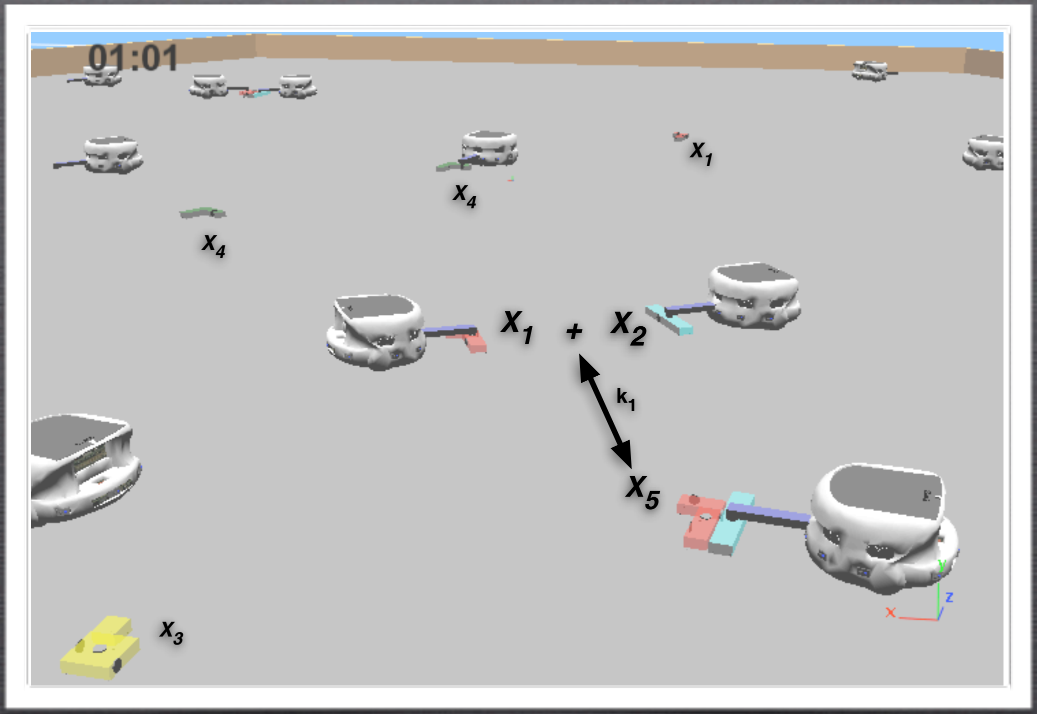
Hybrid Reactions Modeling for Top-down Design

Final Presentation

Loïc Matthey



Supervisors:

Vijay Kumar
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Special contributions:

Spring Berman

Penn University of Pennsylvania

Master Project - MP12 - 09/04/2008

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

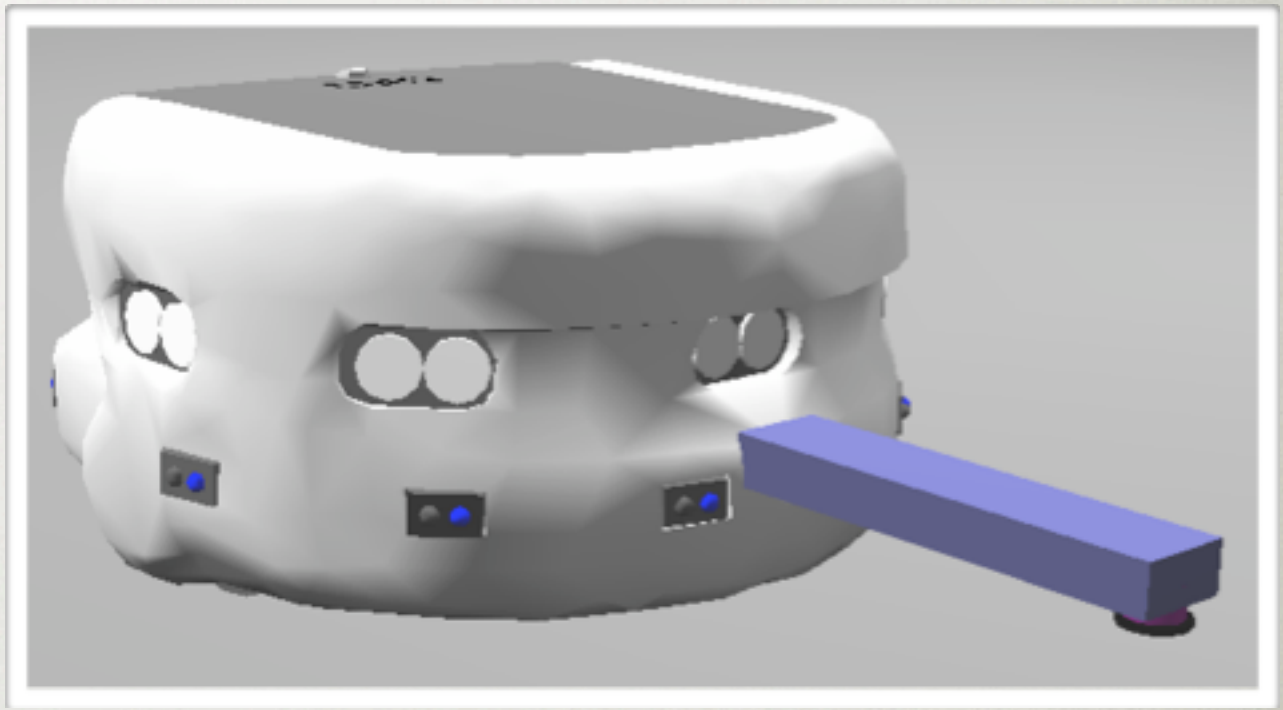
Definition (refined)

- 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 smaller 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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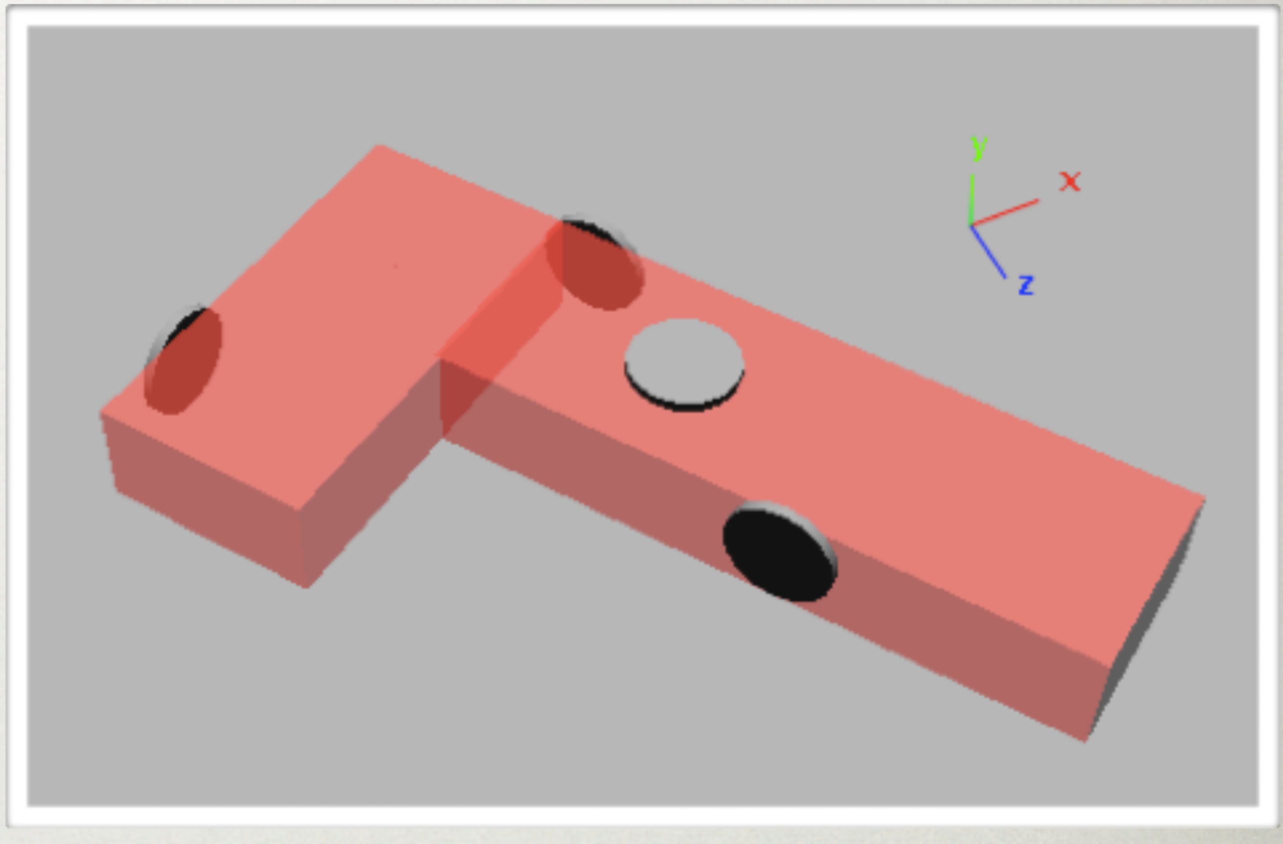

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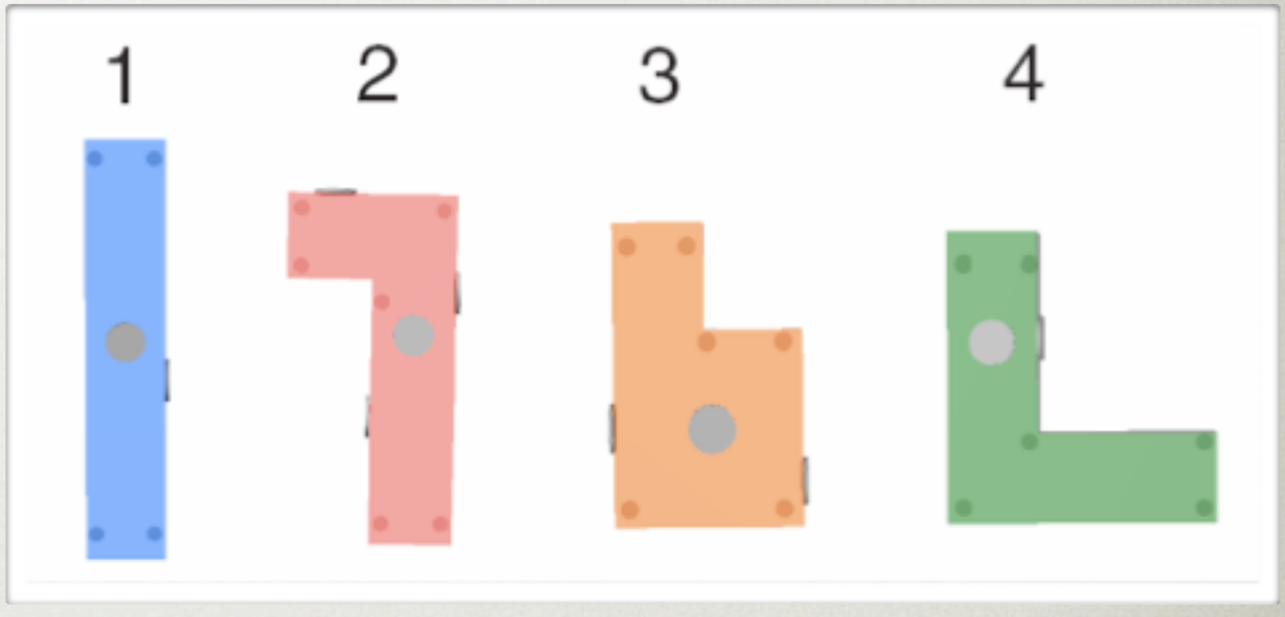

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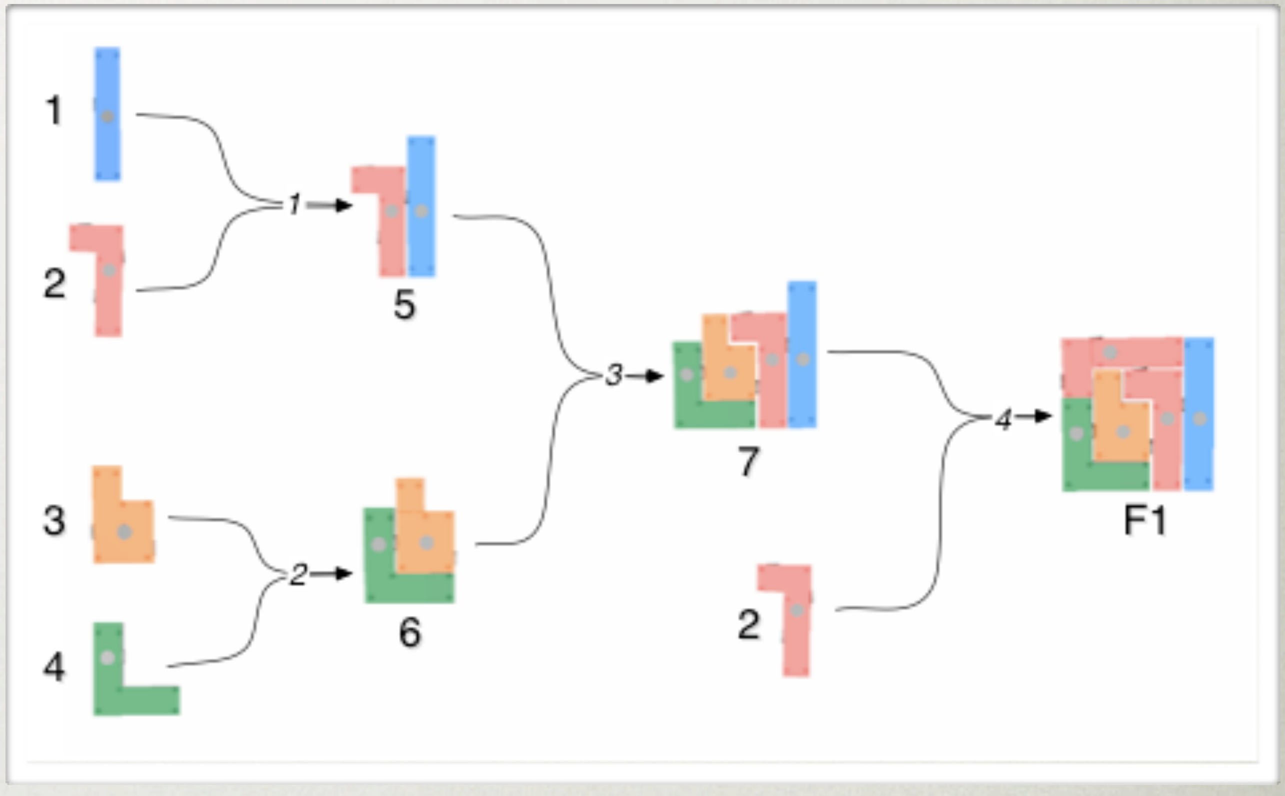

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Realistic platform

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

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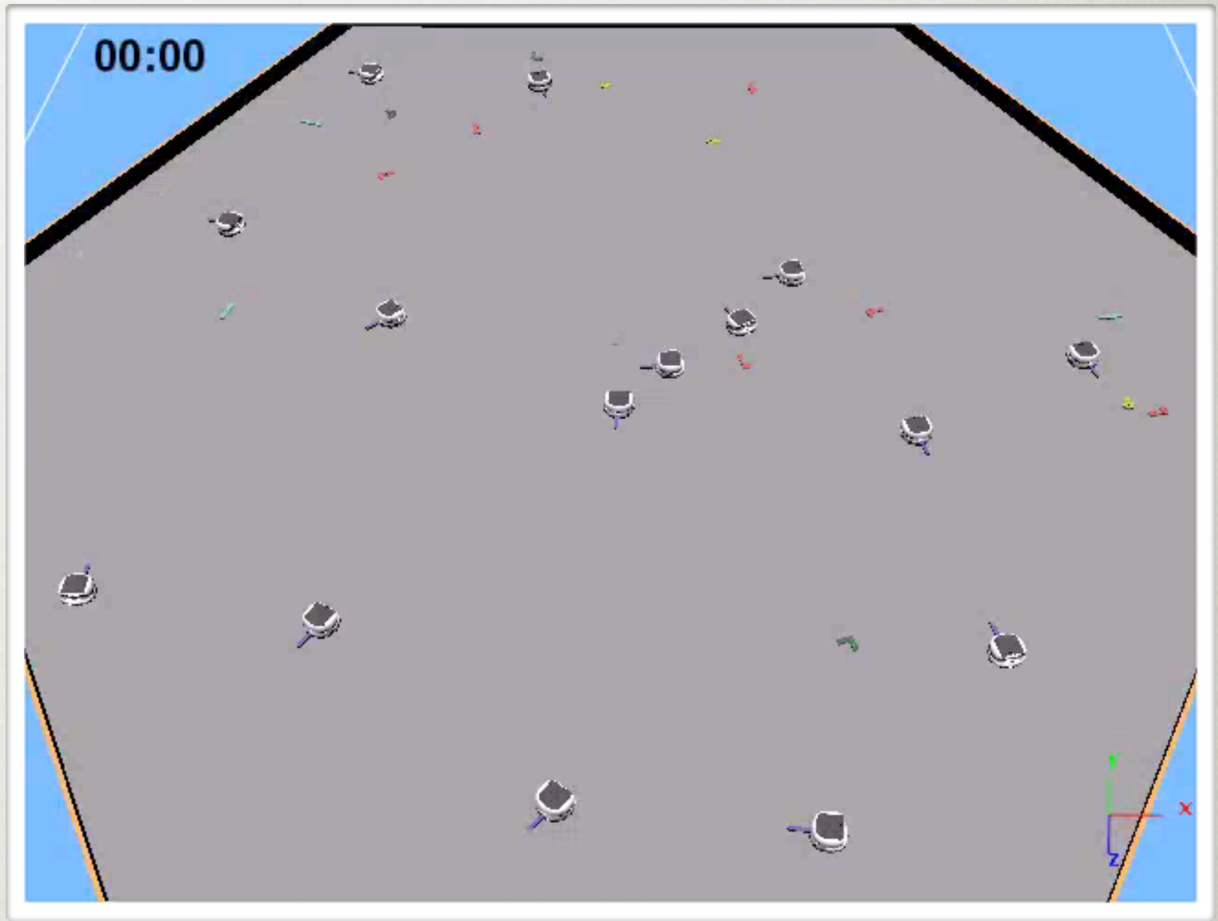

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Chemical reaction networks

- 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.

$$
\begin{array}{lcllcl}
X_R + X_1^f & \xrightarrow{e_1} & X_1 & X_R + X_3^f & \xrightarrow{e_3} & X_3 \\
X_R + X_2^f & \xrightarrow{e_2} & X_2 & X_R + X_4^f & \xrightarrow{e_4} & X_4 \\
X_1 + X_2 & \xrightarrow{k_1} & X_5 + X_R & X_2 + X_7 & \xrightarrow{k_4} & X_{F1} + X_R \\
X_3 + X_4 & \xrightarrow{k_2} & X_6 + X_R & X_2 + X_5 & \xrightarrow{k_5} & X_8 + X_R \\
X_5 + X_6 & \xrightarrow{k_3} & X_7 + X_R & X_6 + X_8 & \xrightarrow{k_6} & X_{F2} + X_R
\end{array}
$$

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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 + \\
 & \quad k_3 x_5 x_6 + k_4 x_2 x_7 + k_5 x_2 x_5 + k_6 x_6 x_8 \\
\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 - k_5 x_2 x_5 \\
\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 - k_5 x_2 x_5 \\
\dot{x_6} &= k_2 x_3 x_4 - k_3 x_5 x_6 - k_6 x_6 x_8 \\
\dot{x_7} &= k_3 x_5 x_6 - k_4 x_2 x_7 \\
\dot{x_8} &= k_5 x_2 x_5 - k_6 x_6 x_8 \\
\dot{x}_{F1} &= k_4 x_2 x_7 \\
\dot{x}_{F2} &= k_6 x_6 x_8
\end{cases}
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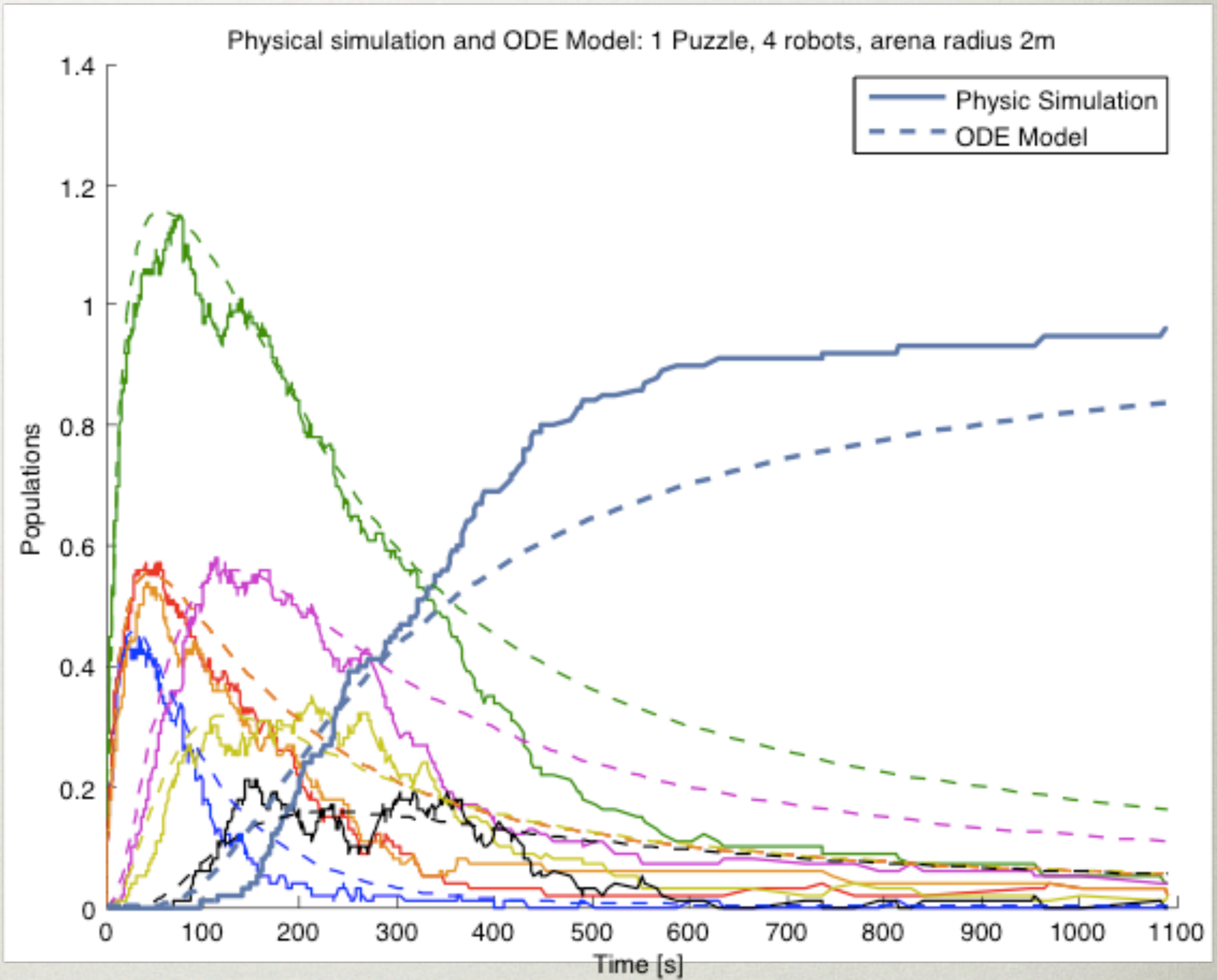

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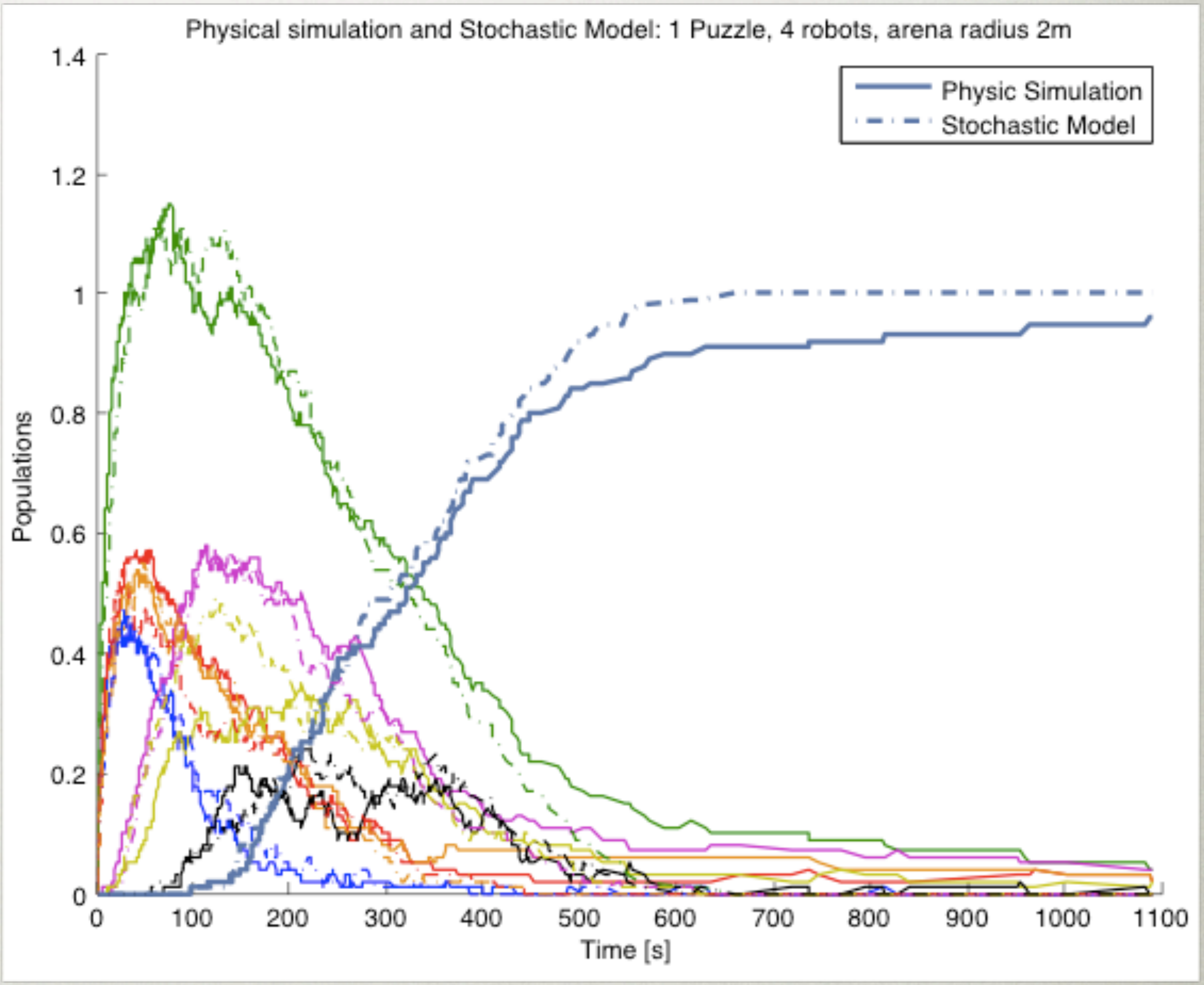

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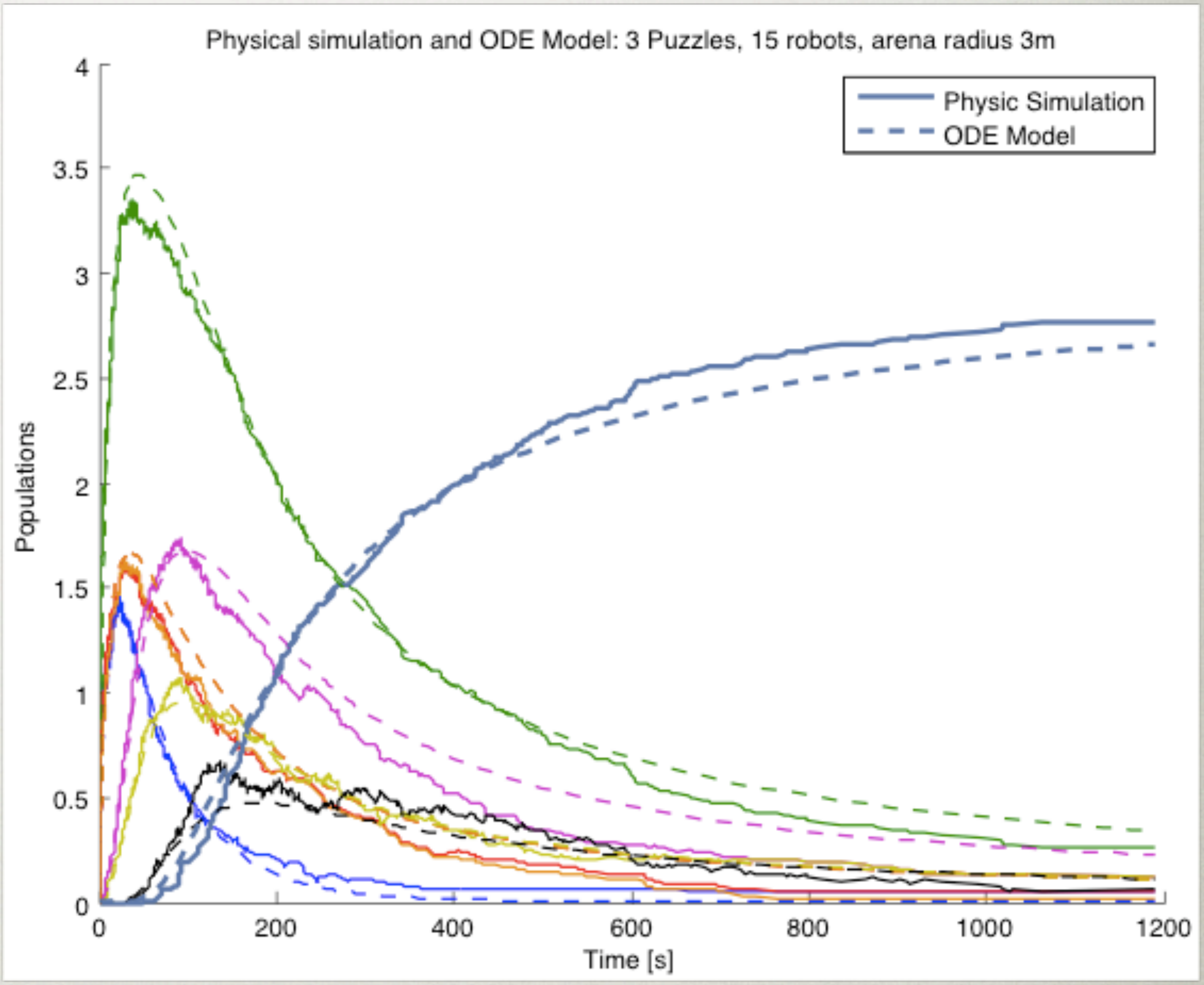

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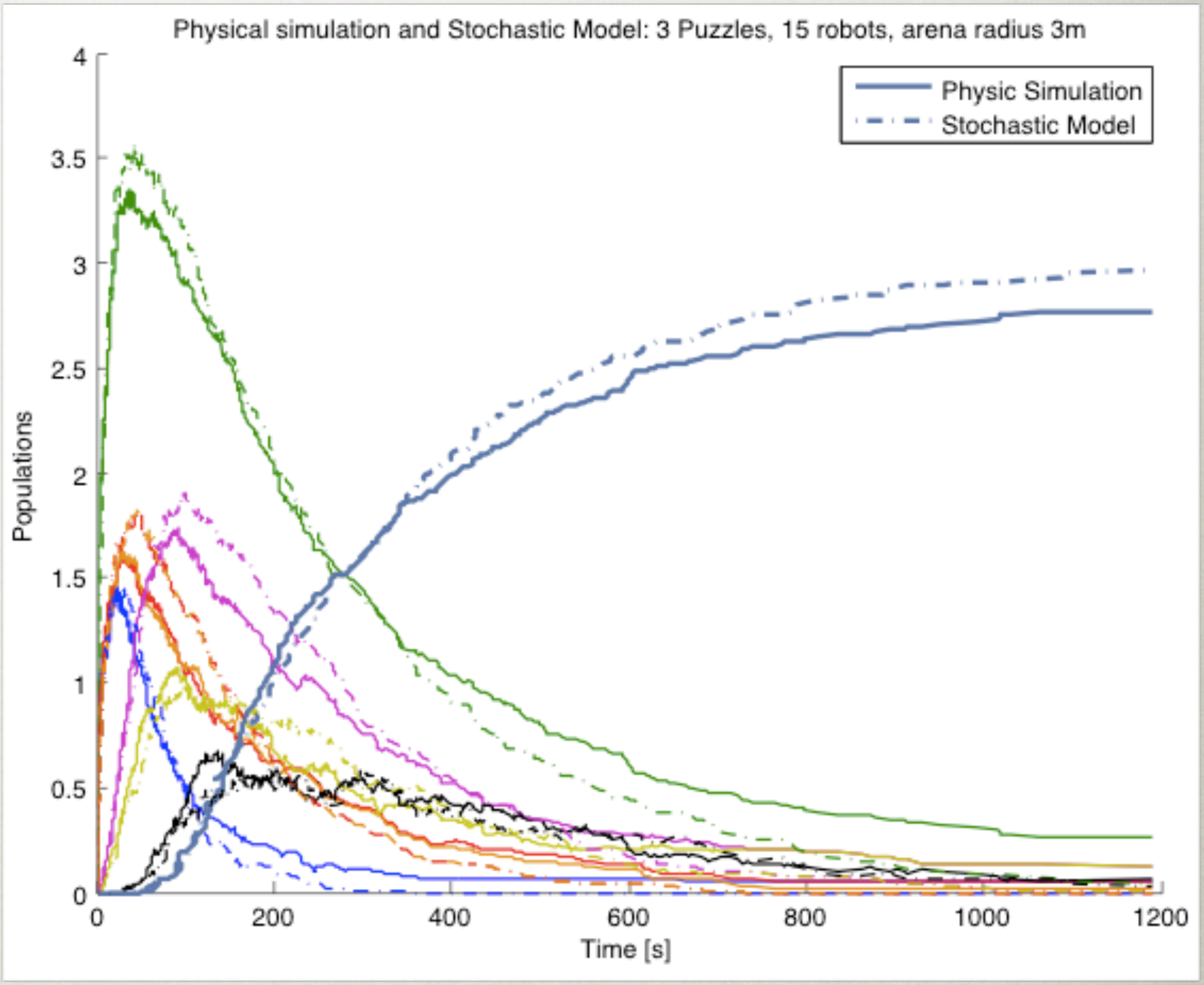


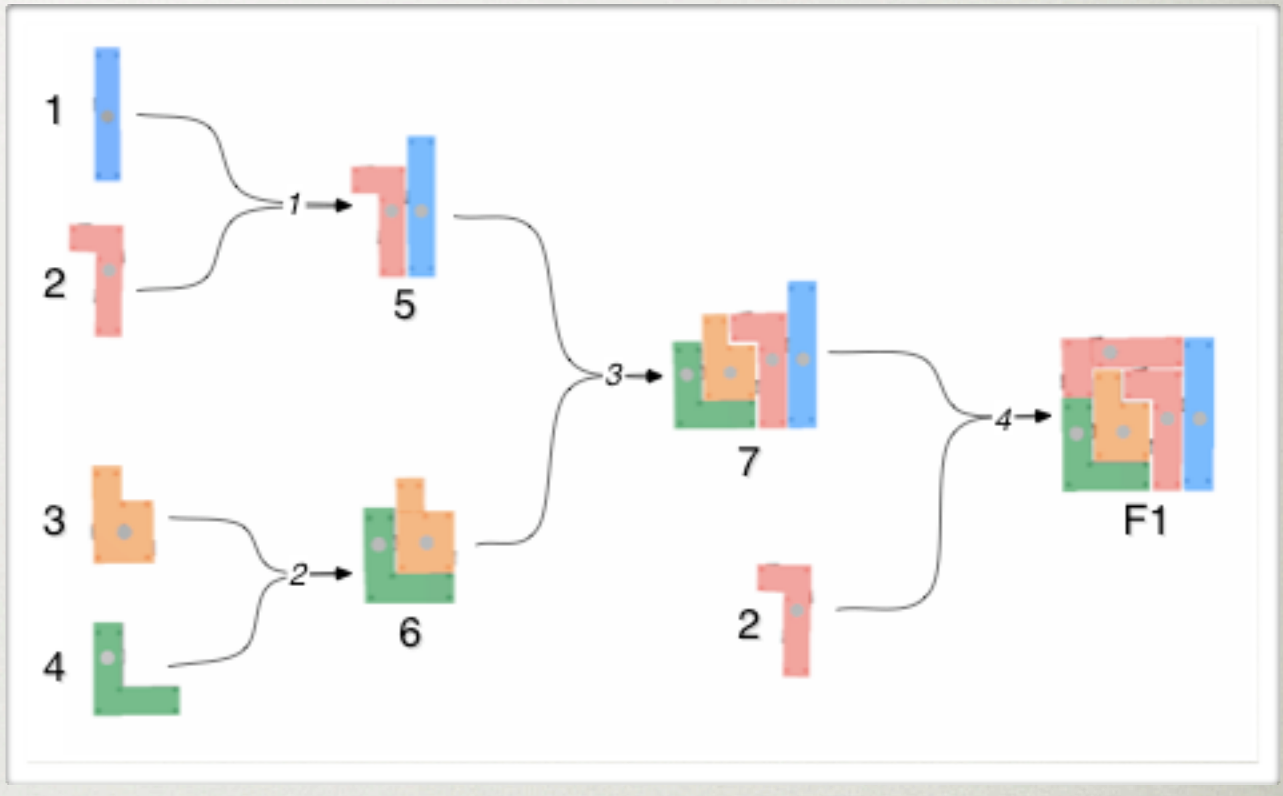
4. State at midterm

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.



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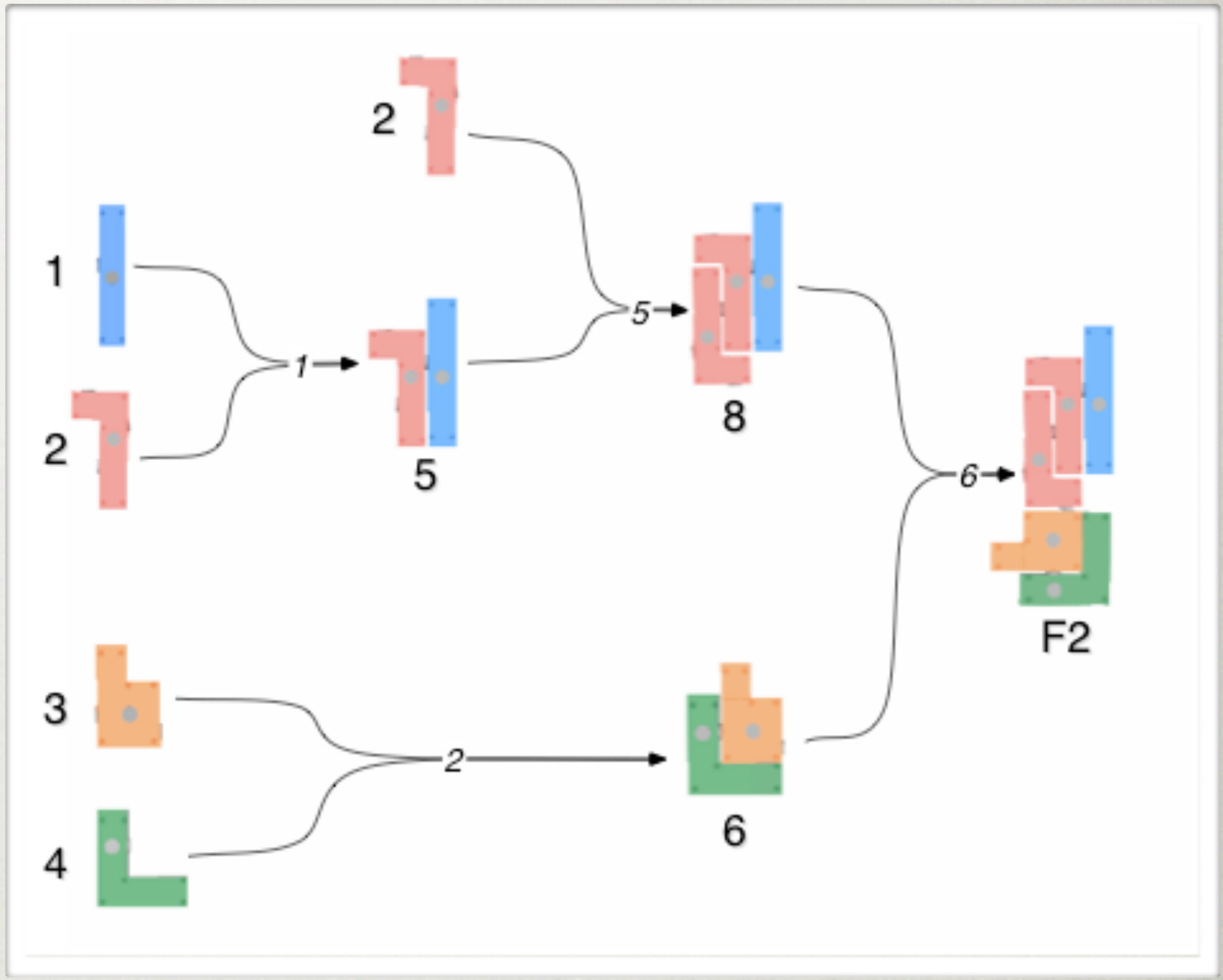

6. CRN Control

Notation

- ODE approximation.
- X_i are discrete number of pieces, x_i are continuous number of pieces.
- ***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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$$
\begin{cases}
\dot{x}_1 & = & -k_1^+ x_1 x_2 + k_1^- x_5 \\
\dot{x}_2 & = & -k_1^+ x_1 x_2 - k_5^+ x_2 x_5 - k_4^+ x_2 x_7 + k_1^- x_5 + k_5^- x_8 + k_4^- x_{F1} \\
\dot{x}_3 & = & -k_2^+ x_3 x_4 + k_2^- x_6 \\
\dot{x}_4 & = & -k_2^+ x_3 x_4 + k_2^- x_6 \\
\dot{x}_5 & = & k_1^+ x_1 x_2 - k_1^- x_5 - k_3^+ x_5 x_6 + k_3^- x_7 - k_5^+ x_2 x_5 + k_5^- x_8 \\
\dot{x}_6 & = & k_2^+ x_3 x_4 - k_2^- x_6 - k_3^+ x_5 x_6 + k_3^- x_7 - k_6^+ x_6 x_8 + k_6^- x_{F2} \\
\dot{x}_7 & = & k_3^+ x_5 x_6 - k_3^- x_7 - k_4^+ x_2 x_7 + k_4^- x_{F1} \\
\dot{x}_8 & = & k_5^+ x_2 x_5 - k_5^- x_8 - k_6^+ x_6 x_8 + k_6^- x_{F2} \\
\dot{x}_{F1} & = & k_4^+ x_2 x_7 - k_4^- x_{F1} \\
\dot{x}_{F2} & = & k_6^+ x_6 x_8 - k_6^- x_{F2}
\end{cases}
$$

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- X_i are discrete number of pieces, x_i are continuous number of pieces.
- 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

- ODE approximation.
- X_i are discrete number of pieces, x_i are continuous number of pieces.
- $\boldsymbol{K}$ 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 extended Deficency One theorem, Feinberg.*
  - *deficiency of network = 0.*
  - *block weakly reversible.*
- Global stability empirically verified, proof under way.

$$\dot{\mathbf{x}} = \mathbf{MKy}(\mathbf{x})$$

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 $\mathbf{y^d}$:

$$\mathbf{MKy^d} = \mathbf{0} \qquad \alpha = \frac{x_{F1}}{x_{F1} + x_{F2}}$$

- Optimize measure of relaxation time for each reaction:

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

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

6. CRN Control

Method

- Two objective functions.

$$f_{ave}(\mathbf{k}) = \tfrac{1}{10}\sum_{j=1}^{10} \tau_j^{-1} \qquad\qquad f_{min}(\mathbf{k}) = \min\{\tau_1^{-1}, \ldots, \tau_{10}^{-1}\}$$

- Two convex programs.

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

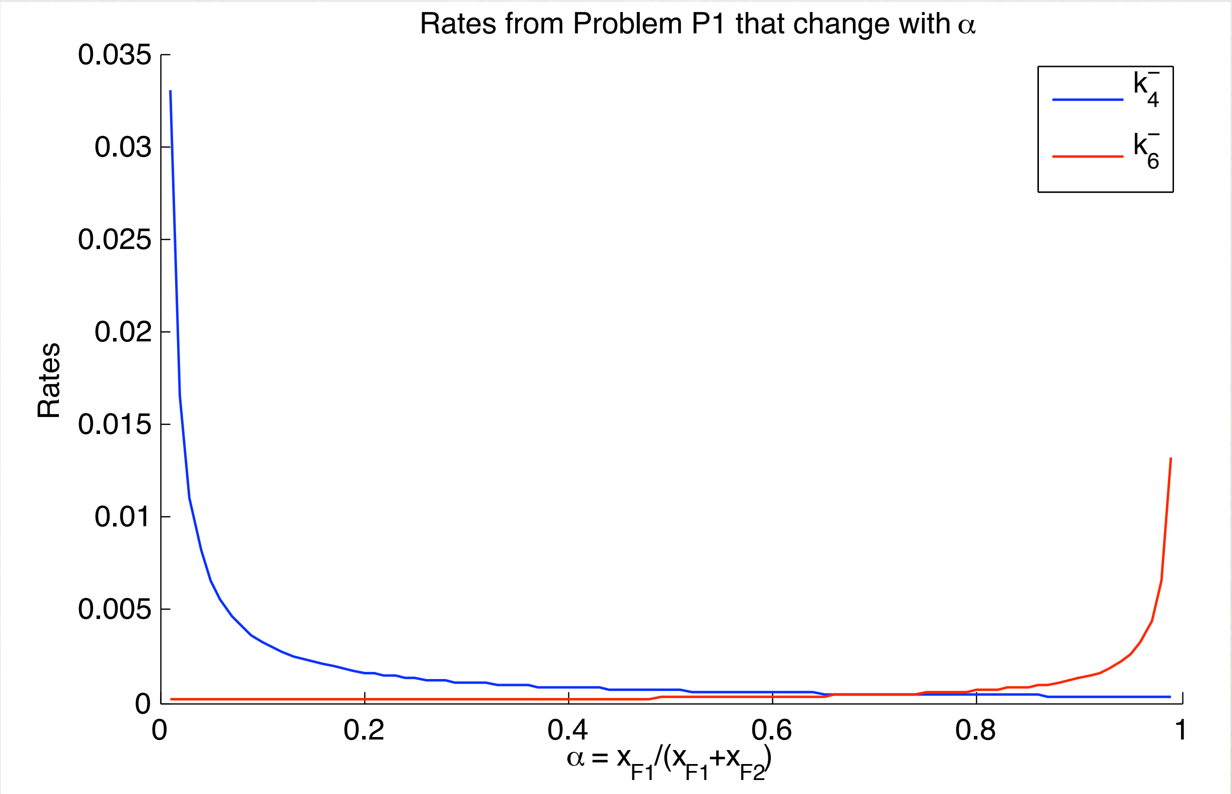
$$\begin{array}{lll} \textbf{P2:} & \text{maximize} & f_{min}(\mathbf{k}(\mathbf{p})) \\ & \text{subject to} & \mathbf{MK}(\mathbf{p})\mathbf{y^d} = \mathbf{0}, \quad \mathbf{0} \le \mathbf{p} \le \mathbf{1}\ . \end{array}$$

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*

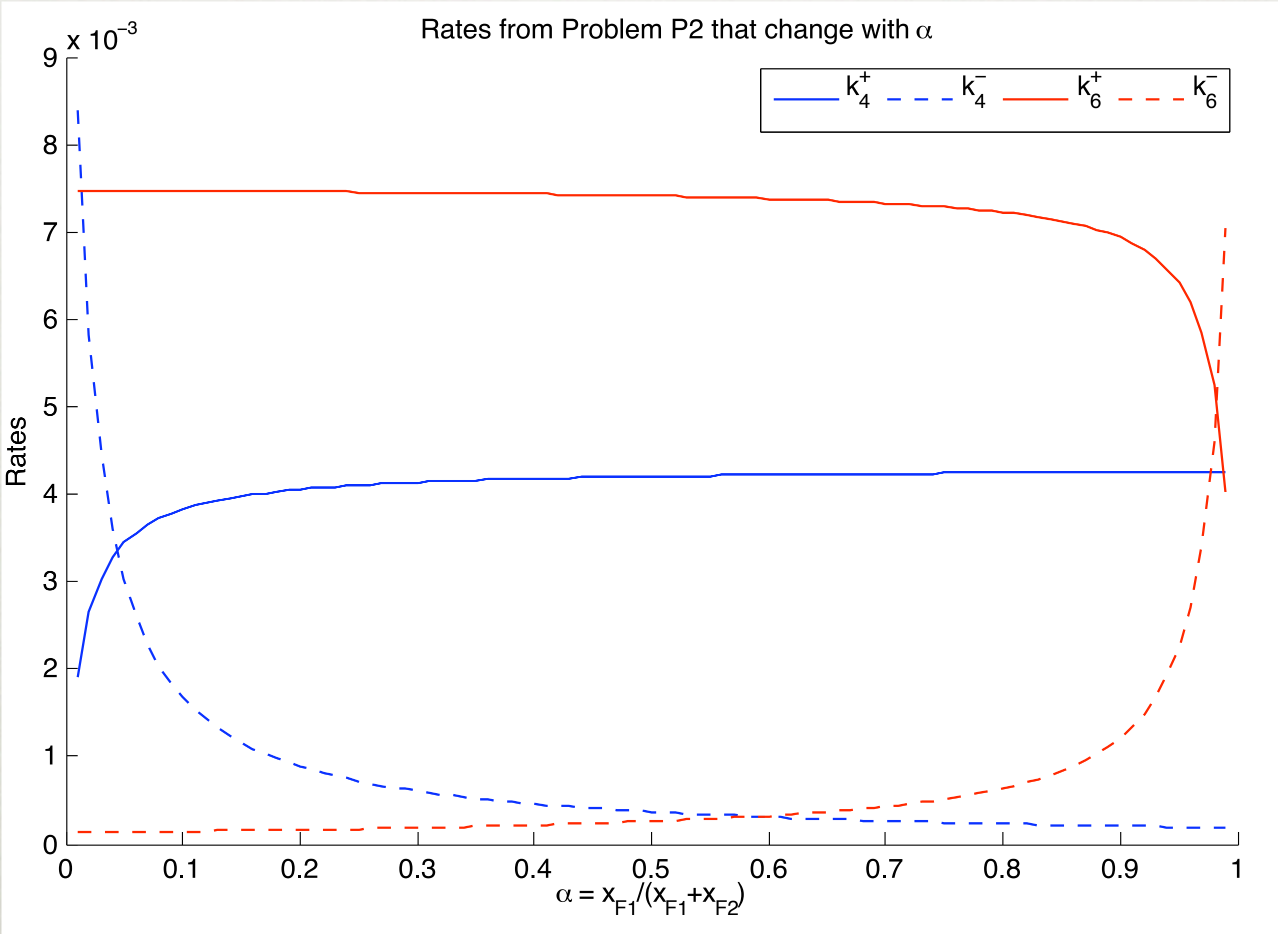


6. CRN Control

Results P2

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

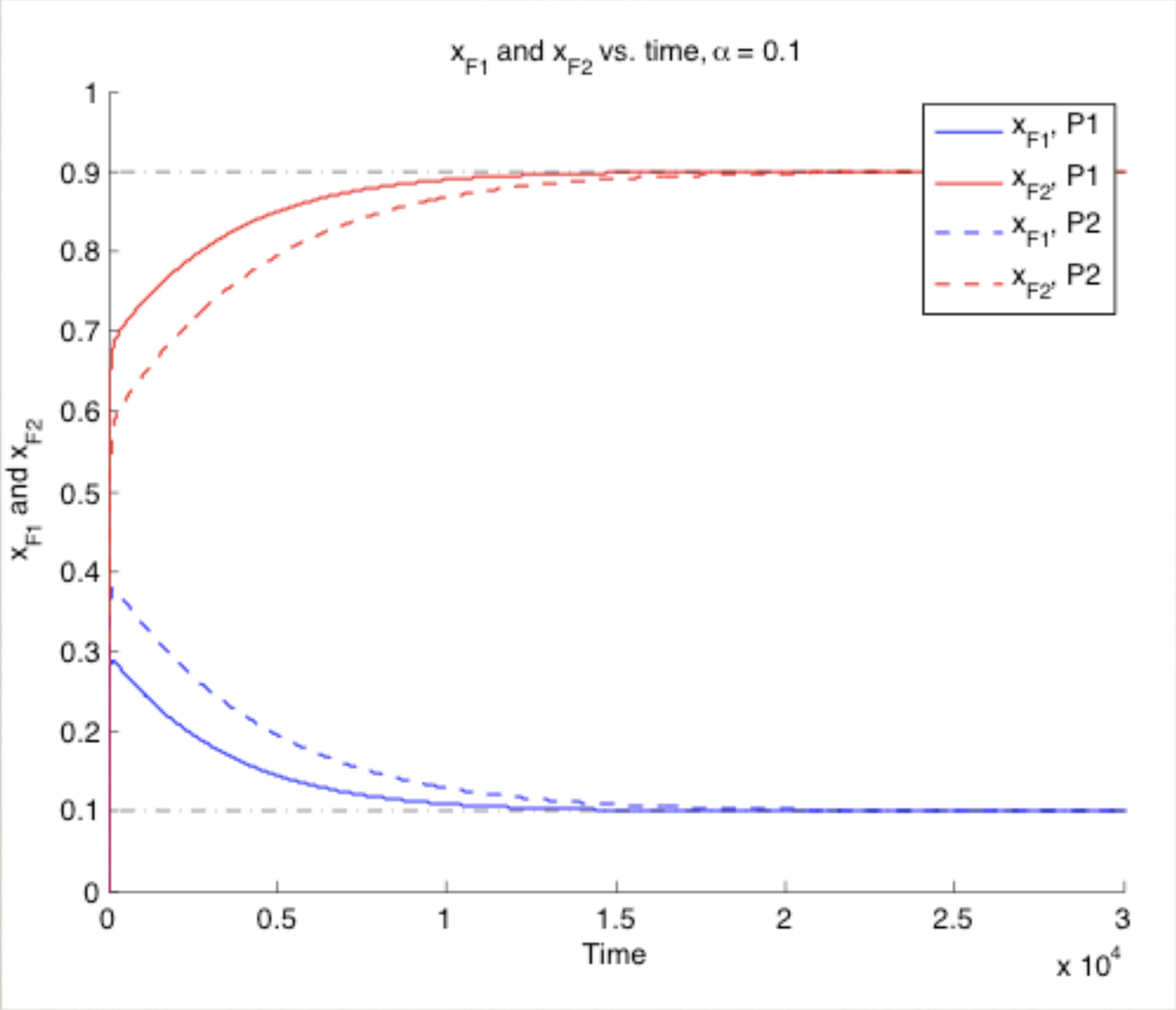
Reaction j	**1**	**2**	**3**	**4**	**5**	**6**
Optimized $\mathbf{p_j^+}$	0.36	0.666	1.0	*continuous*	0.4705	*continuous*
Optimized $\mathbf{p_j^-}$	0.006855	0.005027	0.00377	*continuous*	0.00443	*continuous*



6. CRN Control

Behavior

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



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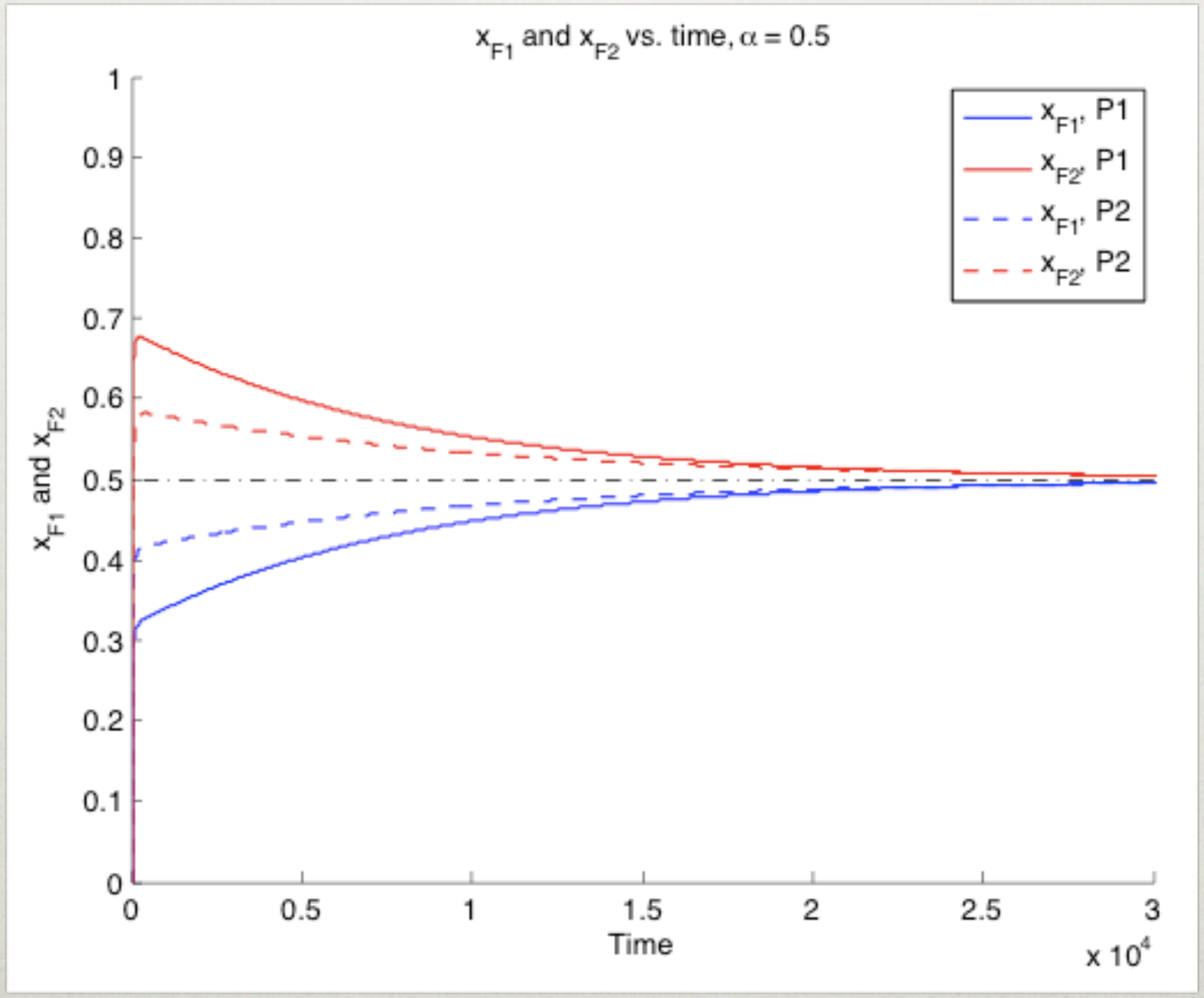

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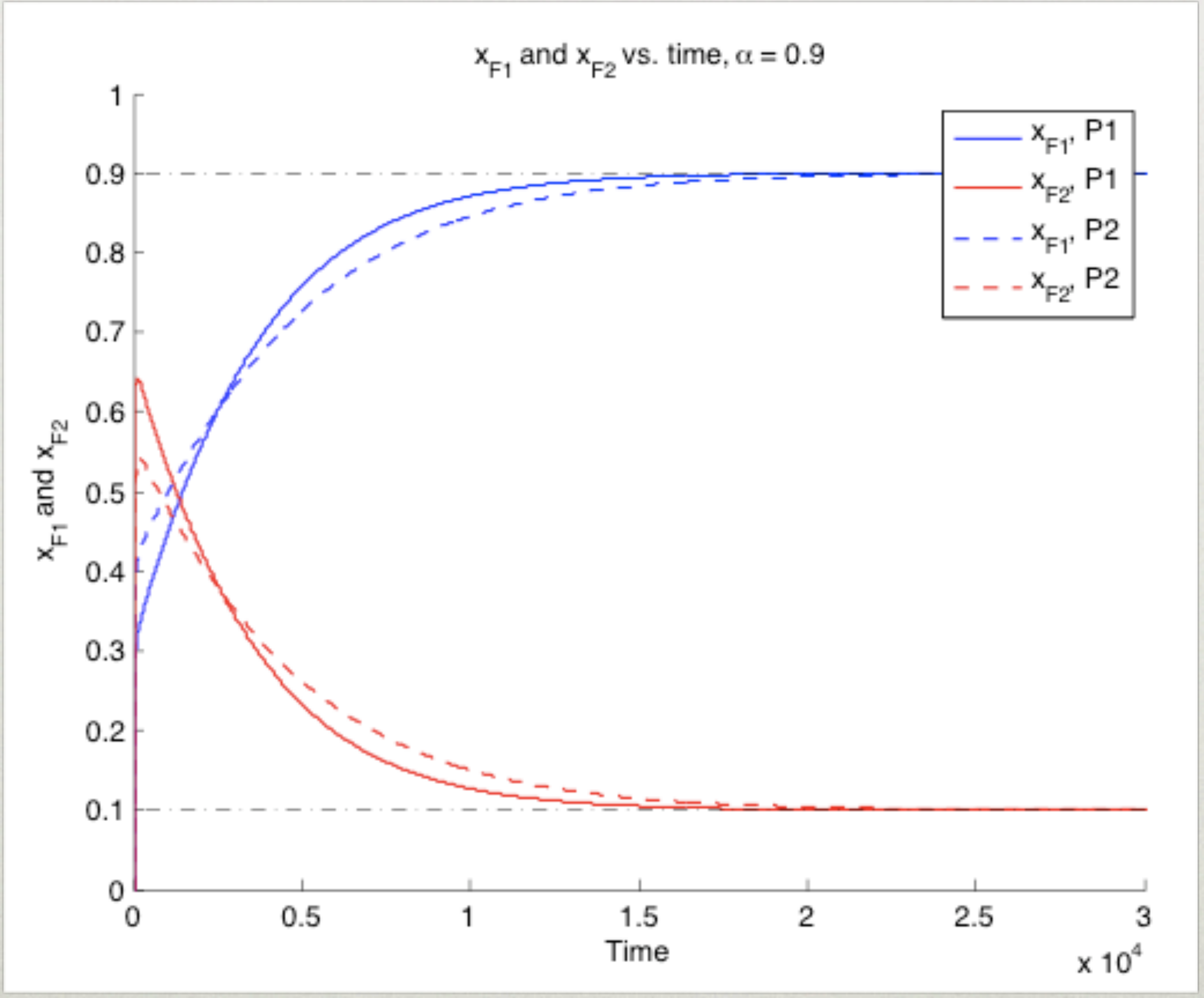

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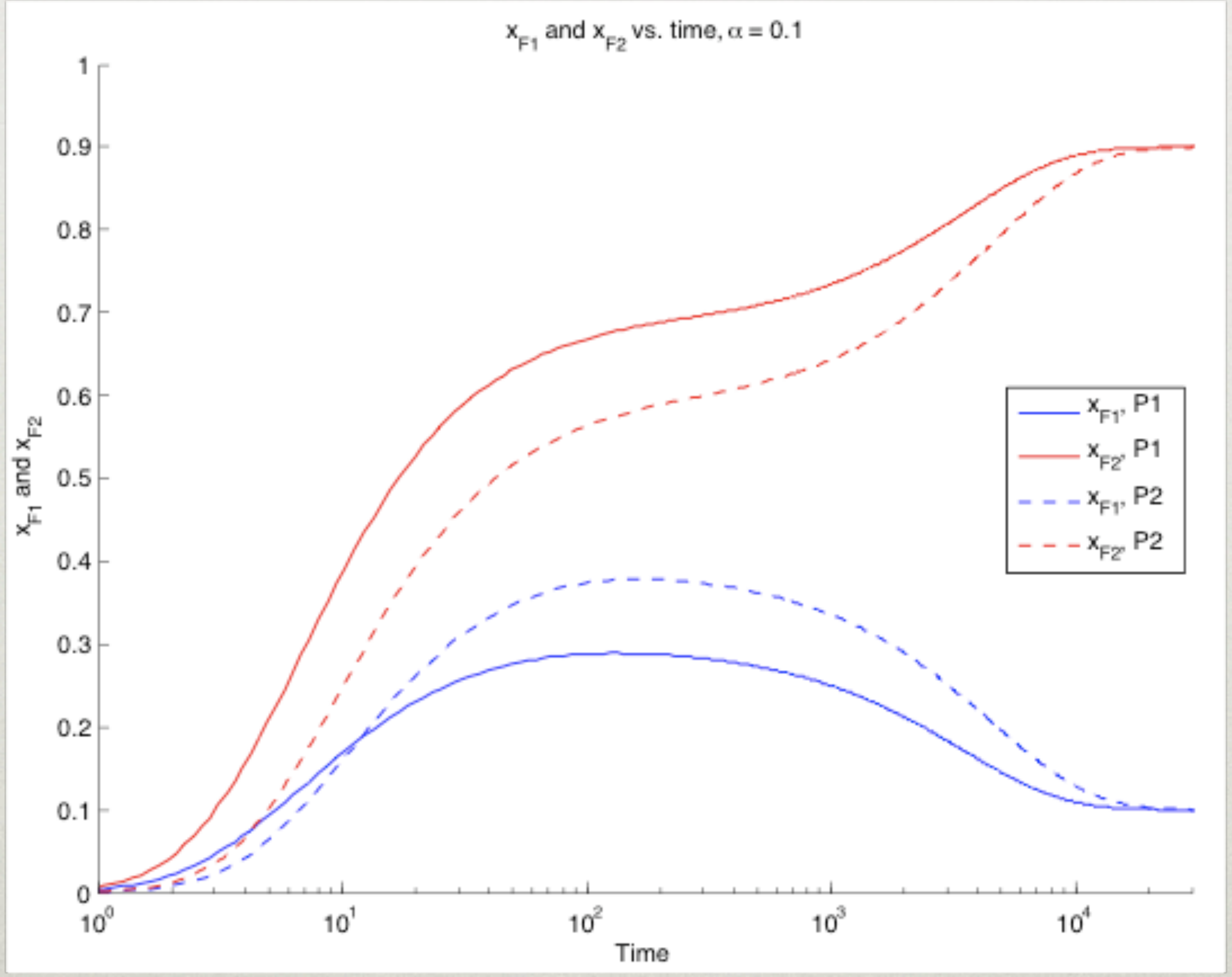
Behavior

- Ratios of final assemblies over time.
- **Log** time scale. Two regimes.



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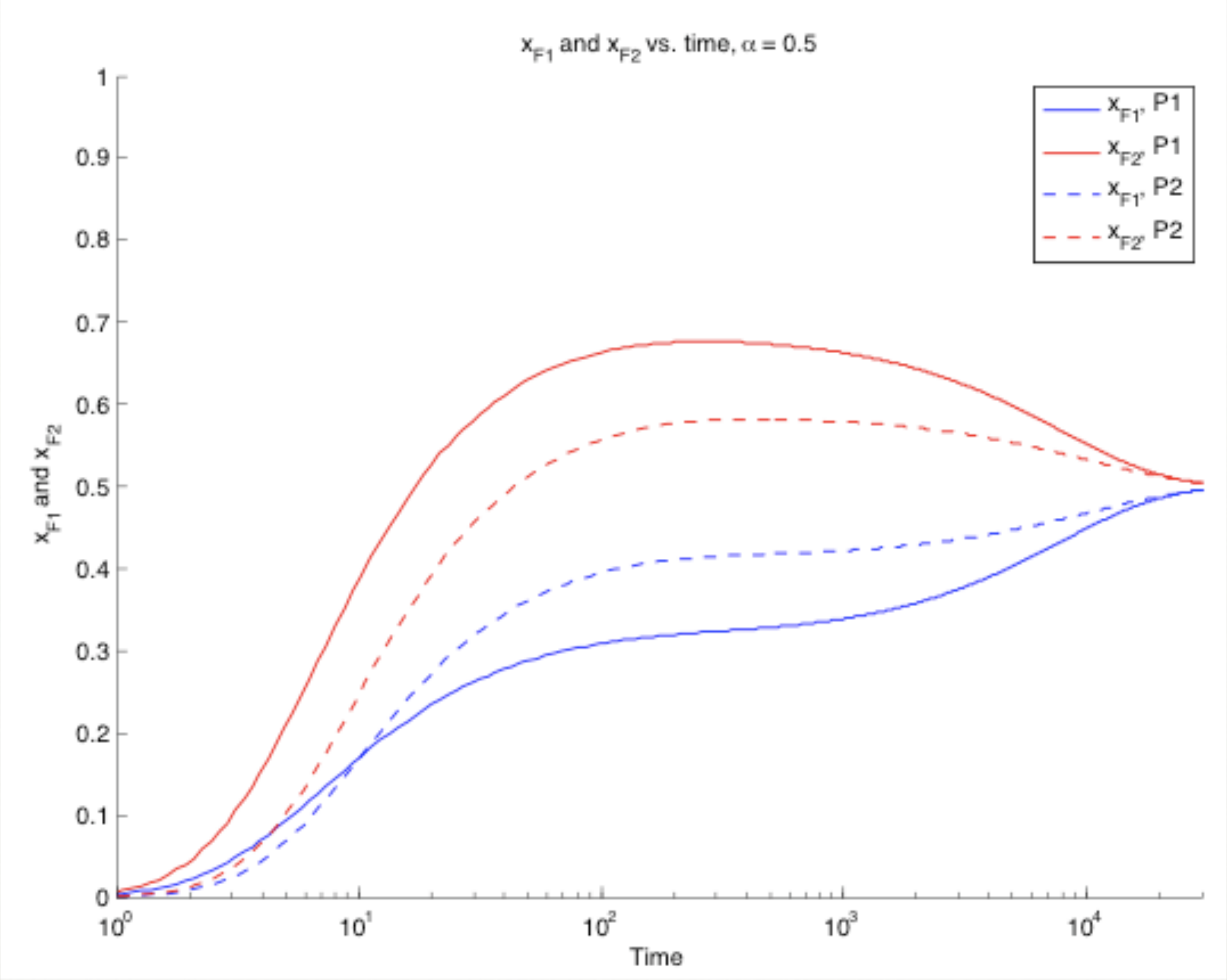

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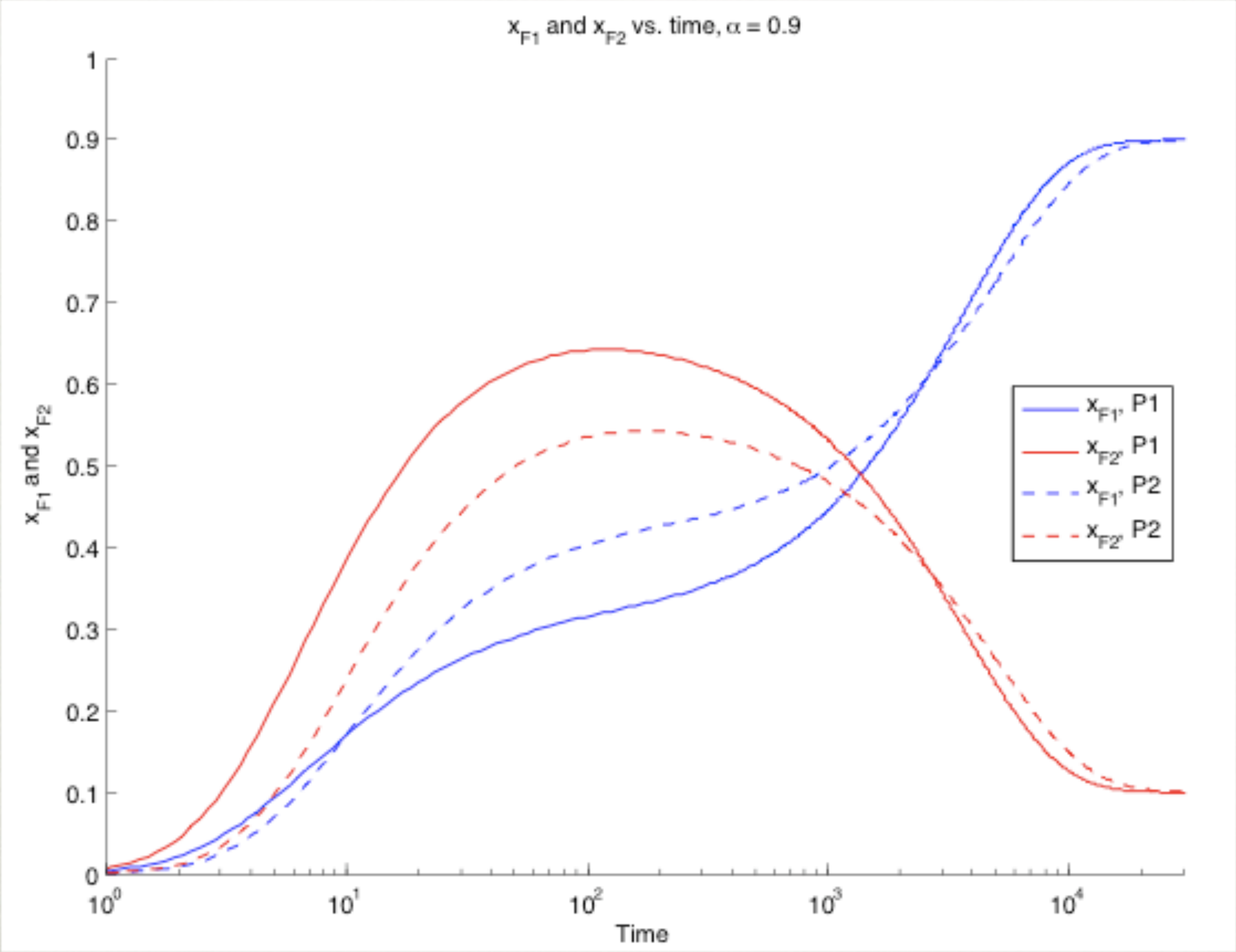
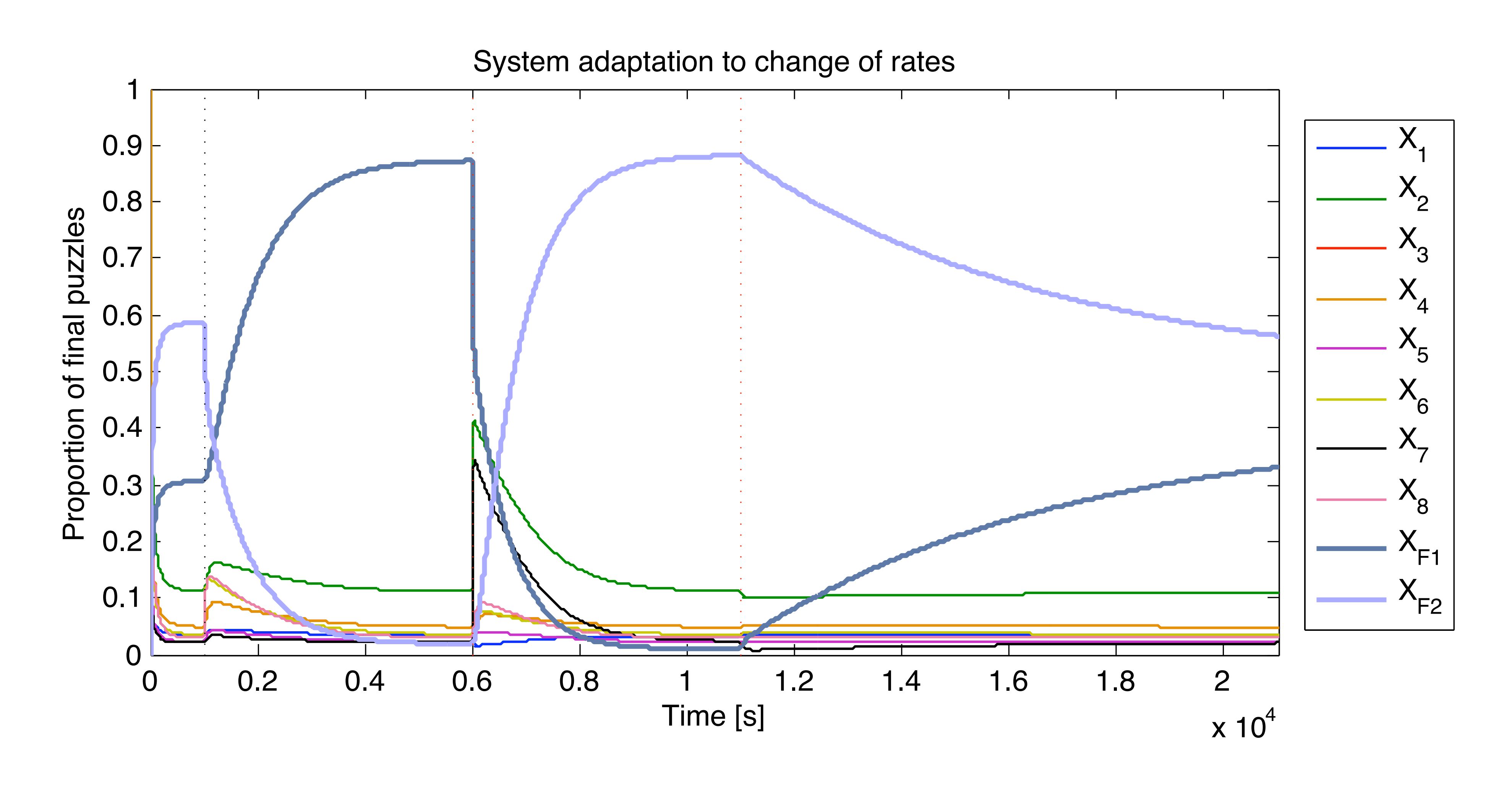


6. CRN Control

Possibilities

- Change of goal over time



- "Green manufactory"

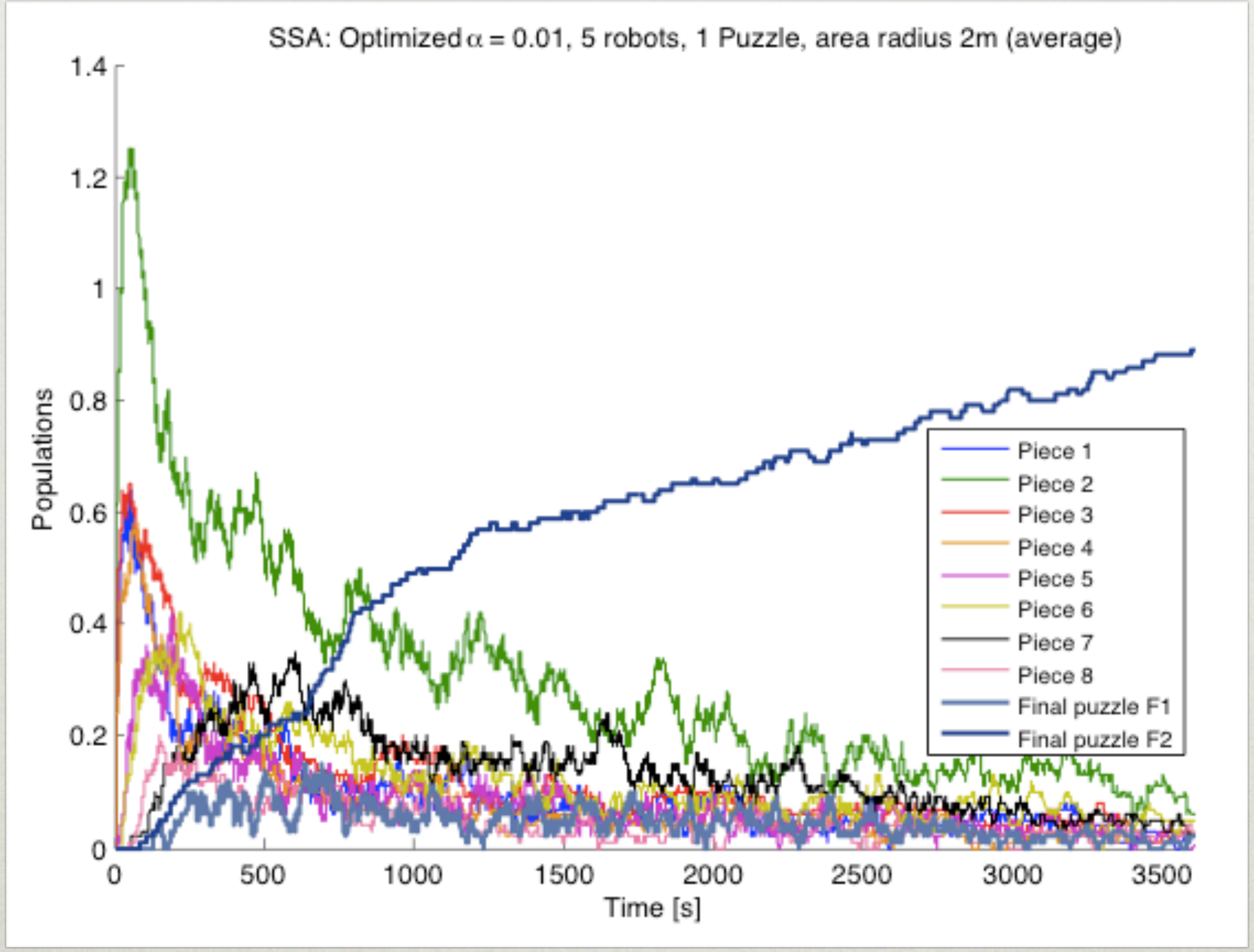
7. Mapping back to Platform

- 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?

7. Mapping back to Platform

Stochastic simulations

- According to stochastic simulations, yes.



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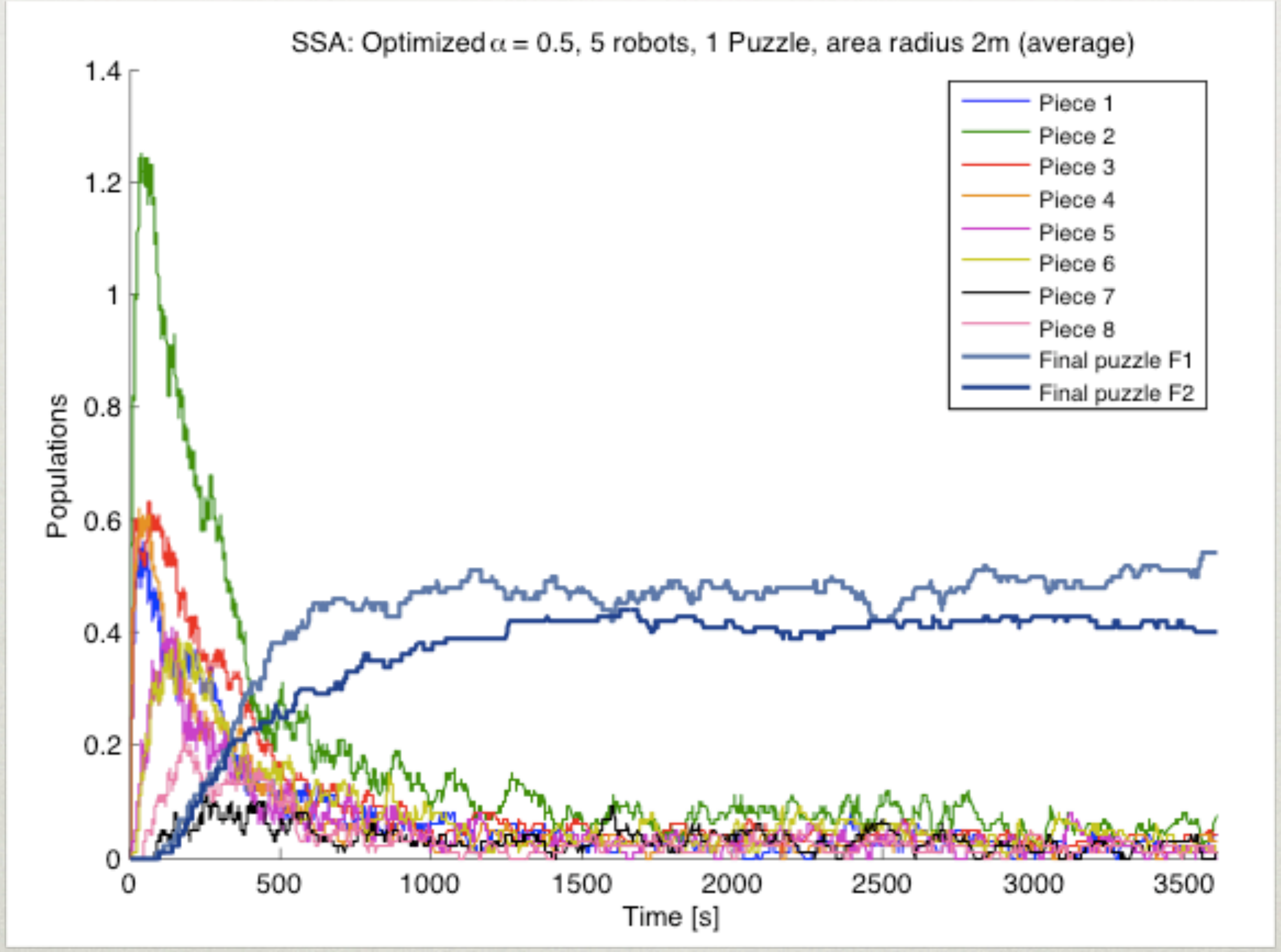

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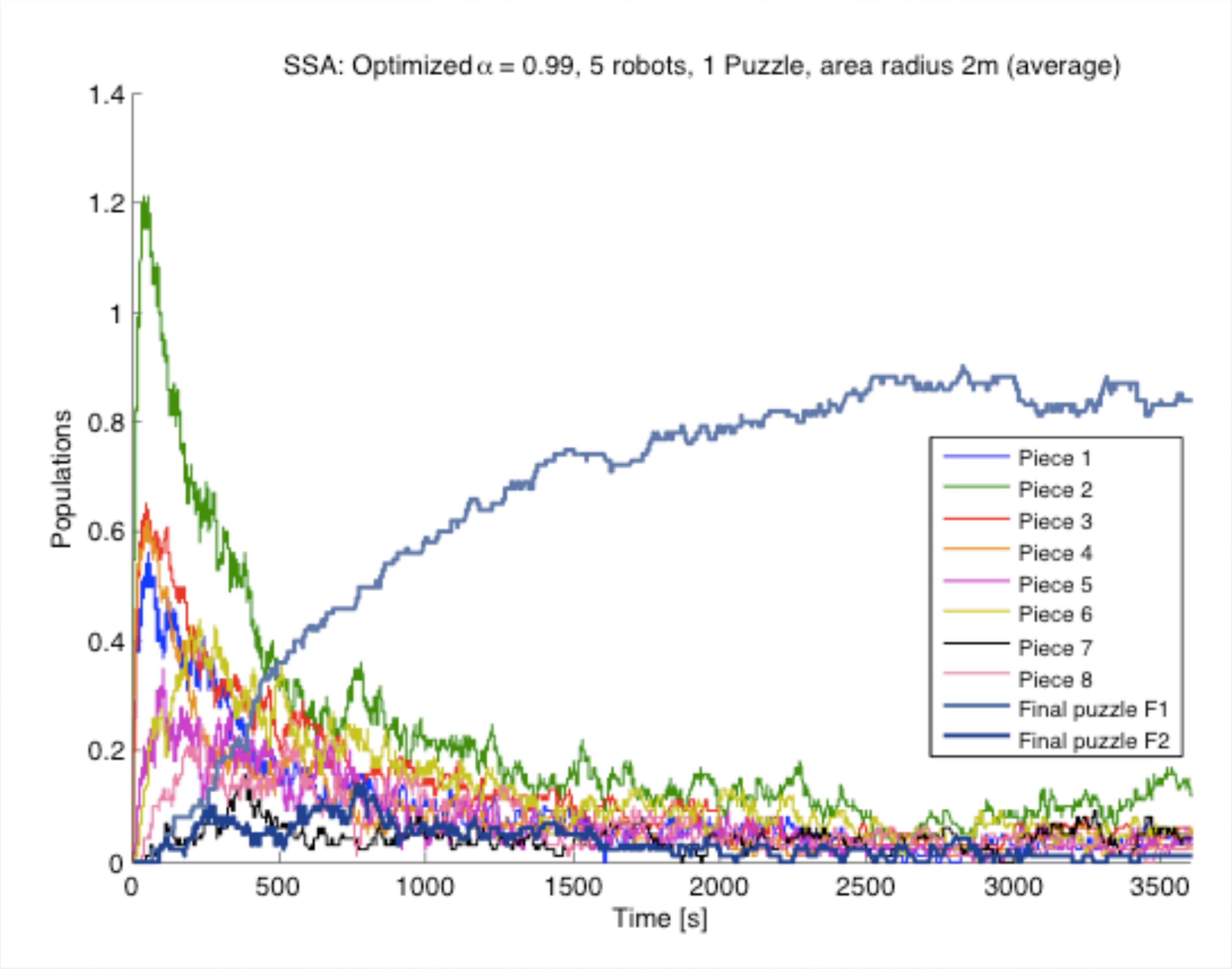
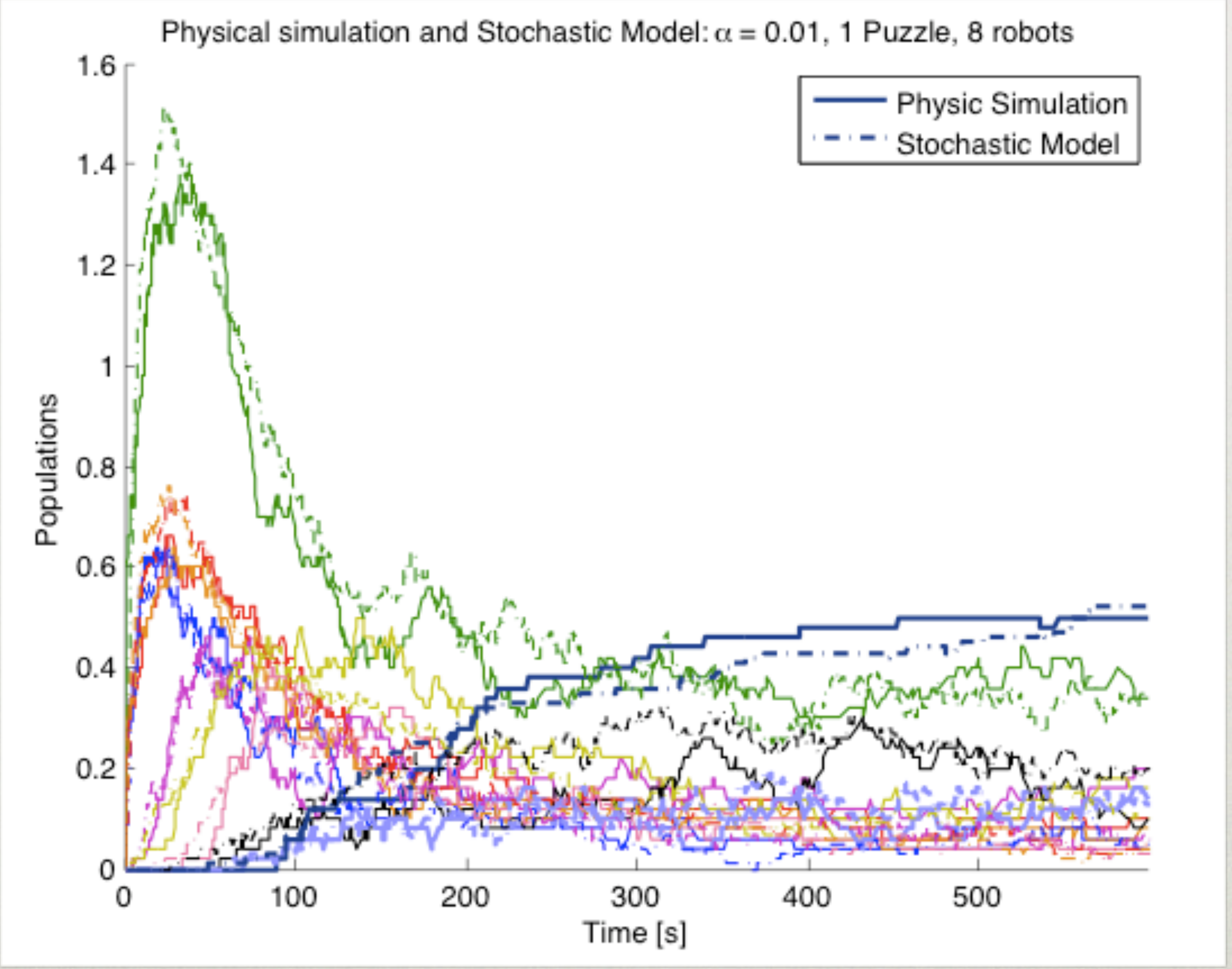


7. Mapping back to Platform

Realistic simulations

- In Webots, more or less...



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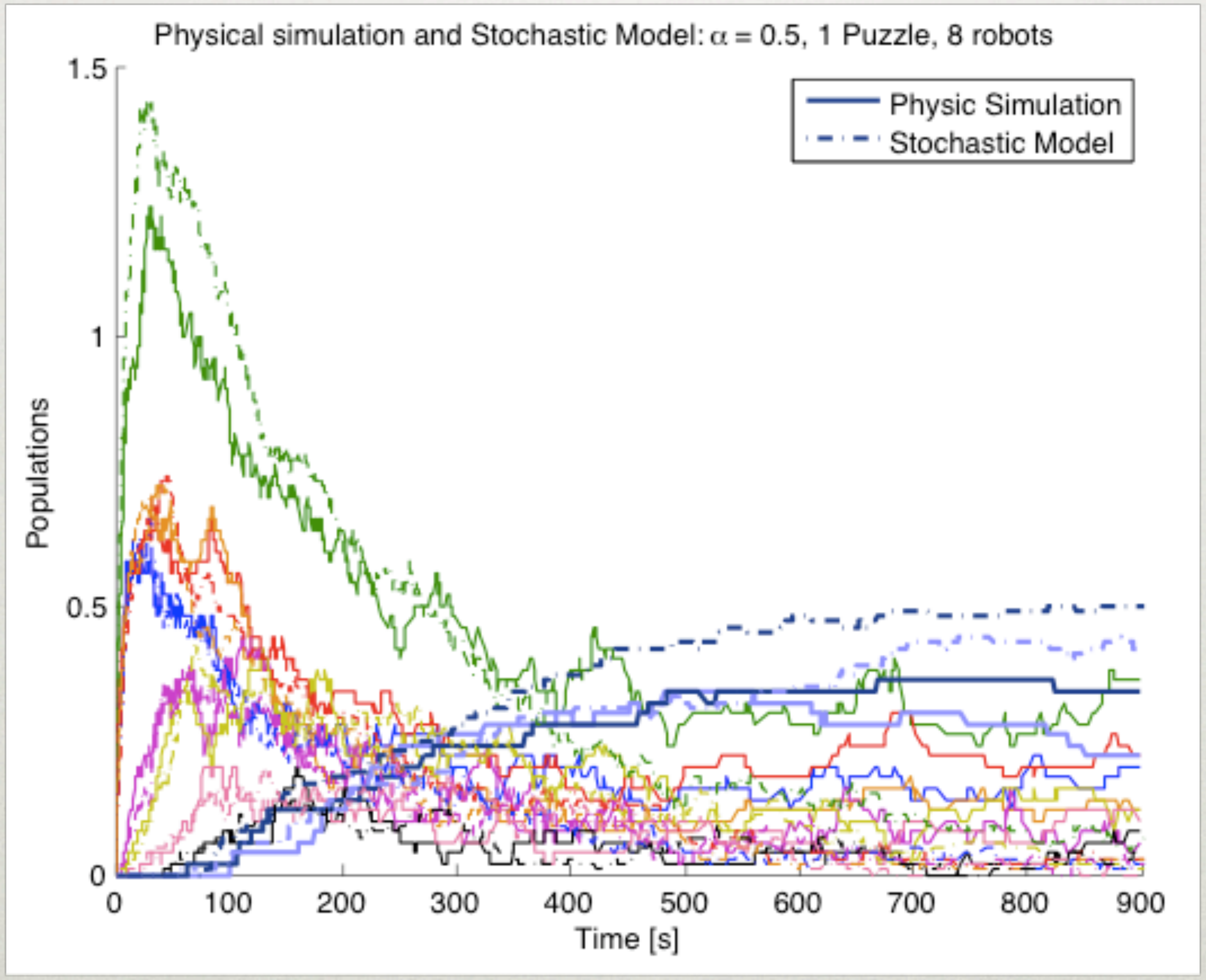

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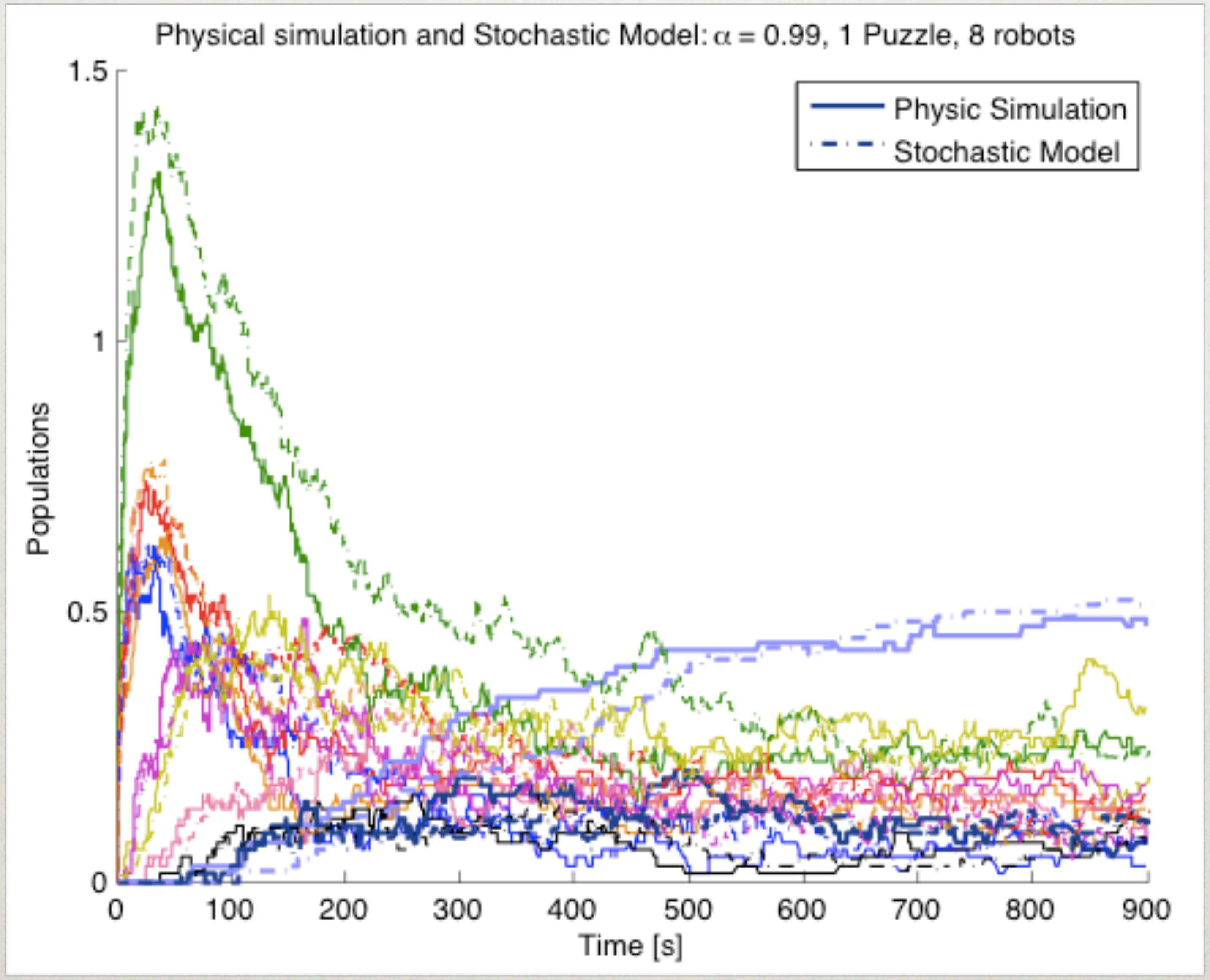


7. Mapping back to Platform

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, maybe due to low number of pieces.

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

- Compare this to a more classical deterministic approach.
- 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:
  - 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.

$$\tau_j = \left(\sum_{i=1}^{12} (-s_{ij}) \frac{dv_j}{dx_i} \right)^{-1}$$

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

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

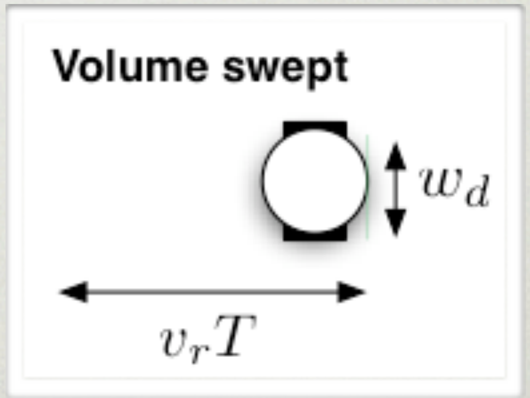
Models

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.

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

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



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.

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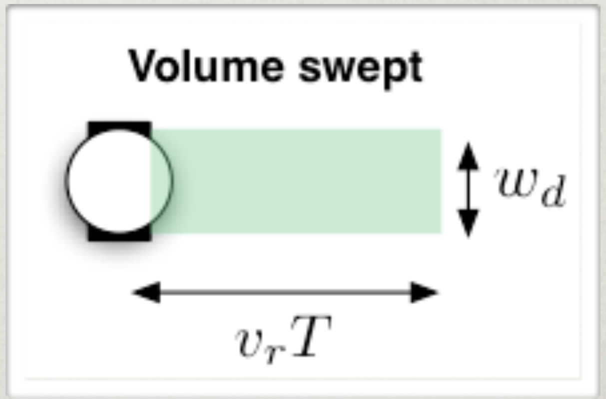
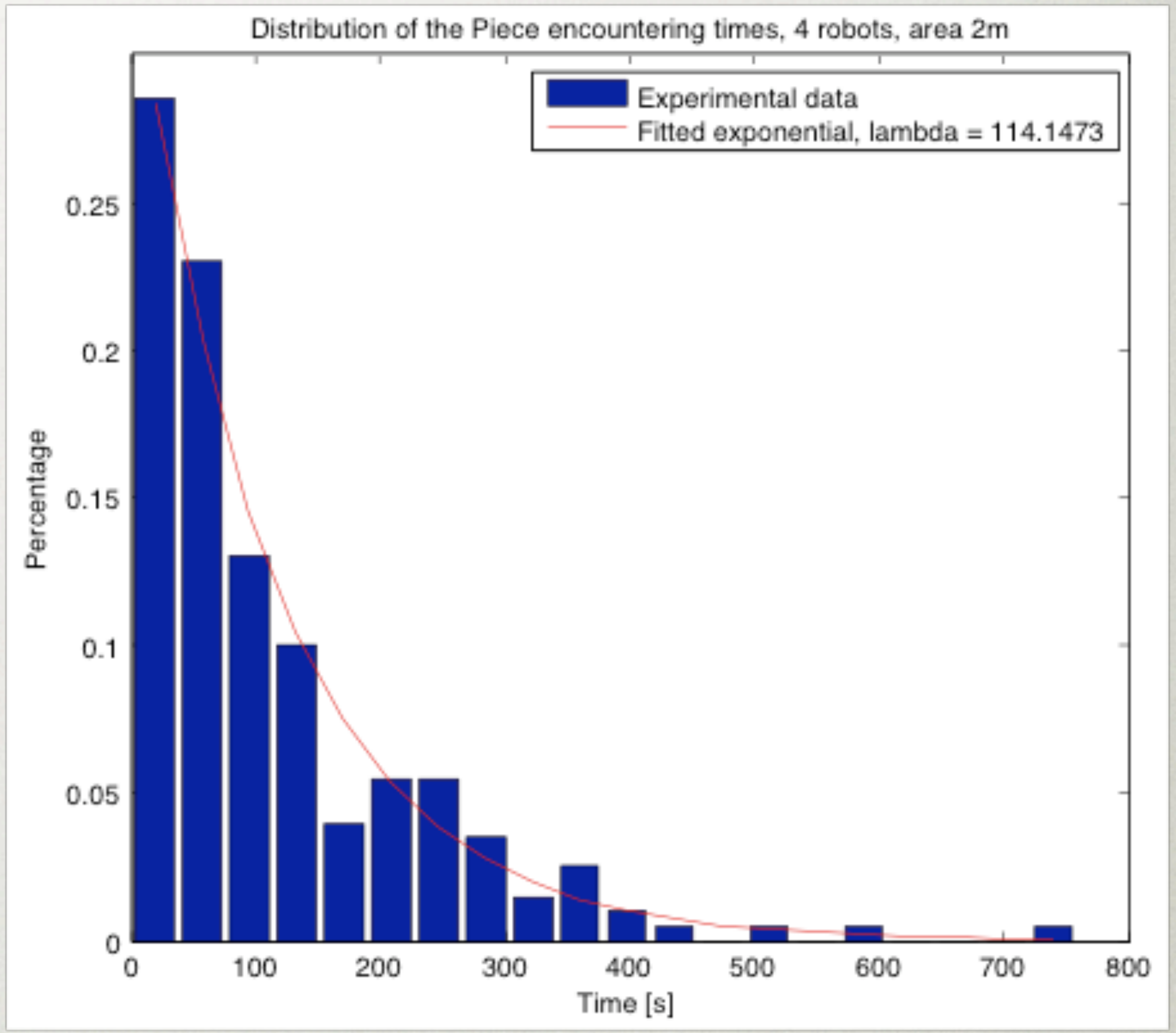


Models

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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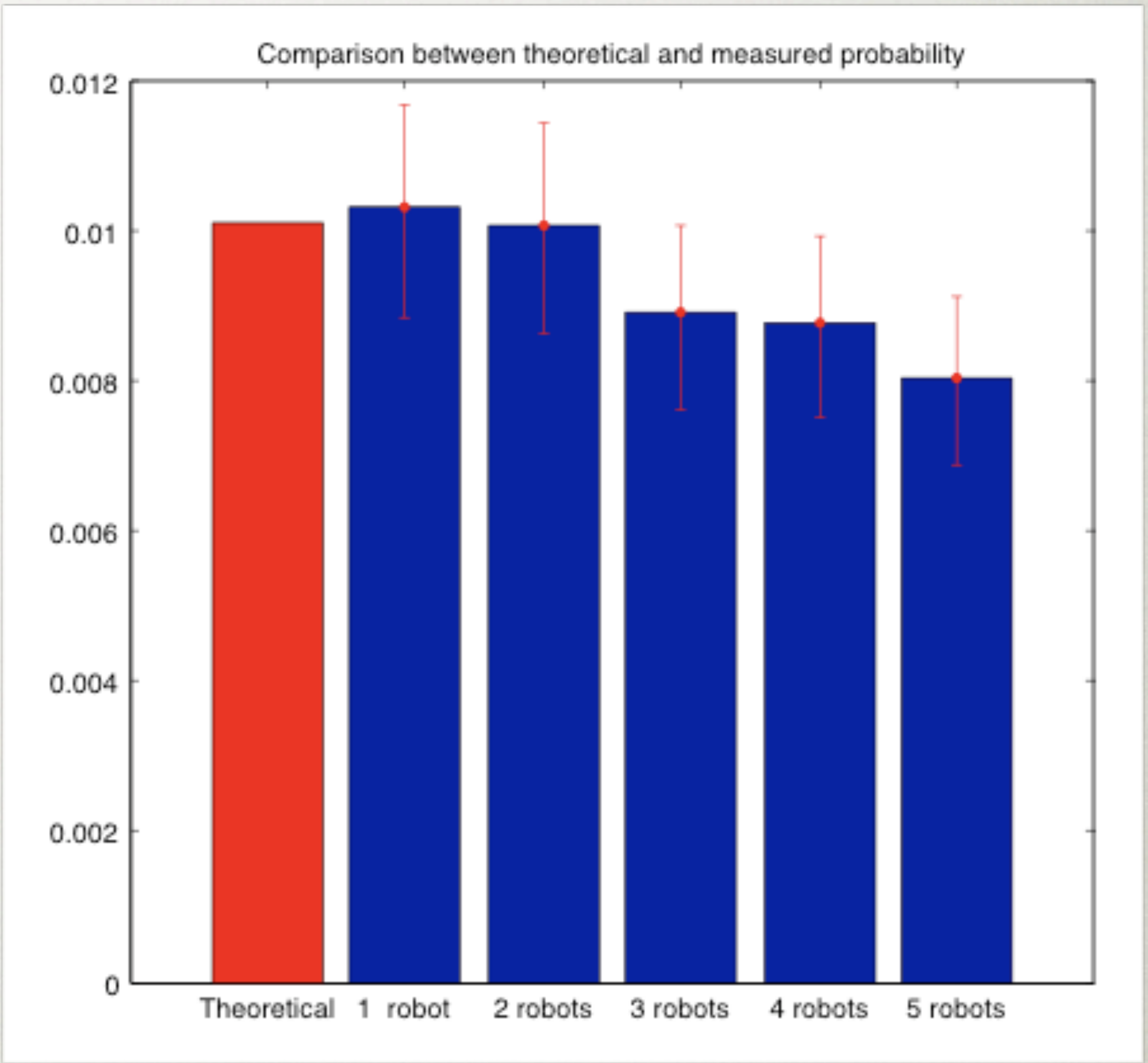

Models

Description

- Chemical Reactions Networks.
- Used for chemical and biological processes.
- Well adapted because of flexibility and versatility.

$$
\begin{aligned}
R + P_i^f &\xrightarrow{k_1} P_i^c \\
P_1^c + P_2^c &\xrightarrow{k_2} P_5^c \\
P_3^c + P_4^c &\underset{k_3'}{\overset{k_3}{\rightleftharpoons}} P_6^c
\end{aligned}
\quad \sim \quad
\begin{aligned}
\dot{R} &= -k_1 R P_i^f \\
\dot{P}_i^f &= -k_1 R P_i^f \\
\dot{P}_1^c &= k_1 R P_1^f - k_2 P_1^c P_2^c \\
\dot{P}_2^c &= k_1 R P_2^f - k_2 P_1^c P_2^c \\
\dot{P}_5^c &= k_2 P_1^c P_2^c \\
\dot{P}_3^c &= k_1 R P_3^f - k_3 P_3^c P_4^c + k_3' P_6^c \\
\dot{P}_4^c &= k_1 R P_4^f - k_3 P_3^c P_4^c + k_3' P_6^c \\
\dot{P}_6^c &= k_3 P_3^c P_4^c - k_3' P_6^c
\end{aligned}
$$

Models

Parameters estimation

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