Rate Equations for Graphs

Vincent Danos[1] Tobias Heindel[2]
Ricardo Honorato-Zimmer[3] Sandro Stucki[4]

[1]CNRS/ENS-PSL/INRIA, France [2]TU Berlin, Germany [3]CINV, Chile [4]GU/Chalmers, Sweden

Virtual CMSB 2020 – Konstanz – 23 Sep 2020

`sandro.stucki@gu.se` `@stuckintheory`

UNIVERSITY OF GOTHENBURG

CHALMERS
UNIVERSITY OF TECHNOLOGY

Mean field approximations (MFAs)

Question

What is the expected value $\mathbb{E}(F)$ of some observable F on a CTMC?

Photo: J Ligero & I Barrios 2013 (Wikipedia).

Mean field approximations (MFAs)

Question

What is the expected value $\mathbb{E}(F)$ of some observable F on a CTMC?

Example (reproduction)

2 🐇 $\xrightharpoonup{k_\alpha}$ 3 🐇

Mean field approximations (MFAs)

Question

What is the expected value $\mathbb{E}(F)$ of some observable F on a CTMC?

Example (reproduction)

$$2B \xrightarrow{k_\alpha} 3B$$

Mean field approximations (MFAs)

Question

What is the expected value $\mathbb{E}(F)$ of some observable F on a CTMC?

Example (reproduction)

$$2B \xrightarrow{k_\alpha} 3B$$

The function $[B]$ counts the number of occurrences of B.

$$\frac{d}{dt}\,\mathbb{E}[B] = k_\alpha\,\mathbb{E}[2B] = k_\alpha\,\mathbb{E}([B]([B]-1)) \qquad \text{(meanfield)}$$

Mean field approximations (MFAs)

Question

What is the expected value $\mathbb{E}(F)$ of some observable F on a CTMC?

Example (reproduction)

$$2B \xrightarrow{k_\alpha} 3B$$

The function $[B]$ counts the number of occurrences of B.

$$\begin{aligned} \tfrac{d}{dt}\,\mathbb{E}[B] &= k_\alpha\,\mathbb{E}[2B] = k_\alpha\,\mathbb{E}([B]([B]-1)) && \text{(meanfield)} \\ &\simeq k_\alpha\,\mathbb{E}([B][B]) \simeq k_\alpha\,\mathbb{E}[B]\,\mathbb{E}[B] && \text{(approximation)} \end{aligned}$$

Mean field approximations (MFAs)

Question

What is the expected value $\mathbb{E}(F)$ of some observable F on a CTMC?

Example (reproduction)

$$2B \xrightarrow{k_\alpha} 3B$$

The function $[B]$ counts the number of occurrences of B.

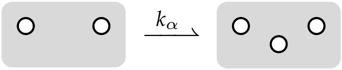
$$\frac{d}{dt}\,\mathbb{E}[B] = k_\alpha\,\mathbb{E}[2B] = k_\alpha\,\mathbb{E}([B]([B]-1)) \quad \text{(meanfield)}$$

$$\simeq k_\alpha\,\mathbb{E}([B][B]) \simeq k_\alpha\,\mathbb{E}[B]\,\mathbb{E}[B] \quad \text{(approximation)}$$

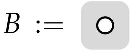
$$\frac{d}{dt}[B] \simeq k_\alpha [B]^2 \quad \text{(thermodynamic limit)}$$

CRNs are Graph Transformation Systems (GTSs)

Reaction/rule

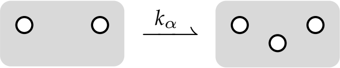


Observable



CRNs are Graph Transformation Systems (GTSs)

Reaction/rule



Observable

$B :=$ 

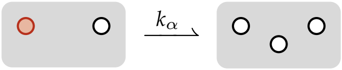
MFA/Rate equation

$\frac{d}{dt}$  $=$

$$\frac{d}{dt}[B] =$$

CRNs are Graph Transformation Systems (GTSs)

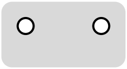
Reaction/rule



Observable

$B :=$ 

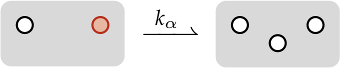
MFA/Rate equation

$\frac{d}{dt}$  $= -k_\alpha$  $+ \cdots$

$$\frac{d}{dt}[B] = -k_\alpha[2B] + \cdots$$

CRNs are Graph Transformation Systems (GTSs)

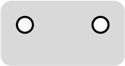
Reaction/rule



Observable

$B :=$ 

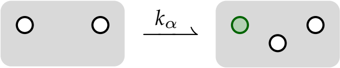
MFA/Rate equation

$\frac{d}{dt}$  $= -2k_\alpha$  $+ \cdots$

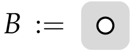
$$\frac{d}{dt}[B] = -2k_\alpha[2B] + \cdots$$

CRNs are Graph Transformation Systems (GTSs)

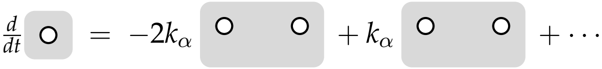
Reaction/rule



Observable



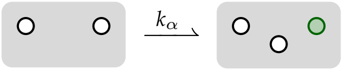
MFA/Rate equation



$$\frac{d}{dt}[B] = -2k_\alpha[2B] + k_\alpha[2B] + \cdots$$

CRNs are Graph Transformation Systems (GTSs)

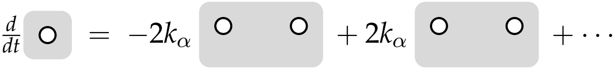
Reaction/rule



Observable

$B :=$ 

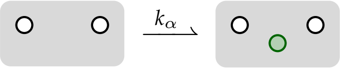
MFA/Rate equation



$$\frac{d}{dt}[B] = -2k_\alpha[2B] + 2k_\alpha[2B] + \cdots$$

CRNs are Graph Transformation Systems (GTSs)

Reaction/rule



Observable

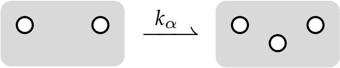
$B :=$ 

MFA/Rate equation

$$\frac{d}{dt}[B] = -2k_\alpha[2B] + 3k_\alpha[2B]$$

CRNs are Graph Transformation Systems (GTSs)

Reaction/rule



Observable

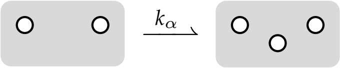
$B :=$ 

MFA/Rate equation

$$\frac{d}{dt}[B] = k_\alpha [2B]$$

CRNs are Graph Transformation Systems (GTSs)

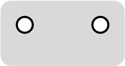
Reaction/rule



Observable

$B :=$ 

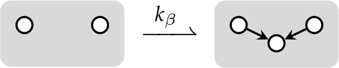
MFA/Rate equation

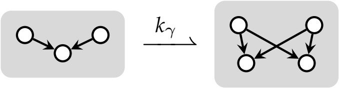
$\frac{d}{dt}$  $= k_\alpha$  $\simeq k_\alpha$  

$$\frac{d}{dt}[B] = k_\alpha[2B] \simeq k_\alpha[B]^2$$

Bunnies with families

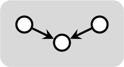
Rules

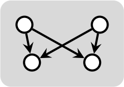




Observables

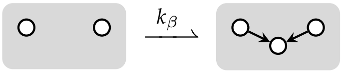
$B :=$ 

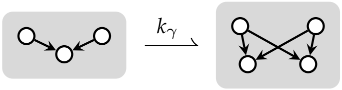
$C :=$ 

$S :=$ 

Bunnies with families

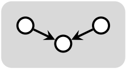
Rules

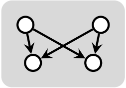




Observables

$B :=$ 

$C :=$ 

$S :=$ 

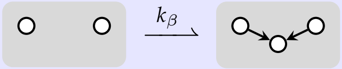
MFA/Rate equation

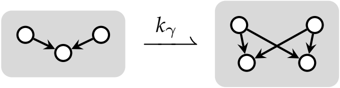
$\frac{d}{dt}$  $=$

$$\frac{d}{dt}[B] =$$

Bunnies with families

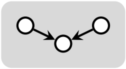
Rules

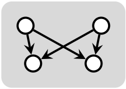




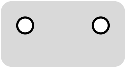
Observables

$B :=$ 

$C :=$ 

$S :=$ 

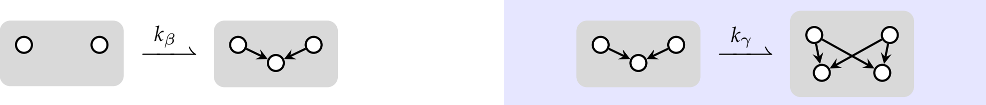
MFA/Rate equation

$\frac{d}{dt}$  $= k_\beta$  $+ \cdots$

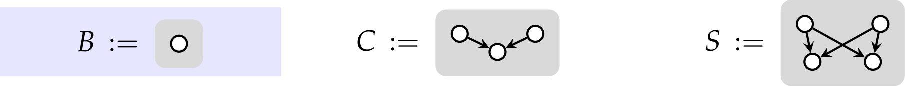
$$\frac{d}{dt}[B] = k_\beta [2B] + \cdots$$

Bunnies with families

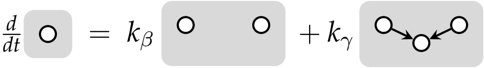
Rules



Observables



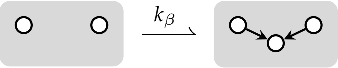
MFA/Rate equation

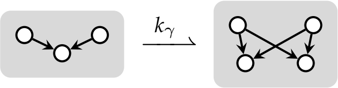


$$\frac{d}{dt}[B] = k_\beta[2B] + k_\gamma[C]$$

Bunnies with families

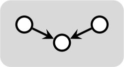
Rules

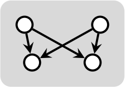




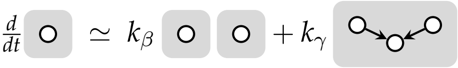
Observables

$B :=$ 

$C :=$ 

$S :=$ 

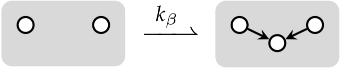
MFA/Rate equation



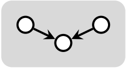
$$\frac{d}{dt}[B] \simeq k_\beta [B]^2 + k_\gamma [C]$$

Bunnies with families (cont.)

Rule

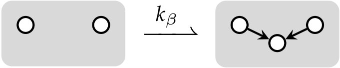


Observable

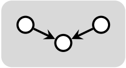
$C :=$ 

Bunnies with families (cont.)

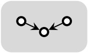
Rule



Observable

$C :=$ 

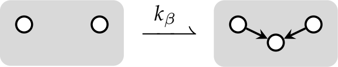
MFA/Rate equation

$\frac{d}{dt}$  $=$

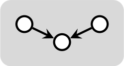
$$\frac{d}{dt}[C] =$$

Bunnies with families (cont.)

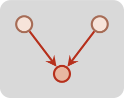
Rule



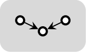
Observable

$C :=$ 

Refinement



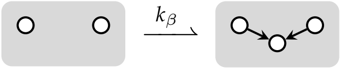
MFA/Rate equation

$\frac{d}{dt}$  $=$

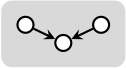
$$\frac{d}{dt}[C] =$$

Bunnies with families (cont.)

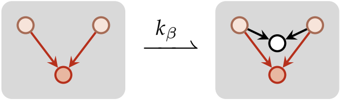
Rule



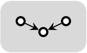
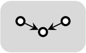
Observable

$C :=$ 

Refinement



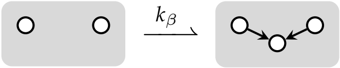
MFA/Rate equation

$\frac{d}{dt}$  $= -k_\beta$  $+ \cdots$

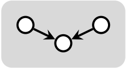
$$\frac{d}{dt}[C] = -k_\beta [C] + \cdots$$

Bunnies with families (cont.)

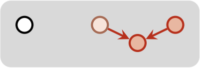
Rule



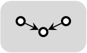
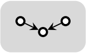
Observable

$C :=$ 

Refinement



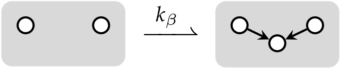
MFA/Rate equation

$\frac{d}{dt}$  $= -k_\beta$  $+ \cdots$

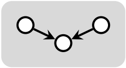
$$\frac{d}{dt}[C] = -k_\beta [C] + \cdots$$

Bunnies with families (cont.)

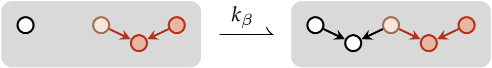
Rule



Observable

$C :=$ 

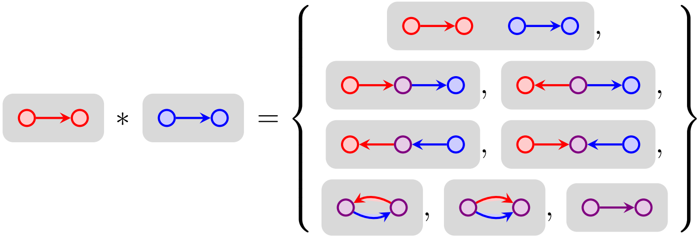
Refinement



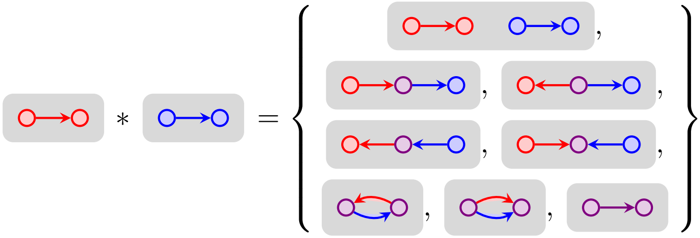
MFA/Rate equation

$$\frac{d}{dt}[C] = -k_\beta[C] - k_\beta[F_0] + \cdots$$

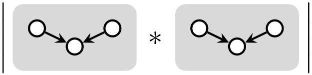
Interlude: minimal gluings (overlaps)



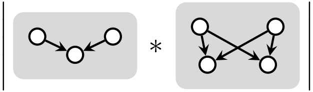
Interlude: minimal gluings (overlaps)



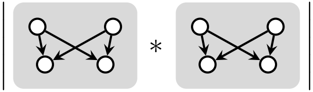
The set of MGs grows quickly, even for small graphs.



$= 44$



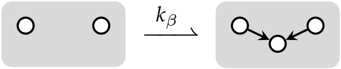
$= 101$



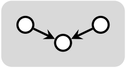
$= 381$

Case 1: irrelevant MGs

Rule



Observable

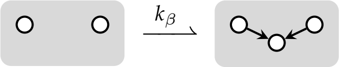
$C :=$ 

MFA/Rate equation

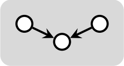
$$\frac{d}{dt}[C] = -k_\beta[C] - k_\beta[F_0] + \cdots$$

Case 1: irrelevant MGs

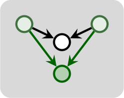
Rule



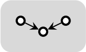
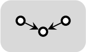
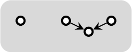
Observable

$C :=$ 

Refinement



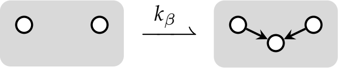
MFA/Rate equation

$\frac{d}{dt}$  $= -k_\beta$  $- k_\beta$  $+ \cdots$

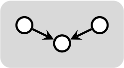
$$\frac{d}{dt}[C] = -k_\beta[C] - k_\beta[F_0] + \cdots$$

Case 1: irrelevant MGs

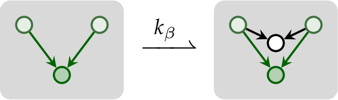
Rule



Observable

$C :=$ 

Refinement

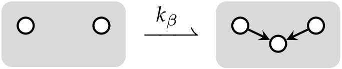


MFA/Rate equation

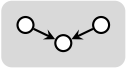
$$\frac{d}{dt}[C] = -k_\beta[C] - k_\beta[F_0] + k_\beta[C] + \cdots$$

Case 1: irrelevant MGs

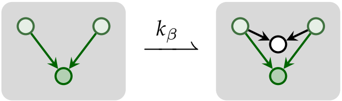
Rule



Observable

$C :=$ 

Refinement

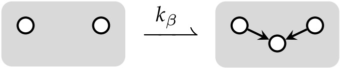


MFA/Rate equation

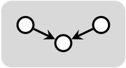
$$\frac{d}{dt}[C] = -k_\beta[F_0] + \cdots$$

Case 1: irrelevant MGs

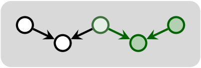
Rule



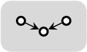
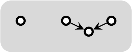
Observable

$C :=$ 

Refinement



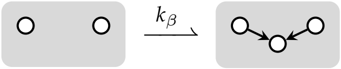
MFA/Rate equation

$\frac{d}{dt}$  $= -k_\beta$  $+ \cdots$

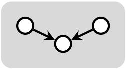
$$\frac{d}{dt}[C] = -k_\beta[F_0] + \cdots$$

Case 1: irrelevant MGs

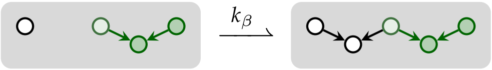
Rule



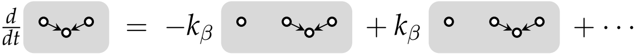
Observable

$C :=$ 

Refinement



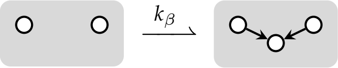
MFA/Rate equation



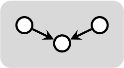
$$\frac{d}{dt}[C] = -k_\beta[F_0] + k_\beta[F_0] + \cdots$$

Case 1: irrelevant MGs

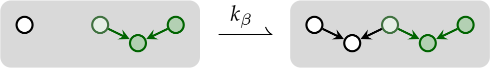
Rule



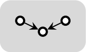
Observable

$C :=$ 

Refinement



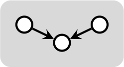
MFA/Rate equation

$\frac{d}{dt}$  $= \cdots$

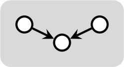
$$\frac{d}{dt}[C] = \cdots$$

Case 2: underivable MGs (RHS only)

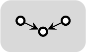
Rule


$\xrightarrow{k_\beta}$


Observable

$C :=$ 

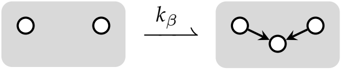
MFA/Rate equation

$\frac{d}{dt}$  $= \cdots$

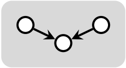
$$\frac{d}{dt}[C] = \cdots$$

Case 2: underivable MGs (RHS only)

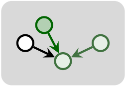
Rule



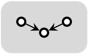
Observable

$C :=$ 

Refinement



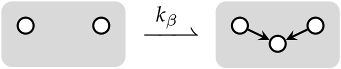
MFA/Rate equation

$\frac{d}{dt}$  $= \cdots$

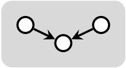
$$\frac{d}{dt}[C] = \cdots$$

Case 2: underivable MGs (RHS only)

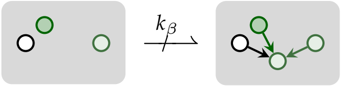
Rule



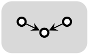
Observable

$C :=$ 

Refinement



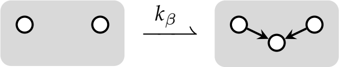
MFA/Rate equation

$\frac{d}{dt}$  $= \cdots$

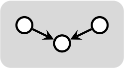
$$\frac{d}{dt}[C] = \cdots$$

Case 2: underivable MGs (RHS only)

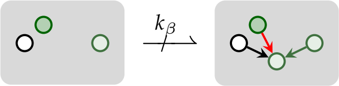
Rule



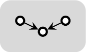
Observable

$C :=$ 

Refinement



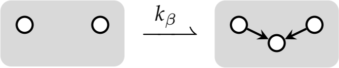
MFA/Rate equation

$\frac{d}{dt}$  $= \cdots$

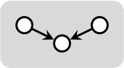
$$\frac{d}{dt}[C] = \cdots$$

Case 3: relevant derivable MGs

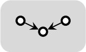
Rule



Observable

$C :=$ 

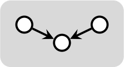
MFA/Rate equation

$\frac{d}{dt}$  $= \cdots$

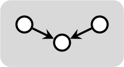
$$\frac{d}{dt}[C] = \cdots$$

Case 3: relevant derivable MGs

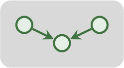
Rule

 $\xrightarrow{k_\beta}$ 

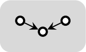
Observable

$C :=$ 

Refinement



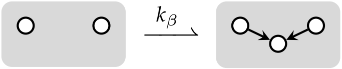
MFA/Rate equation

$\frac{d}{dt}$  $= \cdots$

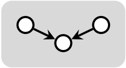
$$\frac{d}{dt}[C] = \cdots$$

Case 3: relevant derivable MGs

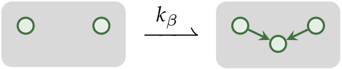
Rule



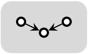
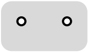
Observable

$C :=$ 

Refinement



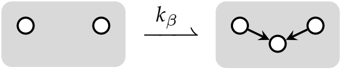
MFA/Rate equation

$\frac{d}{dt}$  $= k_\beta$  $+ \cdots$

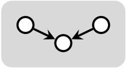
$$\frac{d}{dt}[C] = k_\beta[2B] + \cdots$$

Case 3: relevant derivable MGs

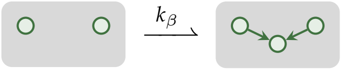
Rule



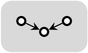
Observable

$C :=$ 

Refinement



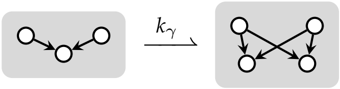
MFA/Rate equation

$\frac{d}{dt}$  $= 2k_\beta$  $+ \cdots$

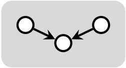
$$\frac{d}{dt}[C] = 2k_\beta[2B] + \cdots$$

Case 3: relevant derivable MGs

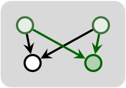
Rule



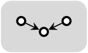
Observable

$C :=$ 

Refinement



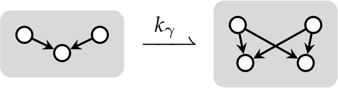
MFA/Rate equation

$\frac{d}{dt}$  $= 2k_\beta$  $+ \cdots$

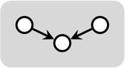
$$\frac{d}{dt}[C] = 2k_\beta[2B] + \cdots$$

Case 3: relevant derivable MGs

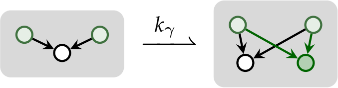
Rule



Observable

$C :=$ 

Refinement

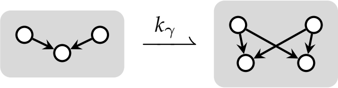


MFA/Rate equation

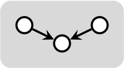
$$\frac{d}{dt}[C] = 2k_\beta[2B] + k_\gamma[C] + \cdots$$

Case 3: relevant derivable MGs

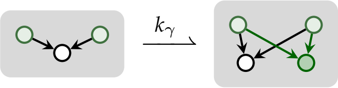
Rule



Observable

$C :=$ 

Refinement

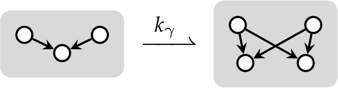


MFA/Rate equation

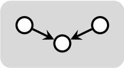
$$\frac{d}{dt}[C] = 2k_\beta[2B] + 2k_\gamma[C]$$

Case 3: relevant derivable MGs

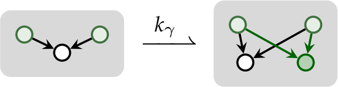
Rule



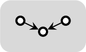
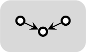
Observable

$C :=$ 

Refinement



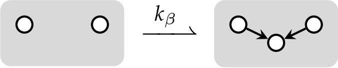
MFA/Rate equation

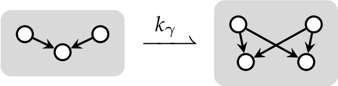
$\frac{d}{dt}$  $\simeq 2k_\beta$   $+ 2k_\gamma$ 

$$\frac{d}{dt}[C] \simeq 2k_\beta[B]^2 + 2k_\gamma[C]$$

Bunnies with families (cont.)

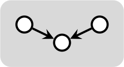
Rules



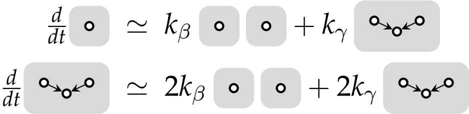


Observables

$B :=$ 

$C :=$ 

MFA/Rate equations



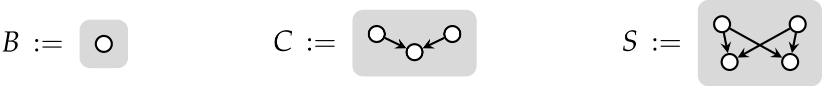
$$\frac{d}{dt}[B] \simeq k_\beta [B]^2 + k_\gamma [C]$$

$$\frac{d}{dt}[C] \simeq 2k_\beta [B]^2 + 2k_\gamma [C]$$

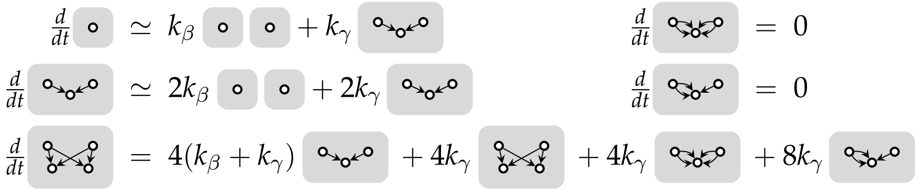
Bunnies with families (cont.)

Rules

Observables

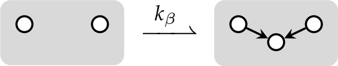


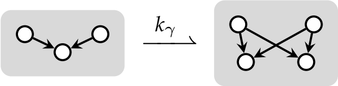
MFA/Rate equations



Bunnies with families (cont.)

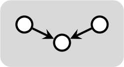
Rules

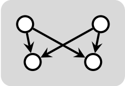




Observables

$B :=$ 

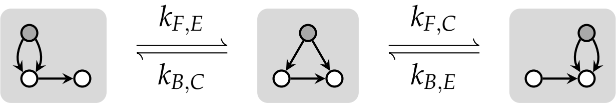
$C :=$ 

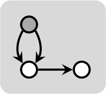
$S :=$ 

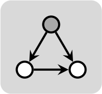
MFA/Rate equations

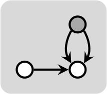
$$
\begin{aligned}
\frac{d}{dt}[B] &\simeq k_\beta[B]^2 + k_\gamma[C] & \frac{d}{dt}[F_1] &= 0 \\
\frac{d}{dt}[C] &\simeq 2k_\beta[B]^2 + 2k_\gamma[C] & \frac{d}{dt}[F_2] &= 0 \\
\frac{d}{dt}[S] &= 4(k_\beta + k_\gamma)[C] + 4k_\gamma[S] + 4k_\gamma[F_1] + 8k_\gamma[F_2]
\end{aligned}
$$

Two-legged DNA walker



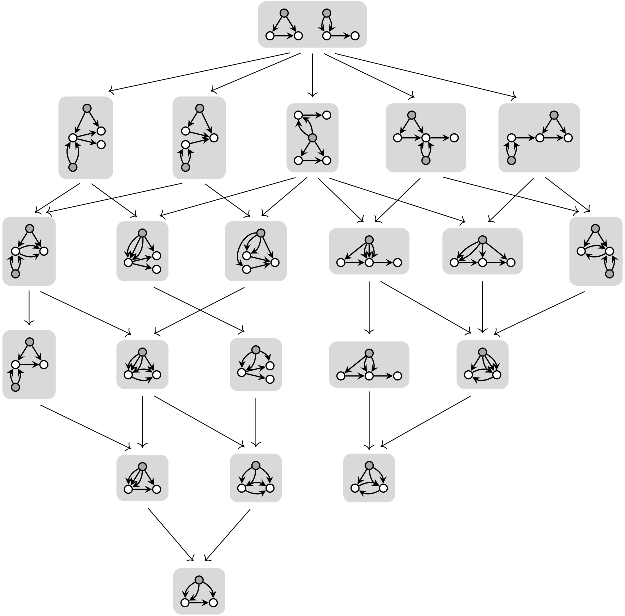
$G_1 :=$ 

$G_2 :=$ 

$G_3 :=$ 

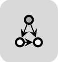
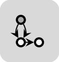
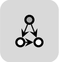
$$V = \frac{1}{2}\left(k_{F,E}\,\mathbb{E}[G_1] + k_{F,C}\,\mathbb{E}[G_2] - k_{B,E}\,\mathbb{E}[G_3] - k_{B,C}\,\mathbb{E}[G_2]\right)$$

Minimal gluings



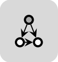
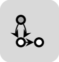
Two-legged DNA walker (cont.)

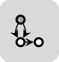
Generate equations using relevant gluings, first try…

$\frac{d}{dt}$  $=\; k_{F,E}$  $-k_{B,C}$  $-\, k_{F,C}$  $+\, k_{B,E}$ 

Two-legged DNA walker (cont.)

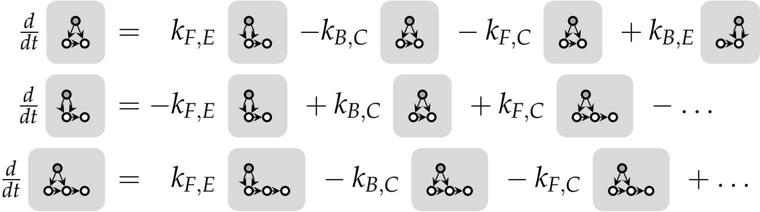
Generate equations using relevant gluings, first try…

$\frac{d}{dt}$  $= k_{F,E}$  $- k_{B,C}$  $- k_{F,C}$  $+ k_{B,E}$ 

$\frac{d}{dt}$  $= -k_{F,E}$  $+ k_{B,C}$  $+ k_{F,C}$  $- \dots$

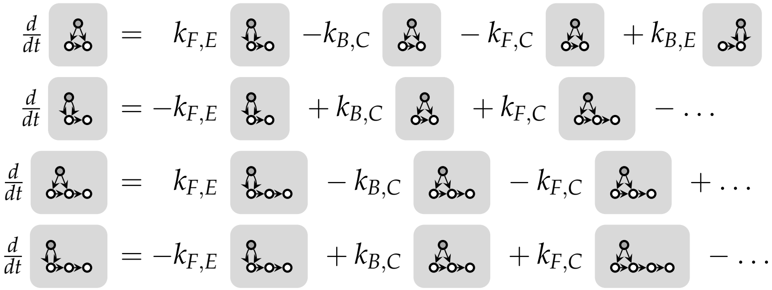
Two-legged DNA walker (cont.)

Generate equations using relevant gluings, first try. . .



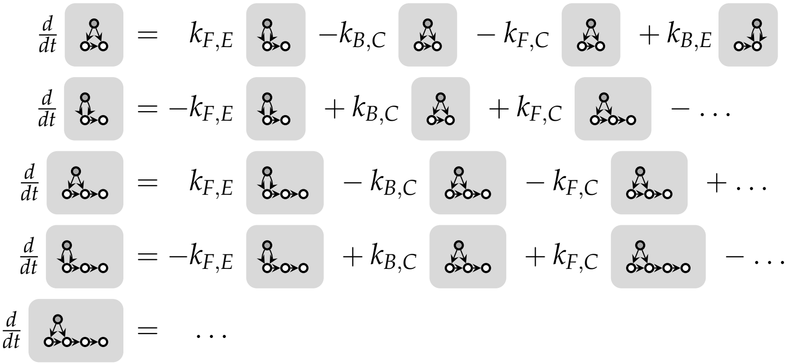
Two-legged DNA walker (cont.)

Generate equations using relevant gluings, first try…

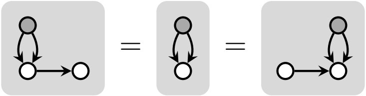


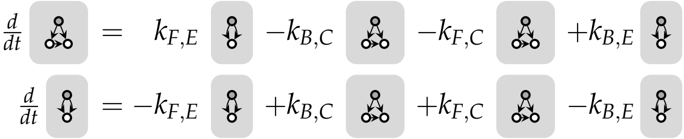
Two-legged DNA walker (cont.)

Generate equations using relevant gluings, first try…

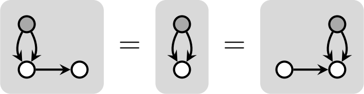


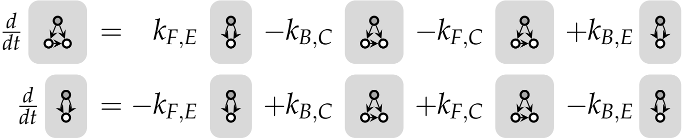
Invariants and Solution





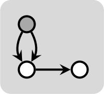
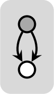
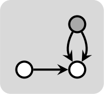
Invariants and Solution



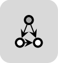


Steady state: $(k_{F,E} + k_{B,E})\,\mathbb{E}[G_0] = (k_{F,C} + k_{B,C})\,\mathbb{E}[G_2]$

Invariants and Solution

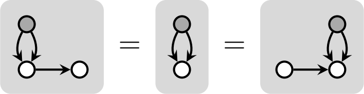
 $=$  $=$ 

$\frac{d}{dt}$  $= \; k_{F,E}$  $-k_{B,C}$  $-k_{F,C}$  $+k_{B,E}$ 

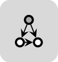
$\frac{d}{dt}$  $= -k_{F,E}$  $+k_{B,C}$  $+k_{F,C}$  $-k_{B,E}$ 

Steady state: $(k_{F,E} + k_{B,E})\, \mathbb{E}[G_0] = (k_{F,C} + k_{B,C})\, \mathbb{E}[G_2]$ $\mathbb{E}[G_0] + \mathbb{E}[G_2] = 1$

Invariants and Solution



$\frac{d}{dt}$  $= k_{F,E}$  $-k_{B,C}$  $-k_{F,C}$  $+k_{B,E}$ 

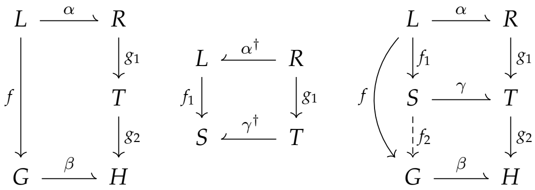
$\frac{d}{dt}$  $= -k_{F,E}$  $+k_{B,C}$  $+k_{F,C}$  $-k_{B,E}$ 

Steady state: $(k_{F,E} + k_{B,E})\,\mathbb{E}[G_0] = (k_{F,C} + k_{B,C})\,\mathbb{E}[G_2]$ $\quad\quad \mathbb{E}[G_0] + \mathbb{E}[G_2] = 1$

$$V = \frac{1}{2}\Big((k_{F,E} - k_{B,E})\,\mathbb{E}[G_0] + (k_{F,C} - k_{B,C})\,\mathbb{E}[G_2]\Big)$$
$$= \frac{(k_{F,C} + k_{B,C})(k_{F,E} - k_{B,E}) + (k_{F,E} + k_{B,E})(k_{F,C} - k_{B,C})}{2(k_{F,E} + k_{B,E} + k_{F,C} + k_{B,C})}$$

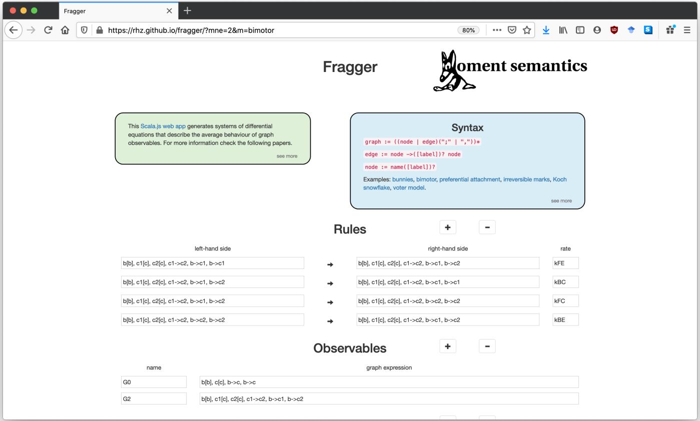
Full details. . .

. . . are in the paper.



$$\frac{d}{dt}\,\mathbb{E}_p[F] = -\sum_{\alpha\in\mathcal{R}} k(\alpha) \sum_{\mu\in\alpha *_L F} \mathbb{E}_p[\hat{\mu}] + \sum_{\alpha\in\mathcal{R}} k(\alpha) \sum_{\mu\in\alpha *_R F} \mathbb{E}_p[\hat{\alpha}^\dagger(\mu_1)].$$

Fragger



Web app `https://rhz.github.io/fragger/`

Source code `https://github.com/rhz/graph-rewriting/`

Related and future work

Site graph rewriting Differential semantics of the Kappa language.

- Derived via abstract interpretation of ground CRN ("fragmentation").
- [Feret et al., 2009, Danos et al., 2010, Harmer et al., 2010].

Moment semantics Generalization to other graph-like structures.

- Direct derivation of MFAs (no ground CRN) incl. higher moments.
- Preliminary: support for negative application conditions (NACs).
- Open problems: truncation; approximate model reduction.
- [Danos et al., 2014, Danos et al., 2015a, Danos et al., 2015b].

Rule algebra Alternative approach leveraging algebraic structure of rules.

- Developed independently by Behr and others.
- Powerful, very general approach based on representation theory.
- Supports irreversible systems and NACs.
- Future work: better understand the relation between the two approaches.
- [Behr et al., 2016, Behr and Krivine, 2020, Behr et al., 2020a, Behr et al., 2020b].

Thank you!

Coauthors

- Vincent Danos, CNRS & ENS-PSL
- Tobias Heindel, TU Berlin
- Ricardo Honorato-Zimmer, CINV



cnrs
ENS
ÉCOLE NORMALE SUPÉRIEURE
TU berlin

CENTRO INTERDISCIPLINARIO DE
Neurociencia de
Valparaíso

UNIVERSITY OF
GOTHENBURG

CHALMERS
UNIVERSITY OF TECHNOLOGY

Checkout the Fragger web-app!

`https://rhz.github.io/fragger/`
`https://github.com/rhz/graph-rewriting/`

Backup slides

Rate equations

For Petri nets:

$$\begin{aligned}\frac{d}{dt}\,\mathbb{E}([A]) = &-\sum_{\alpha\in\mathcal{R}} k(\alpha)\,\rho_\alpha(A) \prod_{(u,n)\in\rho_\alpha} \mathbb{E}(u)^n \\ &+\sum_{\alpha\in\mathcal{R}} k(\alpha)\,\gamma_\alpha(A) \prod_{(u,n)\in\gamma_\alpha} \mathbb{E}(u)^n\end{aligned}$$

Rate equations

For Petri nets:

$$\frac{d}{dt}\,\mathbb{E}([A]) = -\sum_{\alpha\in\mathcal{R}} k(\alpha)\,\rho_\alpha(A) \prod_{(u,n)\in\rho_\alpha} \mathbb{E}(u)^n + \sum_{\alpha\in\mathcal{R}} k(\alpha)\,\gamma_\alpha(A) \prod_{(u,n)\in\gamma_\alpha} \mathbb{E}(u)^n$$

More generally,

- S a countable set (state),
- $\mathbb{R}^S$ probabilities and observables, topology),
- $Q : \mathbb{R}^S \to \mathbb{R}^{S'}$ a continuous linear map (transition matrix).

$$\tfrac{d}{dt} p^T = p^T Q$$

$$\tfrac{d}{dt}\,\mathbb{E}_p(f) = \tfrac{d}{dt} p^T f = p^T Q f = \mathbb{E}_p(Qf)$$

$$(Qf)(x) := \textstyle\sum_y q_{xy}(f(y) - f(x))$$

Rate equations

Suppose

- $\mathcal{A}$ a linear subspace of $\mathbb{R}^S$ with basis $\mathcal{B}$, and
- $\mathcal{B}$ is jump-closed: $Q\mathcal{B} \subseteq \mathcal{A}$.

$$Qg = \sum_{h \in \mathcal{B}} \alpha_{g,h} h$$

$$\frac{d}{dt} \mathbb{E}_p(g) = \sum_{h \in \mathcal{B}} \alpha_{g,h} \mathbb{E}_p(h)$$

- $\mathcal{B}_0 \subseteq \mathcal{B}$ such that $\mathrm{poly}(\mathcal{B}_0) = \mathcal{A}$

$$h = \sum_{\phi \in \mathcal{B}_0} \beta_{h,\phi} \, \phi$$

$$\frac{d}{dt} \mathbb{E}_p(g) \simeq \sum_{h \in \mathcal{B}} \alpha_{g,h} \sum_{\phi \in \mathcal{B}_0} \beta_{h,\phi} \prod_{u \in \phi} \mathbb{E}_p(u)$$

Rate equations

So, in general:

$$\frac{d}{dt}\,\mathbb{E}_p(g) = \sum_{h\in\mathcal{B}} \alpha_{g,h} \sum_{\phi\in\mathcal{B}_0} \beta_{h,\phi} \prod_{u\in\phi} \mathbb{E}_p(u)$$

For Petri nets:

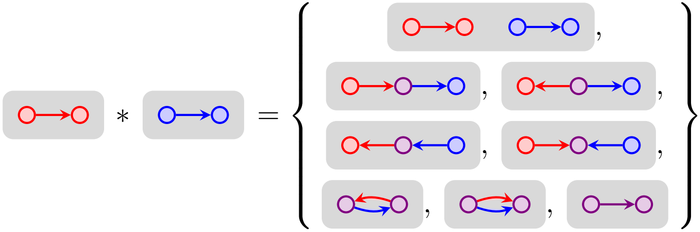
$$\begin{aligned}\frac{d}{dt}\,\mathbb{E}([A]) = &- \sum_{\alpha\in\mathcal{R}} k(\alpha)\,\rho_\alpha(A) \prod_{(u,n)\in\rho_\alpha} \mathbb{E}(u)^n \\ &+ \sum_{\alpha\in\mathcal{R}} k(\alpha)\,\gamma_\alpha(A) \prod_{(u,n)\in\gamma_\alpha} \mathbb{E}(u)^n\end{aligned}$$

- $\mathcal{B}_0$ is the set of species.

Rate equations for graphs

- $\mathcal{B}_0$ is the set of connected graphs

$$\frac{d}{dt}\mathbb{E}([F]) = -\sum_{\alpha\in\mathcal{R}} k(\alpha) \sum_{\mu\in\alpha *_L F} \; \sum_{\phi\in\Phi(\hat{\mu})} \; \prod_{u\in\phi} \mathbb{E}(u) + \sum_{\alpha\in\mathcal{R}} k(\alpha) \sum_{\mu\in\alpha *_R F} \; \sum_{\phi\in\Phi(\hat{\mu}^\dagger)} \; \prod_{u\in\phi} \mathbb{E}(u)$$



Behr, N., Danos, V., and Garnier, I. (2016).
Stochastic mechanics of graph rewriting.
In *Proc. 31st Annual ACM/IEEE Symposium on Logic in Computer Science (LICS 2016), New York, NY, USA*, page 46–55. ACM.

Behr, N., Danos, V., and Garnier, I. (2020a).
Combinatorial conversion and moment bisimulation for stochastic rewriting systems.
Logical Methods in Computer Science, 16.

Behr, N. and Krivine, J. (2020).
Rewriting theory for the life sciences: A unifying framework for CTMC semantics.
In Gadducci, F. and Kehrer, T., editors, *Proc. Graph Transformation, 13th International Conference, (ICGT 2020), Bergen, Norway*, volume 12150 of *LNCS*. Springer.

Behr, N., Saadat, M. G., and Heckel, R. (2020b).
Commutators for stochastic rewriting systems: Theory and implementation in Z3.

CoRR arXiv:2003.11010.

Danos, V., Feret, J., Fontana, W., Harmer, R., and Krivine, J. (2010).
Abstracting the differential semantics of rule-based models: exact and automated model reduction.
In Jouannaud, J.-P., editor, *Proc. 25th Annual IEEE Symposium on Logic in Computer Science (LICS 2010), Edinburgh, Scotland, UK*, volume 0, pages 362–381. IEEE Computer Society.

Danos, V., Heindel, T., Honorato-Zimmer, R., and Stucki, S. (2014).
Approximations for stochastic graph rewriting.
In Merz, S. and Pang, J., editors, *Proc. Formal Methods and Software Engineering – 16th International Conference on Formal Engineering Methods (ICFEM 2014), Luxembourg, Luxembourg*, volume 8829 of *LNCS*, pages 1–10. Springer.

Danos, V., Heindel, T., Honorato-Zimmer, R., and Stucki, S. (2015a).
Computing approximations for graph transformation systems.

In Hildebrandt, T. and Miculan, M., editors, *2nd International Workshop on Meta Models for Process Languages (MeMo 2015), Grenoble, France. Pre-proceedings*, pages 33–43.
Electronic version available at `http://users.dimi.uniud.it/~marino.miculan/Papers/MeMo15-preproc.pdf`.

Danos, V., Heindel, T., Honorato-Zimmer, R., and Stucki, S. (2015b).
Moment semantics for reversible rule-based systems.
In Krivine, J. and Stefani, J., editors, *Proc. Reversible Computation, 7th International Conference (RC 2015), Grenoble, France*, volume 9138 of *LNCS*, pages 3–26. Springer.

Feret, J., Danos, V., Krivine, J., Harmer, R., and Fontana, W. (2009).
Internal coarse-graining of molecular systems.
Proceedings of the National Academy of Sciences, 106(16):6453–6458.

Harmer, R., Danos, V., Feret, J., Krivine, J., and Fontana, W. (2010).
Intrinsic information carriers in combinatorial dynamical systems.
Chaos, 20(3):037108–1–16.