A\}} \cdot (\gamma_i^-(i+1)A_{i+1} - \gamma_i^+(v_A - i)A_i n_b^f)$$
$$+ \mathbf{1}_{\{i>0\}} \cdot (-\gamma_{i-1}^- i A_i + \gamma_{i-1}^+(v_A - i + 1)A_{i-1} n_b^f)$$

$$\gamma_{i,j}^- = \gamma_i^- \qquad \gamma_{i,j}^+ = \gamma_i^+$$

references:
Chaos 20(3) - 2010
PNAS 106 - 2009

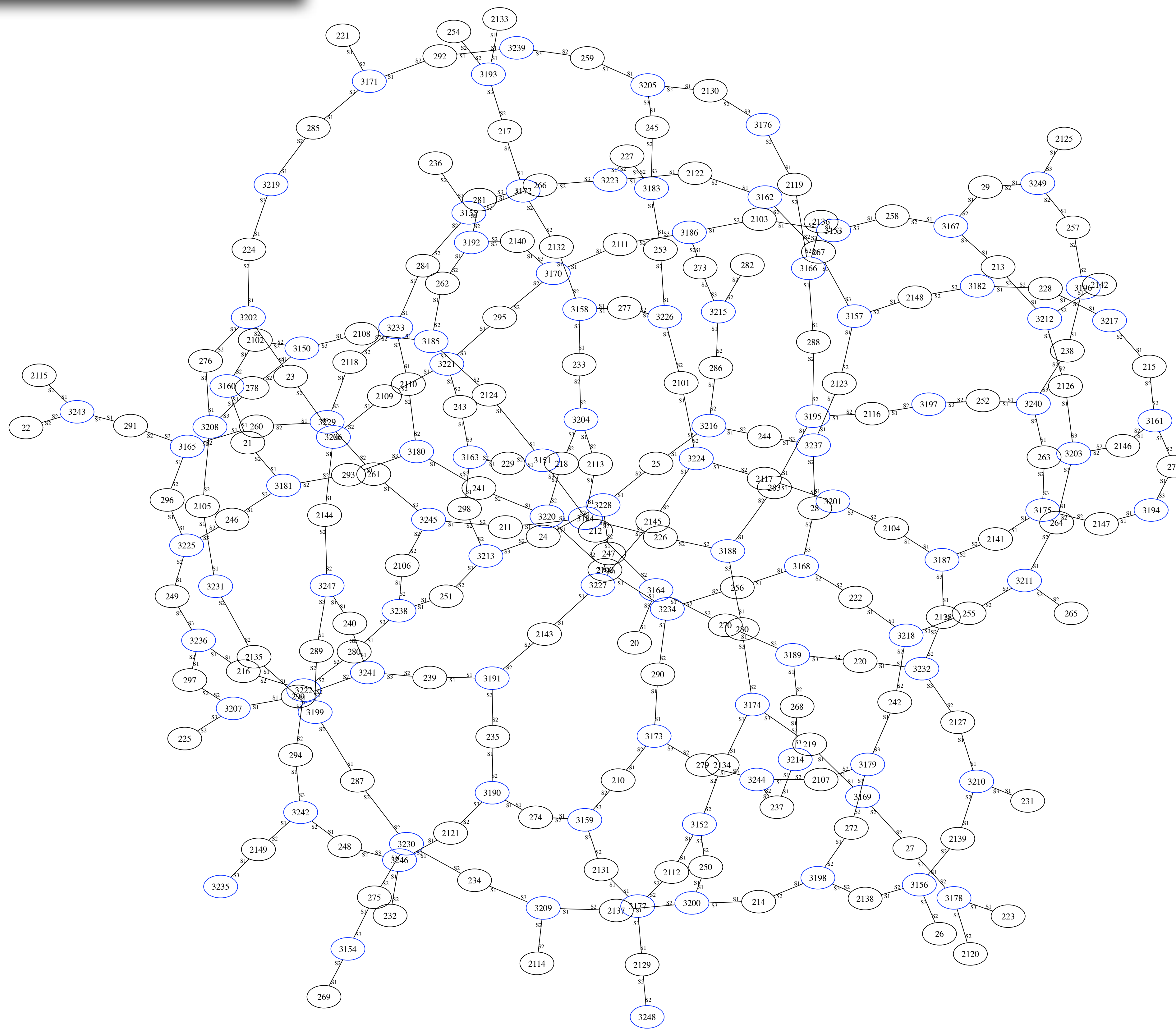
self-consistent / dimension-less

$$a_i = A_i/N,\ a = n_A/N,\ b = n_B/N,\ K_i := \frac{\prod_{0\le k<i} \Gamma_k}{\binom{v_A}{i} N^i}$$

$$K_i \cdot a_i \quad = \quad (a - \sum_{0<k\le v_A} a_k) \cdot (v_B b - \sum_{0\le k\le v_A} k a_k)^i$$

language Kappa/KaSim

Kasim - Snapshot



agents & parameters

```
%agent: B(b1,b2)
%agent: A(a1,a2,a3)

%var: 'vol' 100
%var: 'k_on' 0.1/'vol'

%var: 'k_off'       2
%var: 'k_off_vee'  1/5  * 'k_off'
%var: 'k_off_tee'  1/50 * 'k_off'

%var: 'n_A' (1000 * 'vol')
%var: 'n_B' (1500 * 'vol')

%init: 'n_A' (A(a1,a2,a3))
%init: 'n_B' (B(b1,b2))
```

rules ...

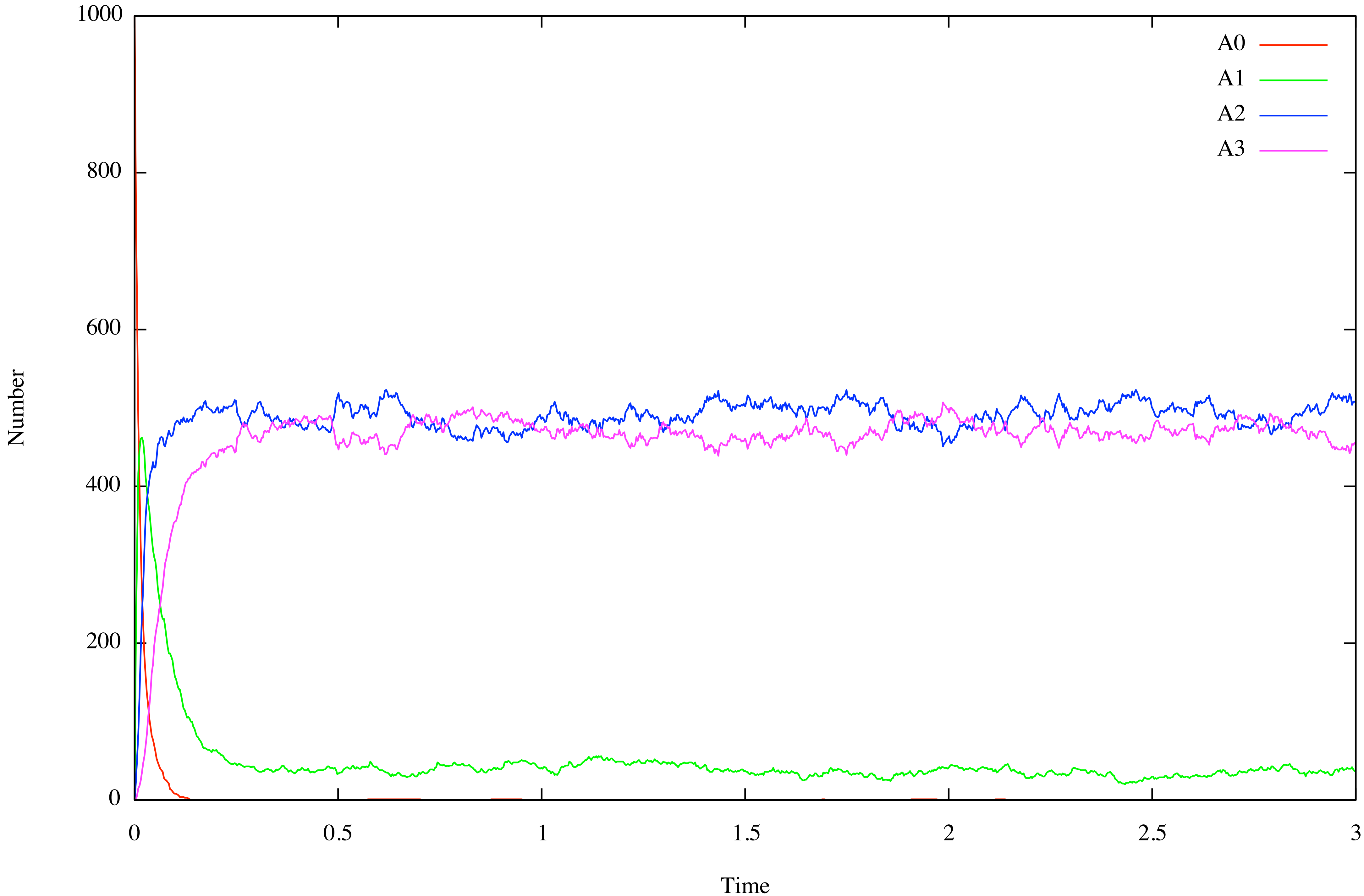
```
'b2-a1-11' B(b2), A(a1,a2!_,a3!_) -> B(b2!0), A(a1!0,a2!_,a3!_)@ 'k_on'
'b2-a1-10' B(b2), A(a1,a2!_,a3  ) -> B(b2!0), A(a1!0,a2!_,a3  )@ 'k_on'
'b2-a1-01' B(b2), A(a1,a2  ,a3!_) -> B(b2!0), A(a1!0,a2  ,a3!_)@ 'k_on'
'b2-a1-00' B(b2), A(a1,a2  ,a3  ) -> B(b2!0), A(a1!0,a2  ,a3  )@ 'k_on'

'b2 a1-11' B(b2!0), A(a1!0,a2!_,a3!_) -> B(b2), A(a1,a2!_,a3!_)@ 'k_off_tee'
'b2 a1-10' B(b2!0), A(a1!0,a2!_,a3  ) -> B(b2), A(a1,a2!_,a3  )@ 'k_off_vee'
'b2 a1-01' B(b2!0), A(a1!0,a2  ,a3!_) -> B(b2), A(a1,a2  ,a3!_)@ 'k_off_vee'
'b2 a1-00' B(b2!0), A(a1!0,a2  ,a3  ) -> B(b2), A(a1,a2  ,a3  )@ 'k_off'
```

observables ...

```
%var: 'A0' A(a1,a2,a3)

%var: 'a1' A(a1!_,a2,a3)
%var: 'a2' A(a1,a2!_,a3)
%var: 'a3' A(a1,a2,a3!_)

%var: 'A1' 'a1' + 'a2' + 'a3'

%var: 'a1a2' A(a1!_,a2!_,a3)
%var: 'a1a3' A(a1!_,a2,a3!_)
%var: 'a2a3' A(a1,a2!_,a3!_)

%var: 'A2' 'a1a2' + 'a1a3' + 'a2a3'

%var: 'A3' A(a1!_,a2!_,a3!_)

%plot: 'A0'
%plot: 'A1'
%plot: 'A2'
%plot: 'A3'
```

KaSim - Simulations

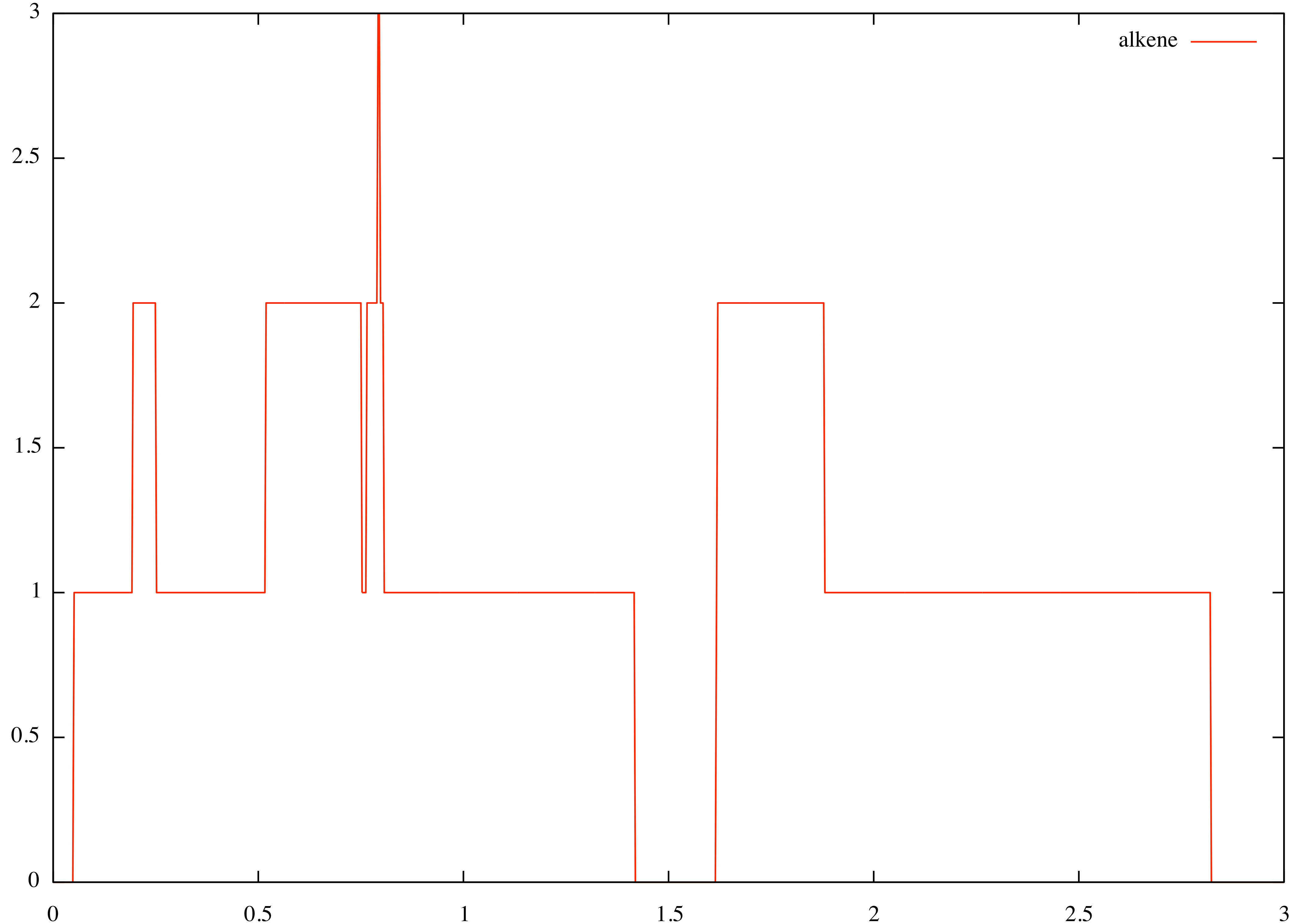
29/0/2011 percoop



alkenes

```
# double bonds/alkenes [2;3] = 6
%var: 'Ba1a2' B(b1!1,b2!2),A(a1!1,a2!2)
%var: 'Ba2a1' B(b1!1,b2!2),A(a1!2,a2!1)
%var: 'Ba1a3' B(b1!1,b2!2),A(a1!1,a3!2)
%var: 'Ba3a1' B(b1!1,b2!2),A(a1!2,a3!1)
%var: 'Ba2a3' B(b1!1,b2!2),A(a2!1,a3!2)
%var: 'Ba3a2' B(b1!1,b2!2),A(a2!2,a3!1)

%var: 'alkene' 'Ba1a2'+ 'Ba2a1' + 'Ba1a3' + 'Ba3a1' + 'Ba2a3' + 'Ba3a2'

%plot: 'alkene'
```

alkenes



energy II

stat phys of communicating processes

idea 1:
distributed task = deadlock-escape + local heuristics

reversible communicating processes

$$\begin{array}{ll} \Theta, \Gamma \cdot (p, q) & \to^f \Theta, \Gamma 0 \cdot p, \Gamma 1 \cdot q \\ \Theta, \Gamma \cdot (ap + q), \Gamma' \cdot (a'p' + q') & \to^s \Theta, \Gamma(a, \Gamma', q) \cdot p, \Gamma'(a', \Gamma, q') \cdot p' \end{array}$$

idea II:
exhaustive search/probabilistic equilibrium
= must succeed + almost surely finite time

probabilistic reversible communicating processes

$$\begin{aligned}
\Theta, \Gamma \cdot (p, q) &\rightarrow^{f} \Theta, \Gamma 0 \cdot p, \Gamma 1 \cdot q \\
\Theta, \Gamma \cdot (ap + q), \Gamma' \cdot (a'p' + q') &\rightarrow^{s} \Theta, \Gamma(a, \Gamma', q) \cdot p, \Gamma'(a', \Gamma, q') \cdot p'
\end{aligned}$$

$$\rho(x, y) = \frac{k_a^\star}{k_a} \cdot \frac{1}{\mu(ap)} \cdot \frac{1}{\mu(a'p')}$$

Probabilistic equilibrium (CTMC) =
detailed balance/thermo consistency+ convergence

$$p(x) \quad = \quad \frac{e^{-V(x)}}{\sum_y \qquad e^{-V(y)}}$$

aka grand canonical ensemble

explosive growths

		event horizon	nb of complete matchings
$q \to^{f}$	$0 \cdot p(a), 1 \cdot p(\bar{a})$	$1, 1$	1
$\to^{fs}$	$0a0 \cdot p(a), 0a1 \cdot p(a), 1\bar{a}0 \cdot p(\bar{a}), 1\bar{a}1 \cdot p(\bar{a})$	$2, 2$	2
$=$	$0a0 \cdot a(p(a), p(a)), 0a1 \cdot a(p(a), p(a)),$		
	$1\bar{a}0 \cdot \bar{a}(p(\bar{a}), p(\bar{a})), 1\bar{a}1 \cdot \bar{a}(p(\bar{a}), p(\bar{a}))$		
$\to^{fs}$	$0a0a0 \cdot p(a), 0a0a1 \cdot p(a), 0a1a0 \cdot p(a), 0a1a1 \cdot p(a),$	$4, 4$	$4!$
	$1\bar{a}0\bar{a}0 \cdot p(\bar{a}), 1\bar{a}0\bar{a}1 \cdot p(\bar{a}), 1\bar{a}1\bar{a}0 \cdot p(\bar{a}), 1\bar{a}1\bar{a}1 \cdot p(\bar{a})$		
$\ldots$			
$\to^{fs}$	$\prod_{w \in 2^k} 0w(a) \cdot p(a), \prod_{w \in 2^k} 1w(\bar{a}) \cdot p(\bar{a})$	$2^k, 2^k$	$2^k!$

is there a "concurrent" potential that controls the above?

a "concurrent" potential:

$$V_2(p) = \sum_{\theta \in p, \mathbf{a} \in \mathcal{A}^{\leq \alpha}} \langle \xi_{\mathbf{a}}, \text{nb of } \mathbf{a} \text{ in the stack of } \theta \rangle$$

fork/energy balance

$$\Theta, \Gamma \cdot (p, q) \to^f \Theta, \Gamma 0 \cdot p, \Gamma 1 \cdot q$$
$$\Delta V_1 = V_1(\Gamma) + \eta = \ln(k^\star / k)$$

$$k \;=\; \exp(-\eta \,-\, V_1(\Gamma))$$

synch

$$\Theta, \Gamma \cdot (ap + q), \Gamma' \cdot (a'p' + q') \to^s \Theta, \Gamma(a, \Gamma', q) \cdot p, \Gamma'(a', \Gamma, q') \cdot p'$$

$$\Delta V_1 = \epsilon_a$$

$$k_a \;=\; \exp(-\epsilon_a)$$

Sufficient Condition for Equilibrium

Proposition 1 *Let p_0 be a α-way synchronising process with max thread creation $\leq 1+\delta$ with $\delta > 0$, and suppose $\epsilon_m := \min \epsilon_{\boldsymbol{a}} > \delta\alpha^2 \ln(4(\delta+1))$, then:*

$$Z(p_0) := \sum_{q\in\Omega(p_0)} e^{-V(q)} < +\infty$$

where $\Omega(p_0)$ is the set of processes reachable from $\varnothing \cdot p_0$.

Corollary 1 *Consider a reversible process $\varnothing \cdot p_0$ equipped with rate constants $k^{\pm}_{\boldsymbol{a}}$, $k^{\pm}_{f}$ compatible with the V_2 potential; if $\epsilon_m > \delta\alpha^2 \ln(4(\delta+1))$, then p_0 has an equilibrium on $\Omega(p_0)$ defined as $\pi(q) = e^{-V(q)}/Z(p_0)$.*

Idea III:
energy-based programming/distributed Metropolis
code = statics/potential + transition/moves + compatible kinetics

$$\mathrm{argmax}\,\xi.\,\sum_{q\in\partial X} p^\star(\xi,q) = \int \mathbf{1}_{\partial X}\,dp^\star$$

machine learning

Modeling complex systems in the life sciences

Clean and powerful mathematical/computational tools

Combinatorial dynamics

Causality analysis

New means of encoding info

Self-organised energy-based dynamics

... stochastic machine learning

kappalanguage.org - tools

rulebase.org on-line playable models

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