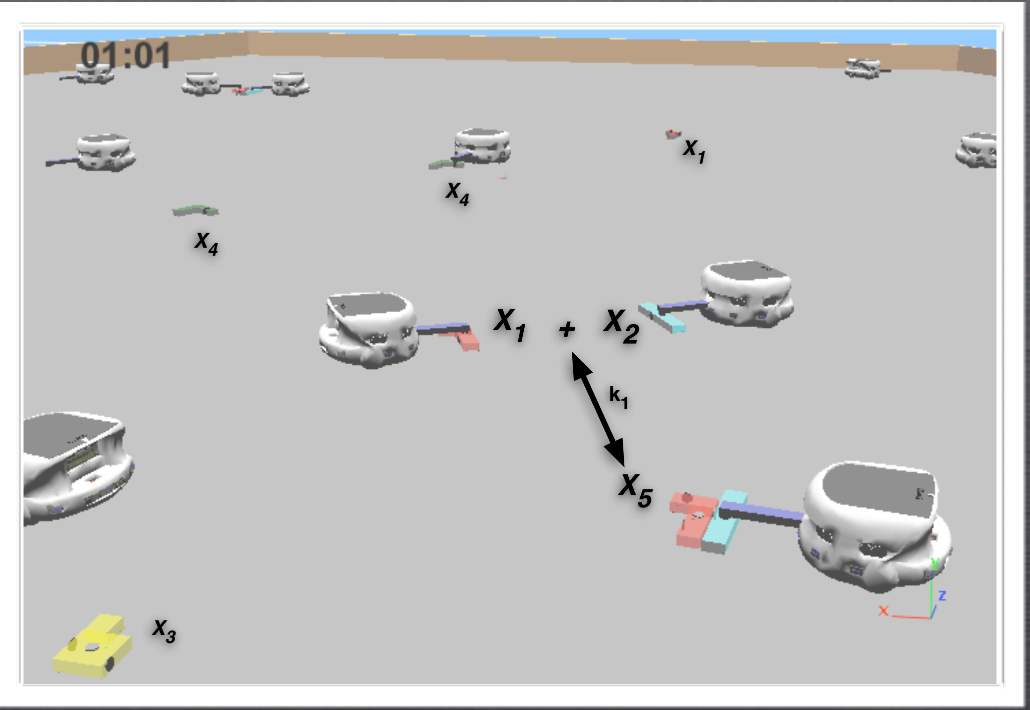
Hybrid Reactions Modeling for Top-down Design

Final Presentation

Loïc Matthey



Supervisors:

Grégory Mermoud
Vijay Kumar
Alcherio Martinoli

Special contributions:

Spring Berman

Penn University of Pennsylvania

Master Project - MP12 - 09/16/2008

EPFL École Polytechnique Fédérale de Lausanne

Contents

1. Introduction

Context

- Joint work with the GRASP Lab from University of Pennsylvania (Penn), Prof. Vijay Kumar.
- Considered problem:
  - **Stochastic assembly of products**
- Solving for poor yield: add agents to the initial system or modify the behavior to improve performance.
  - **Augmented system.**

2. Goals

- Propose a theoretical framework for the Augmented System problem.
- Validation using a higher-level assembly task (biological scale).
  - Realistic physics simulation with Webots.
- Develop mathematical models and simulations fitting the tasks.
  - Use a chemical reaction network (CRN) formalism.
- Optimize the chemical reaction network model and map it back on the realistic platform.

3. Stochastic Assembly

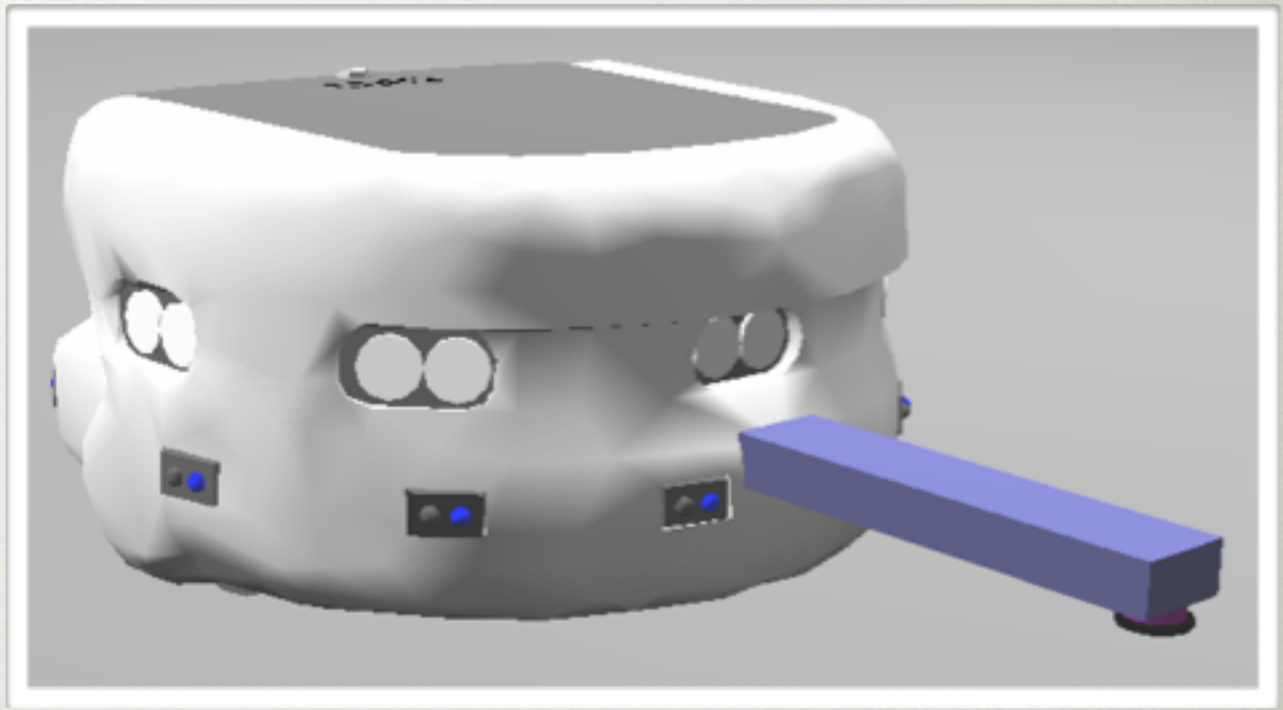
Definition (refined)

- Let M_i pieces of different types, assembling with bi-directional connections.
- Let those pieces move and assemble randomly in an arena of size A.
- Let the final assembled products be known as S_j.
- Let a system of reactions R describe the plan of assembly of pieces via their connections. These reactions can contain disassembling reactions too.
- Then this system will create a certain amount $|S_j|$ after a time T_f.
  - Goal: obtain the bigger $|S_j|$ after the smallest T_f, while controlling the ratios between $|S_j|$.

4. State at midterm

Realistic platform

- Realistic multi-robot platform in Webots.
- Simplification of an assembly task.
- Components:
  - Connections with "magnets"
  - Robot with protruding arm, rotating connector. Moving randomly.
  - Heterogeneous pieces.
  - Unique puzzle target plan.



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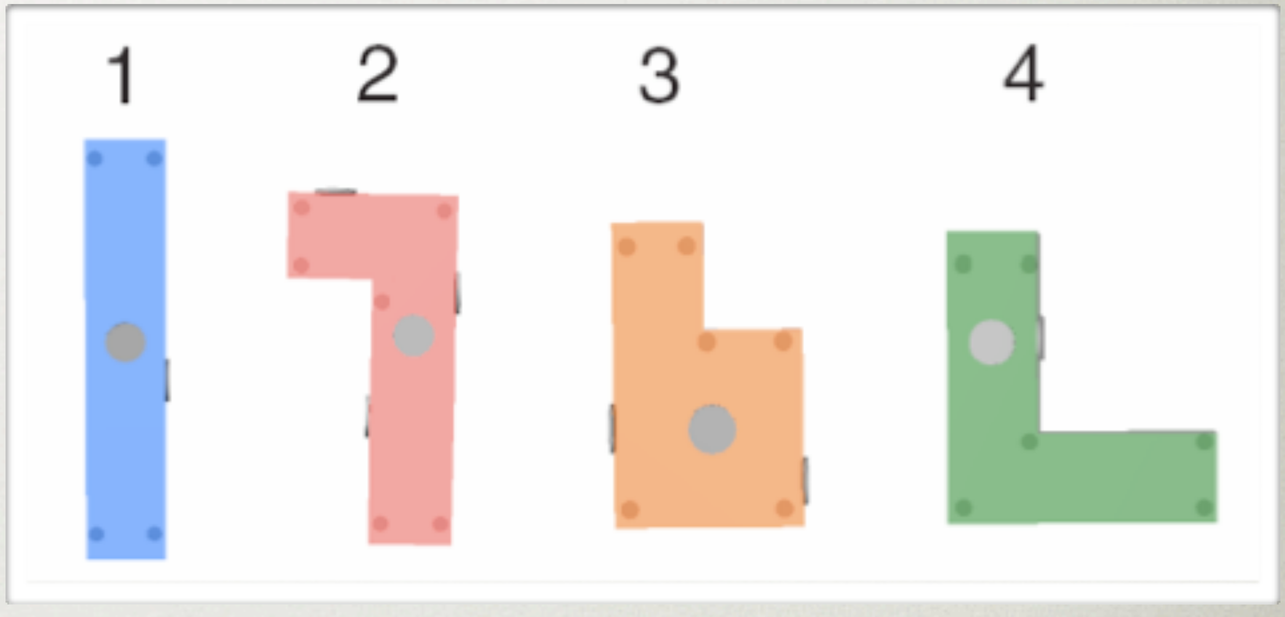

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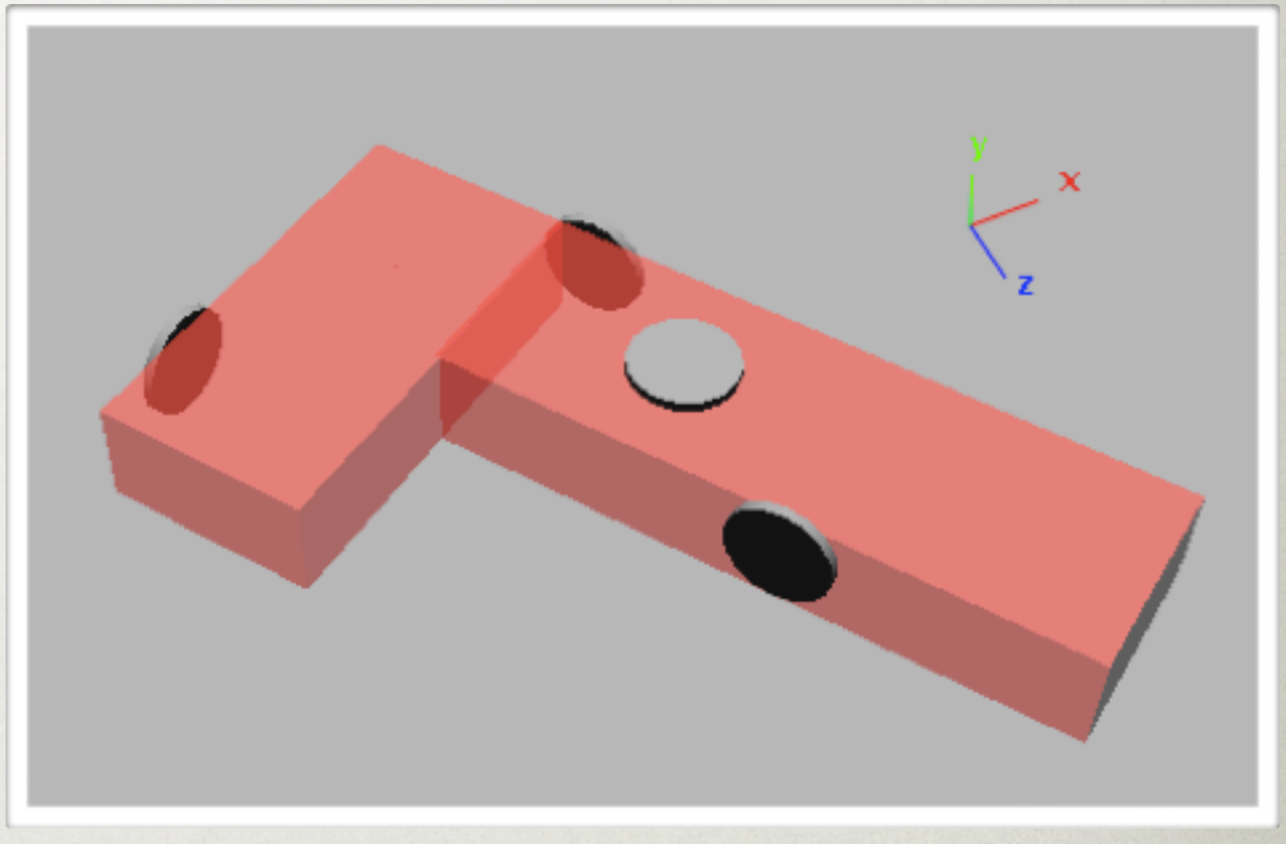

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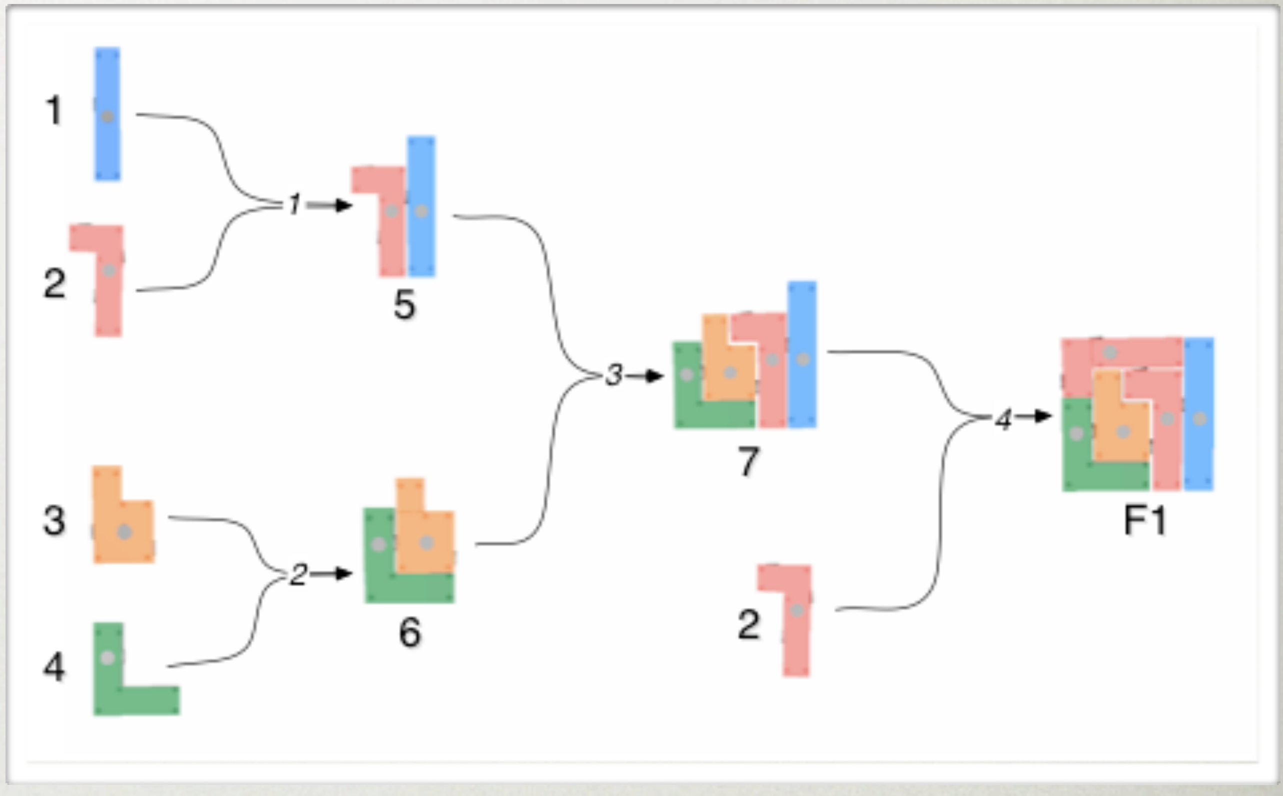

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Realistic platform

- All local communications.
- Experimental platform.
  - Random positions.
  - Several experiments.

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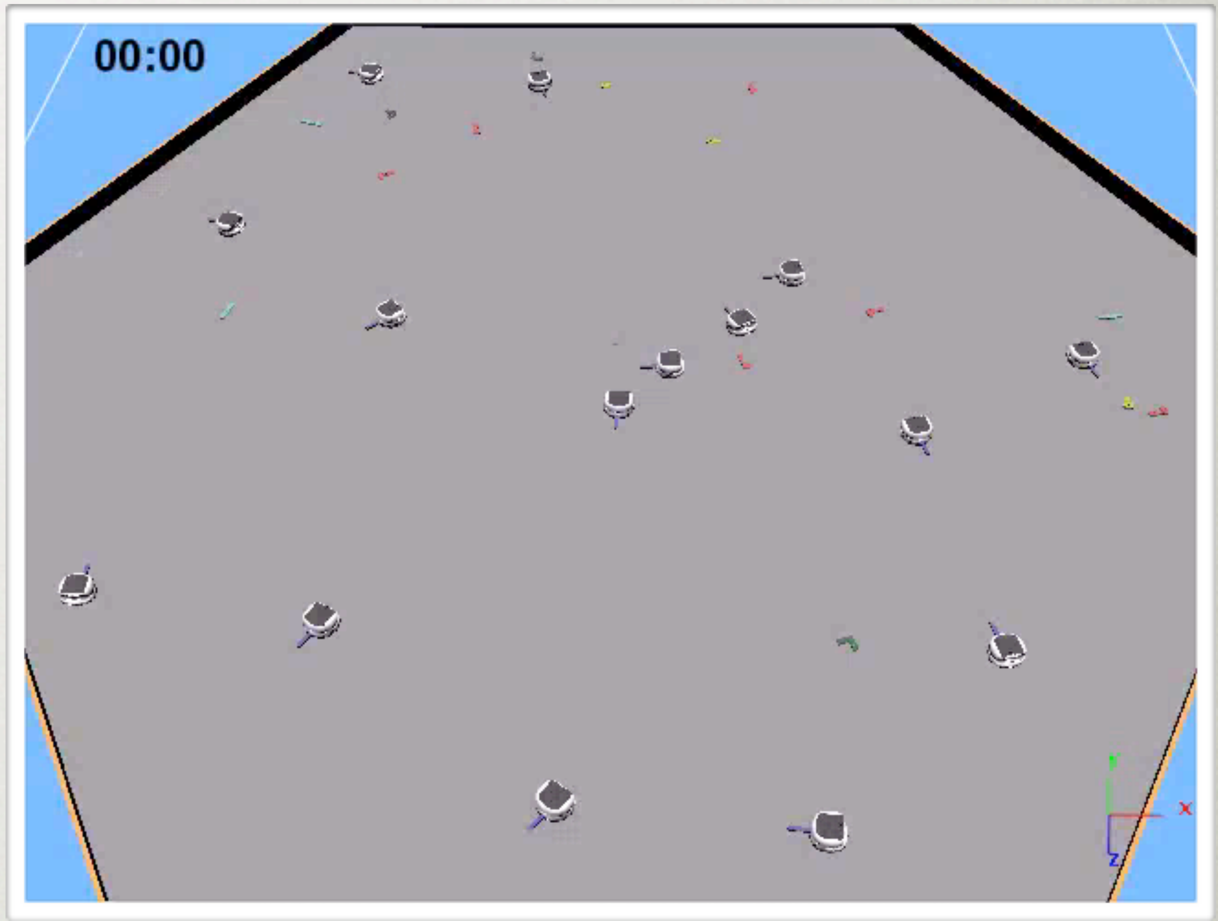

4. State at midterm

Chemical reaction networks

- Chemical reaction networks model.
  - Guessed and fitted parameters.
  - ODE simulations and stochastic simulations.
  - Quantitative fit to the experimental data.
    - 100 experiments, 20min maximum, initial positions and orientations.

$$
\begin{array}{lcl}
X_R + X_1^u & \xrightarrow{e_1} & X_1^c \\
X_R + X_2^u & \xrightarrow{e_2} & X_2^c \\
X_R + X_3^u & \xrightarrow{e_3} & X_3^c \\
X_R + X_4^u & \xrightarrow{e_4} & X_4^c
\end{array}
\qquad
\begin{array}{lcl}
X_R + X_5^u & \xrightarrow{e_5} & X_5^c \\
X_R + X_6^u & \xrightarrow{e_6} & X_6^c \\
X_R + X_7^u & \xrightarrow{e_7} & X_7^c
\end{array}
$$

$$
\begin{array}{ll}
X_1^c + X_2^c \xrightarrow{k_1^+} X_5^c + X_R & \qquad X_5^c + X_6^c \xrightarrow{k_3^+} X_7^c + X_R \\
X_3^c + X_4^c \xrightarrow{k_2^+} X_6^c + X_R & \qquad X_2^c + X_7^c \xrightarrow{k_4^+} X_{F1}^c + X_R
\end{array}
$$

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$$
\begin{cases}
\dot{x}_R &= -\sum_{l=1}^{4} e_l x_R x_l^f + k_1 x_1 x_2 + k_2 x_3 x_4 + \\
 & \qquad k_3 x_5 x_6 + k_4 x_2 x_7 \\
\dot{x}_1^f &= -e_1 x_R x_1^f \\
\dot{x}_2^f &= -e_2 x_R x_2^f \\
\dot{x}_3^f &= -e_3 x_R x_3^f \\
\dot{x}_4^f &= -e_4 x_R x_4^f \\
\dot{x}_1 &= e_1 x_R x_1^f - k_1 x_1 x_2 \\
\dot{x}_2 &= e_2 x_R x_2^f - k_1 x_1 x_2 - k_4 x_2 x_7 \\
\dot{x}_3 &= e_3 x_R x_3^f - k_2 x_3 x_4 \\
\dot{x}_4 &= e_4 x_R x_4^f - k_2 x_3 x_4 \\
\dot{x}_5 &= k_1 x_1 x_2 - k_3 x_5 x_6 \\
\dot{x}_6 &= k_2 x_3 x_4 - k_3 x_5 x_6 \\
\dot{x}_7 &= k_3 x_5 x_6 - k_4 x_2 x_7 \\
\dot{x}_{F1} &= k_4 x_2 x_7
\end{cases}
$$

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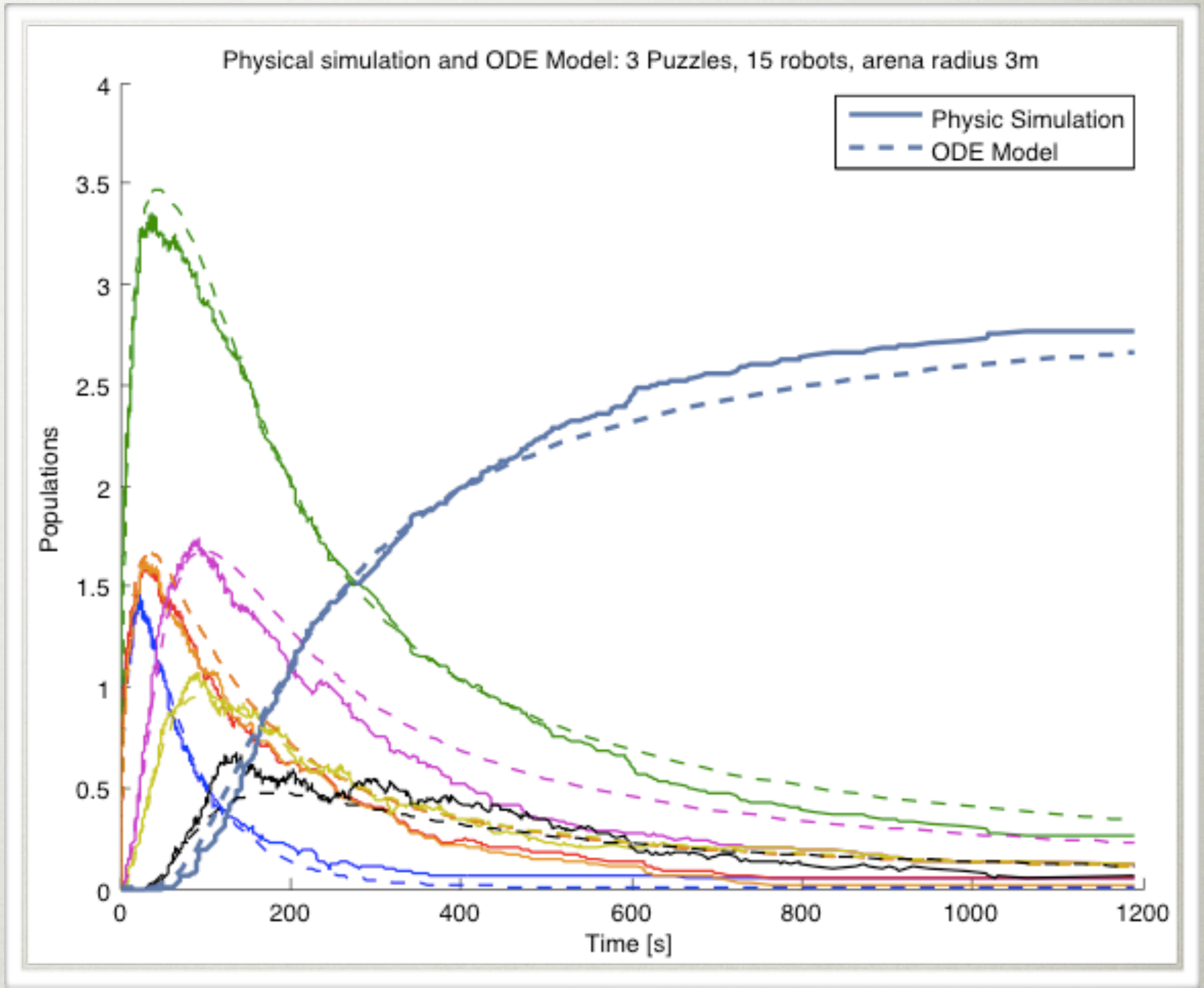

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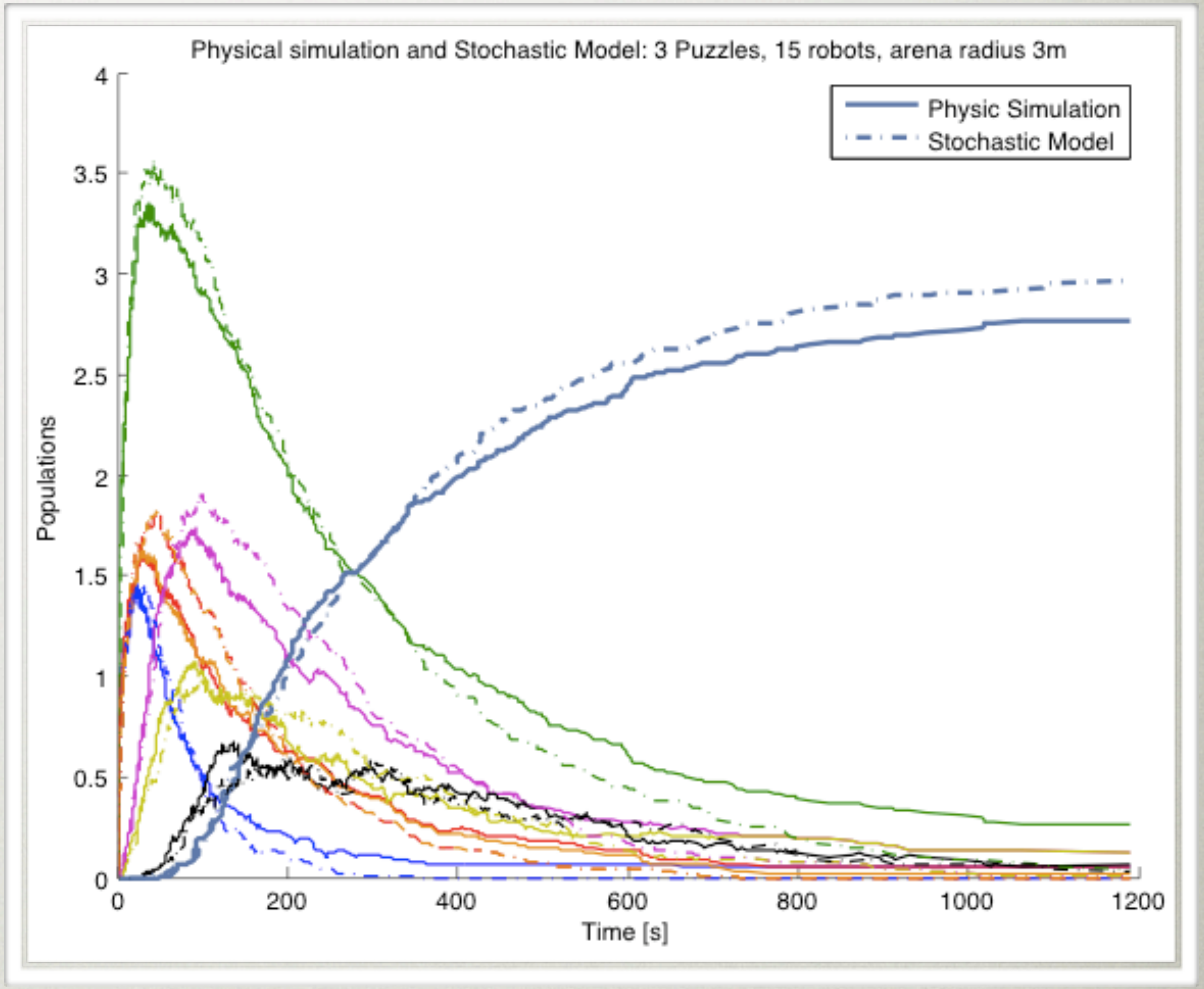
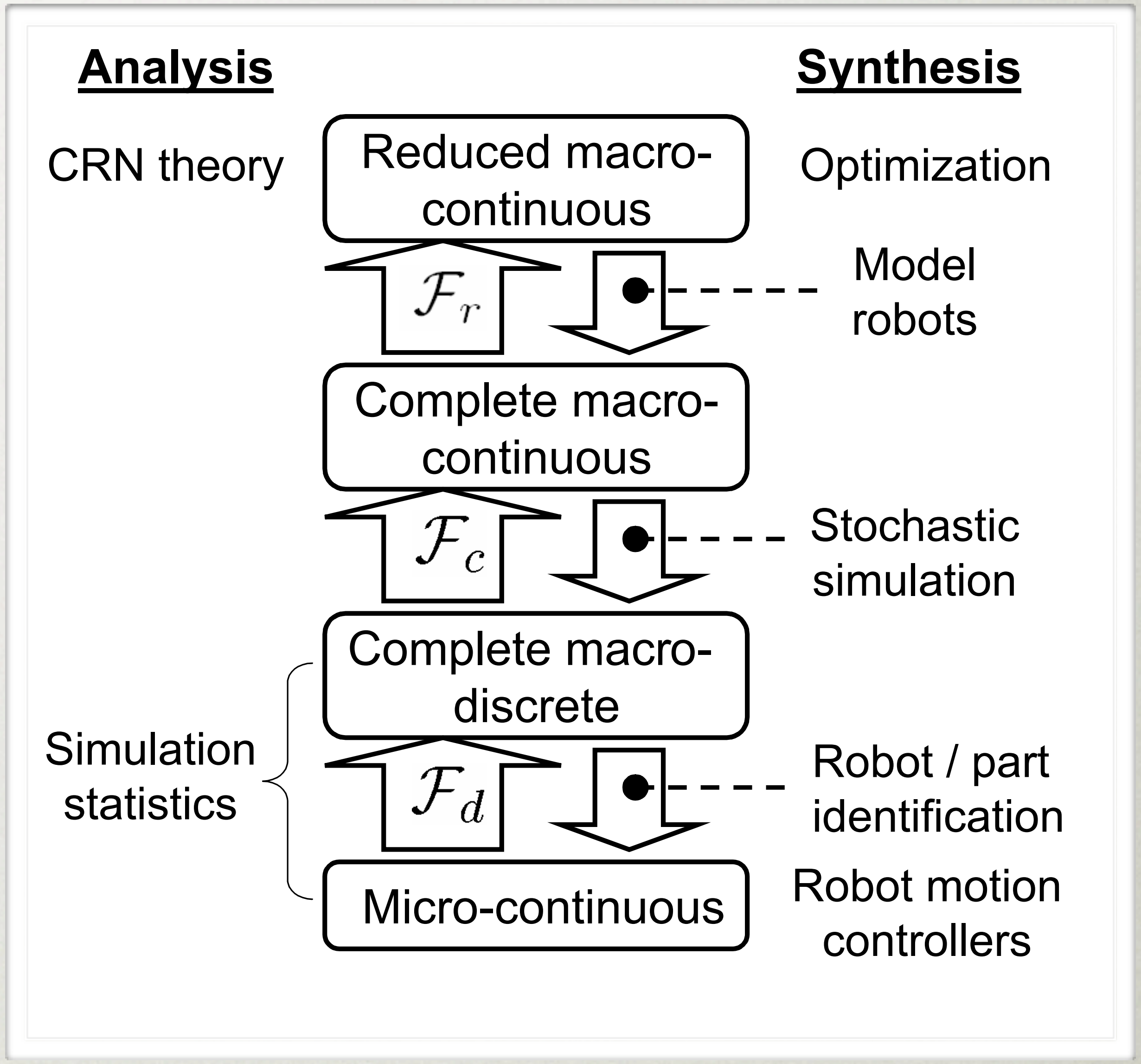


4. State at midterm

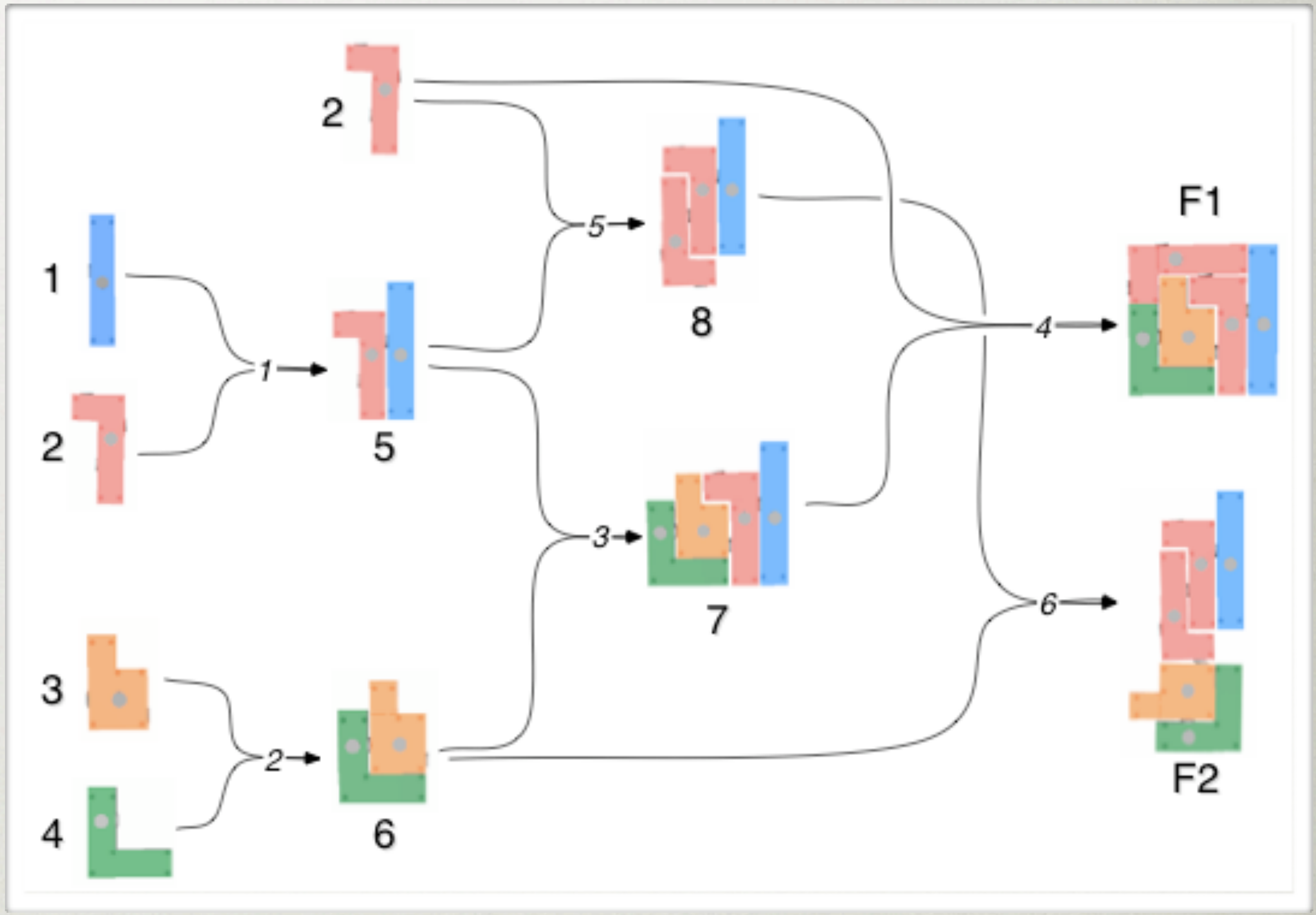
What now?

- Optimize the system.
  - What framework?
  - Nonlinear multi-affine system.
- Map back this optimization on the realistic platform.
  - Model "back-fitting".
  - Discrepancies.
- Other applications.



5. Extended plans

- Goal: control the ratio of different puzzles produced by the system.
- Several target puzzles needed.
- Same building blocks, new reactions only.
- Similar models and results.



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X_5^c \xrightarrow{k_1^-} X_1^c + X_2^u & & X_{F1}^c \xrightarrow{k_4^-} X_7^c + X_2^u \\
X_6^c \xrightarrow{k_2^-} X_3^c + X_4^u & & X_8^c \xrightarrow{k_5^-} X_5^c + X_2^u \\
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- Goal: control the ratio of different puzzles produced by the system.
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$$e_i = p^e \qquad k_i^+ = p^e \cdot p_i^a \cdot p_i^+ \qquad k_i^- = p_i^-$$

$$p^e \approx \frac{vTw}{A} \qquad p_i^a \text{ measured} \qquad p_i^+, p_i^- \quad \textit{tunable}$$

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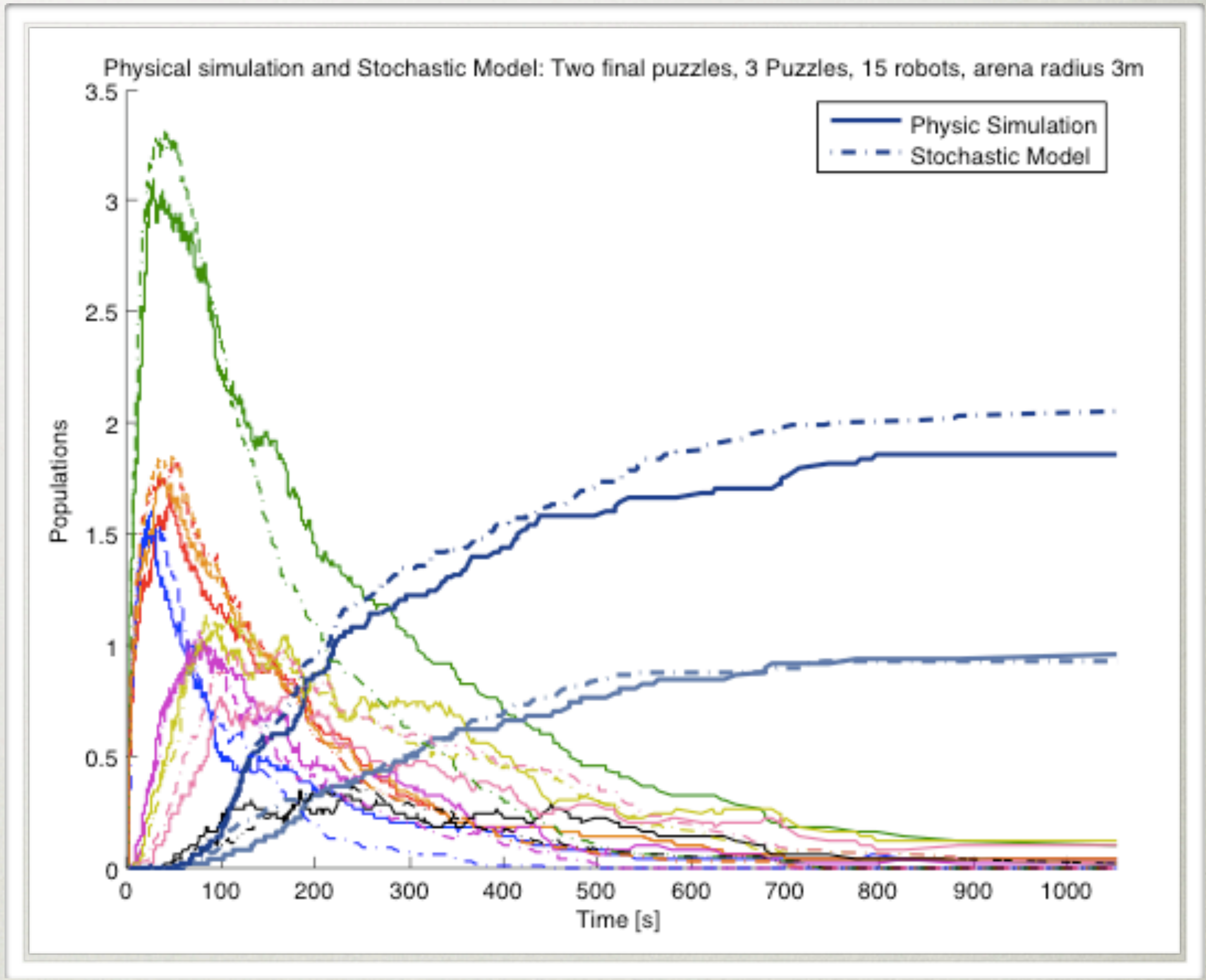
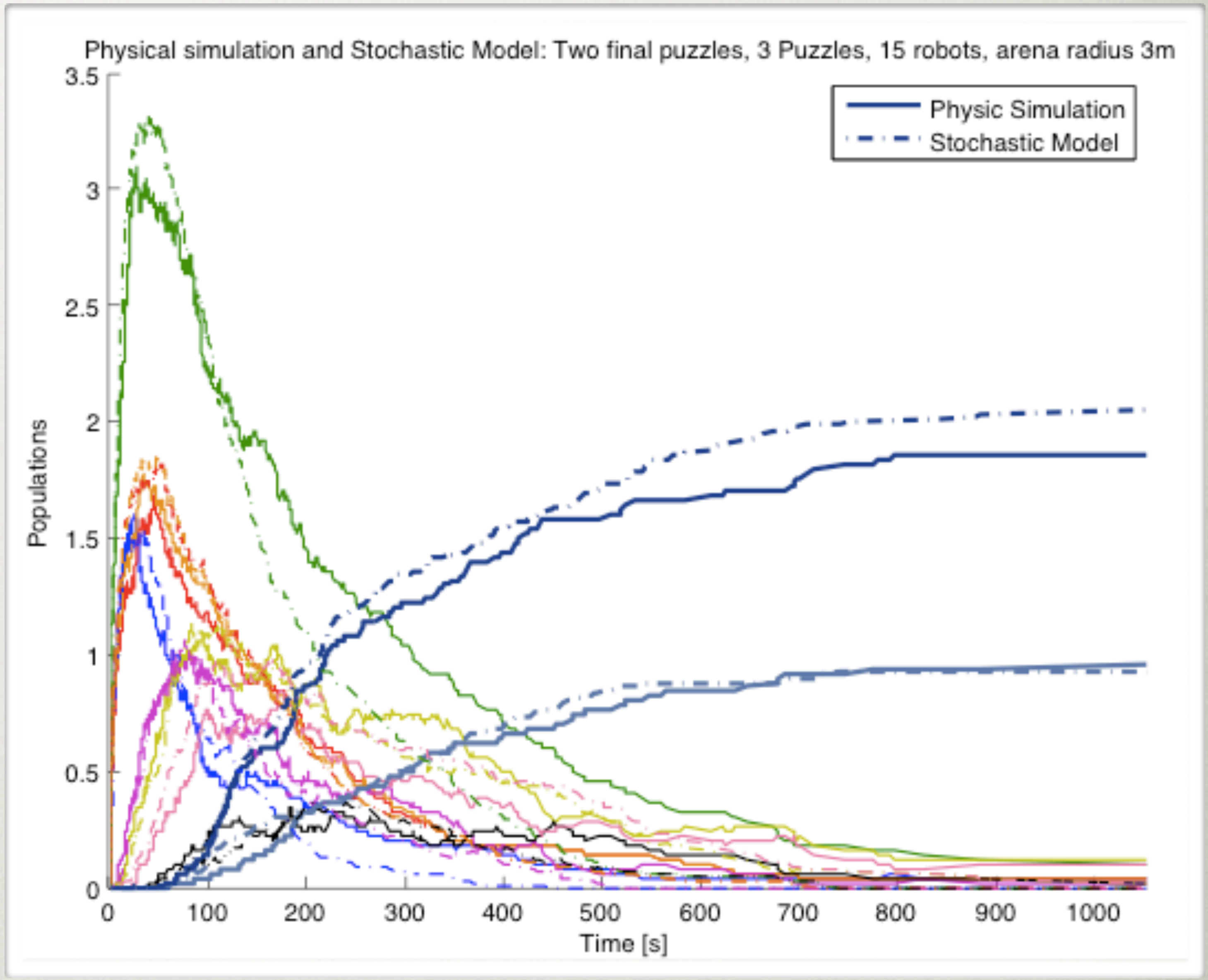


6. CRN Control

Idea

- Control the ratio of different puzzles produced by the system.
- Tunable parameters



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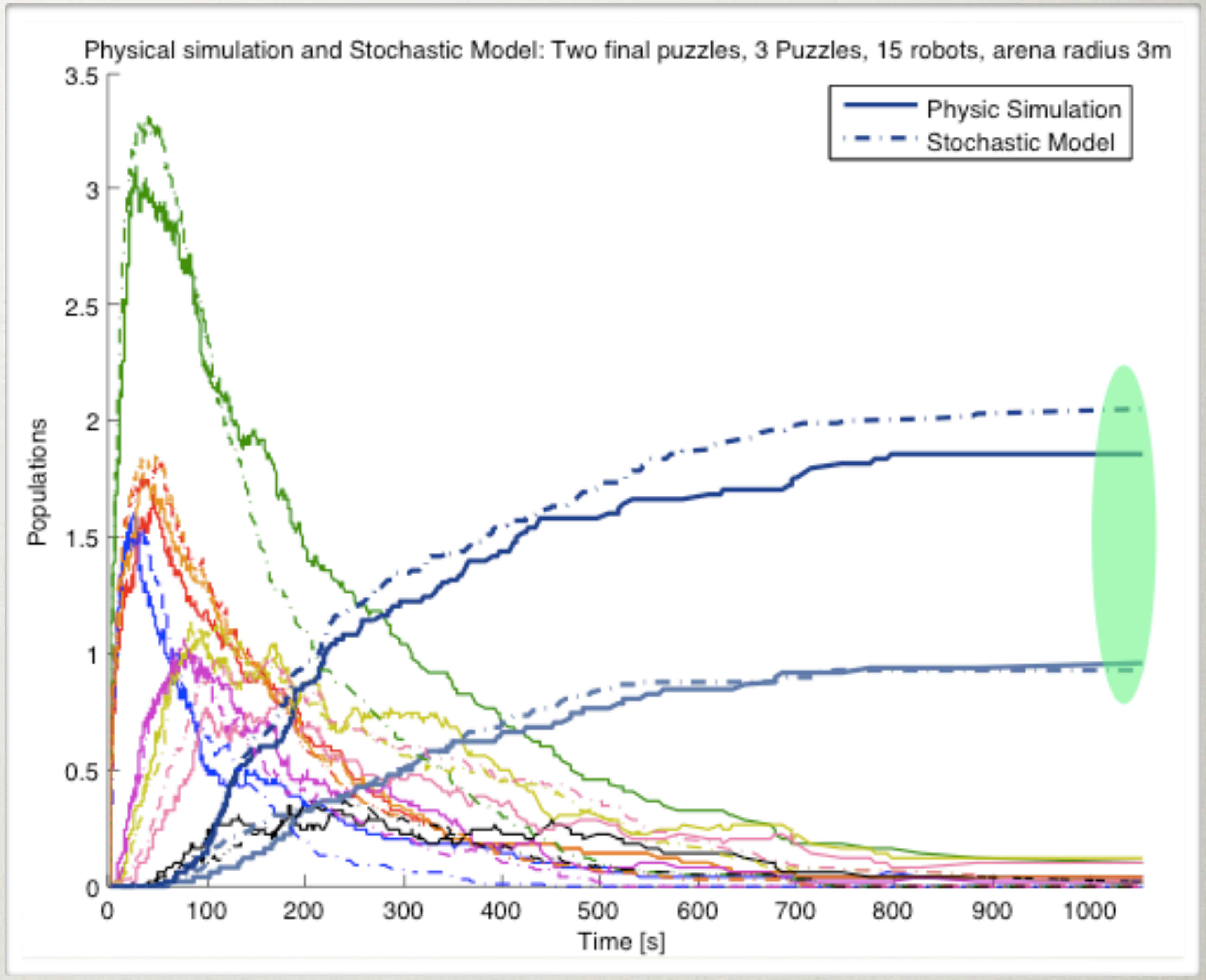

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6. CRN Control

Notation

- Remove robots and lying pieces, reduced model.
- ODE approximation.
- ***K*** is the matrix of rates. **y(x)** the complexes.

$$X_1 + X_2 \underset{k_1^-}{\overset{k_1^+}{\rightleftharpoons}} X_5 \qquad X_2 + X_7 \underset{k_4^-}{\overset{k_4^+}{\rightleftharpoons}} X_{F1}$$

$$X_3 + X_4 \underset{k_2^-}{\overset{k_2^+}{\rightleftharpoons}} X_6 \qquad X_2 + X_5 \underset{k_5^-}{\overset{k_5^+}{\rightleftharpoons}} X_8$$

$$X_5 + X_6 \underset{k_3^-}{\overset{k_3^+}{\rightleftharpoons}} X_7 \qquad X_6 + X_8 \underset{k_6^-}{\overset{k_6^+}{\rightleftharpoons}} X_{F2}$$

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$$
\left\{
\begin{array}{lcl}
\dot{x}_1 & = & -k_1^+ x_1 x_2 + k_1^- x_5 \\
\dot{x}_2 & = & -k_1^+ x_1 x_2 - k_5^+ x_2 x_5 - k_4^+ x_2 x_7 + k_1^- x_5 + k_5^- x_8 + k_4^- x_{F1} \\
\dot{x}_3 & = & -k_2^+ x_3 x_4 + k_2^- x_6 \\
\dot{x}_4 & = & -k_2^+ x_3 x_4 + k_2^- x_6 \\
\dot{x}_5 & = & k_1^+ x_1 x_2 - k_1^- x_5 - k_3^+ x_5 x_6 + k_3^- x_7 - k_5^+ x_2 x_5 + k_5^- x_8 \\
\dot{x}_6 & = & k_2^+ x_3 x_4 - k_2^- x_6 - k_3^+ x_5 x_6 + k_3^- x_7 - k_6^+ x_6 x_8 + k_6^- x_{F2} \\
\dot{x}_7 & = & k_3^+ x_5 x_6 - k_3^- x_7 - k_4^+ x_2 x_7 + k_4^- x_{F1} \\
\dot{x}_8 & = & k_5^+ x_2 x_5 - k_5^- x_8 - k_6^+ x_6 x_8 + k_6^- x_{F2} \\
\dot{x}_{F1} & = & k_4^+ x_2 x_7 - k_4^- x_{F1} \\
\dot{x}_{F2} & = & k_6^+ x_6 x_8 - k_6^- x_{F2}
\end{array}
\right.
$$

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- Remove robots and lying pieces, reduced model.
- ODE approximation.
- *K* is the matrix of rates. **y(x)** the complexes.

$$\dot{\mathbf{x}} = \mathbf{MKy}(\mathbf{x})$$
$$\mathbf{y}(\mathbf{x}) = [x_1x_2 \quad x_5 \quad x_3x_4 \quad x_6 \quad x_2x_7 \quad x_{F1} \quad x_5x_6 \quad x_7 \quad x_2x_5 \quad x_8 \quad x_6x_8 \quad x_{F2}]^T$$

6. CRN Control

Notation

- Remove robots and lying pieces, reduced model.
- ODE approximation.
- *K* is the matrix of rates. **y(x)** the complexes.

$$\begin{cases} x_3 - x_4 & = & N_1 \\ x_1 + x_5 + x_7 + x_8 + x_{F1} + x_{F2} & = & N_2 \\ x_2 + x_5 + x_7 + 2(x_8 + x_{F1} + x_{F2}) & = & N_3 \\ x_3 + x_6 + x_7 + x_{F1} + x_{F2} & = & N_4 \end{cases}$$

6. CRN Control
Convergence

- Theorem 1: System has an unique equilibrium $\bar{\mathbf{x}} > \mathbf{0}$.
- *Proof: uses Deficency Zero theorem, Feinberg:*
    - *deficiency of network $\delta = 0$. (complexes - linkage classes - rank).*
    - *weakly reversible.*
  - *Then: System has one asymptotically stable equilibrium*
  - *Extension to globally asymptotically stable equilibrium, Siegel:*
    - *no boundary equilibria.*
- Our system has only one equilibrium, globally asymptotically stable, independent of initial state.

6. CRN Control

Method

- System has only one equilibrium: we can design *K* such that it converge to our goal!
- Optimize *K* under constraints for the equilibrium $\mathbf{y^d}$:

$$\mathbf{MKy^d} = \mathbf{0}$$

$$\alpha = \frac{x_{F1}}{x_{F1} + x_{F2}}$$

- Needs to set all components of $\mathbf{y^d}$.

$$\mathbf{y}(\mathbf{x}) = [x_1x_2 \quad x_5 \quad x_3x_4 \quad x_6 \quad x_2x_7 \quad x_{F1} \quad x_5x_6 \quad x_7 \quad x_2x_5 \quad x_8 \quad x_6x_8 \quad x_{F2}]^T$$

6. CRN Control
Method

- Optimize measure of relaxation time for each reaction.
  - Exact formula only for simple cases...
- Reformulate as a linearization around the equilibrium point for independent reactions.

$$\mathrm{X}_k + X_l \underset{k_j^-}{\overset{k_j^+}{\rightleftharpoons}} X_m$$

- Use an estimate of the time to go back to equilibrium when disturbed (Heinrich).

$$\tau_j = (k_j^+(x_k^d + x_l^d) + k_j^-)^{-1}$$

6. CRN Control

Method

- Two objective functions.

$$f_{ave}(\mathbf{k}) = \frac{1}{6}\sum_{j=1}^{6} \tau_j^{-1}$$

$$f_{min}(\mathbf{k}) = \min\{\tau_1^{-1}, \ldots, \tau_{10}^{-1}\}$$

- Two linear programs.

$$\begin{array}{lll} \mathbf{P1:} & \text{maximize} & f_{ave}(\mathbf{k}(\mathbf{p})) \\ & \text{subject to} & \mathbf{MK}(\mathbf{p})\mathbf{y^d} = \mathbf{0}, \quad \mathbf{0} \le \mathbf{p} \le \mathbf{1}\ . \end{array}$$

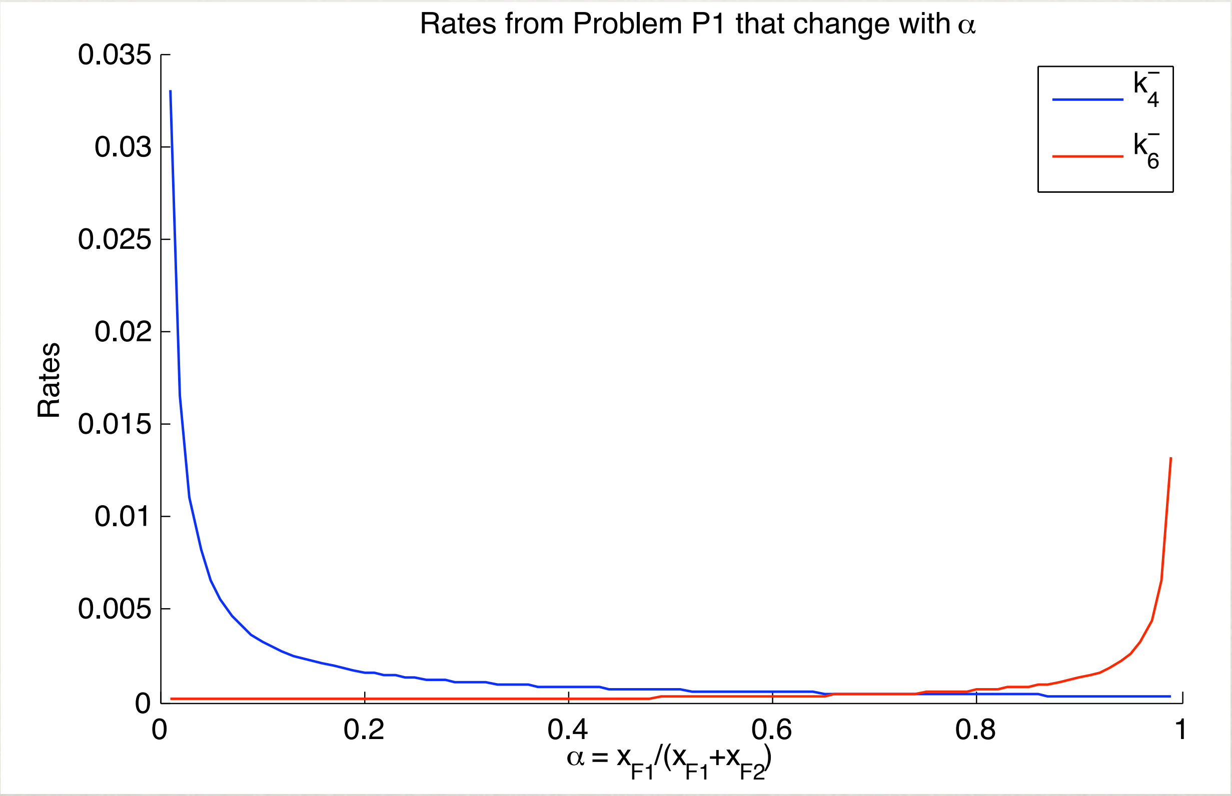
$$\begin{array}{lll} \mathbf{P2:} & \text{maximize} & f_{min}(\mathbf{k}(\mathbf{p})) \\ & \text{subject to} & \mathbf{MK}(\mathbf{p})\mathbf{y^d} = \mathbf{0}, \quad \mathbf{0} \le \mathbf{p} \le \mathbf{1}\ . \end{array}$$

6. CRN Control

Results P1

- $\mathbf{x^d}$ with conservation laws and $\alpha \in \{0.01, 0.02, 0.03, \ldots, 0.99\}$
- Forward maximum. Only final reactions change.

Reaction j	1	2	3	4	5	6
Optimized $\mathbf{p_j^+}$	1.0					
Optimized $\mathbf{p_j^-}$	0.01885	0.00754	0.00377	*continuous*	0.00942	*continuous*

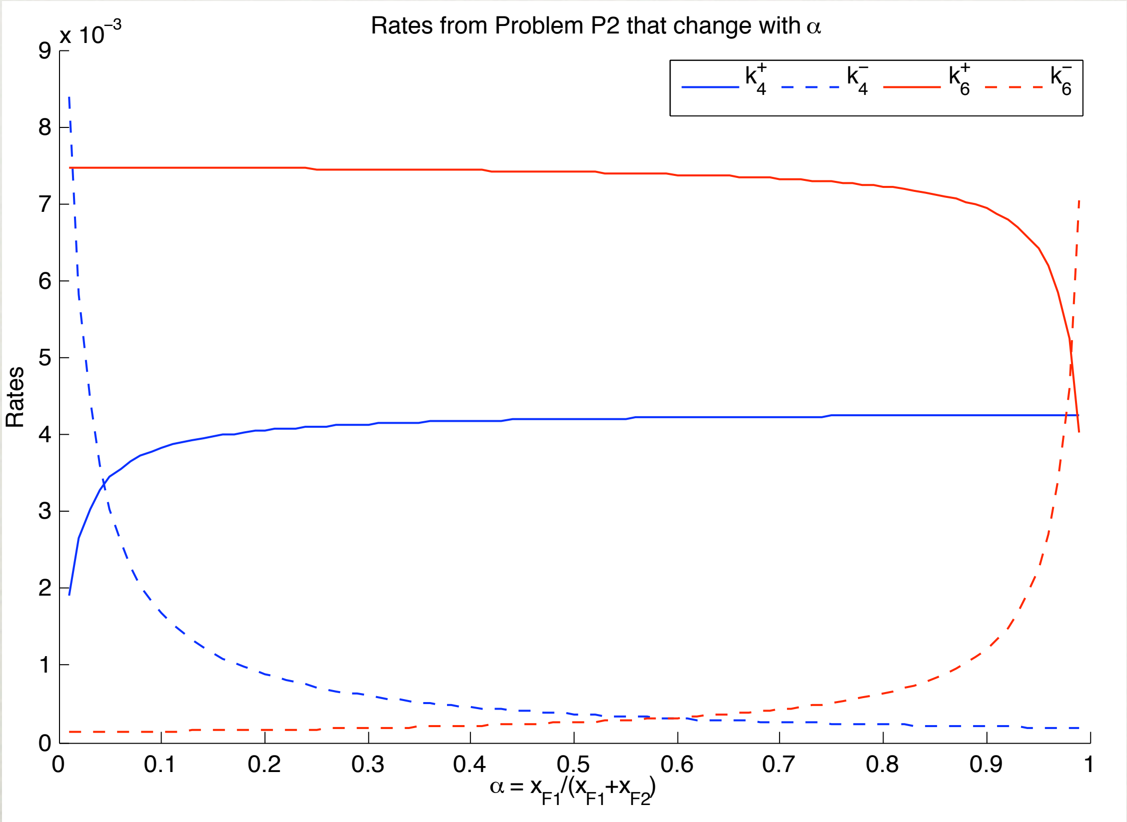


6. CRN Control

Results P2

- $\mathbf{x}^{\mathbf{d}}$ with conservation laws and $\alpha \in \{0.01, 0.02, 0.03, \ldots, 0.99\}$
- Similar to P1. Final reactions cutting.

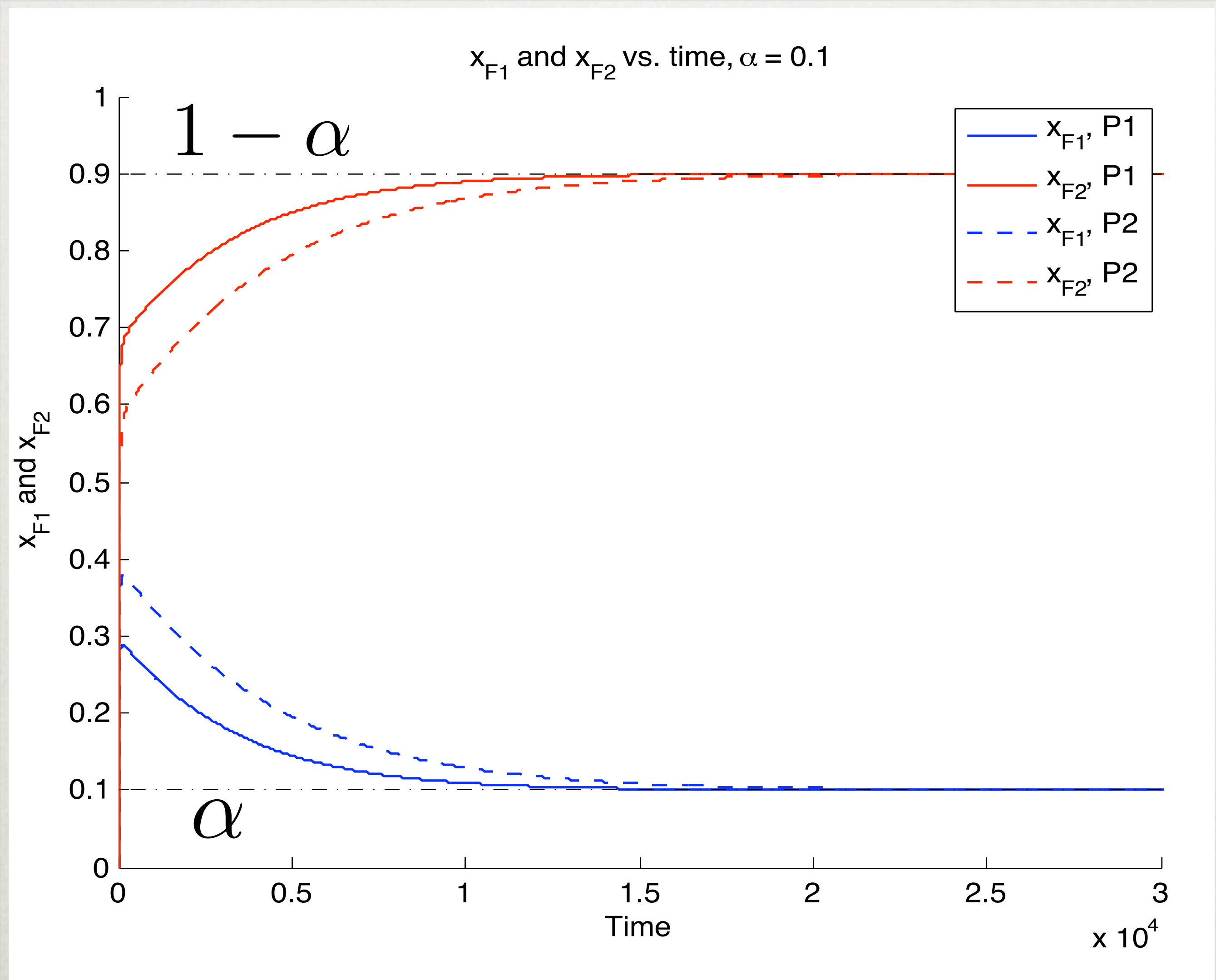
Reaction j	1	2	3	4	5	6
Optimized $\mathbf{p}_j^+$	0.36	0.666	1.0	*continuous*	0.4705	*continuous*
Optimized $\mathbf{p}_j^-$	0.006855	0.005027	0.00377	*continuous*	0.00443	*continuous*



6. CRN Control

Behavior

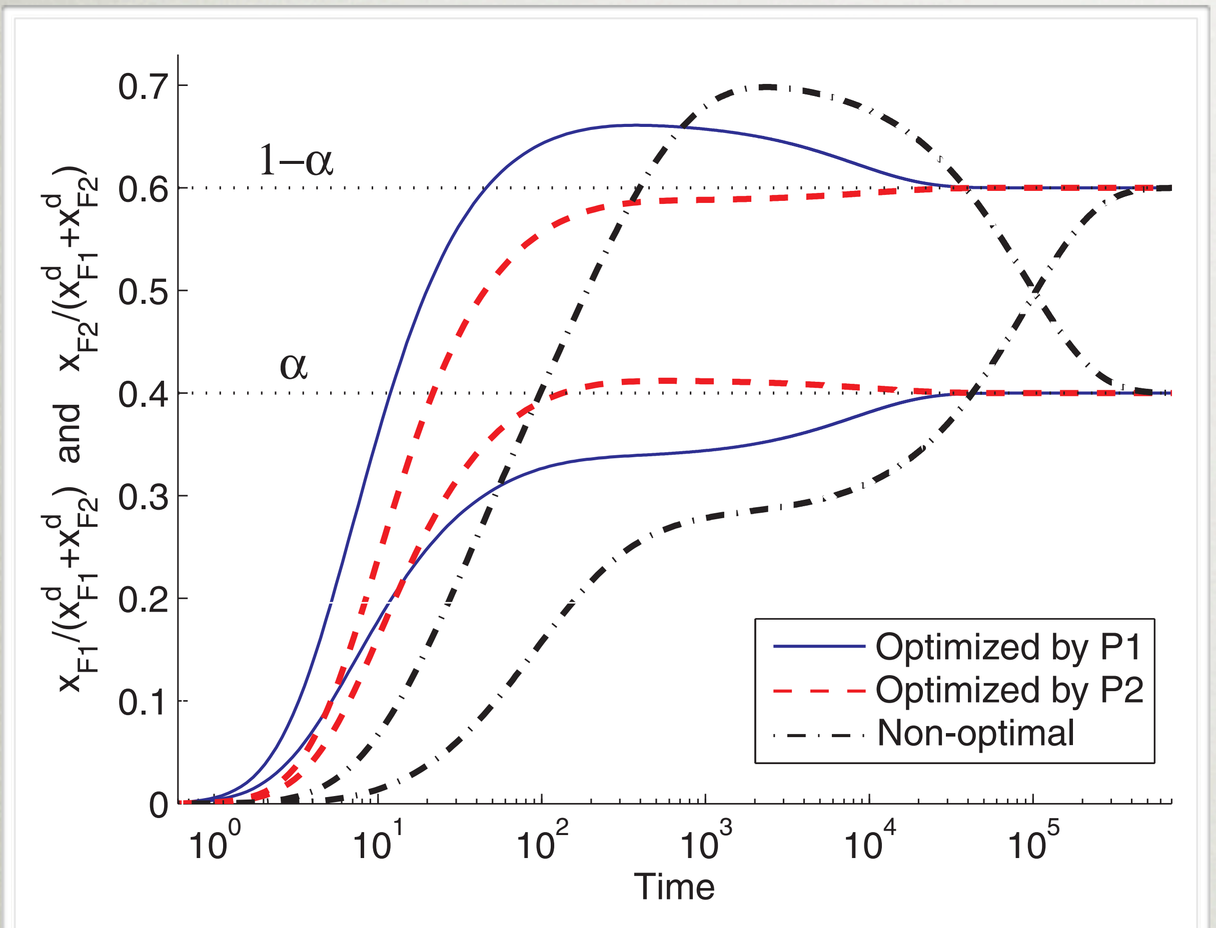
- Ratios of final assemblies over time.
- Linear time scale.

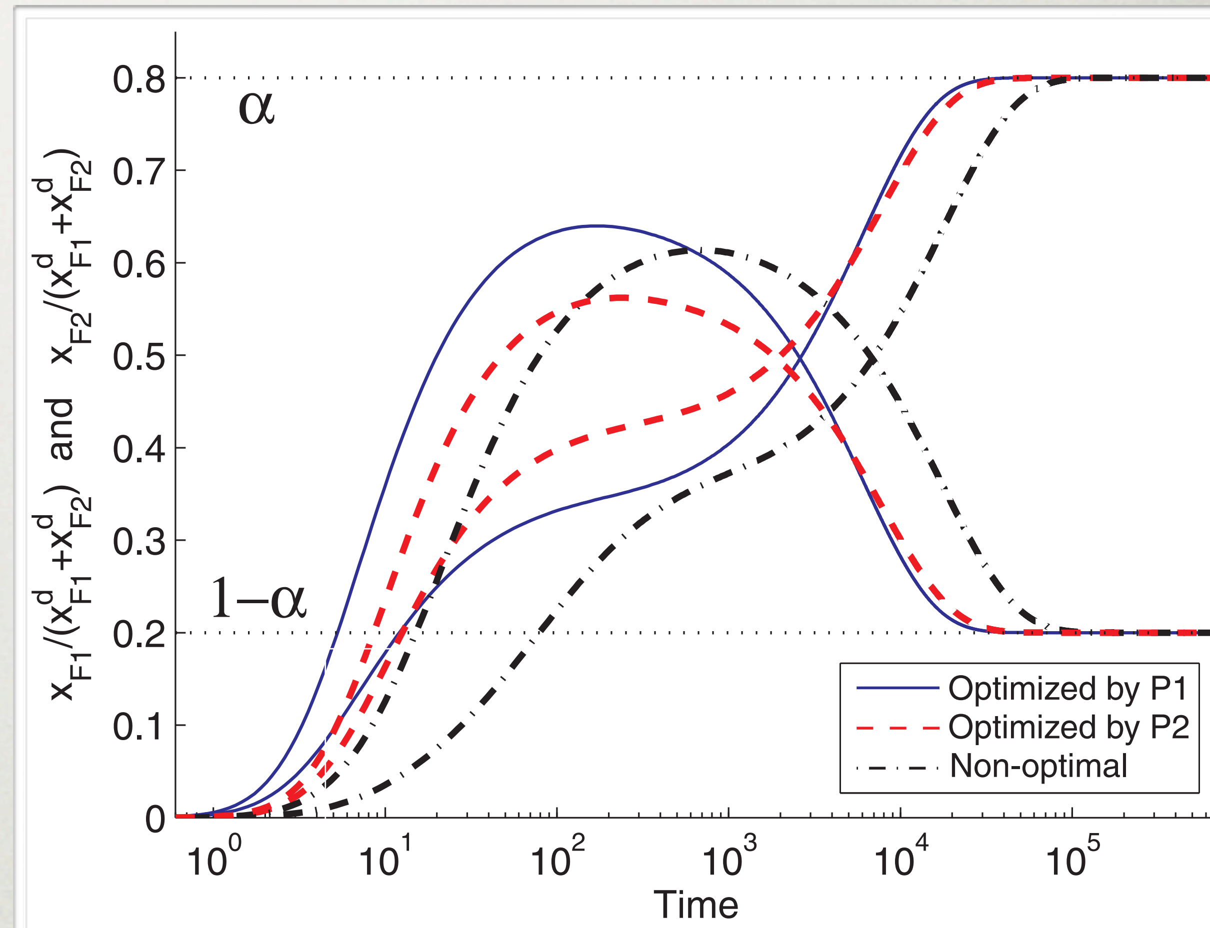


6. CRN Control

Behavior

- Time log-scale.
- Comparison with non-optimal set of rates.

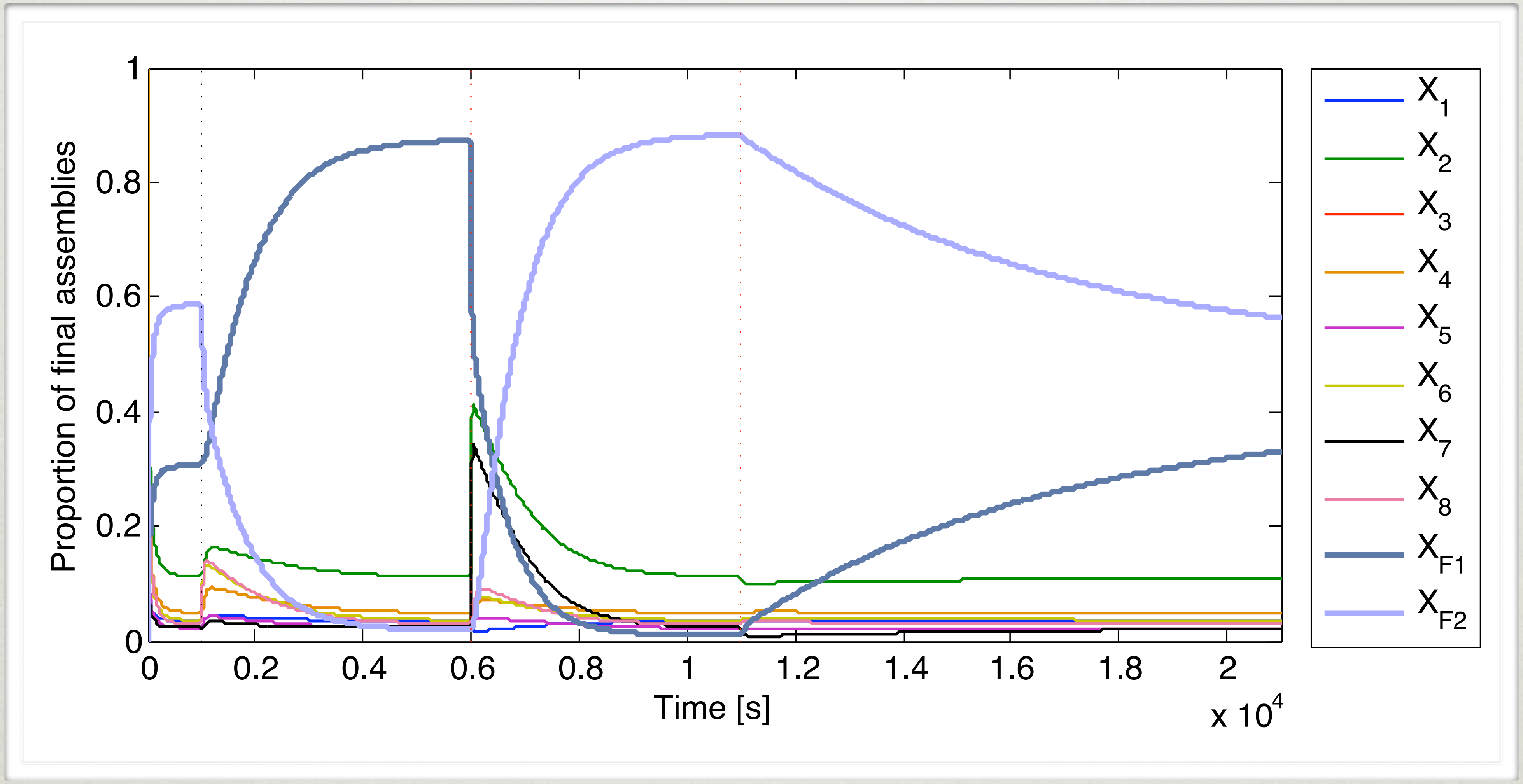




6. CRN Control

Possibilities

- Change of goal over time, abrupt change of rates.



- "Green manufactory"

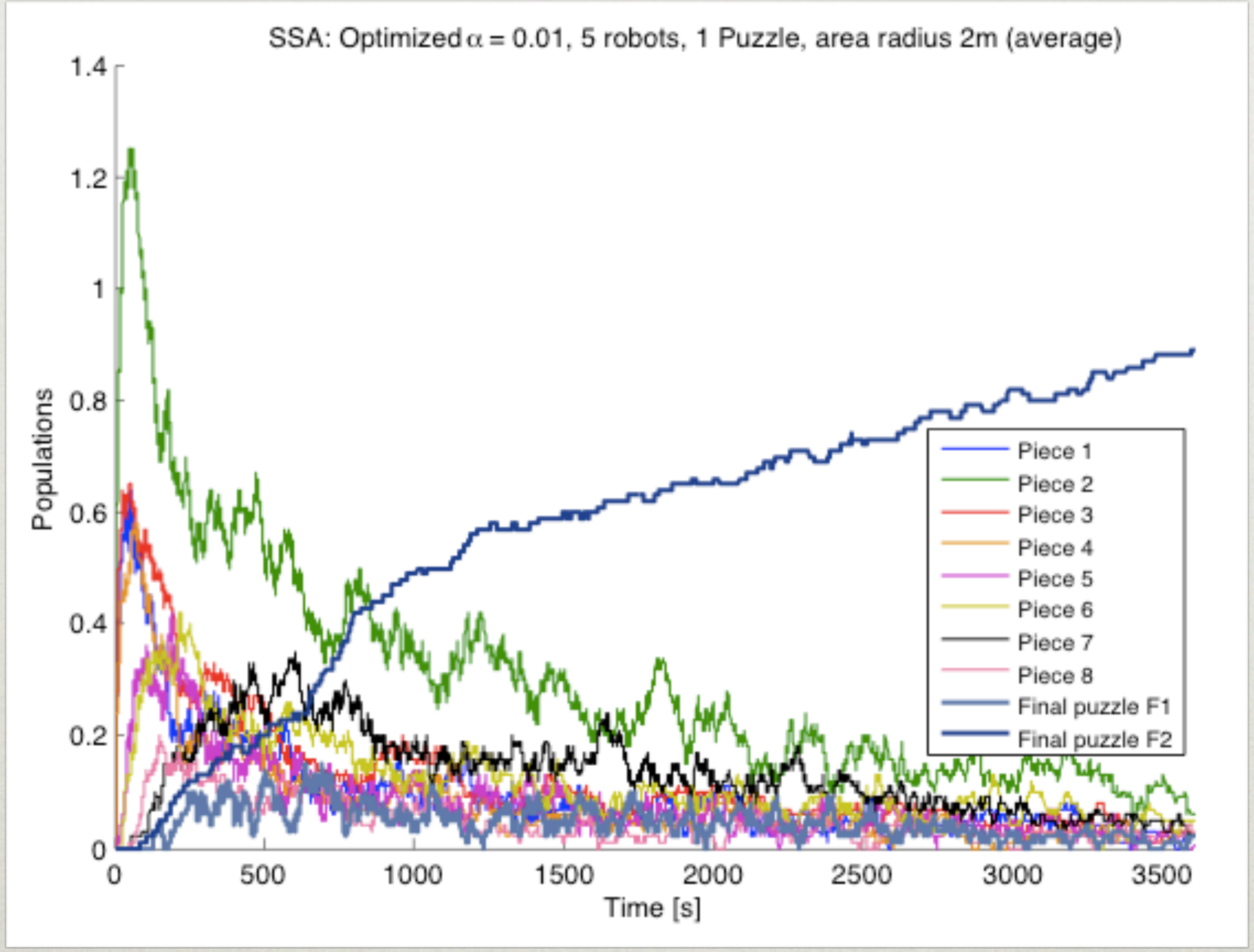
7. Mapping back to Platform

- Easy for us:
  - Forward rate: probability to start an assembly.
  - Backward rate: probability to disassemble the current piece.
- But our model was more complicated, with robots. Still working?
  - Optimization on reduced model, maybe does not adapt to the complete model and the realistic platform.

7. Mapping back to Platform

Stochastic simulations

- According to stochastic simulations, yes.



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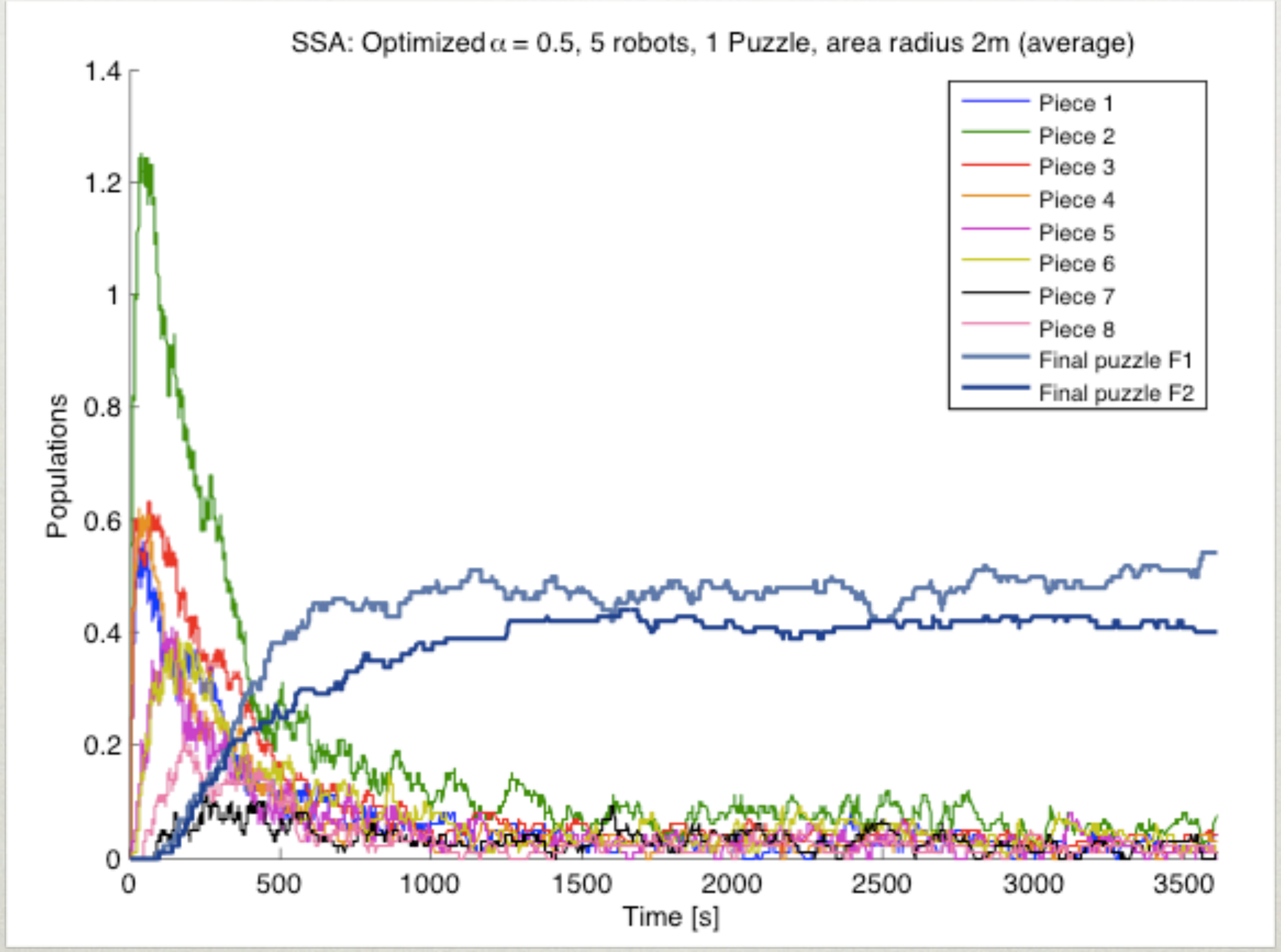

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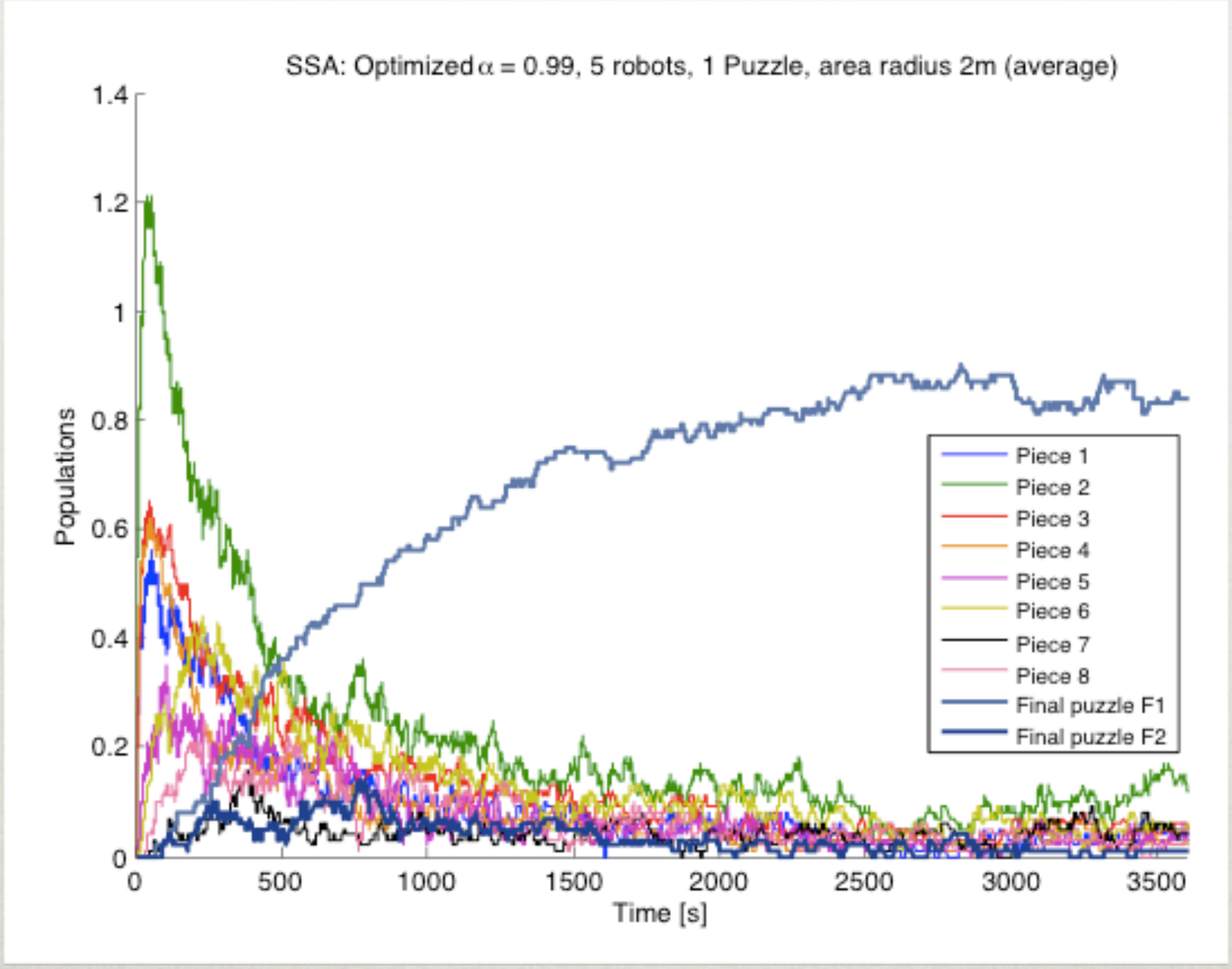

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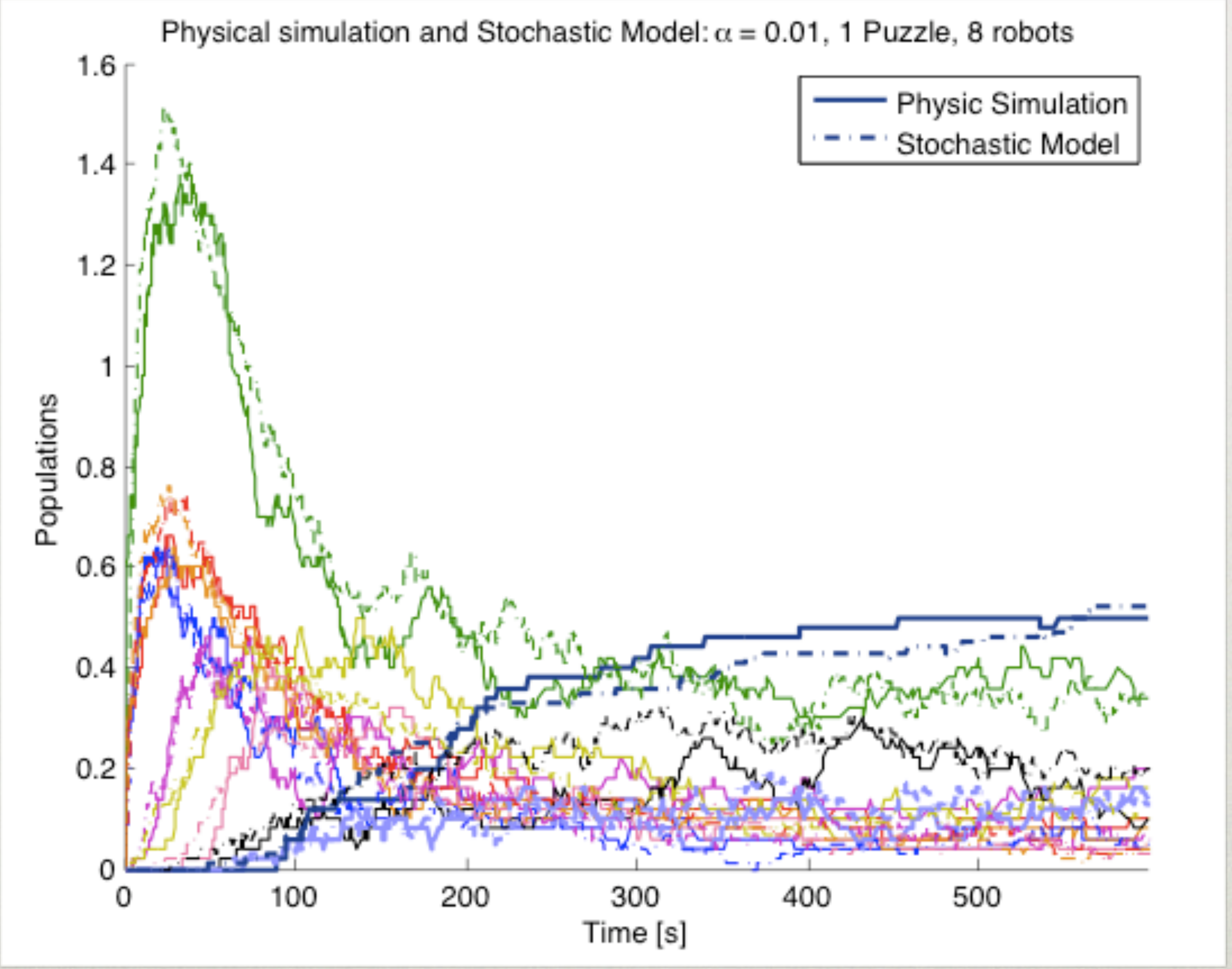
Realistic simulations

- In Webots, more or less...



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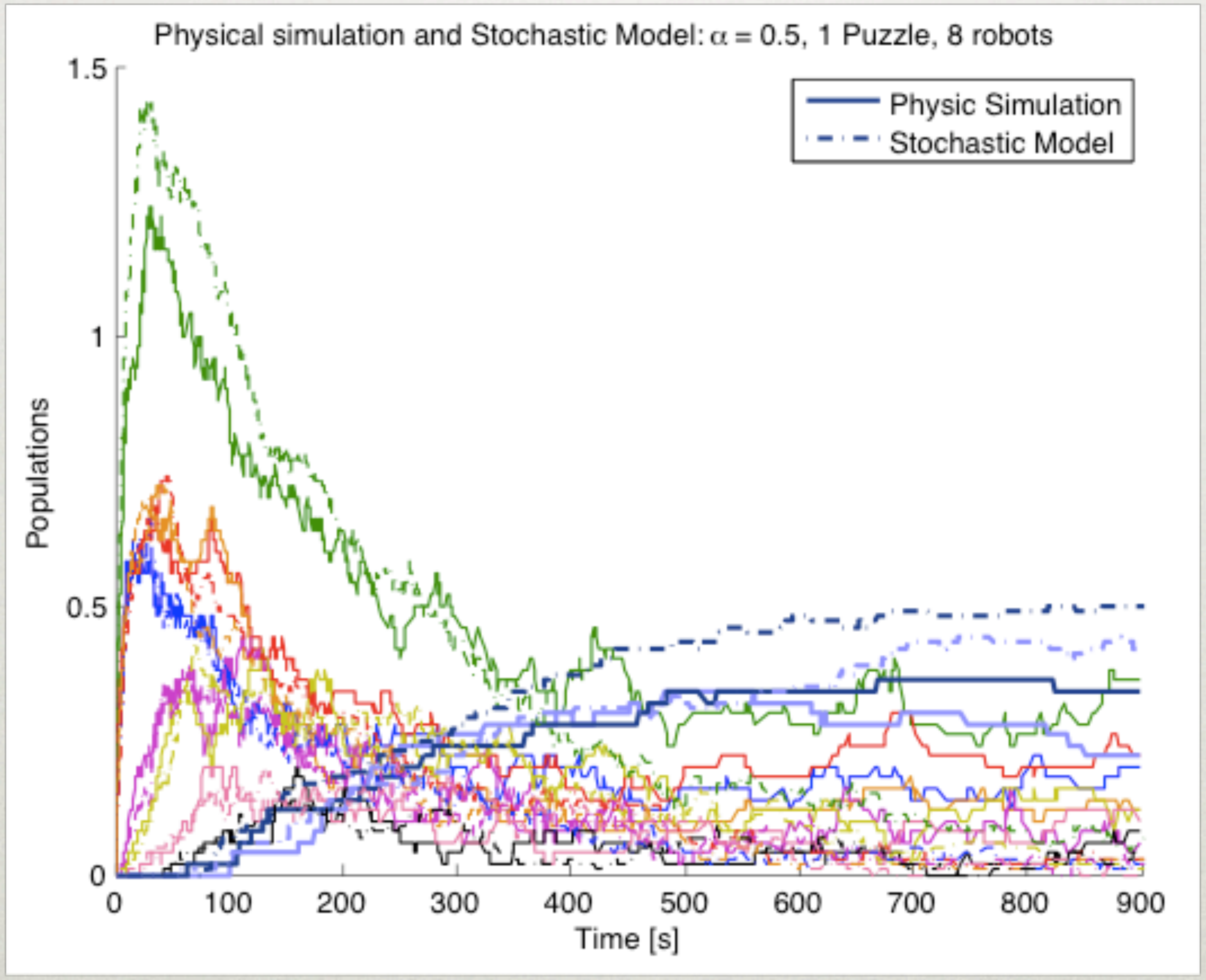

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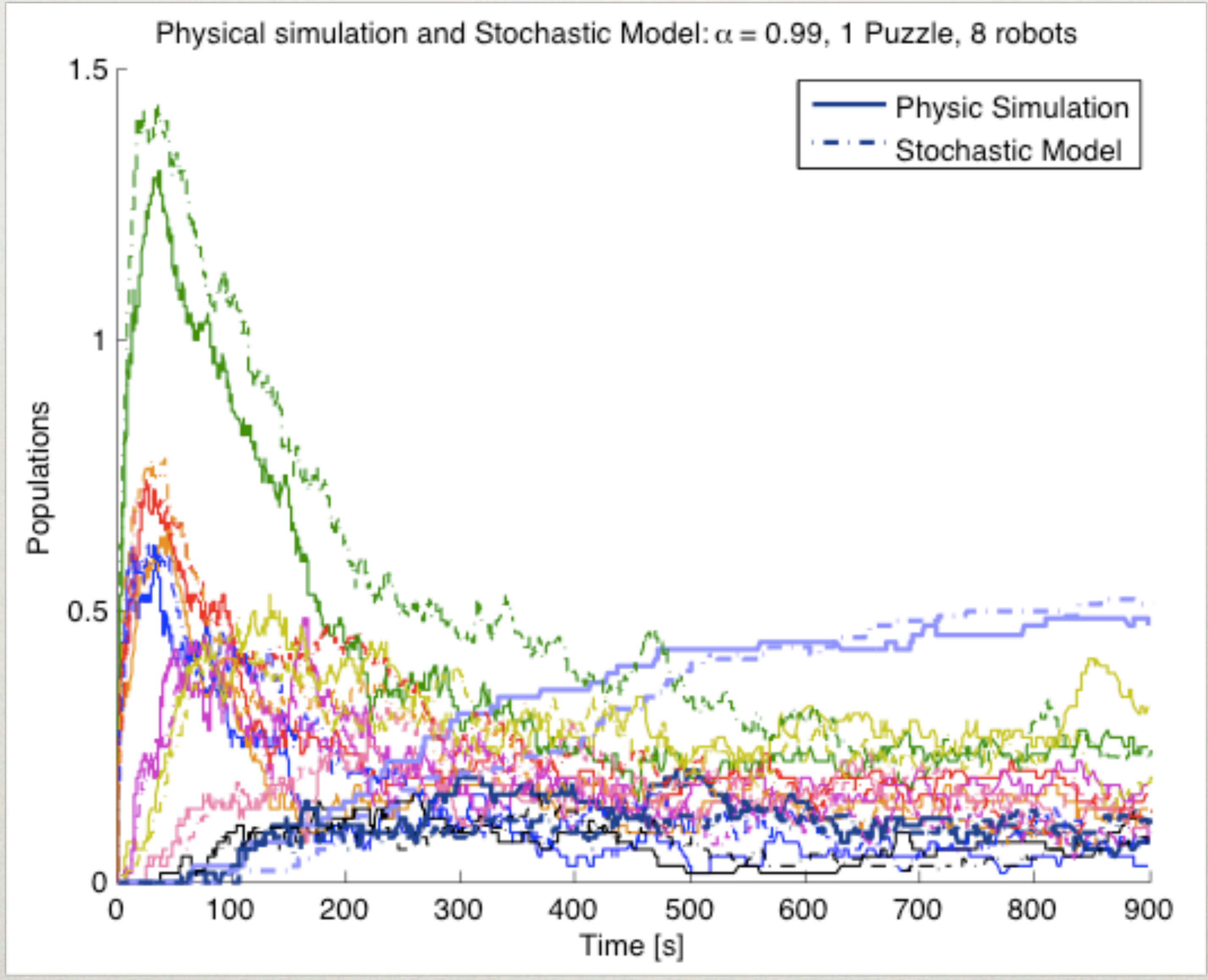
Realistic simulations

- In Webots, more or less...



7. Mapping back to Platform

Realistic simulations

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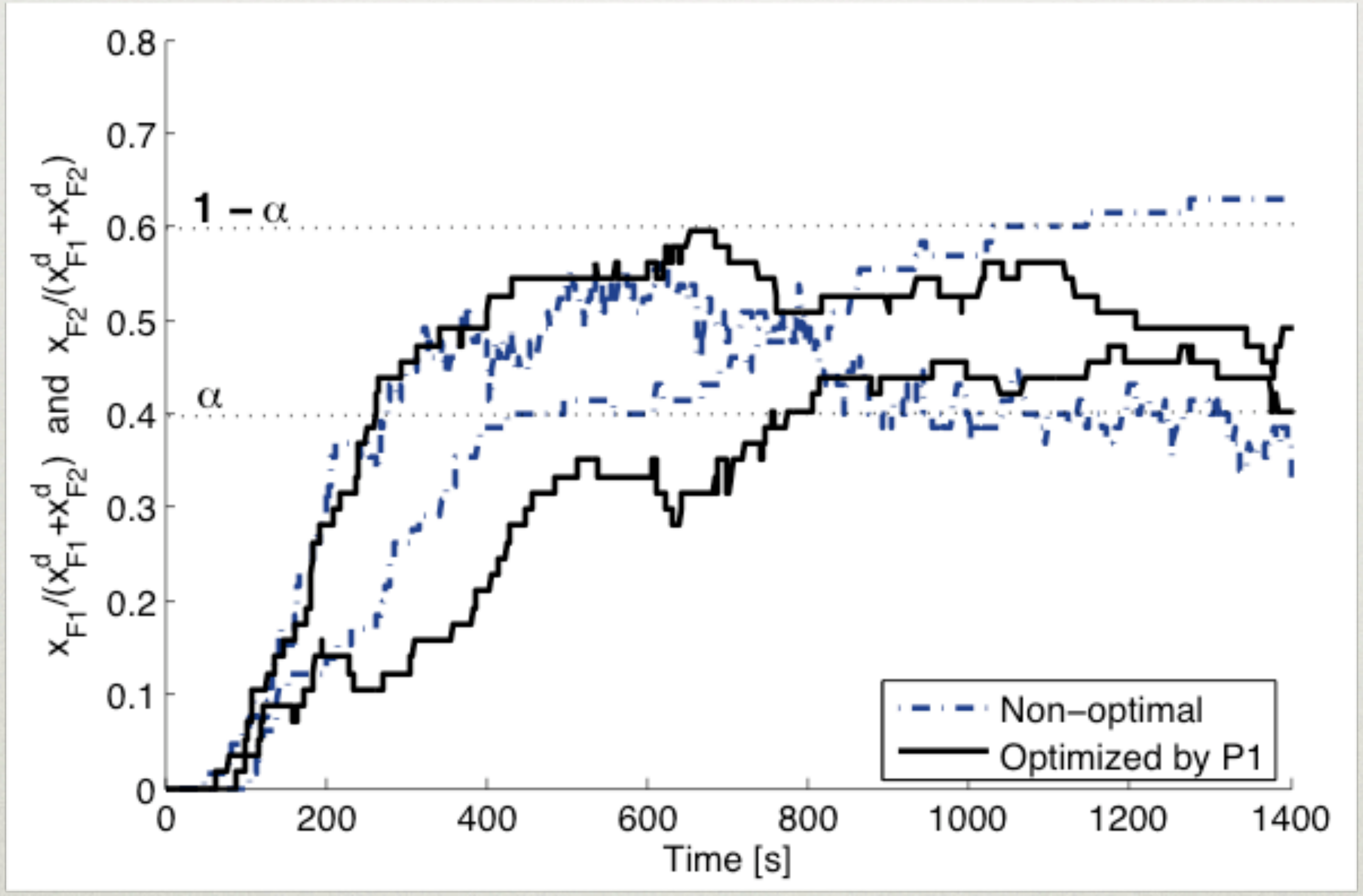


7. Mapping back to Platform

Problems

- Several problems arise:
  - Time to carry a piece is too big. Workaround by adding robots.
  - Well-mixed property is violated after disassembly. Pieces lie around.
- Rates are not precise anymore, iterative process needed.
- Sub-optimal results, due to simulations errors (one piece stuck = one full assembly impossible).

8. Conclusion

- Successfully developed a Top-down control design using a different language.
- Realistic simulations in Webots.
- Close fitting of the model to the experimental data. Good for predictions.
- Promising first control results. Possibility to design the system for high-level goals.

9. Further work

- Extend the framework to bigger assembly plans.
  - Possibility to optimize directly the plans!
- Try other optimizations schemes for the rates.
- Apply framework to new realistic problems.

- Acknowledgements:
  - Grégory Mermoud, Alcherio Martinoli.
  - Spring Berman, Vijay Kumar.

Thank you

Any Questions ?

Control

- R. Heinrich, S. Schuster, and H.-G. Holzhutter, "Mathematical analysis of enzymic reaction systems using optimization principles", Eur. J. Biochem., vol. 201, pp. 1–21, 1991.

$$\tau_j = \left(\sum_{i=1}^{10} (-s_{ij}) \frac{dv_j}{dx_i} \right)^{-1}_{x=x^d}$$

$$v_j = k_j^+ x_k x_l - k_j^- x_m$$

$$\tau_j = (k_j^+ (x_k^d + x_l^d) + k_j^-)^{-1}$$

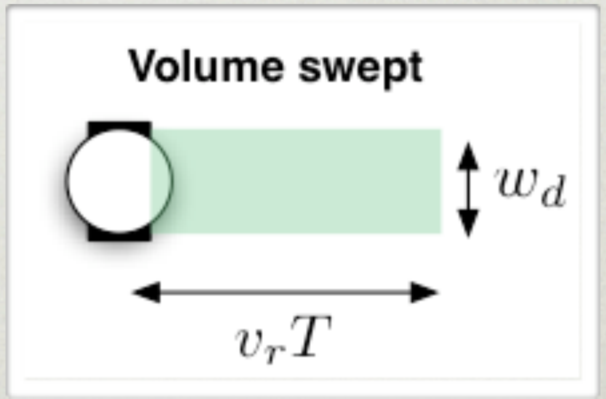
Models

Parameters estimation

- Reaction rates depends on encountering probabilities.
  - Measure them in Webots
  - A-priori guess using theoretical informations
- Chose to use the geometric probabilities, like N. Correll did.
  - Actually is the exact application of a chemical simulation formula to large-scale robots.

$$k_i = p_i^e \cdot p_i^a$$

$$p_e \sim \frac{1}{A_{total}} v_r T w_d$$



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Models

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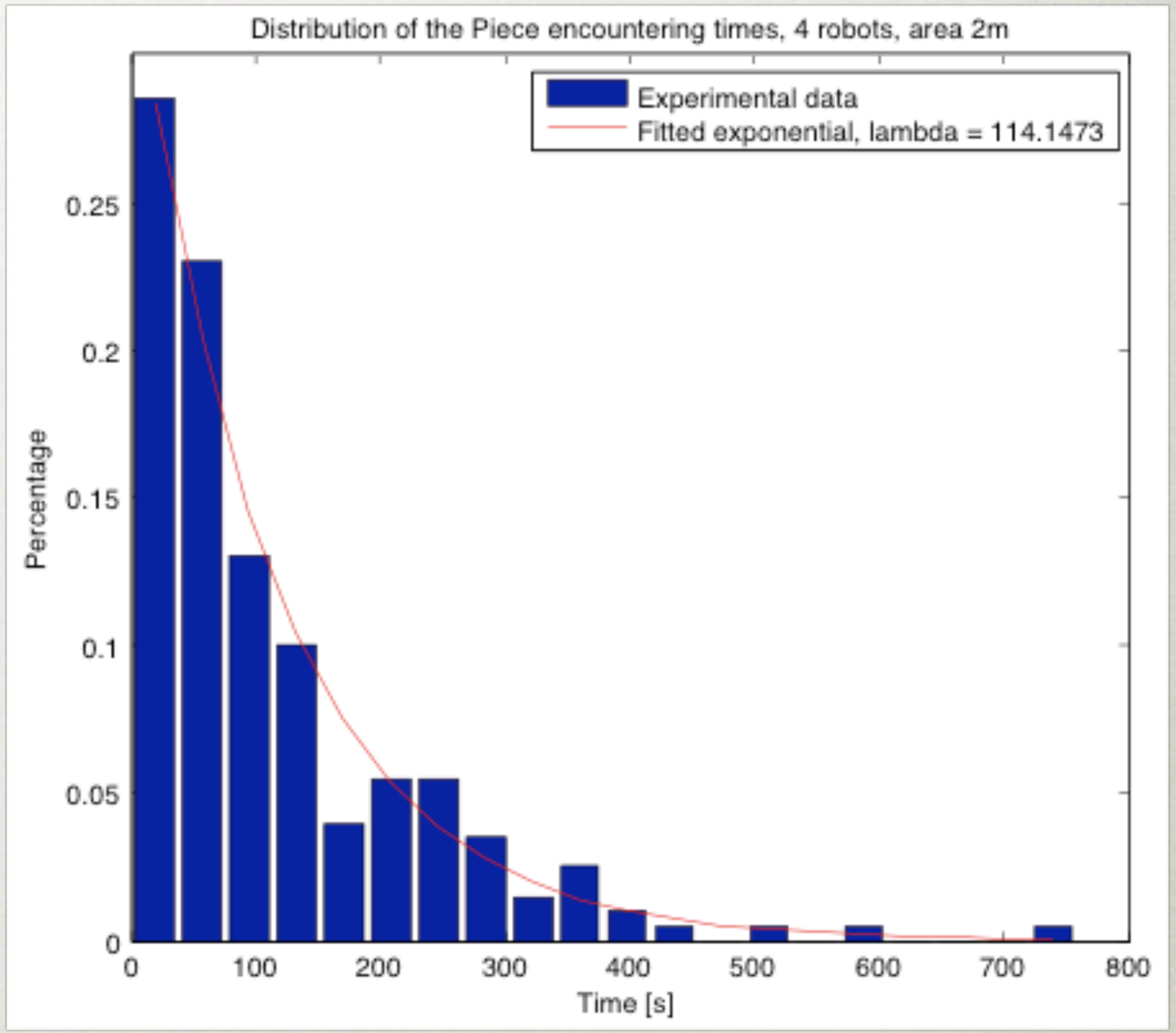
$$
\begin{aligned}
X_R + X_1^u &\xrightarrow{e_1} X_1^c & X_R + X_5^u &\xrightarrow{e_5} X_5^c \\
X_R + X_2^u &\xrightarrow{e_2} X_2^c & X_R + X_6^u &\xrightarrow{e_6} X_6^c \\
X_R + X_3^u &\xrightarrow{e_3} X_3^c & X_R + X_7^u &\xrightarrow{e_7} X_7^c \\
X_R + X_4^u &\xrightarrow{e_4} X_4^c & & \\
X_1^c + X_2^c &\xrightarrow{k_1^+} X_5^c + X_R & X_5^c + X_6^c &\xrightarrow{k_3^+} X_7^c + X_R \\
X_3^c + X_4^c &\xrightarrow{k_2^+} X_6^c + X_R & X_2^c + X_7^c &\xrightarrow{k_4^+} X_{F1}^c + X_R \\
X_5^c &\xrightarrow{k_1^-} X_1^c + X_2^u & X_7^c &\xrightarrow{k_3^-} X_6^c + X_5^u \\
X_6^c &\xrightarrow{k_2^-} X_3^c + X_4^u & X_{F1}^c &\xrightarrow{k_4^-} X_7^c + X_2^u
\end{aligned}
$$

Models

Parameters estimation

- Rates verifications
- Webots experiments
  - Sample the times to event.
  - 100 experiments.
  - Fit an exponential distribution in Matlab.
- Verify effect of adding "dummy" robots.



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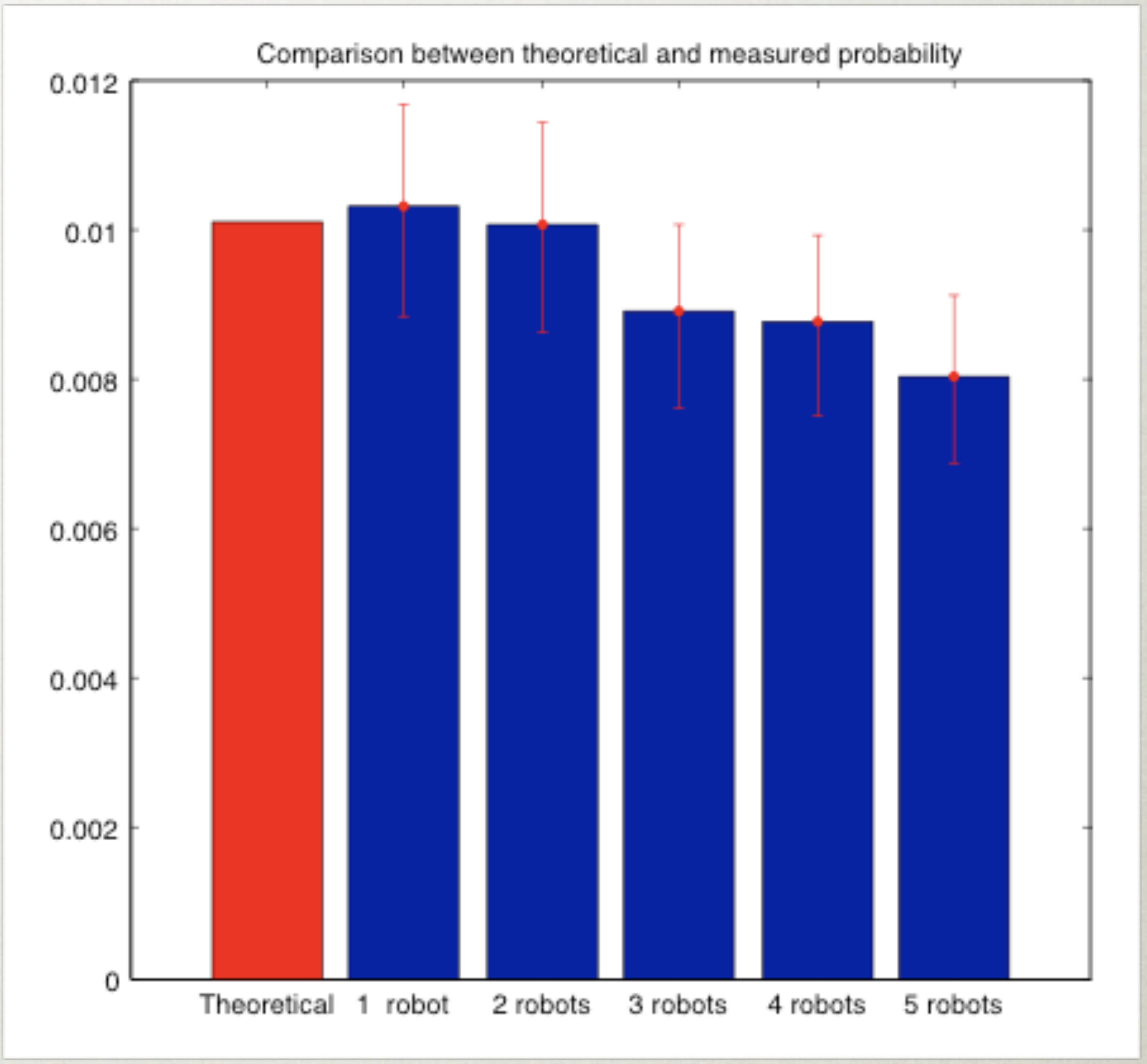

Models

Parameters estimation

- Hypothesis:
  - System should be well-mixed.
- Enforced by chemotaxis-like movement of robots.
- We can make non-spatiality assumption then.