

Rate Equations for Graphs

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Virtual CMSB 2020 – Konstanz – 23 Sep 2020

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UNIVERSITY OF TECHNOLOGY

Mean field approximations (MFAs)

Question

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



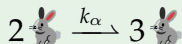
Photo: J Ligeró & I Barrios 2013 (Wikipedia).

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Example (reproduction)

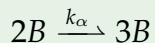


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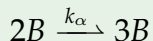


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Example (reproduction)



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

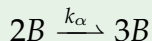
$$\frac{d}{dt} \mathbb{E}[B] = k_\alpha \mathbb{E}[2B] = k_\alpha \mathbb{E}([B]([B] - 1)) \quad (\text{meanfield})$$

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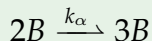
$$\begin{aligned} \frac{d}{dt} \mathbb{E}[B] &= k_\alpha \mathbb{E}[2B] = k_\alpha \mathbb{E}([B]([B] - 1)) && \text{(meanfield)} \\ &\simeq k_\alpha \mathbb{E}([B][B]) \simeq k_\alpha \mathbb{E}[B] \mathbb{E}[B] && \text{(approximation)} \end{aligned}$$

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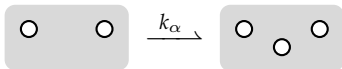


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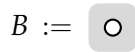
$$\begin{aligned} \frac{d}{dt} \mathbb{E}[B] &= k_\alpha \mathbb{E}[2B] = k_\alpha \mathbb{E}([B]([B] - 1)) && \text{(meanfield)} \\ &\simeq k_\alpha \mathbb{E}([B][B]) \simeq k_\alpha \mathbb{E}[B] \mathbb{E}[B] && \text{(approximation)} \\ \frac{d}{dt} [B] &\simeq k_\alpha [B]^2 && \text{(thermodynamic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

CRNs are Graph Transformation Systems (GTSs)

Reaction/rule

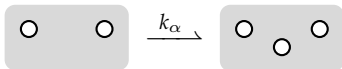


Observable

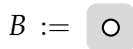


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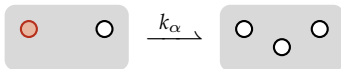
MFA/Rate equation

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

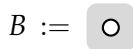
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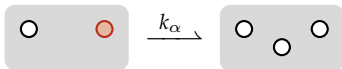
MFA/Rate equation

$$\frac{d}{dt} \text{[red circle]} = -k_\alpha \text{[red circle, white circle]} + \dots$$

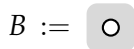
$$\frac{d}{dt}[B] = -k_\alpha[2B] + \dots$$

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Observable



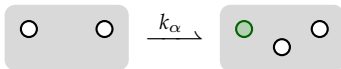
MFA/Rate equation

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

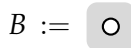
$$\frac{d}{dt}[B] = -2k_\alpha[2B] + \dots$$

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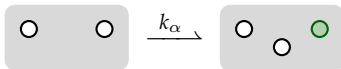
MFA/Rate equation

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

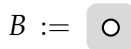
$$\frac{d}{dt} [B] = -2k_\alpha [2B] + k_\alpha [2B] + \dots$$

CRNs are Graph Transformation Systems (GTSs)

Reaction/rule



Observable



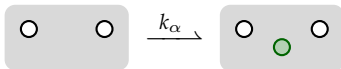
MFA/Rate equation

$$\frac{d}{dt} \text{[} \text{○} \text{]} = -2k_\alpha \text{[} \text{○} \text{ } \text{○} \text{]} + 2k_\alpha \text{[} \text{○} \text{ } \text{○} \text{]} + \dots$$

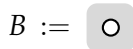
$$\frac{d}{dt} [B] = -2k_\alpha [2B] + 2k_\alpha [2B] + \dots$$

CRNs are Graph Transformation Systems (GTSs)

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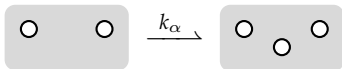
MFA/Rate equation


$$\frac{d}{dt} \text{○} = -2k_\alpha \text{○ ○} + 3k_\alpha \text{○ ○}$$

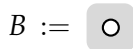
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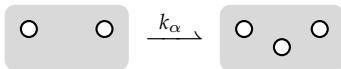
MFA/Rate equation

$$\frac{d}{dt} \text{○} = k_\alpha \text{○ ○}$$

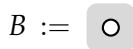
$$\frac{d}{dt} [B] = k_\alpha [2B]$$

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MFA/Rate equation

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

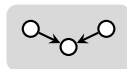
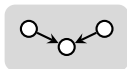
$$\frac{d}{dt}[B] = k_\alpha[2B] \simeq k_\alpha[B]^2$$

Bunnies with families

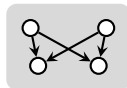
Rules



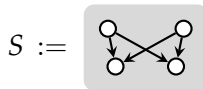
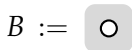
k_β



k_γ



Observables

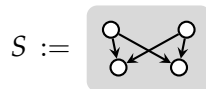
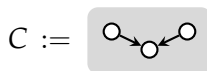
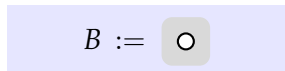


Bunnies with families

Rules



Observables



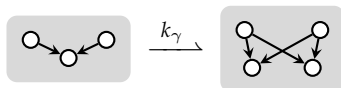
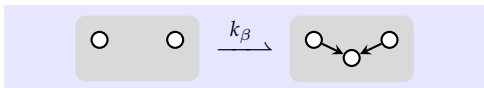
MFA/Rate equation

$$\frac{d}{dt} \text{○} =$$

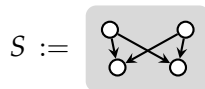
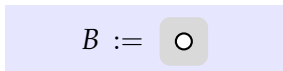
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Bunnies with families

Rules



Observables



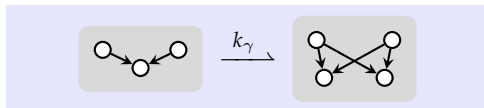
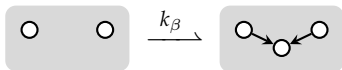
MFA/Rate equation

$$\frac{d}{dt} \text{ } = k_\beta \text{ } + \dots$$

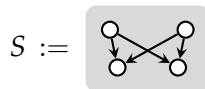
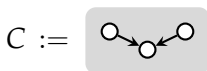
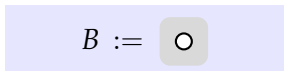
$$\frac{d}{dt} [B] = k_\beta [2B] + \dots$$

Bunnies with families

Rules



Observables



MFA/Rate equation



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

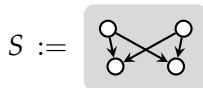
Bunnies with families

Rules



Observables

$$B := \text{○}$$



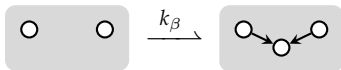
MFA/Rate equation

$$\frac{d}{dt} \text{○} \simeq k_\beta \text{○} \text{○} + k_\gamma \text{○} \rightarrow \text{○} \leftarrow \text{○}$$

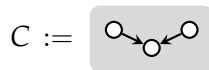
$$\frac{d}{dt}[B] \simeq k_\beta[B]^2 + k_\gamma[C]$$

Bunnies with families (cont.)

Rule

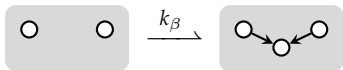


Observable

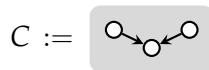


Bunnies with families (cont.)

Rule



Observable



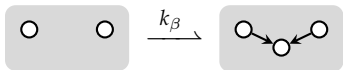
MFA/Rate equation

$$\frac{d}{dt} \text{[Diagram]} =$$

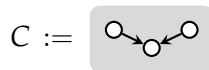
$$\frac{d}{dt} [C] =$$

Bunnies with families (cont.)

Rule




Observable



Refinement



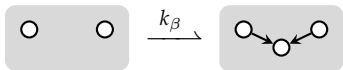
MFA/Rate equation

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

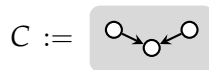
$$\frac{d}{dt} [C] =$$

Bunnies with families (cont.)

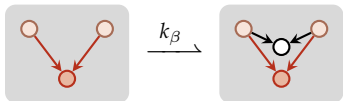
Rule



Observable



Refinement



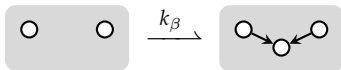
MFA/Rate equation

$$\frac{d}{dt} \text{○} \rightarrow \text{○} \leftarrow \text{○} = -k_\beta \text{○} \rightarrow \text{○} \leftarrow \text{○} + \dots$$

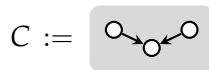
$$\frac{d}{dt}[C] = -k_\beta[C] + \dots$$

Bunnies with families (cont.)

Rule



Observable



Refinement



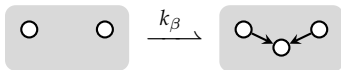
MFA/Rate equation

$$\frac{d}{dt} \langle \text{Observable} \rangle = -k_\beta \langle \text{Observable} \rangle + \dots$$

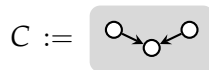
$$\frac{d}{dt} [C] = -k_\beta [C] + \dots$$

Bunnies with families (cont.)

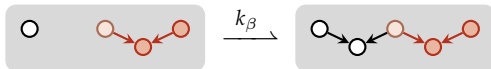
Rule



Observable



Refinement

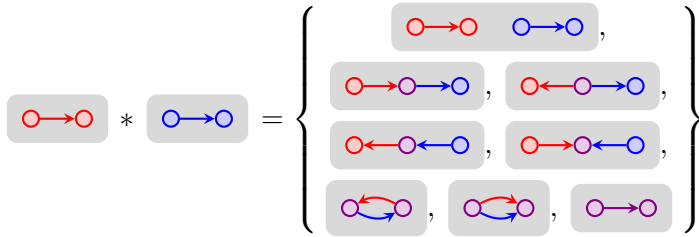


MFA/Rate equation

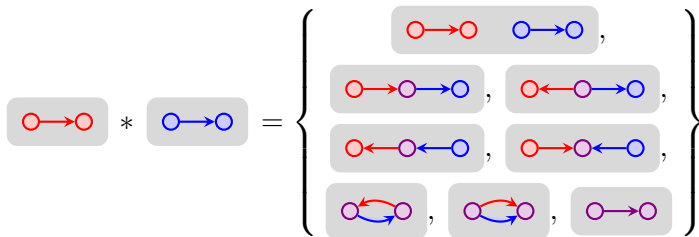
$$\frac{d}{dt} \text{[Observable]} = -k_\beta \text{[Observable]} - k_\beta \text{[Family]} + \dots$$

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

Interlude: minimal gluings (overlaps)



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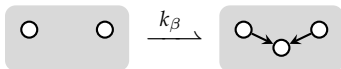
The set of MGs grows quickly, even for small graphs.

$$\left| \begin{array}{c} \text{Graph 1} \\ \text{Graph 2} \end{array} * \begin{array}{c} \text{Graph 1} \\ \text{Graph 1} \end{array} \right| = 44 \qquad \left| \begin{array}{c} \text{Graph 1} \\ \text{Graph 2} \end{array} * \begin{array}{c} \text{Graph 2} \\ \text{Graph 2} \end{array} \right| = 101$$

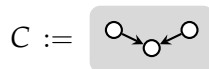
$$\left| \begin{array}{c} \text{Graph 2} \\ \text{Graph 2} \end{array} * \begin{array}{c} \text{Graph 2} \\ \text{Graph 2} \end{array} \right| = 381$$

Case 1: irrelevant MGs

Rule



Observable



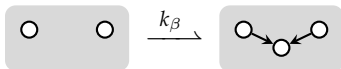
MFA/Rate equation

$$\frac{d}{dt} \langle \text{Complex} \rangle = -k_\beta \langle \text{Complex} \rangle - k_\beta \langle \text{Free} \rangle + \dots$$

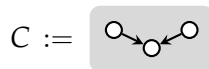
$$\frac{d}{dt} [C] = -k_\beta [C] - k_\beta [F_0] + \dots$$

Case 1: irrelevant MGs

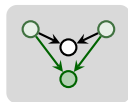
Rule



Observable



Refinement



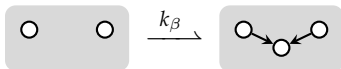
MFA/Rate equation

$$\frac{d}{dt} \langle \text{Complex} \rangle = -k_\beta \langle \text{Complex} \rangle - k_\beta \langle \text{F}_0 \rangle + \dots$$

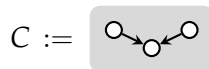
$$\frac{d}{dt} [C] = -k_\beta [C] - k_\beta [F_0] + \dots$$

Case 1: irrelevant MGs

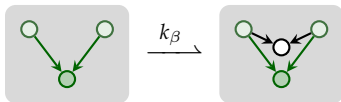
Rule



Observable



Refinement



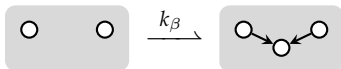
MFA/Rate equation

$$\frac{d}{dt} \text{[V-shape]} = -k_\beta \text{[V-shape]} - k_\beta \text{[F0]} + k_\beta \text{[C]} + \dots$$

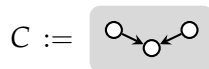
$$\frac{d}{dt} [C] = -k_\beta [C] - k_\beta [F_0] + k_\beta [C] + \dots$$

Case 1: irrelevant MGs

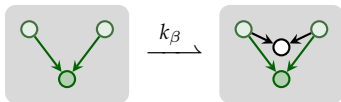
Rule



Observable



Refinement



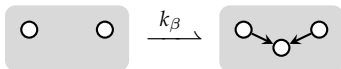
MFA/Rate equation

$$\frac{d}{dt} \circ \leftarrow \circ \rightarrow \circ = -k_\beta \circ \quad \circ \leftarrow \circ \rightarrow \circ + \dots$$

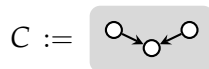
$$\frac{d}{dt}[C] = -k_\beta[F_0] + \dots$$

Case 1: irrelevant MGs

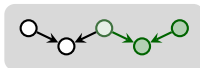
Rule



Observable



Refinement



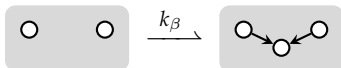
MFA/Rate equation

$$\frac{d}{dt} \langle \text{bound pair} \rangle = -k_\beta \langle \text{two free particles} \rangle + \dots$$

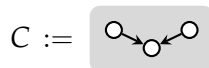
$$\frac{d}{dt} [C] = -k_\beta [F_0] + \dots$$

Case 1: irrelevant MGs

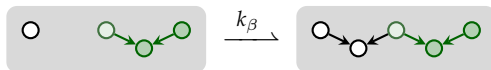
Rule



Observable



Refinement



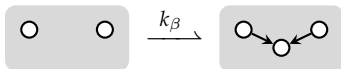
MFA/Rate equation

$$\frac{d}{dt} \circ \leftarrow \circ \rightarrow \circ = -k_\beta \circ \quad \circ \leftarrow \circ \rightarrow \circ + k_\beta \circ \quad \circ \leftarrow \circ \rightarrow \circ + \dots$$

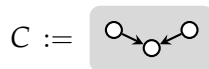
$$\frac{d}{dt} [C] = -k_\beta [F_0] + k_\beta [F_0] + \dots$$

Case 1: irrelevant MGs

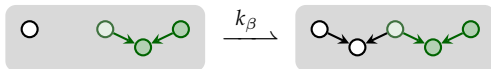
Rule



Observable



Refinement



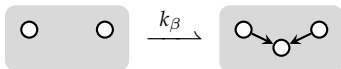
MFA/Rate equation

$$\frac{d}{dt} \left[\text{Observable} \right] = \dots$$

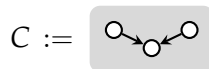
$$\frac{d}{dt} [C] = \dots$$

Case 2: underivable MGs (RHS only)

Rule



Observable



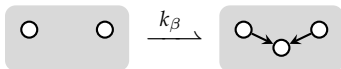
MFA/Rate equation

$$\frac{d}{dt} \text{○} \leftarrow \text{○} \rightarrow \text{○} = \dots$$

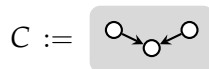
$$\frac{d}{dt}[C] = \dots$$

Case 2: underivable MGs (RHS only)

Rule



Observable



Refinement



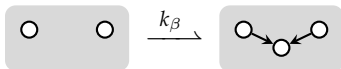
MFA/Rate equation

$$\frac{d}{dt} \text{[Complex of 3 particles]} = \dots$$

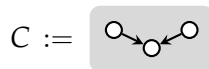
$$\frac{d}{dt} [C] = \dots$$

Case 2: underivable MGs (RHS only)

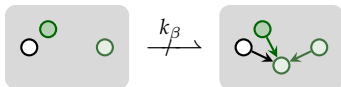
Rule



Observable



Refinement



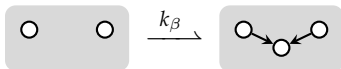
MFA/Rate equation

$$\frac{d}{dt} \text{[Diagram]} = \dots$$

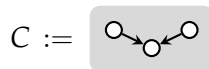
$$\frac{d}{dt} [C] = \dots$$

Case 2: underivable MGs (RHS only)

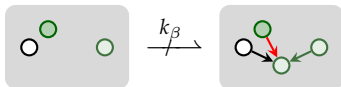
Rule



Observable



Refinement



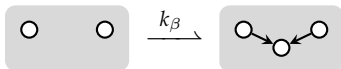
MFA/Rate equation

$$\frac{d}{dt} \text{[Diagram]} = \dots$$

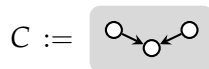
$$\frac{d}{dt} [C] = \dots$$

Case 3: relevant derivable MGs

Rule



Observable



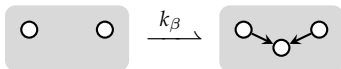
MFA/Rate equation

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

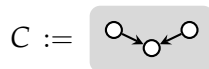
$$\frac{d}{dt}[C] = \dots$$

Case 3: relevant derivable MGs

Rule



Observable



Refinement



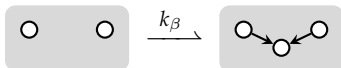
MFA/Rate equation

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

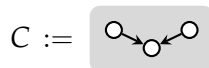
$$\frac{d}{dt} [C] = \dots$$

Case 3: relevant derivable MGs

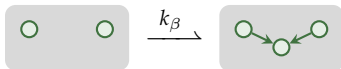
Rule



Observable



Refinement



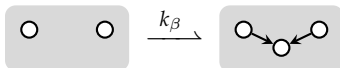
MFA/Rate equation

$$\frac{d}{dt} \begin{array}{c} \circ \quad \circ \\ \searrow \quad \swarrow \\ \circ \end{array} = k_\beta \begin{array}{c} \circ \quad \circ \\ \searrow \quad \swarrow \\ \circ \end{array} + \dots$$

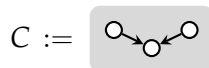
$$\frac{d}{dt}[C] = k_\beta[2B] + \dots$$

Case 3: relevant derivable MGs

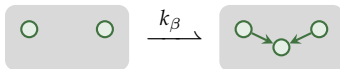
Rule



Observable



Refinement



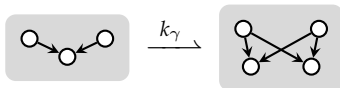
MFA/Rate equation

$$\frac{d}{dt} \text{[Central Circle]} = 2k_\beta \text{[Two Circles]} + \dots$$

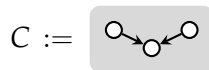
$$\frac{d}{dt} [C] = 2k_\beta [2B] + \dots$$

Case 3: relevant derivable MGs

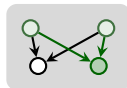
Rule



Observable



Refinement



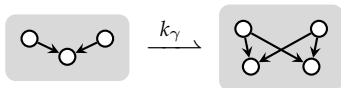
MFA/Rate equation

$$\frac{d}{dt} \text{[Observable]} = 2k_{\beta} \text{[Refined]} + \dots$$

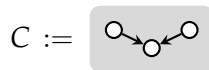
$$\frac{d}{dt} [C] = 2k_{\beta} [2B] + \dots$$

Case 3: relevant derivable MGs

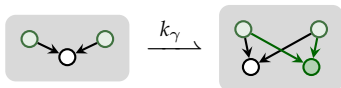
Rule



Observable



Refinement



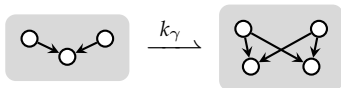
MFA/Rate equation

$$\frac{d}{dt} \text{[Observable State]} = 2k_\beta \text{[Two Nodes]} + k_\gamma \text{[Observable State]} + \dots$$

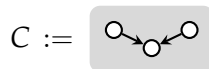
$$\frac{d}{dt} [C] = 2k_\beta [2B] + k_\gamma [C] + \dots$$

Case 3: relevant derivable MGs

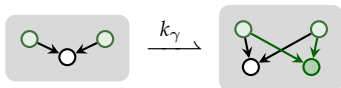
Rule



Observable



Refinement



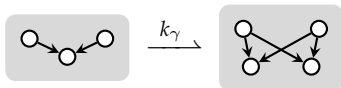
MFA/Rate equation

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

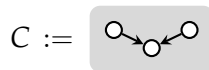
$$\frac{d}{dt}[C] = 2k_{\beta}[2B] + 2k_{\gamma}[C]$$

Case 3: relevant derivable MGs

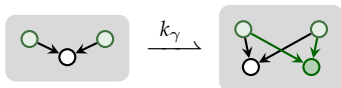
Rule



Observable



Refinement



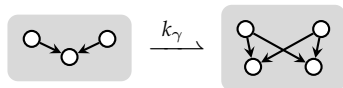
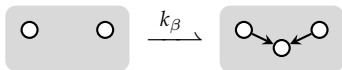
MFA/Rate equation

$$\frac{d}{dt} \text{[graph with 3 nodes]} \simeq 2k_\beta \text{[graph with 2 nodes]} + 2k_\gamma \text{[graph with 3 nodes]}$$

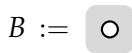
$$\frac{d}{dt}[C] \simeq 2k_\beta[B]^2 + 2k_\gamma[C]$$

Bunnies with families (cont.)

Rules



Observables



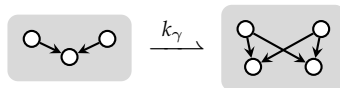
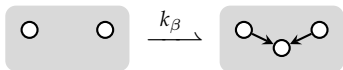
MFA/Rate equations

$$\begin{aligned} \frac{d}{dt} \circ &\simeq k_\beta \circ \quad \circ + k_\gamma \begin{array}{c} \circ \quad \circ \\ \searrow \quad \swarrow \\ \circ \end{array} \\ \frac{d}{dt} \begin{array}{c} \circ \quad \circ \\ \searrow \quad \swarrow \\ \circ \end{array} &\simeq 2k_\beta \circ \quad \circ + 2k_\gamma \begin{array}{c} \circ \quad \circ \\ \searrow \quad \swarrow \\ \circ \end{array} \end{aligned}$$

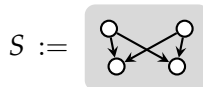
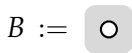
$$\begin{aligned} \frac{d}{dt} [B] &\simeq k_\beta [B]^2 + k_\gamma [C] \\ \frac{d}{dt} [C] &\simeq 2k_\beta [B]^2 + 2k_\gamma [C] \end{aligned}$$

Bunnies with families (cont.)

Rules



Observables



MFA/Rate equations

$$\frac{d}{dt} \circ \simeq k_\beta \circ \circ + k_\gamma \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \end{array}$$

$$\frac{d}{dt} \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \end{array} = 0$$

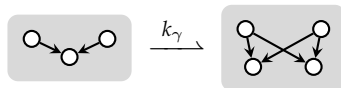
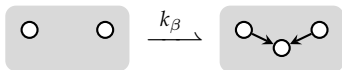
$$\frac{d}{dt} \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \end{array} \simeq 2k_\beta \circ \circ + 2k_\gamma \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \end{array}$$

$$\frac{d}{dt} \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \end{array} = 0$$

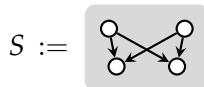
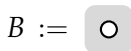
$$\frac{d}{dt} \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \\ \circ & & \circ \end{array} = 4(k_\beta + k_\gamma) \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \end{array} + 4k_\gamma \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \\ \circ & & \circ \end{array} + 4k_\gamma \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \end{array} + 8k_\gamma \begin{array}{ccc} \circ & \circ & \\ \circ & & \circ \end{array}$$

Bunnies with families (cont.)

Rules



Observables



MFA/Rate equations

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

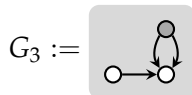
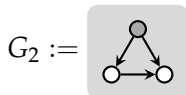
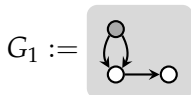
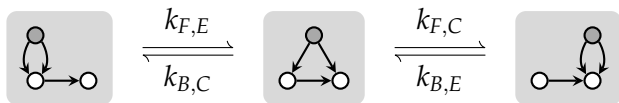
$$\frac{d}{dt}[F_1] = 0$$

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

$$\frac{d}{dt}[F_2] = 0$$

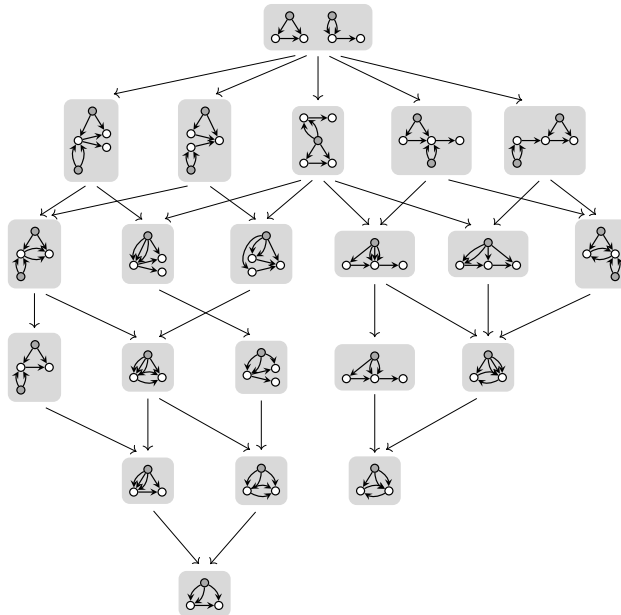
$$\frac{d}{dt}[S] = 4(k_\beta + k_\gamma)[C] + 4k_\gamma[S] + 4k_\gamma[F_1] + 8k_\gamma[F_2]$$

Two-legged DNA walker



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

Minimal gluings



Two-legged DNA walker (cont.)

Generate equations using relevant gluings, first try...

$$\frac{d}{dt} \text{[Diagram 1]} = k_{F,E} \text{[Diagram 2]} - k_{B,C} \text{[Diagram 3]} - k_{F,C} \text{[Diagram 4]} + k_{B,E} \text{[Diagram 5]}$$

Two-legged DNA walker (cont.)

Generate equations using relevant gluings, first try...

$$\begin{aligned} \frac{d}{dt} \text{[Diagram 1]} &= k_{F,E} \text{[Diagram 2]} - k_{B,C} \text{[Diagram 3]} - k_{F,C} \text{[Diagram 4]} + k_{B,E} \text{[Diagram 5]} \\ \frac{d}{dt} \text{[Diagram 2]} &= -k_{F,E} \text{[Diagram 1]} + k_{B,C} \text{[Diagram 3]} + k_{F,C} \text{[Diagram 4]} - \dots \end{aligned}$$

Two-legged DNA walker (cont.)

Generate equations using relevant gluings, first try...

$$\begin{aligned} \frac{d}{dt} \text{[Walker with 2 legs]} &= k_{F,E} \text{[Walker with 1 leg]} - k_{B,C} \text{[Walker with 2 legs]} - k_{F,C} \text{[Walker with 2 legs]} + k_{B,E} \text{[Walker with 1 leg]} \\ \frac{d}{dt} \text{[Walker with 1 leg]} &= -k_{F,E} \text{[Walker with 1 leg]} + k_{B,C} \text{[Walker with 2 legs]} + k_{F,C} \text{[Walker with 2 legs]} - \dots \\ \frac{d}{dt} \text{[Walker with 0 legs]} &= k_{F,E} \text{[Walker with 0 legs]} - k_{B,C} \text{[Walker with 0 legs]} - k_{F,C} \text{[Walker with 0 legs]} + \dots \end{aligned}$$

Two-legged DNA walker (cont.)

Generate equations using relevant gluings, first try...

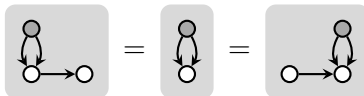
$$\begin{aligned}
 \frac{d}{dt} \text{[Walker with 2 legs]} &= k_{F,E} \text{[Walker with 1 leg]} - k_{B,C} \text{[Walker with 2 legs]} - k_{F,C} \text{[Walker with 2 legs]} + k_{B,E} \text{[Walker with 2 legs]} \\
 \frac{d}{dt} \text{[Walker with 1 leg]} &= -k_{F,E} \text{[Walker with 1 leg]} + k_{B,C} \text{[Walker with 2 legs]} + k_{F,C} \text{[Walker with 2 legs]} - \dots \\
 \frac{d}{dt} \text{[Walker with 2 legs]} &= k_{F,E} \text{[Walker with 1 leg]} - k_{B,C} \text{[Walker with 2 legs]} - k_{F,C} \text{[Walker with 2 legs]} + \dots \\
 \frac{d}{dt} \text{[Walker with 3 legs]} &= -k_{F,E} \text{[Walker with 3 legs]} + k_{B,C} \text{[Walker with 2 legs]} + k_{F,C} \text{[Walker with 2 legs]} - \dots
 \end{aligned}$$

Two-legged DNA walker (cont.)

Generate equations using relevant gluings, first try...

$$\begin{aligned}
 \frac{d}{dt} \text{[Walker with 2 legs, 1 step]} &= k_{F,E} \text{[Walker with 2 legs, 0 steps]} - k_{B,C} \text{[Walker with 2 legs, 1 step]} - k_{F,C} \text{[Walker with 2 legs, 1 step]} + k_{B,E} \text{[Walker with 2 legs, 2 steps]} \\
 \frac{d}{dt} \text{[Walker with 2 legs, 0 steps]} &= -k_{F,E} \text{[Walker with 2 legs, 0 steps]} + k_{B,C} \text{[Walker with 2 legs, 1 step]} + k_{F,C} \text{[Walker with 2 legs, 1 step]} - \dots \\
 \frac{d}{dt} \text{[Walker with 2 legs, 1 step]} &= k_{F,E} \text{[Walker with 2 legs, 0 steps]} - k_{B,C} \text{[Walker with 2 legs, 1 step]} - k_{F,C} \text{[Walker with 2 legs, 1 step]} + \dots \\
 \frac{d}{dt} \text{[Walker with 2 legs, 2 steps]} &= -k_{F,E} \text{[Walker with 2 legs, 1 step]} + k_{B,C} \text{[Walker with 2 legs, 2 steps]} + k_{F,C} \text{[Walker with 2 legs, 2 steps]} - \dots \\
 \frac{d}{dt} \text{[Walker with 2 legs, 3 steps]} &= \dots
 \end{aligned}$$

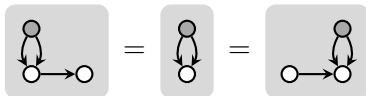
Invariants and Solution



$$\frac{d}{dt} \begin{array}{c} \bullet \\ \circ \end{array} = k_{F,E} \begin{array}{c} \bullet \\ \bullet \end{array} - k_{B,C} \begin{array}{c} \bullet \\ \circ \end{array} - k_{F,C} \begin{array}{c} \bullet \\ \circ \end{array} + k_{B,E} \begin{array}{c} \bullet \\ \bullet \end{array}$$

$$\frac{d}{dt} \begin{array}{c} \bullet \\ \bullet \end{array} = -k_{F,E} \begin{array}{c} \bullet \\ \bullet \end{array} + k_{B,C} \begin{array}{c} \bullet \\ \circ \end{array} + k_{F,C} \begin{array}{c} \bullet \\ \circ \end{array} - k_{B,E} \begin{array}{c} \bullet \\ \bullet \end{array}$$

Invariants and Solution

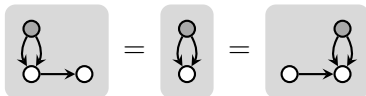


$$\frac{d}{dt} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Molecule on Left]} \end{array} = k_{F,E} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Empty]} \end{array} - k_{B,C} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Molecule on Left]} \end{array} - k_{F,C} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Molecule on Left]} \end{array} + k_{B,E} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Empty]} \end{array}$$

$$\frac{d}{dt} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Empty]} \end{array} = -k_{F,E} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Empty]} \end{array} + k_{B,C} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Molecule on Left]} \end{array} + k_{F,C} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Molecule on Left]} \end{array} - k_{B,E} \begin{array}{c} \text{[Molecule on Left]} \\ \text{[Empty]} \end{array}$$

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

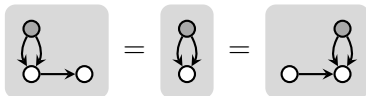
Invariants and Solution



$$\begin{aligned} \frac{d}{dt} \begin{array}{c} \circ \\ \circ \end{array} &= k_{F,E} \begin{array}{c} \circ \\ \circ \end{array} - k_{B,C} \begin{array}{c} \circ \\ \circ \end{array} - k_{F,C} \begin{array}{c} \circ \\ \circ \end{array} + k_{B,E} \begin{array}{c} \circ \\ \circ \end{array} \\ \frac{d}{dt} \begin{array}{c} \circ \\ \circ \end{array} &= -k_{F,E} \begin{array}{c} \circ \\ \circ \end{array} + k_{B,C} \begin{array}{c} \circ \\ \circ \end{array} + k_{F,C} \begin{array}{c} \circ \\ \circ \end{array} - k_{B,E} \begin{array}{c} \circ \\ \circ \end{array} \end{aligned}$$

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



$$\begin{aligned} \frac{d}{dt} \begin{array}{c} \circ \\ \circ \end{array} &= k_{F,E} \begin{array}{c} \circ \\ \circ \end{array} - k_{B,C} \begin{array}{c} \circ \\ \circ \end{array} - k_{F,C} \begin{array}{c} \circ \\ \circ \end{array} + k_{B,E} \begin{array}{c} \circ \\ \circ \end{array} \\ \frac{d}{dt} \begin{array}{c} \circ \\ \circ \end{array} &= -k_{F,E} \begin{array}{c} \circ \\ \circ \end{array} + k_{B,C} \begin{array}{c} \circ \\ \circ \end{array} + k_{F,C} \begin{array}{c} \circ \\ \circ \end{array} - k_{B,E} \begin{array}{c} \circ \\ \circ \end{array} \end{aligned}$$

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

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

Full details...

...are in the paper.

$$\begin{array}{ccc}
 \begin{array}{ccc} L & \xrightarrow{\alpha} & R \\ \downarrow f & & \downarrow g_1 \\ & & T \\ & & \downarrow g_2 \\ G & \xrightarrow{\beta} & H \end{array} &
 \begin{array}{ccc} L & \xleftarrow{\alpha^\dagger} & R \\ f_1 \downarrow & & \downarrow g_1 \\ S & \xleftarrow{\gamma^\dagger} & T \end{array} &
 \begin{array}{ccc} L & \xrightarrow{\alpha} & R \\ \downarrow f_1 & & \downarrow g_1 \\ S & \xrightarrow{\gamma} & T \\ \downarrow f_2 & & \downarrow g_2 \\ G & \xrightarrow{\beta} & H \end{array}
 \end{array}$$

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

Fragger

The screenshot shows the Fragger web application in a browser window. The URL is <https://rhz.github.io/fragger/?mne=2&m=bimotor>. The page features the Fragger logo and the text "Moment semantics".

Syntax

```
graph := [(node | edge){":" | ","}]>
edge := node =>{[label]?} node
node := name{[label]?}
```

Examples: bunny, bimotor, preferential attachment, irreversible marks, Koch snowflake, voter model.

Rules

left-hand side	right-hand side	rate
<input type="text" value="b[b], e1[e], e2[e], e1->e2, b->c1, b->c1"/>	<input type="text" value="b[b], e1[e], e2[e], e1->e2, b->c1, b->c2"/>	<input type="text" value="kFE"/>
<input type="text" value="b[b], e1[e], e2[e], e1->e2, b->c1, b->c2"/>	<input type="text" value="b[b], e1[e], e2[e], e1->e2, b->c1, b->c1"/>	<input type="text" value="kBC"/>
<input type="text" value="b[b], e1[e], e2[e], e1->e2, b->c1, b->c2"/>	<input type="text" value="b[b], e1[e], e2[e], e1->e2, b->c2, b->c2"/>	<input type="text" value="kFC"/>
<input type="text" value="b[b], e1[e], e2[e], e1->e2, b->c2, b->c2"/>	<input type="text" value="b[b], e1[e], e2[e], e1->e2, b->c1, b->c2"/>	<input type="text" value="kBE"/>

Observables

name	graph expression
<input type="text" value="G0"/>	<input type="text" value="b[b], e[e], b->c, b->c"/>
<input type="text" value="G2"/>	<input type="text" value="b[b], e1[e], e2[e], e1->e2, b->c1, b->c2"/>

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!

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- Tobias Heindel, TU Berlin
- Ricardo Honorato-Zimmer, CINV



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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:

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

More generally,

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

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

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

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

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 $\text{poly}(\mathcal{B}_0) = \mathcal{A}$

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

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

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:

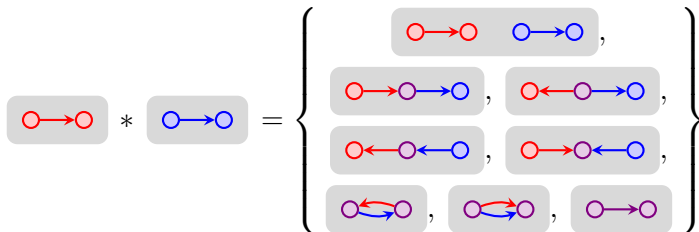
$$\begin{aligned} \frac{d}{dt} \mathbb{E}([A]) &= - \sum_{\alpha \in \mathcal{R}} k(\alpha) \rho_{\alpha}(A) \prod_{(u,n) \in \rho_{\alpha}} \mathbb{E}(u)^n \\ &+ \sum_{\alpha \in \mathcal{R}} k(\alpha) \gamma_{\alpha}(A) \prod_{(u,n) \in \gamma_{\alpha}} \mathbb{E}(u)^n \end{aligned}$$





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

Rate equations for graphs




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

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



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[//users.dimi.uniud.it/~marino.miculan/Papers/MeMo15-preproc.pdf](http://users.dimi.uniud.it/~marino.miculan/Papers/MeMo15-preproc.pdf).



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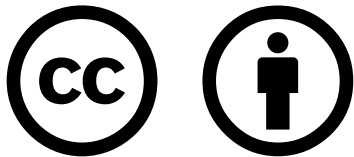
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