Rule-based Modeling of Nano Devices

What we have been doing in the interdisciplinary project "CompReNDe: Compositional and executable Representations of Nano Devices"

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(based on joint work with Cristian Versari)

Rule-based Modeling of Nano Devices

A presentation of how computer science modeling techniques can be applied to the modeling of Nano Devices

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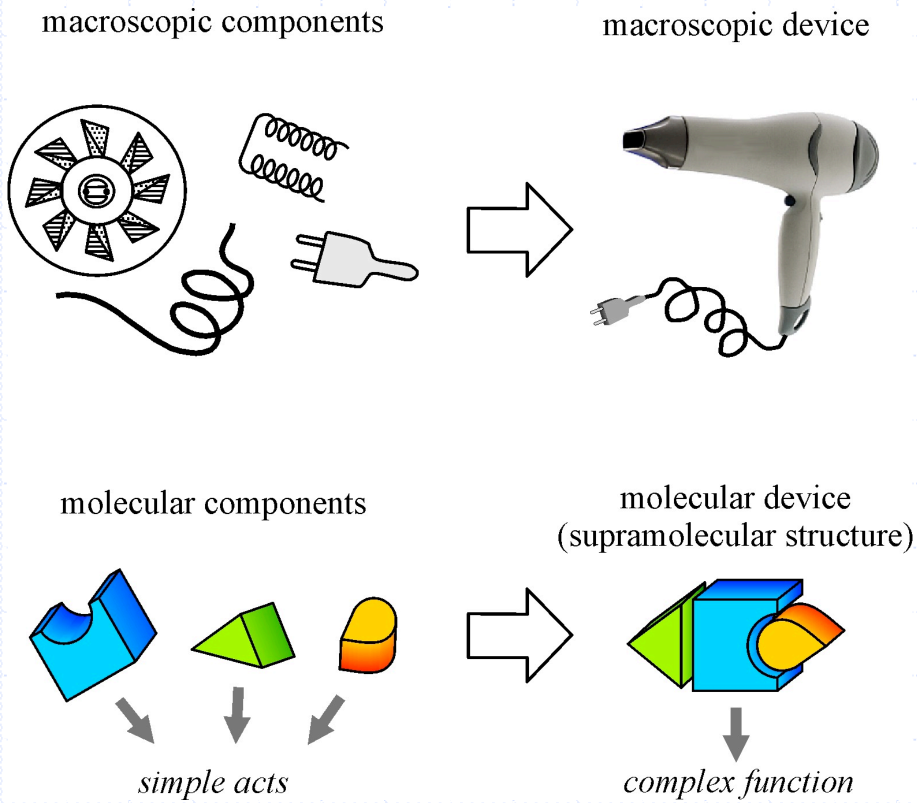
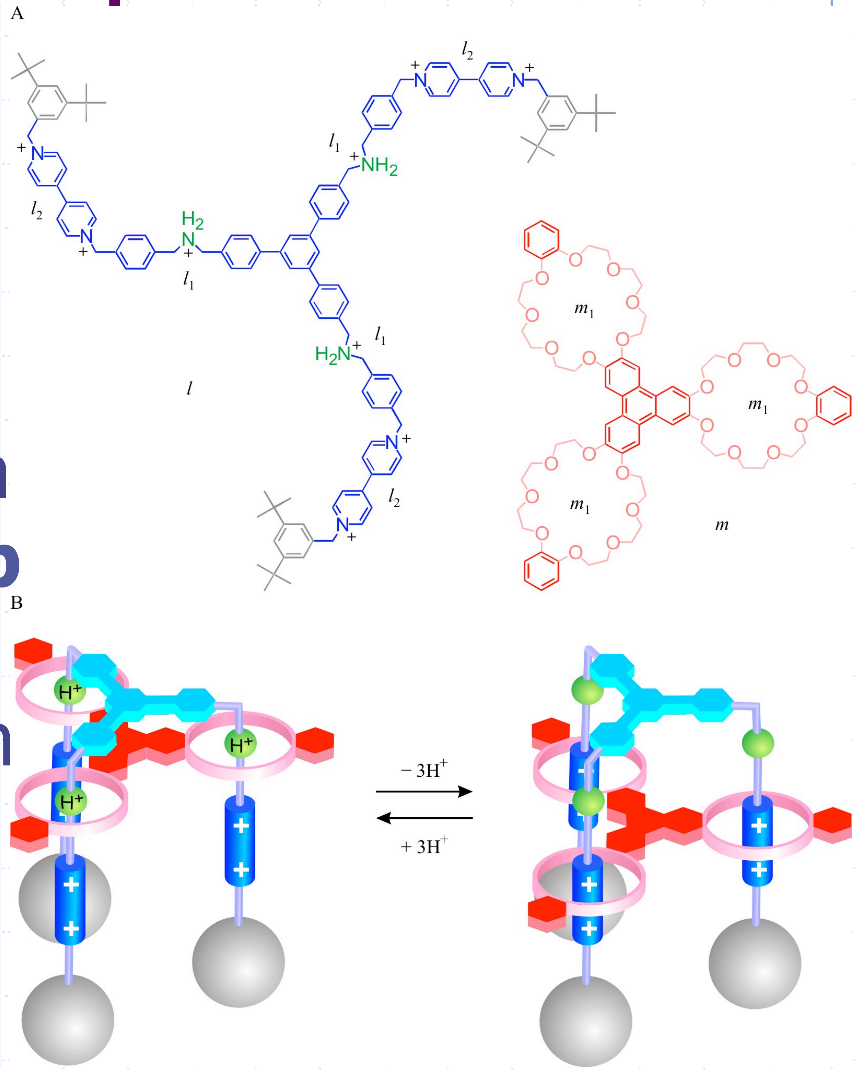
Nano Devices

- **Bottom-up** assembly of supramolecular structures
- Complex functions are then obtained by **composing** “programmed” molecules



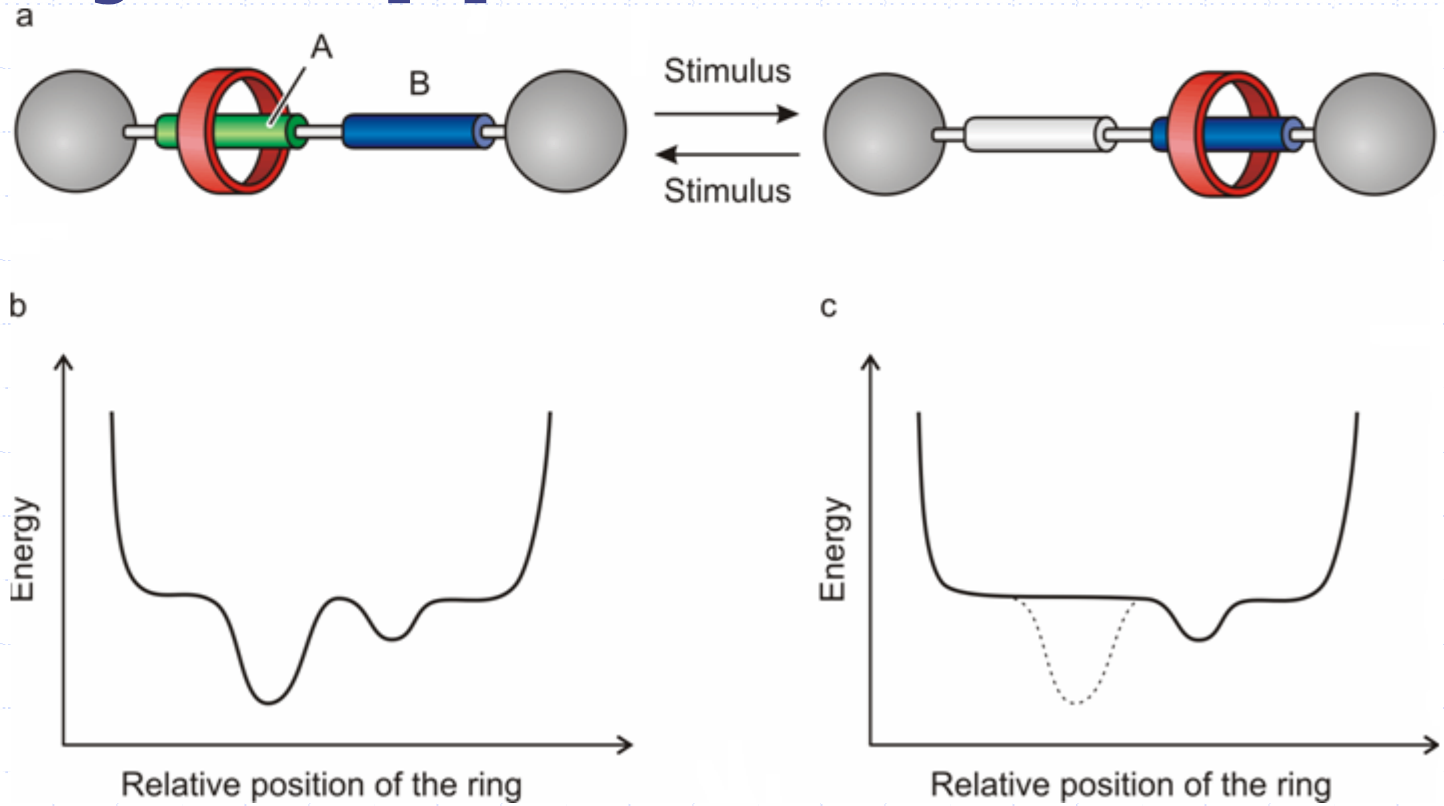
An (running) Example

- **Nano-Elevator**:
  - Three legs
  - Joined on top
  - Intermediary platform that can be moved **up** and **down** by adding or removing hydrogen ions to the top-part of the legs



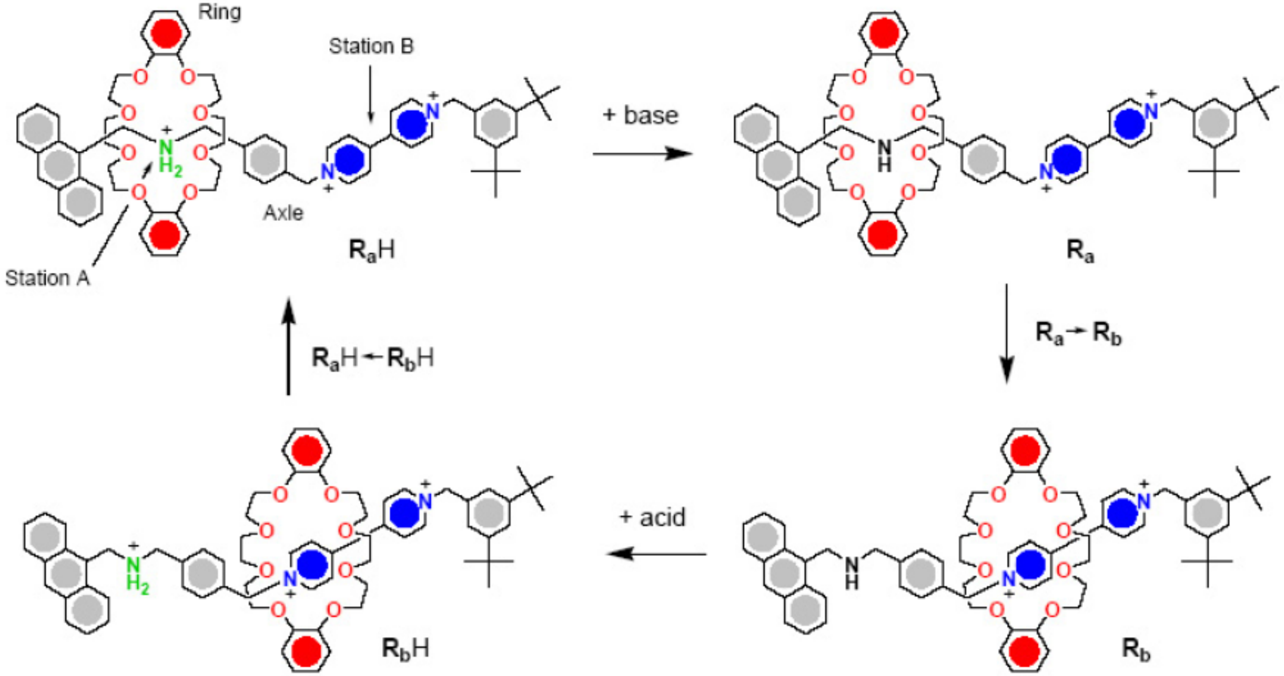
Modeling the legs

- Legs are "[2]Rotaxanes"



Modeling the legs

- More precisely rotaxane RaH

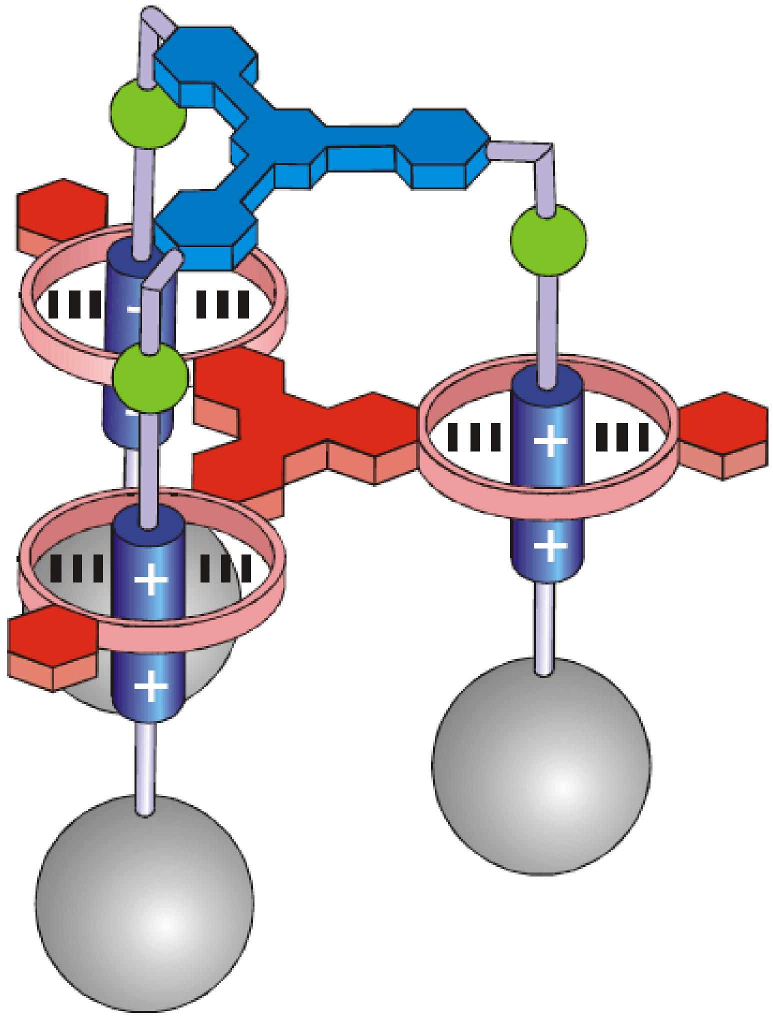


RaH+base → Ra+baseH   Ra → Rb

Rb+acidH → RbH+acid   RbH→ RaH

From the Rotaxane to the Nano Elevator

- Three rotaxanes connected
- How many states?
  - $4^3 = 64$
- How many different reactions?
  - ???
- Need for Compositional Modeling



Plan of the talk

- Model of RaH with Kappa-calculus
- Administrative instantaneous rules
- K_F: Kappa + complex functional rates
- Model of the Nano-Elevator
- Conclusion and Future Work

Plan of the talk

- **Model of RaH with Kappa-calculus**
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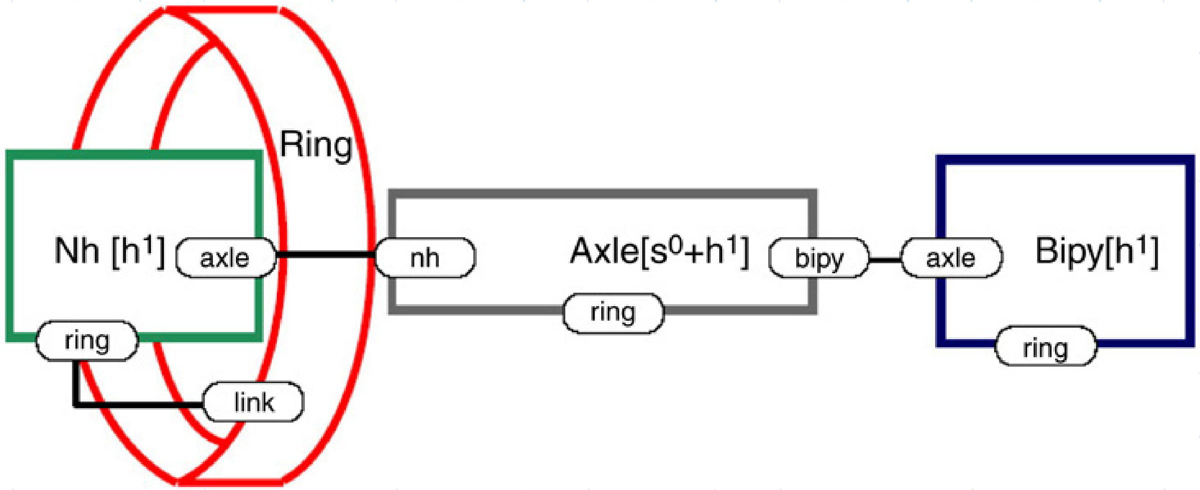
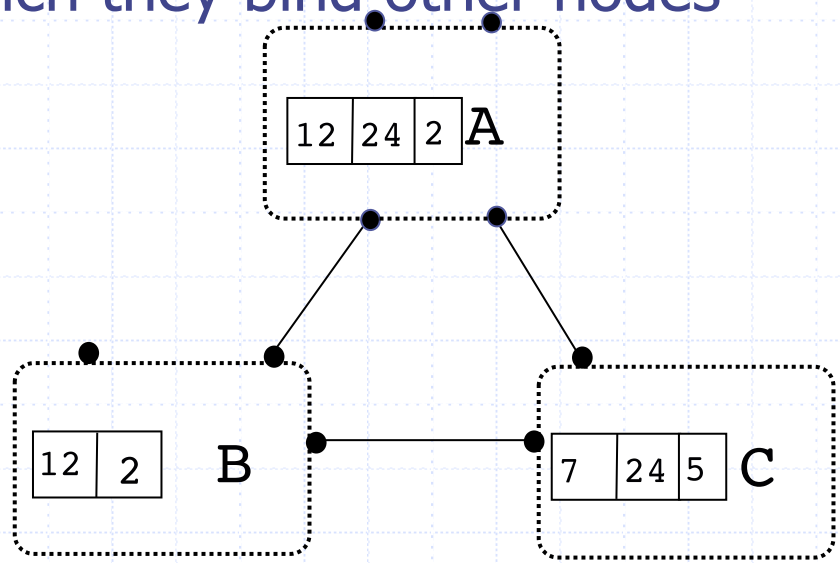
Easy things first… [TCS08]

- Compositional modeling of [2]rotaxane
  - we want to represent the **components** of the device



K-calculus: the nodes

- K is a **graph-rewriting** system where nodes
  - carry **state information** (about phosphorilation, shape,…)
  - have **sites** through which they bind other nodes
- A **complex**:



and its syntactic description:

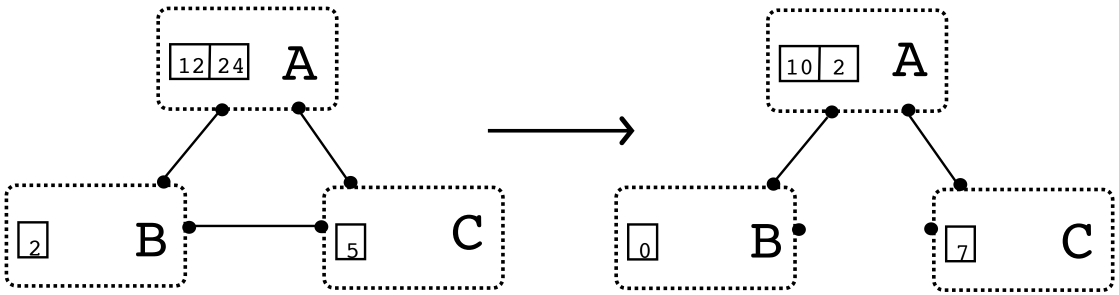
$A[1^{12}+2^{24}+3^{2}](1^{x}+2^{y}+3+4)$, $B[1^{12}+2^{2}](1+2^{x}+3^{z})$, $C[1^{7}+2^{24}+3^{5}](1^{z}+2^{y})$

K-calculus: the reactions

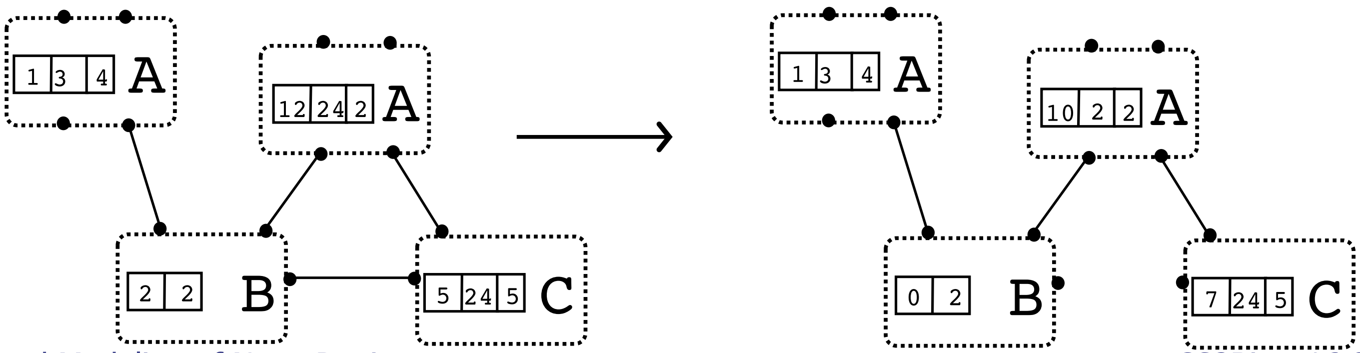
- A reaction rule:

$$A[1^{12}+2^{24}](1^x+2^y),\ B[1^2](2^x+3^z),\ C[1^5](1^z+2^y)$$

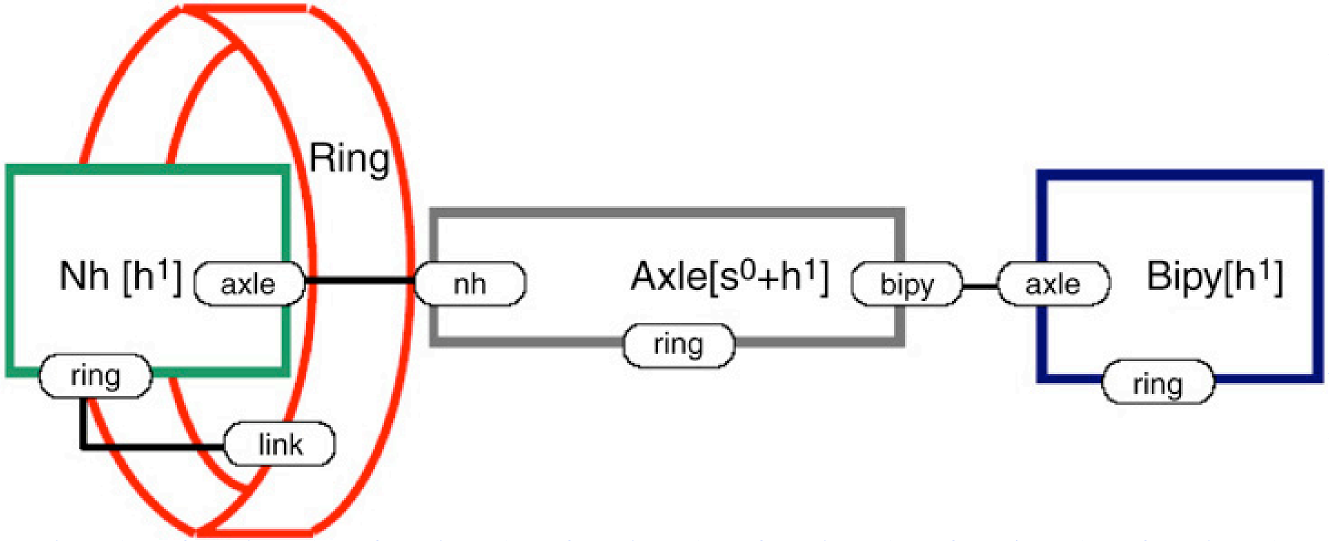
$$\rightarrow A[1^{10}+2^2](1^x+2^y),\ B[1^0](2^x+3),\ C[1^7](1+2^y)$$



and a possible instantiation:



RaH modeled in K: the initial state



$$Nh[h^1](axle^s + ring^x)\,, \qquad Axle[s^0 + h^1](nh^s + bipy^r + ring)\,,$$
$$Bipy[h^1](axle^r + ring)\,, \qquad Ring\,(link^x)$$

RaH modeled in K: some reaction rules (forward move)

- Ion donation:

$$Nh[h^1],\, Base[h^0] \underset{base\_nh}{\overset{nh\_base}{\rightleftharpoons}} Nh[h^0],\, Base[h^1]$$

- Disconnection:

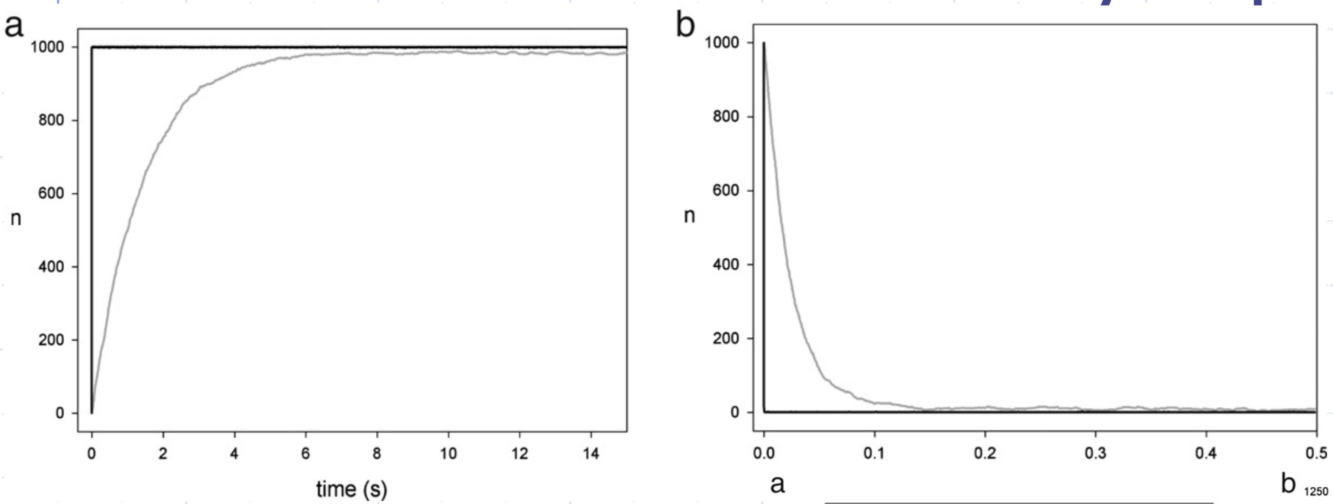
$$Nh[h^0](axle^s + ring^x)\,, Axle[s^0](nh^s + ring) \xrightarrow{\infty} Nh[h^0](axle^s + ring)\,, Axle[s^0](nh^s + ring^x)$$

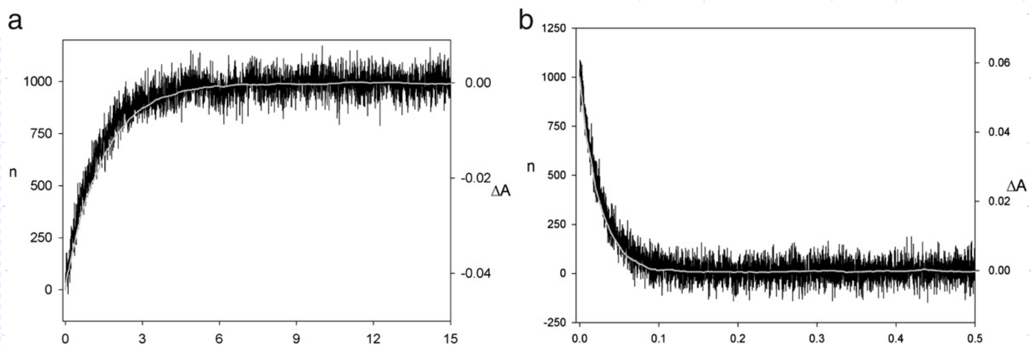
- Connection:

$$Axle[s^0](bipy^r + ring^x)\,, Bipy[h^0](axle^r + ring) \underset{unlink\_bipy}{\overset{link\_bipy}{\rightleftharpoons}} Axle[s^1](bipy^r + ring)\,, Bipy[h^0](axle^r + ring^x)$$

Simulation results

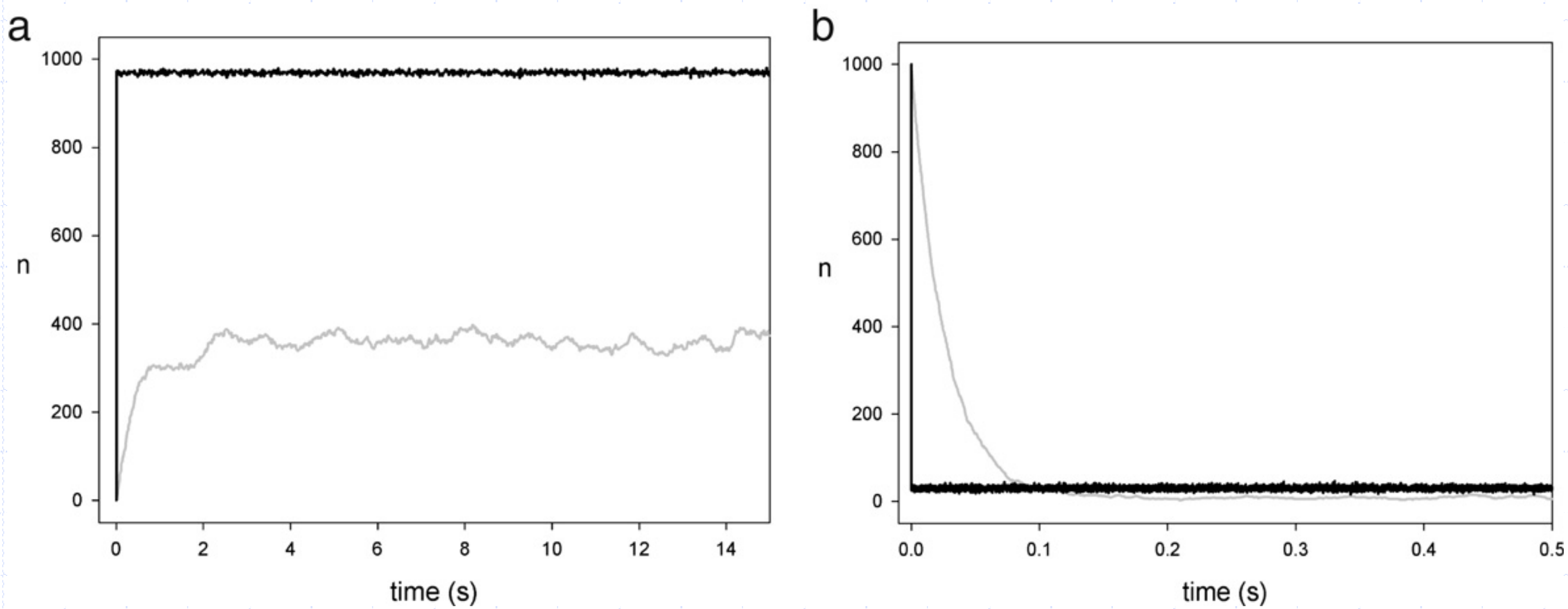
- Simulation of the model, by using rates obtained from laboratory experiments





Some (initially) unexpected simulation results

- Simulation of the model assuming **low** concentrations



- Follows from the **competition** between the ion-exchange and shuttling reactions

Plan of the talk

- Model of RaH with Kappa-calculus
- **Administrative instantaneous rules**
- K_F: Kappa + complex functional rates
- Model of the Nano-Elevator
- Conclusion and Future Work

The price to pay for compositionality

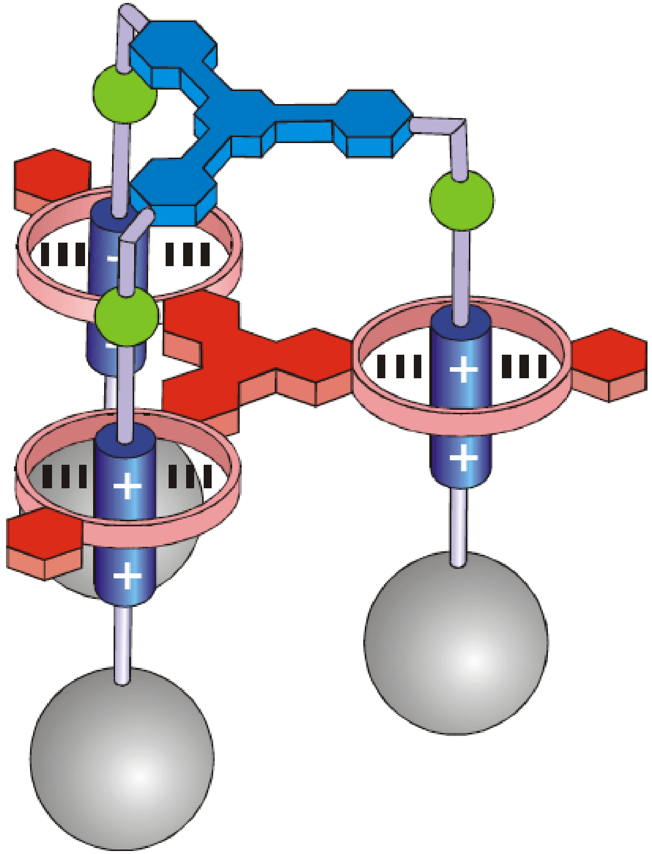
- The model is compositional but…
- …we had to extend Kappa with **instantaneous** reactions, e.g.

$$Nh[h^0](axle^s + ring^x), Axle[s^0](nh^s + ring) \xrightarrow{\infty} Nh[h^0](axle^s + ring), Axle[s^0](nh^s + ring^x)$$

- "Administrative" reactions used to model the **influence** of one component on the behaviour of other components

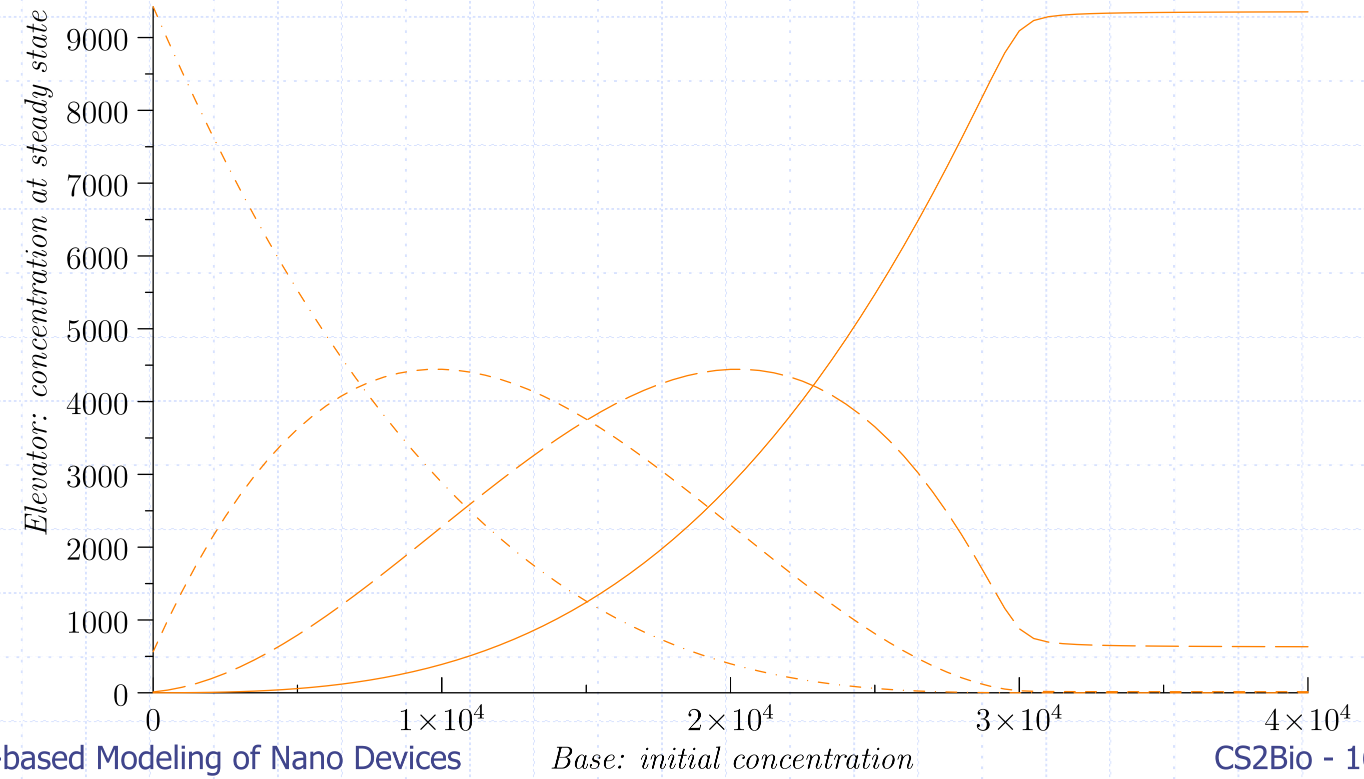
From the Rotaxane to the Nano-Elevator

- First attempt:
  - Consider 3 rotaxanes
  - Connect the three Nhs
  - Connect the three Rings



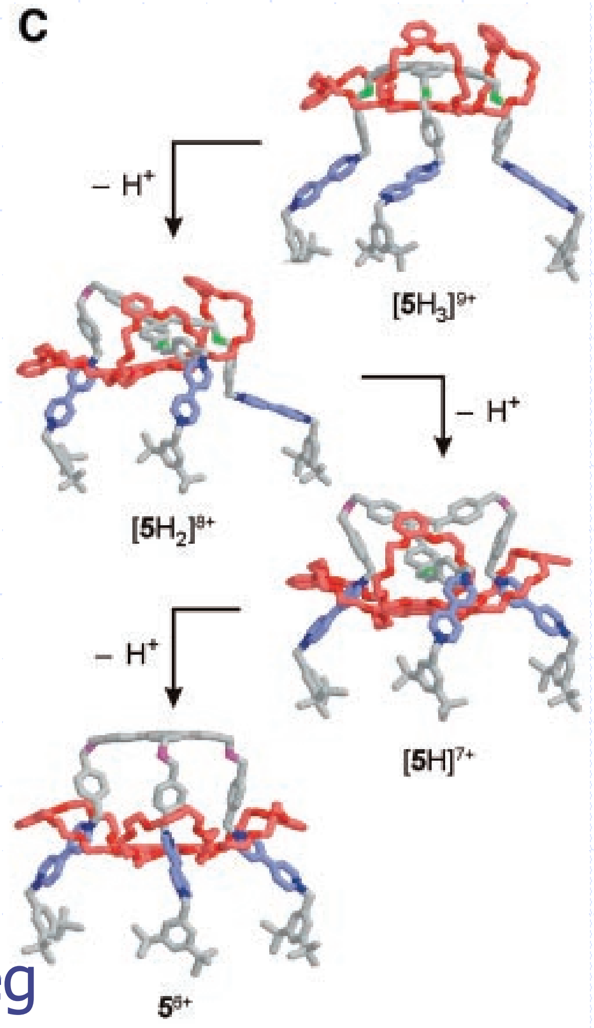
Simulation results

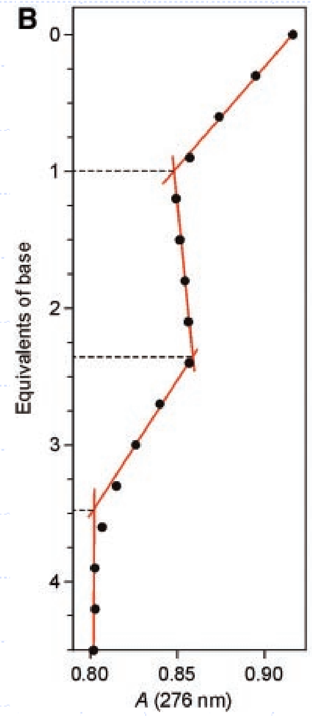
- We have investigated (at steady state) the distributions of the three **kinds** of Nano-Elevators (depending on base concentration)



Simulation is not faithful

- Laboratory experiments proved that there are **three** distinct phases in the platform movement
  - first (almost) all nano-elevators moves **one** leg
  - then they move the **second** leg
  - and finally the **third** leg





Chemical interpretation

- Upon donation of the ion of one of the rotaxanes…
- …the **rate** of donation for the other rotaxanes is decreased!
- In other words: the behaviour of the rotaxanes is **influenced** by the state of the other rotaxanes in the same device!

Model with "administrative" reactions

$$Nh(\overline{ph}+0), B_1(ph) \xrightarrow{fast} Nh(ph+1), B_1(\overline{ph})$$
$$Nh(\overline{ph}+1), B_2(ph) \xrightarrow{fast} Nh(ph+2), B_2(\overline{ph})$$
$$Nh(\overline{ph}+2), B_3(ph) \xrightarrow{fast} Nh(ph+3), B_3(\overline{ph})$$

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$$Nh(\overline{ph}+1), Nh(ph+3) \xrightarrow{fast} Nh(ph+1), Nh(\overline{ph}+3)$$

$$Nh(X+axis^x)\,,\ Axis(Y \neq X+up^x)$$
$$\xrightarrow{\infty} Nh(X+axis^x)\,,\ Axis(X+up^x)$$

$$Axis(X+down^x)\,,\ Bipy(Y \neq X+axis^x)$$
$$\xrightarrow{\infty} Axis(X+down^x)\,,\ Bipy(X+axis^x)$$

$$Nh(ph), H() \xrightarrow{fast} Nh(\overline{ph})$$

$$Nh(t^x+disk)\,,\ Top(n_j^x+\overline{r_j})$$
$$\xrightarrow{\infty+} Nh(t^x+disk), Top(n_j^x+r_j)$$
$$Nh(t^x+disk^*)\,,\ Top(n_j^x+r_j)$$
$$\xrightarrow{\infty+} Nh(t^x+disk^*), Top(n_j^x+\overline{r_j})$$
$$Nh(t^x+X\neq 0)\,,\ Top(n_j^x+\{r_1,r_2,r_3\}=\{h,h,h\})$$
$$\xrightarrow{\infty} Nh(t^x+0), Top(n_j^x+(r_j))$$
$$Nh(t^x+X\neq 1)\,,\ Top(n_j^x+\{r_1,r_2,r_3\}=\{v,h,h\})$$
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$$Nh(t^x+X\neq 2)\,,\ Top(n_j^x+\{r_1,r_2,r_3\}=\{v,v,h\})$$
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$$Nh(t^x+X\neq 3)\,,\ Top(n_j^x+\{r_1,r_2,r_3\}=\{v,v,v\})$$
$$\xrightarrow{\infty} Nh(t^x+3), Top(n_j^x+(r_j))$$

$$Nh(ph+disk^x), Ring(up^x) \xrightarrow{fast+} Nh(ph+disk), Ring(up)$$
$$Bipy(disk+X), Ring(up+down) \xrightarrow{k_X} Bipy(disk^x+X), Ring(up+dow$$

$$Nh(\overline{ph}+disk+X), Ring(up) \xrightarrow{k'_X} Nh(\overline{ph}+disk^x+X), Ring(up^x)$$
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  - One third of them represents the same phenomenon, but are needed to define the different rates

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Model with “administrative” reactions

- **Unsatisfactory** model!
  - Too many rules
  - Half of them are “administrative”
  - One third of them represents the same phenomena, but are needed to define the different rates
  - No **compositionality**: the previous model of the rotaxane represents a very small part of the new model

Plan of the talk

- Model of RaH with Kappa-calculus
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Recovery plan

- In the light of our initial failure, we decided to change our direction of work
  - **Complex Functional rates**: associate to the K-rules a rate which depends on the state of the other components in the same complex

K_F-calculus

- Syntax:
$$\begin{array}{rcl} \mathrm{S} & ::= & \textsc{Mol} \quad | \quad \mathrm{S},\mathrm{S} \\ \textsc{Mol} & ::= & \mathrm{A}[u](\sigma) \end{array}$$

- Example: remember the rotaxane

$$Nh[h^1](axle^s + ring^x)\,, \qquad Axle[s^0 + h^1](nh^s + bipy^r + ring)\,,$$
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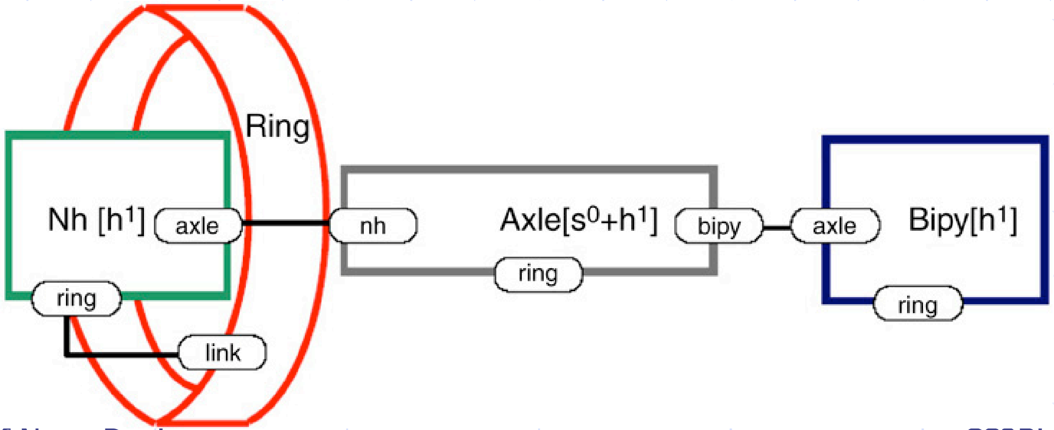
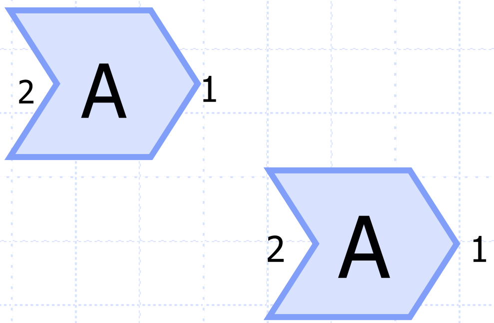


Complex Functional Rate

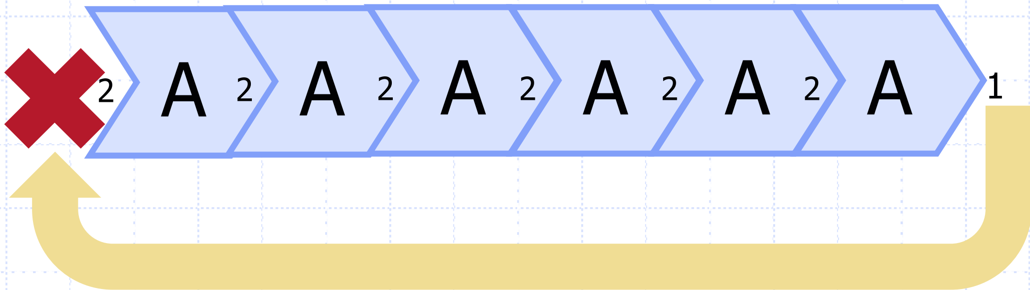
- We express it by using **colored** reactions
- An example: linear polymerization
  - Monomer association: $\mathrm{A}(1), \mathrm{A}(2) \xrightarrow{f} \mathrm{A}(1^x), \mathrm{A}(2^x)$
  - Monomer dissociation: $\mathrm{A}(1^x), \mathrm{A}(2^x) \xrightarrow{f'} \mathrm{A}(1), \mathrm{A}(2)$



Self-association

- Assume we want to avoid self-association

$$A(1), A(2) \xrightarrow{f} A(1^x), A(2^x)$$



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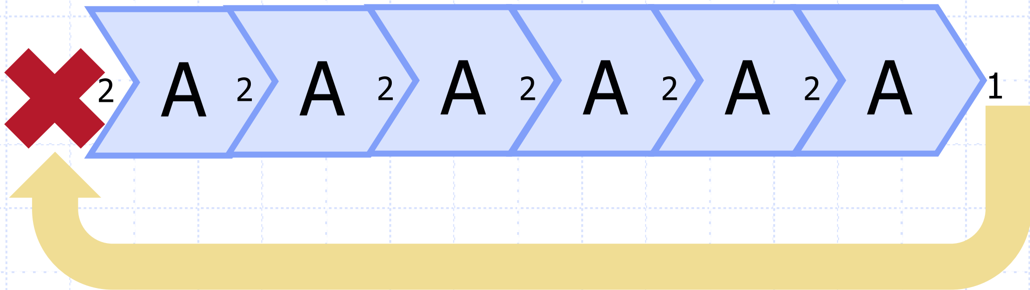

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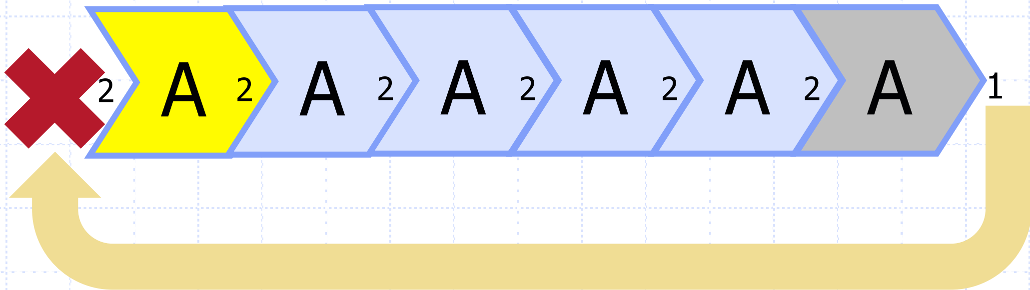

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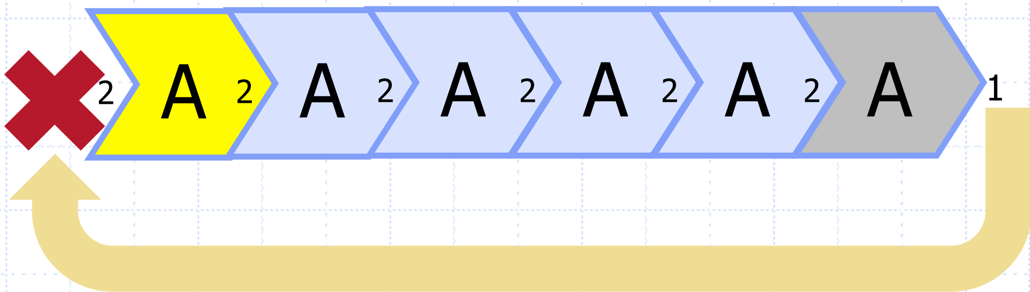

$$f(\mathrm{S}^{\tilde{c}}) \;=\; \text{if S contains two complexes then } \lambda \text{ else } 0$$

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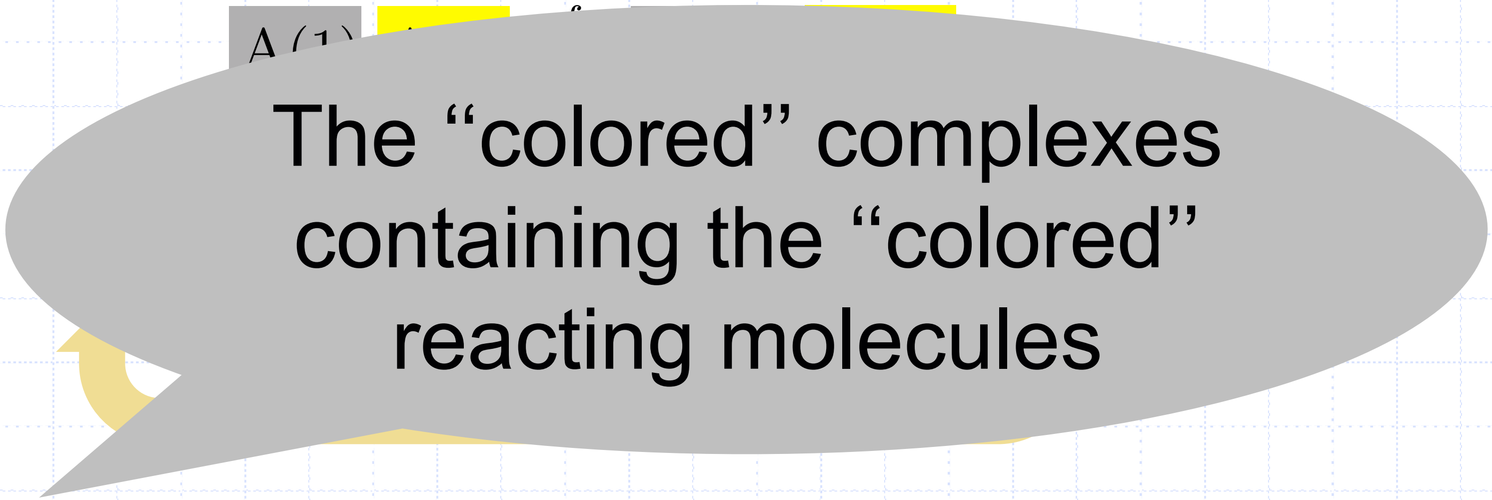

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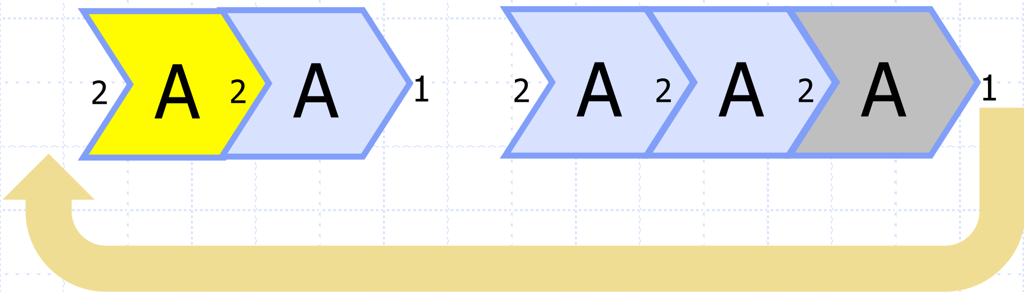
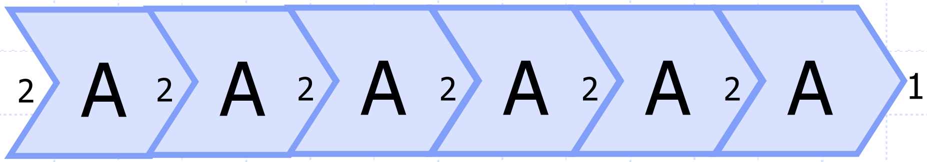


$$f(\mathrm{S}^{\tilde{c}}) \ = \ \text{if S contains two complexes then } \lambda \text{ else } 0$$

Dissociation

- Assume that monomers close to the ends dissociate more easily

$$\mathrm{A}(1^x), \mathrm{A}(2^x) \xrightarrow{f'} \mathrm{A}(1), \mathrm{A}(2)$$



Dissociation

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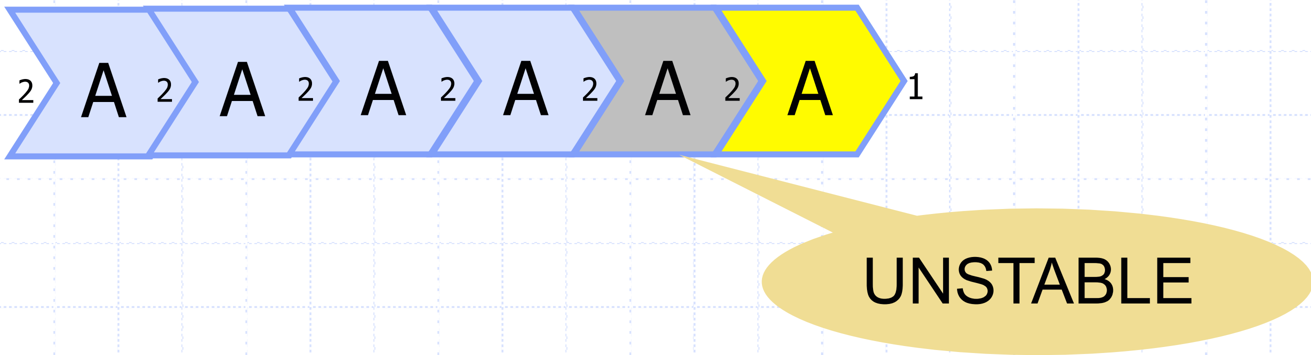
$$\mathrm{A}(1^x), \mathrm{A}(2^x) \xrightarrow{f'} \mathrm{A}(1), \mathrm{A}(2)$$



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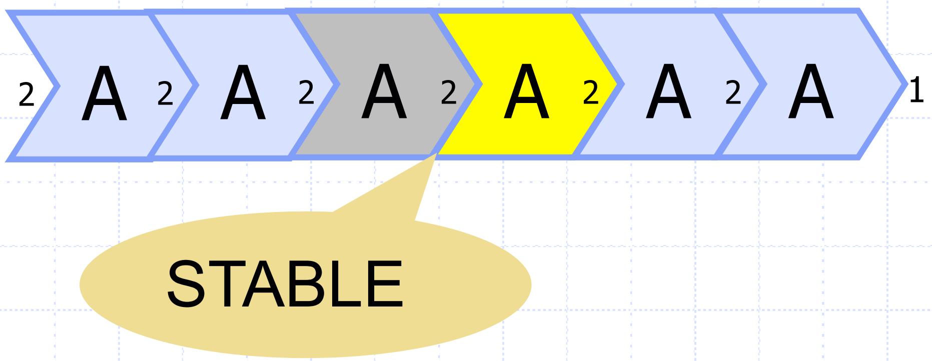

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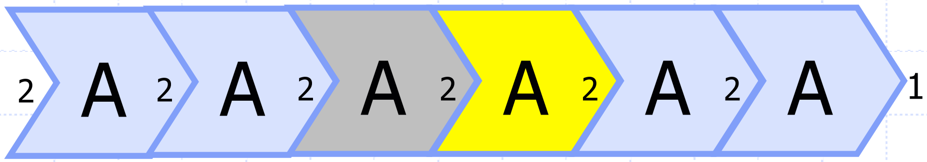


$$f'(\mathrm{S}^{\tilde{c}}) = \frac{\lambda}{min\{dist(\mathrm{S}^{\tilde{c}}, c_1, end_2), dist(\mathrm{S}^{\tilde{c}}, c_2, end_1)\}}$$

A more realistic polymerization example

- Long polymers have a **greater mass**, then have a **lower speed**, hence also **smaller reaction propensity**
  - Following the [Gillespie77] approach, we considered the following functional rate

$$\lambda \cdot \sqrt{\frac{2}{\left(\frac{M_1 \cdot M_2}{M_1 + M_2}\right)}}$$

where M_1 and M_2 are the masses of the two attaching polymers

The model

- The usual rules

$$A(1), A(2) \xrightarrow{f_m} A(1^x), A(2^x)$$

$$A(1^x), A(2^x) \xrightarrow{f'_m} A(1), A(2)$$

- With the **mass dependent** functional rate

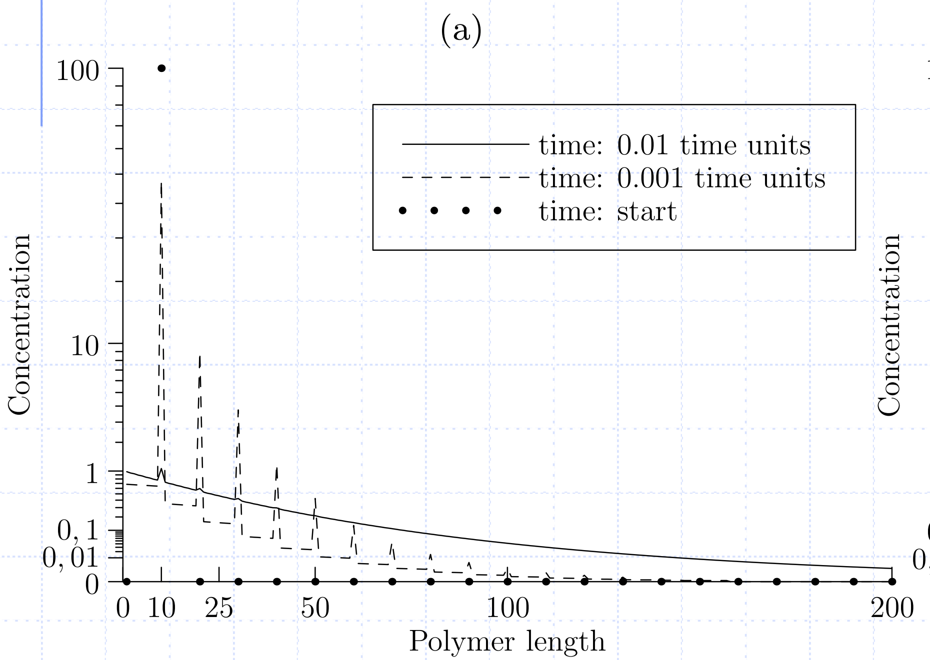
$$
\begin{aligned}
f_m(\mathrm{S}^{\tilde{c}}) \;=\; & \text{if S contains two complexes then} \\
& \quad \text{let } \mathrm{S}_1, \mathrm{S}_2 \text{ be two complexes in S in} \\
& \quad \text{let } M_1 = \textstyle\sum_{\mathrm{A}[1^m](\sigma)\in \mathrm{S}_1} \mathfrak{m}(m) \quad \text{in} \\
& \quad \text{let } M_2 = \textstyle\sum_{\mathrm{A}[1^m](\sigma)\in \mathrm{S}_2} \mathfrak{m}(m) \quad \text{in} \\
& \quad \text{let } M_{12} = \frac{M_1 \cdot M_2}{M_1 + M_2} \quad \text{in} \\
& \qquad \lambda \cdot \sqrt{\frac{2}{M_{12}}} \\
& \text{else } 0 \\
f'_m(\mathrm{S}^{\tilde{c}}) \;=\; & \lambda'
\end{aligned}
$$

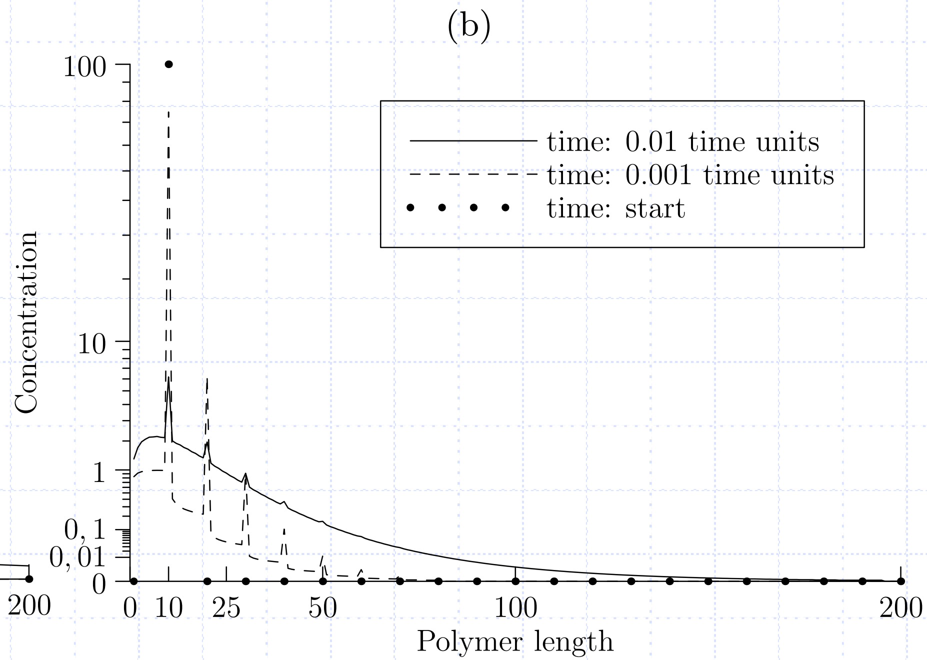
Simulation results

- Initial state 100 polymers of legth 10:

constant rate

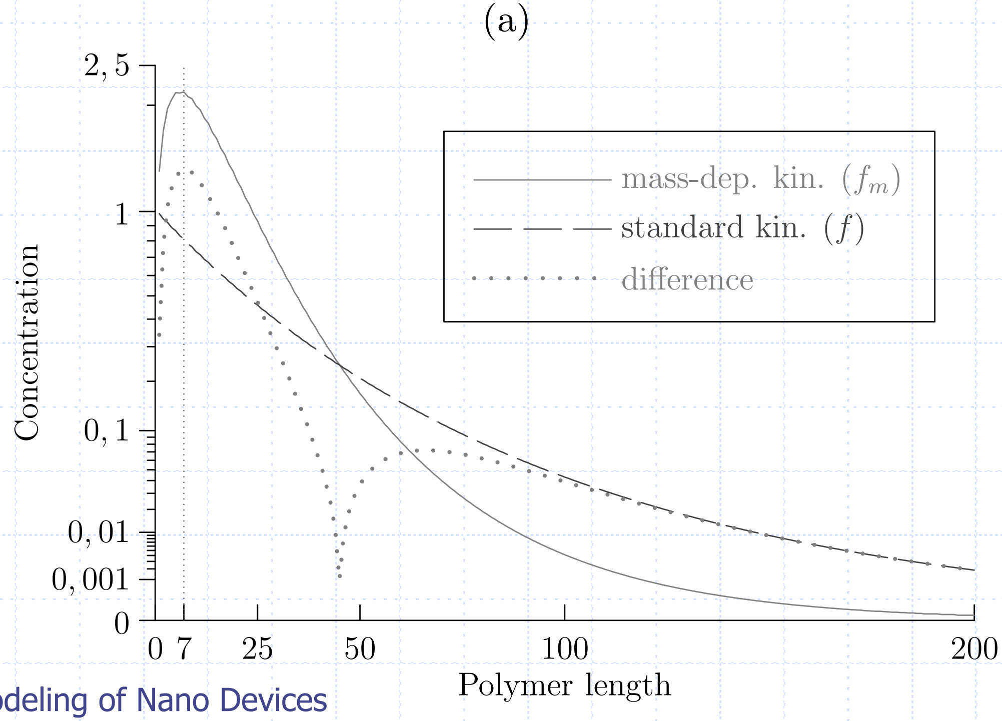
mass-dependent rate





Simulation results

comparison of the two models
at steady state



Plan of the talk

- Model of RaH with Kappa-calculus
- Administrative instantaneous rules
- K_F: Kappa + complex functional rates
- **Model of the Nano-Elevator**
- Conclusion and Future Work

New model for the Nano-Elevator

- Three connected rotaxanes:

$$Top(l^{t_1} + nh^{s_1} + r^{t_2}), Top(l^{t_2} + nh^{s_2} + r^{t_3}), Top(l^{t_3} + nh^{s_3} + r^{t_1}),$$
$$Nh[h^1](top^{s_1} + bipy^{r_1} + ring^{x_1}), Ring(l^{p_1} + link^{x_1} + r^{p_2}), Bipy(nh^{r_1} + ring),$$
$$Nh[h^1](top^{s_2} + bipy^{r_2} + ring^{x_2}), Ring(l^{p_2} + link^{x_2} + r^{p_3}), Bipy(nh^{r_2} + ring),$$
$$Nh[h^1](top^{s_3} + bipy^{r_3} + ring^{x_3}), Ring(l^{p_3} + link^{x_3} + r^{p_1}), Bipy(nh^{r_3} + ring)$$

- Movement reaction:

$$Nh(bipy^{r_1} + ring^{x_1})^{c_1}, Ring(link^{x_1})^{c_2}, Bipy(nh^{r_1} + ring)^{c_3} \xleftrightarrow{f_{\mathrm{mov}}}$$
$$Nh(bipy^{r_1} + ring)^{c_1}, Ring(link^{x_1})^{c_2}, Bipy(nh^{r_1} + ring^{x_1})^{c_3}$$

$$\begin{aligned} f_{\mathrm{mov}}(\mathrm{S}^{\tilde{c}}) \;=\; & \text{let } Nh[h^x](ring^y + \sigma)^{c_1} \in \mathrm{S}^{\tilde{c}} \quad \text{in} \\ & \text{if } y = \varepsilon \text{ then} \\ & \quad \text{if } x = 0 \text{ then } \lambda^1_{\mathrm{mov}} \text{ else } \lambda^2_{\mathrm{mov}} \\ & \text{else} \\ & \quad \text{if } x = 0 \text{ then } \lambda^3_{\mathrm{mov}} \text{ else } \lambda^4_{\mathrm{mov}} \end{aligned}$$

New model for the Nano-Elevator

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$$Nh[h^1](top^{s_1} + bipy^{r_1} + ring^{x_1}), Ring(l^{p_1} + link^{x_1} + r^{p_2}), Bipy(nh^{r_1} + ring),$$
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- Ion-exchange reaction:

$$Nh[h^1], Base[h^0] \quad \underset{f_{\text{b-prot}}}{\overset{f_{\text{b-deprot}}}{\rightleftarrows}} \quad Nh[h^0], Base[h^1]$$

$$Nh[h^0], Acid[h^1] \quad \underset{f_{\text{a-prot}}}{\overset{f_{\text{a-deprot}}}{\rightleftarrows}} \quad Nh[h^1], Acid[h^0]$$

$$f_{\mathrm{k}}(\mathrm{S}^{\tilde{c}}) \quad = \quad \text{let } P = \sum_{Nh[h^x](\sigma)\in \mathrm{S}^{\tilde{c}}} x \quad \text{in} \quad (\lambda_{\mathrm{k}}) \cdot 10^{s_{\mathrm{k}} \cdot P}$$

for $\mathrm{k} \in \{\text{b-deprot}, \text{b-prot}, \text{a-deprot}, \text{a-prot}\}$

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$$Nh[h^1](top^{s_2} + bipy^{r_2} + ring^{x_2}), Ring(l^{p_2} + link^{x_2} + r^{p_3}), Bipy(nh^{r_2} + ring),$$
$$Nh[h^1](top^{s_3} + bipy^{r_3} + ring^{x_3}), Ring(l^{p_3} + link^{x_3} + r^{p_1}), Bipy(nh^{r_3} + ring)$$

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for $\text{k} \in \{\text{b-deprot}, \text{b-prot}, \text{a-deprot}, \text{a-prot}\}$

Simulation of the Nano-Elevator

- We have translated the model into a Chemical Reaction Network
  - Automatic **generation** of all the possible complexes
  - Automatic generation of all the possible **reactions**, and computation of the corresponding rates

The complexes:

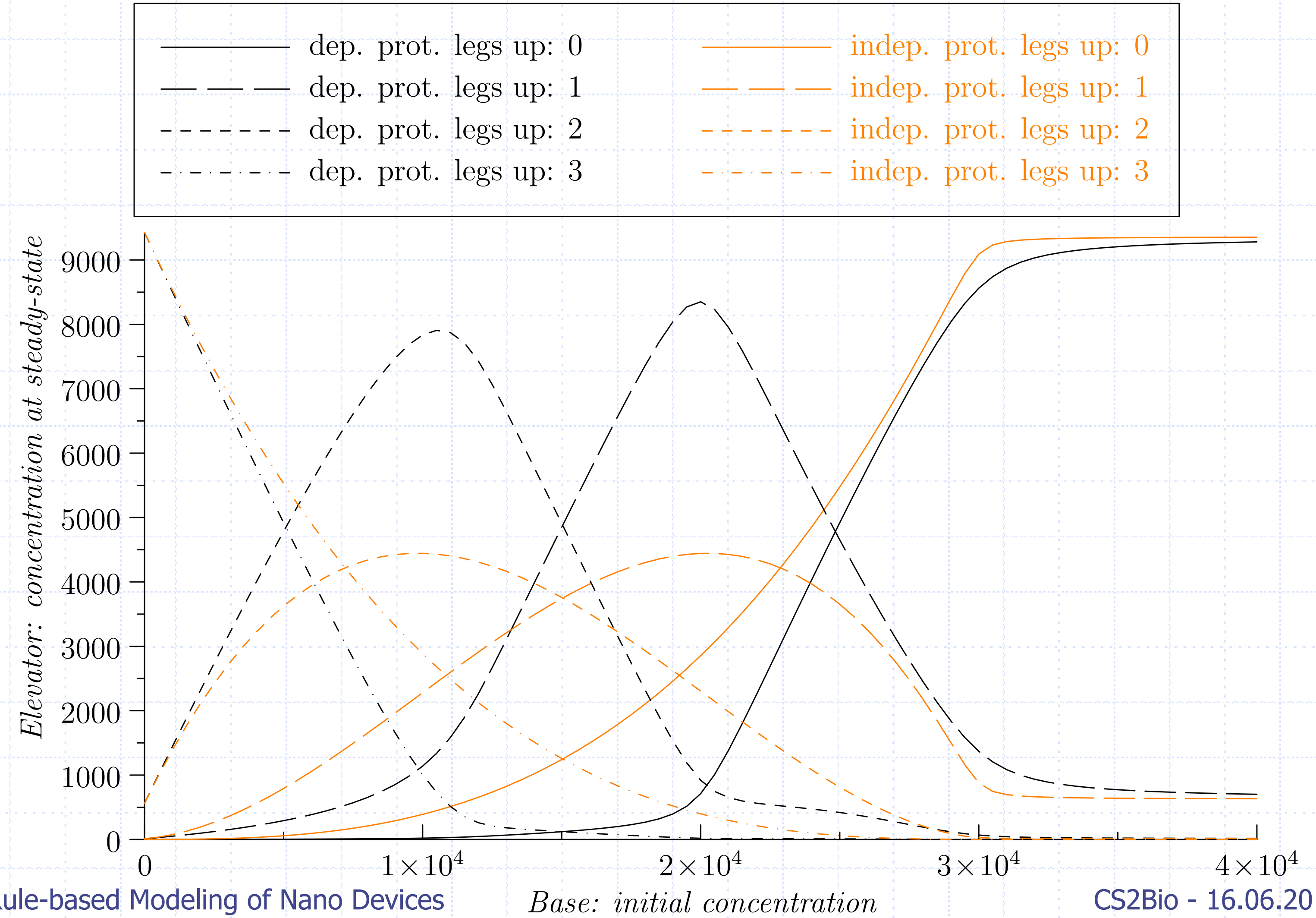
24 elevator configurations + 2 for acid/base

```
Kappa definition of complexes:
Complex ID: S1
    Rot(h~1, ring~1, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~1, ring~1, toplink~0!4, comp~0),
    Rot(h~1, ring~1, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S2
    AB(h~0, comp~0)

Complex ID: S3
    Rot(h~0, ring~1, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~1, ring~1, toplink~0!4, comp~0),
    Rot(h~1, ring~1, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S4
    AB(h~1, comp~0)

Complex ID: S5
    Rot(h~1, ring~0, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~1, ring~1, toplink~0!4, comp~0),
    Rot(h~1, ring~1, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S6
    Rot(h~1, ring~1, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~0, ring~1, toplink~0!4, comp~0),
    Rot(h~0, ring~1, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S7
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~1, ring~1, toplink~0!4, comp~0),
    Rot(h~1, ring~1, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S8
    Rot(h~0, ring~1, toplink~0!1, comp~0),
    Rot(h~1, ring~0, toplink~0!2, comp~0),
    Rot(h~1, ring~1, toplink~0!3, comp~0),
    Top(leg~0!1, prev~0!4, next~0!5),
    Top(leg~0!2, prev~0!6, next~0!4),
    Top(leg~0!3, prev~0!5, next~0!6)

Complex ID: S9
    Rot(h~0, ring~1, toplink~0!1, comp~0),
    Rot(h~1, ring~0, toplink~0!2, comp~0),
    Rot(h~1, ring~1, toplink~0!3, comp~0),
    Top(leg~0!1, prev~0!4, next~0!5),
    Top(leg~0!2, prev~0!5, next~0!6),
    Top(leg~0!3, prev~0!6, next~0!4)

Complex ID: S10
    Rot(h~1, ring~1, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~1, ring~0, toplink~0!4, comp~0),
    Rot(h~1, ring~0, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S11
    Rot(h~0, ring~1, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~0, ring~1, toplink~0!4, comp~0),
    Rot(h~0, ring~1, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S12
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Rot(h~0, ring~1, toplink~0!2, comp~0),
    Rot(h~1, ring~1, toplink~0!3, comp~0),
    Top(leg~0!1, prev~0!4, next~0!5),
    Top(leg~0!2, prev~0!5, next~0!6),
    Top(leg~0!3, prev~0!6, next~0!4)

Complex ID: S13
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Rot(h~0, ring~1, toplink~0!2, comp~0),
    Rot(h~1, ring~1, toplink~0!3, comp~0),
    Top(leg~0!1, prev~0!4, next~0!5),
    Top(leg~0!2, prev~0!6, next~0!4),
    Top(leg~0!3, prev~0!5, next~0!6)

Complex ID: S14
    Rot(h~1, ring~0, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~0, ring~1, toplink~0!4, comp~0),
    Rot(h~0, ring~1, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S15
    Rot(h~1, ring~1, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~1, ring~0, toplink~0!4, comp~0),
    Rot(h~1, ring~0, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S16
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Rot(h~1, ring~0, toplink~0!2, comp~0),
    Rot(h~1, ring~1, toplink~0!3, comp~0),
    Top(leg~0!1, prev~0!4, next~0!5),
    Top(leg~0!2, prev~0!5, next~0!6),
    Top(leg~0!3, prev~0!6, next~0!4)

Complex ID: S17
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Rot(h~1, ring~0, toplink~0!2, comp~0),
    Rot(h~1, ring~1, toplink~0!3, comp~0),
    Top(leg~0!1, prev~0!4, next~0!5),
    Top(leg~0!2, prev~0!6, next~0!4),
    Top(leg~0!3, prev~0!5, next~0!6)

Complex ID: S18
    Rot(h~1, ring~0, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~1, ring~0, toplink~0!4, comp~0),
    Rot(h~1, ring~0, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S19
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~0, ring~1, toplink~0!4, comp~0),
    Rot(h~0, ring~1, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S20
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Rot(h~0, ring~1, toplink~0!2, comp~0),
    Rot(h~1, ring~0, toplink~0!3, comp~0),
    Top(leg~0!1, prev~0!4, next~0!5),
    Top(leg~0!2, prev~0!6, next~0!4),
    Top(leg~0!3, prev~0!5, next~0!6)

Complex ID: S21
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Rot(h~0, ring~1, toplink~0!2, comp~0),
    Rot(h~1, ring~0, toplink~0!3, comp~0),
    Top(leg~0!1, prev~0!4, next~0!5),
    Top(leg~0!2, prev~0!5, next~0!6),
    Top(leg~0!3, prev~0!6, next~0!4)

Complex ID: S22
    Rot(h~1, ring~1, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~0, ring~0, toplink~0!4, comp~0),
    Rot(h~0, ring~0, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S23
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~1, ring~0, toplink~0!4, comp~0),
    Rot(h~1, ring~0, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S24
    Rot(h~0, ring~1, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~0, ring~0, toplink~0!4, comp~0),
    Rot(h~0, ring~0, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S25
    Rot(h~1, ring~0, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~0, ring~0, toplink~0!4, comp~0),
    Rot(h~0, ring~0, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)

Complex ID: S26
    Rot(h~0, ring~0, toplink~0!1, comp~0),
    Top(leg~0!1, prev~0!2, next~0!3),
    Top(leg~0!4, prev~0!3, next~0!5),
    Rot(h~0, ring~0, toplink~0!4, comp~0),
    Rot(h~0, ring~0, toplink~0!6, comp~0),
    Top(leg~0!6, prev~0!5, next~0!2)
```

The reactions: 143 reactions

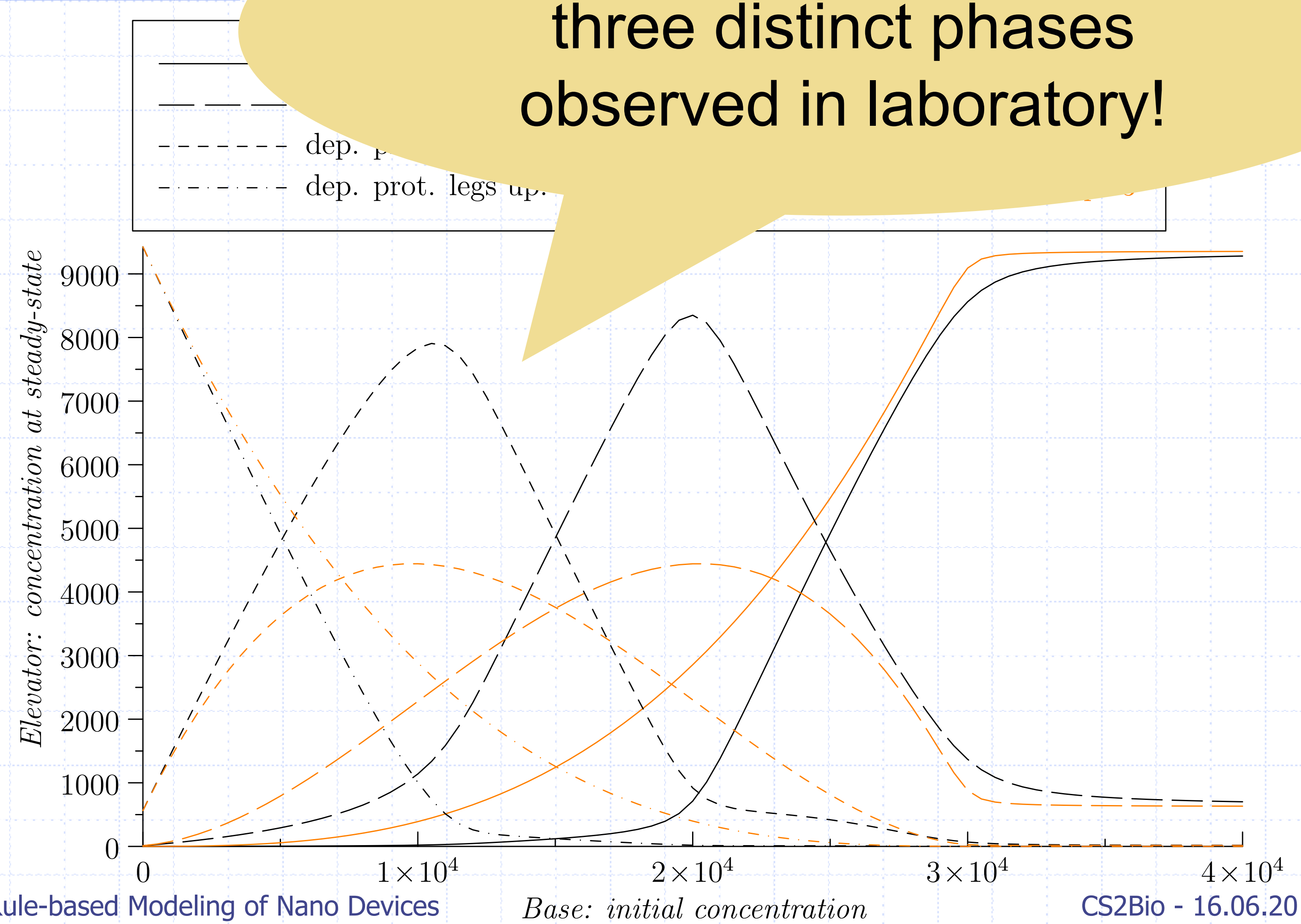
```
// Reactions:
R_3_5_4: S1 => S5; 3 * Rate0 * S1;
R_1_2_0: S1 + S2 => S3 + S4; 3 * Rate1 * S1 * S2;
R_7_6: S2 + S3 => S4 + S6; 3 * Rate6 * S2 * S3;
R_9: S2 + S5 => S4 + S7; Rate1 * S2 * S5;
R_10: S2 + S5 => S4 + S8; Rate1 * S2 * S5;
R_11: S2 + S5 => S4 + S9; Rate1 * S2 * S5;
R_18: S2 + S6 => S4 + S11; Rate5 * S2 * S6;
R_22: S2 + S7 => S4 + S12; Rate6 * S2 * S7;
R_23: S2 + S7 => S4 + S13; Rate4 * S2 * S7;
R_25: S2 + S8 => S4 + S12; Rate6 * S2 * S8;
R_26: S2 + S8 => S4 + S14; Rate6 * S2 * S8;
R_28: S2 + S9 => S4 + S13; Rate6 * S2 * S9;
R_29: S2 + S9 => S4 + S14; Rate6 * S2 * S9;
R_30: S2 + S10 => S4 + S15; Rate1 * S2 * S10;
R_31: S2 + S10 => S4 + S16; Rate1 * S2 * S10;
R_32: S2 + S10 => S4 + S17; Rate1 * S2 * S10;
R_53: S2 + S12 => S4 + S19; Rate5 * S2 * S12;
R_56: S2 + S13 => S4 + S19; Rate5 * S2 * S13;
R_57: S2 + S14 => S4 + S19; Rate5 * S2 * S14;
R_61: S2 + S15 => S4 + S20; Rate6 * S2 * S15;
R_62: S2 + S15 => S4 + S21; Rate6 * S2 * S15;
R_65: S2 + S16 => S4 + S20; Rate6 * S2 * S16;
R_64: S2 + S16 => S4 + S22; Rate6 * S2 * S16;
R_68: S2 + S17 => S4 + S21; Rate6 * S2 * S17;
R_67: S2 + S17 => S4 + S22; Rate6 * S2 * S17;
R_71_69_70: S2 + S18 => S4 + S23; 3 * Rate1 * S2 * S18;
R_101: S2 + S20 => S4 + S24; Rate5 * S2 * S20;
R_104: S2 + S21 => S4 + S24; Rate5 * S2 * S21;
R_105: S2 + S22 => S4 + S24; Rate5 * S2 * S22;
R_109_110: S2 + S23 => S4 + S25; 2 * Rate6 * S2 * S23;
R_129: S2 + S25 => S4 + S26; Rate5 * S2 * S25;
R_12: S3 => S7; Rate1 * S3;
R_14: S3 => S8; Rate0 * S3;
R_13: S3 => S9; Rate0 * S3;
R_8: S3 + S4 => S1 + S2; Rate4 * S3 * S4;
R_19_20: S4 + S6 => S2 + S3; 2 * Rate3 * S4 * S6;
R_21: S4 + S7 => S2 + S5; Rate4 * S4 * S7;
R_24: S4 + S8 => S2 + S5; Rate4 * S4 * S8;
R_27: S4 + S9 => S2 + S5; Rate4 * S4 * S9;
R_49_50_48: S4 + S11 => S2 + S6; 2 * Rate2 * S4 * S11;
R_52: S4 + S12 => S2 + S7; Rate3 * S4 * S12;
R_51: S4 + S12 => S2 + S8; Rate3 * S4 * S12;
R_55: S4 + S13 => S2 + S7; Rate3 * S4 * S13;
R_54: S4 + S13 => S2 + S9; Rate3 * S4 * S13;
R_59: S4 + S14 => S2 + S8; Rate3 * S4 * S14;
R_58: S4 + S14 => S2 + S9; Rate3 * S4 * S14;
R_60: S4 + S15 => S2 + S10; Rate4 * S4 * S15;
R_63: S4 + S16 => S2 + S10; Rate4 * S4 * S16;
R_66: S4 + S17 => S2 + S10; Rate4 * S4 * S17;
R_98: S4 + S19 => S2 + S12; Rate2 * S4 * S19;
R_97: S4 + S19 => S2 + S13; Rate2 * S4 * S19;
R_96: S4 + S19 => S2 + S14; Rate2 * S4 * S19;
R_99: S4 + S20 => S2 + S15; Rate3 * S4 * S20;
R_100: S4 + S20 => S2 + S16; Rate3 * S4 * S20;
R_102: S4 + S21 => S2 + S15; Rate3 * S4 * S21;
R_103: S4 + S21 => S2 + S17; Rate3 * S4 * S21;
R_107: S4 + S22 => S2 + S16; Rate3 * S4 * S22;
R_106: S4 + S22 => S2 + S17; Rate3 * S4 * S22;
R_108: S4 + S23 => S2 + S18; Rate4 * S4 * S23;
R_128: S4 + S24 => S2 + S20; Rate2 * S4 * S24;
R_127: S4 + S24 => S2 + S21; Rate2 * S4 * S24;
R_126: S4 + S24 => S2 + S22; Rate2 * S4 * S24;
R_131_130: S4 + S25 => S2 + S23; 2 * Rate3 * S4 * S25;
R_139_138_140: S4 + S26 => S2 + S25; 3 * Rate2 * S4 * S26;
R_15: S5 => S1; Rate1 * S5;
R_17_16: S5 => S10; 2 * Rate0 * S5;
R_34: S6 => S12; Rate1 * S6;
R_35: S6 => S13; Rate1 * S6;
R_33: S6 => S14; Rate0 * S6;
R_36: S7 => S3; Rate0 * S7;
R_37: S7 => S16; Rate0 * S7;
R_38: S7 => S17; Rate0 * S7;
R_40: S8 => S3; Rate1 * S8;
R_41: S8 => S15; Rate0 * S8;
R_39: S8 => S17; Rate1 * S8;
R_43: S9 => S3; Rate1 * S9;
R_44: S9 => S15; Rate0 * S9;
R_42: S9 => S16; Rate1 * S9;
R_47_46: S10 => S5; 2 * Rate1 * S10;
R_45: S10 => S18; Rate0 * S10;
R_73_74_72: S11 => S19; 3 * Rate1 * S11;
R_75: S12 => S6; Rate0 * S12;
R_77: S12 => S21; Rate0 * S12;
R_76: S12 => S22; Rate1 * S12;
R_78: S13 => S6; Rate0 * S13;
R_80: S13 => S20; Rate0 * S13;
R_79: S13 => S22; Rate1 * S13;
R_81: S14 => S6; Rate1 * S14;
R_83: S14 => S20; Rate1 * S14;
R_82: S14 => S21; Rate1 * S14;
R_85: S15 => S8; Rate1 * S15;
R_86: S15 => S9; Rate1 * S15;
R_84: S15 => S23; Rate1 * S15;
R_88: S16 => S7; Rate1 * S16;
R_87: S16 => S9; Rate0 * S16;
R_89: S16 => S23; Rate0 * S16;
R_91: S17 => S7; Rate1 * S17;
R_90: S17 => S8; Rate0 * S17;
R_92: S17 => S23; Rate0 * S17;
R_95_93_94: S18 => S10; 3 * Rate1 * S18;
R_111: S19 => S11; Rate0 * S19;
R_113_112: S19 => S24; 2 * Rate1 * S19;
R_116: S20 => S13; Rate1 * S20;
R_114: S20 => S14; Rate0 * S20;
R_115: S20 => S25; Rate1 * S20;
R_119: S21 => S12; Rate1 * S21;
R_117: S21 => S14; Rate0 * S21;
R_118: S21 => S25; Rate1 * S21;
R_122: S22 => S12; Rate0 * S22;
R_121: S22 => S13; Rate0 * S22;
R_120: S22 => S25; Rate0 * S22;
R_123: S23 => S15; Rate0 * S23;
R_125: S23 => S16; Rate1 * S23;
R_124: S23 => S17; Rate1 * S23;
R_133_134: S24 => S19; 2 * Rate0 * S24;
R_132: S24 => S26; Rate1 * S24;
R_136: S25 => S20; Rate0 * S25;
R_137: S25 => S21; Rate0 * S25;
R_135: S25 => S22; Rate1 * S25;
R_143_141_142: S26 => S24; 2 * Rate0 * S26;
```

Simulation results



Simulatio

Simulation now reflects the three distinct phases observed in laboratory!



Plan of the talk

- Model of RaH with Kappa-calculus
- Administrative instantaneous rules
- K_F: Kappa + complex functional rates
- Model of the Nano-Elevator
- **Conclusion and Future Work**

Conclusion

- We have (successfully) experimented the following approach for the modeling of Nano Devices
  - Functional behaviour:
    modeled compositionally using **Kappa rules** (“don’t care don’t write” approach)
  - Quantitative aspects:
    complex functional rates (capture non compositional properties of Nano Devices)

Conclusion

- We have developed an automatic translator from Kappa with functional rates to Chemical Reaction Networks
  - One **species** for each **complex**
  - Not applicable to the entire Kappa-calculus as **inifinitely** many complexes can be generated…
  - …but applicable to Nano Devices (**boundedly** many configurations)

Related work

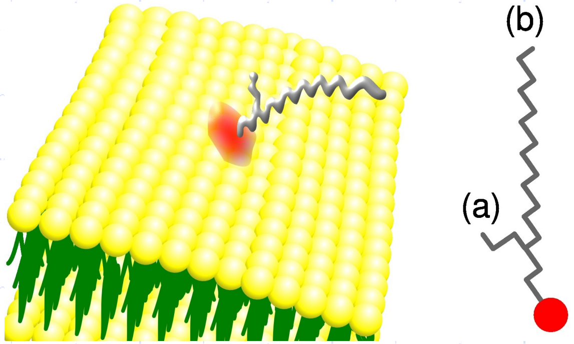
- **KaSIM**: Kappa-calculus stochastic simulator
  - Rules with two rates:
    one used if the reactants belong to the same complex, another one otherwise
  - Useful, e.g. in the case of polymers that do not form rings

Related work

- Kappa **rule refinement** [FMSB08]:
  - Replace one rule with a set of rules that applies in more specific cases
  - Automatic calculation of the rates for the refined rules in such a way that the overall system stochasticity is not altered
  - Syntax-less definition based on a categorical language

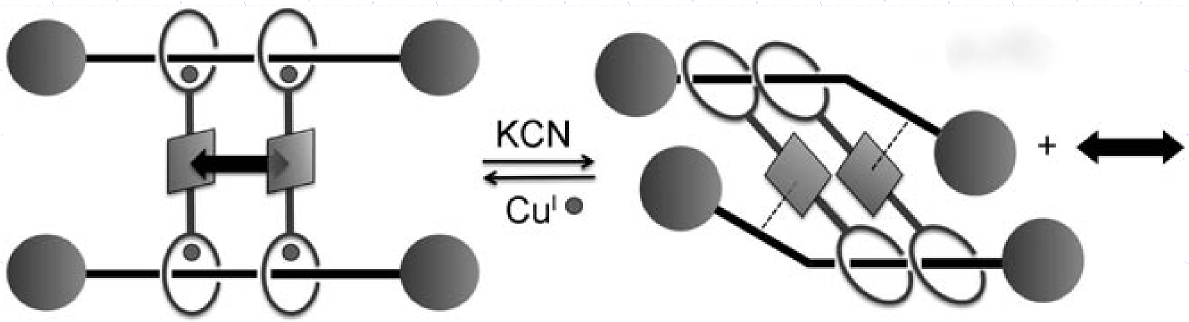
Related work

- **NFSim**: simulator for the BioNetGen language
  - **Global** functional rates:
    rates depends on global variables
  - **Local** functional rates:
    similar to our “complex functional rate” but without the spatial localization



Future work

- Consider also cases in which the number of possible complexes is **unbounded**
  - **dynamic** generation of the chemical rules
- Apply our approach to model **other** Nano Devices, e.g., a [4]rotaxane…



Future work

- …used as a "switchable molecular receptor" (forming a rigid scaffold from a collapsed structure)

  [AngewandteChemie10]