Analyzing robustness of biological reaction systems

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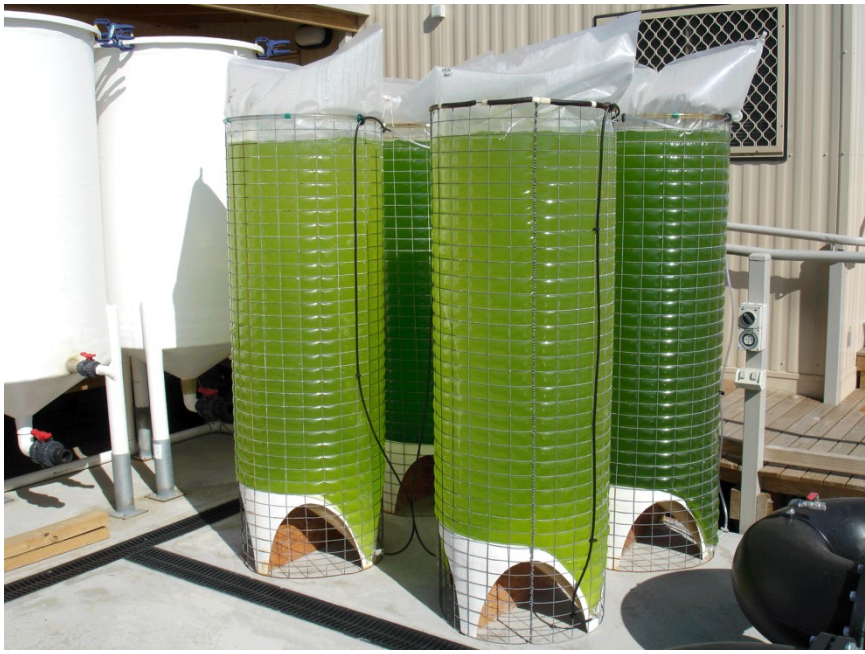
sybila
systems biology laboratory

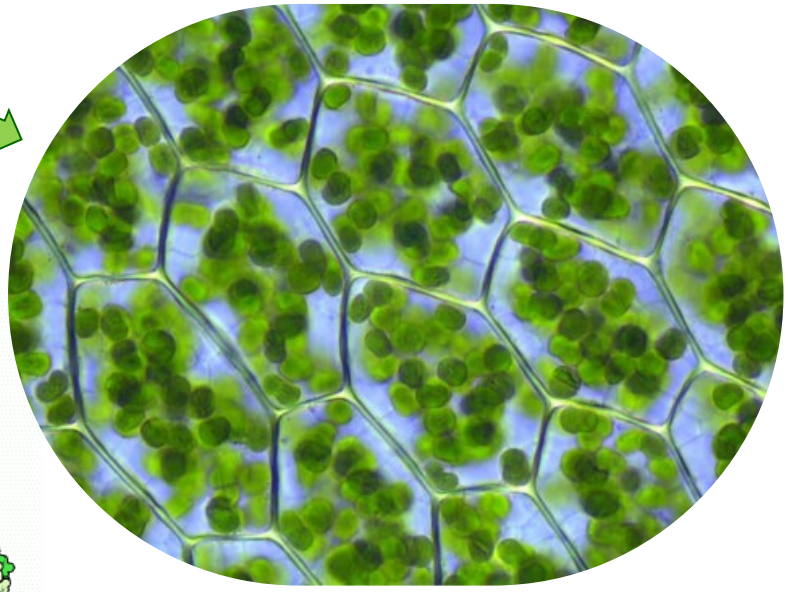
Contents

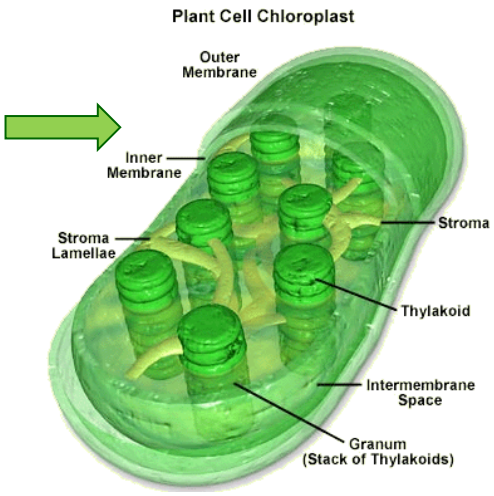
- What is Robustness?
- Dynamic reaction systems
- Behavior and properties
- Computing robustness

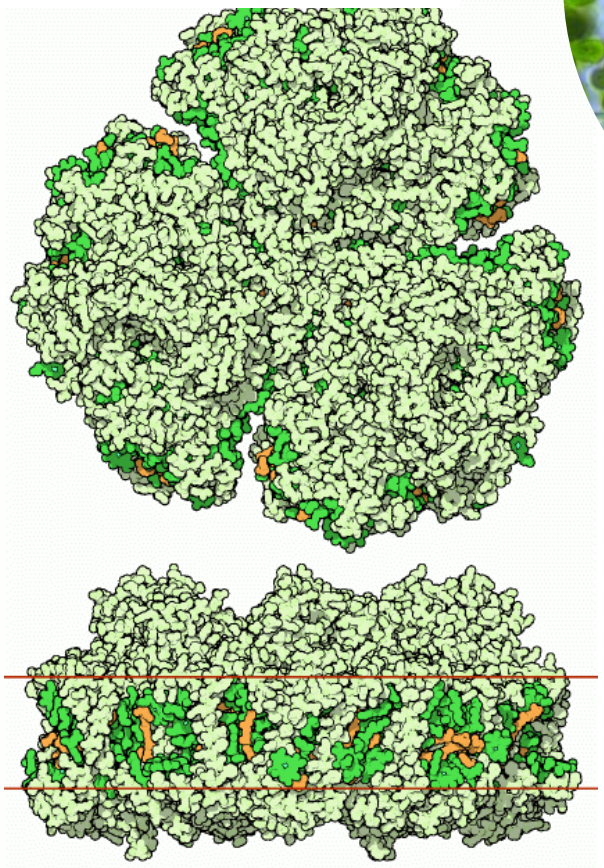
Motivation / Bioreactors



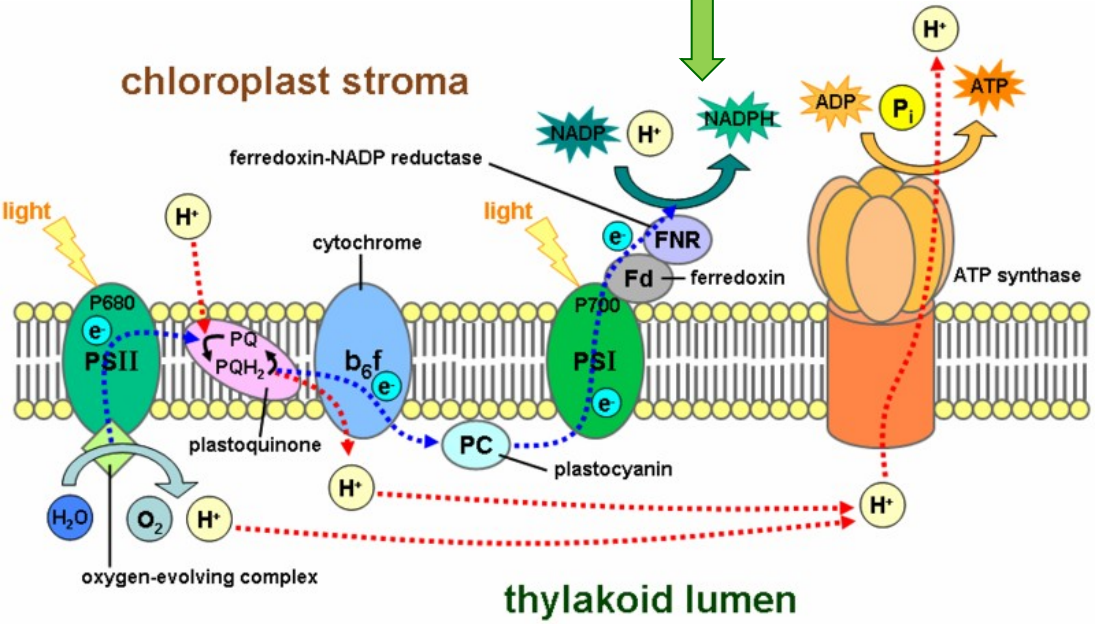
Motivation / Photosynthesis



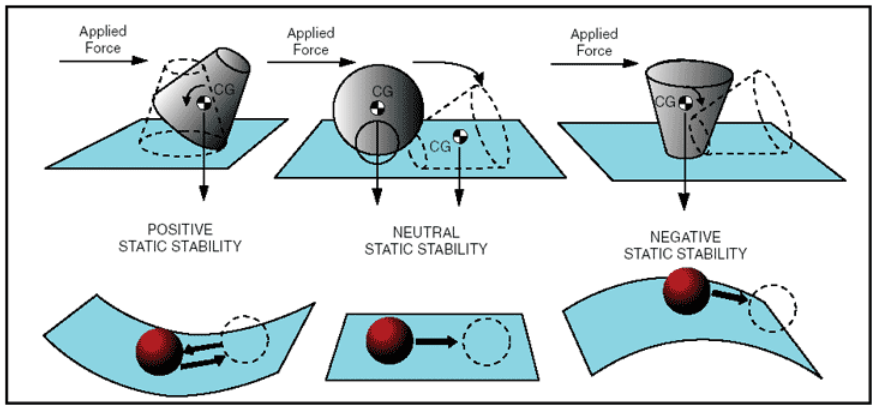


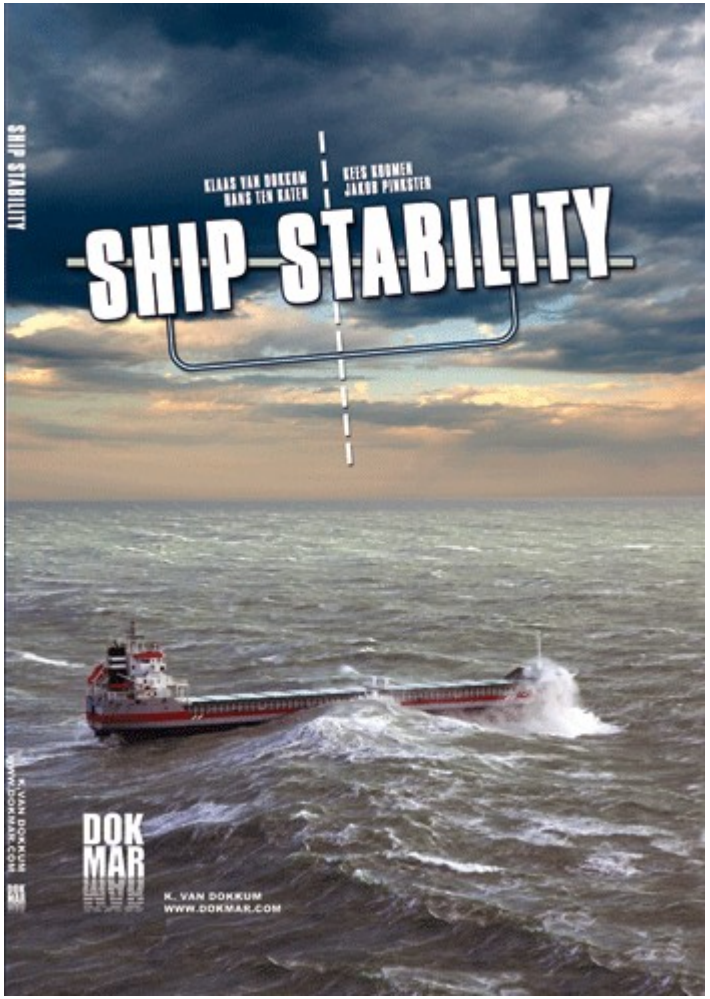


photosystem I - PSI

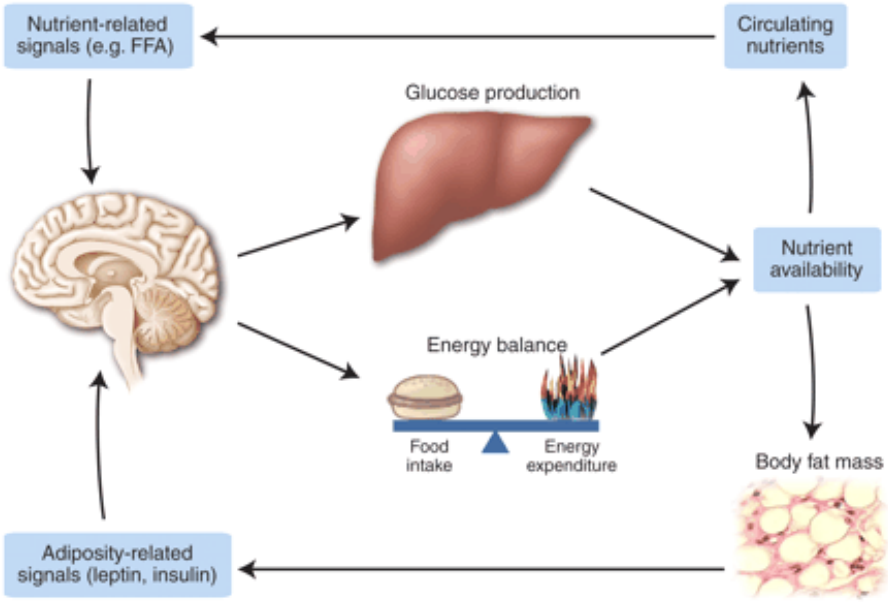


Is stability robustness?





Is homeostasis robustness?



What is robustness

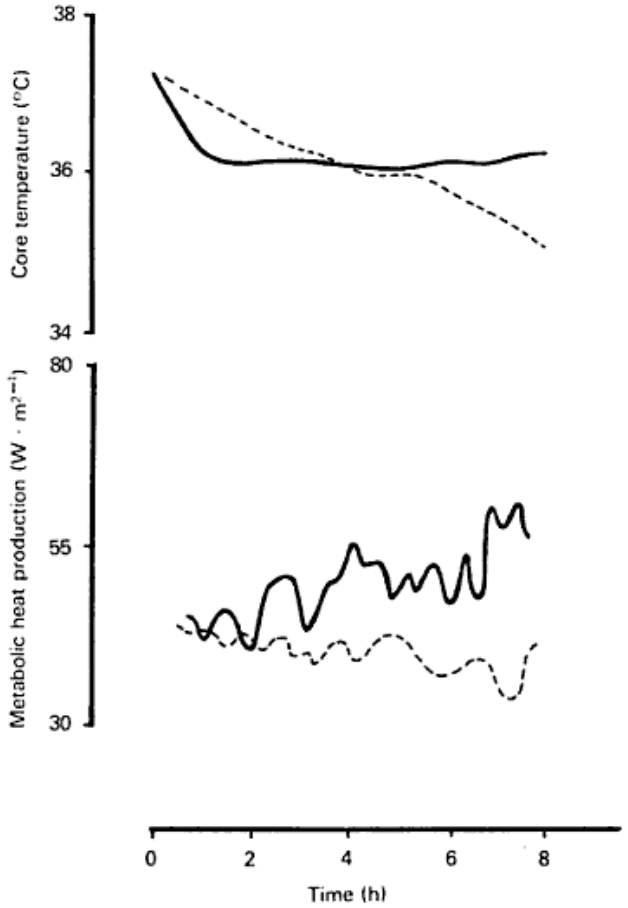
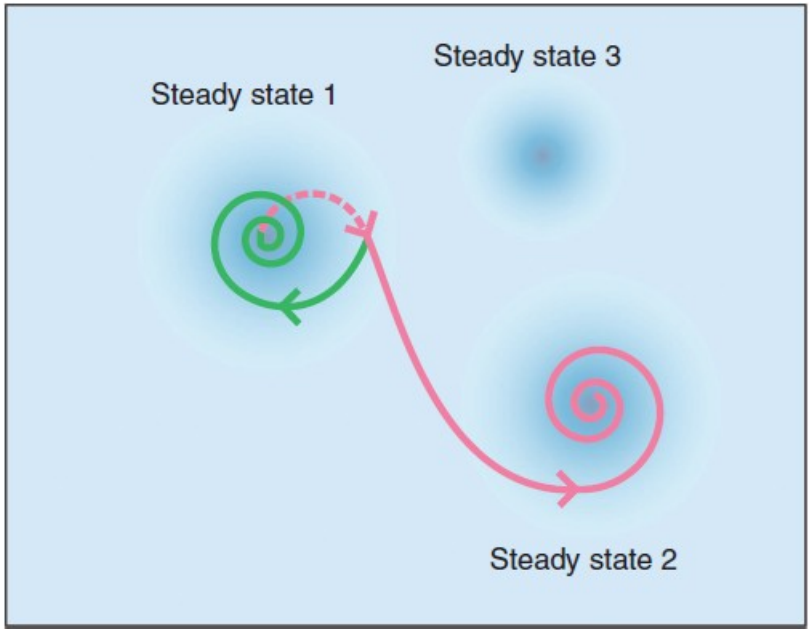


Fig. 5.4 Reduced body temperature in man. Response of a group of male Aborigines (– – –) and Europeans (——) to a night of moderate cold exposure. From Richards, S.A. (1973). *Temperature Regulation*, Wykeham Publications, Taylor & Francis: London.

What is robustness

Is
multistability or instability
robustness?



What is robustness?

Robustness is a property that allows a system to maintain its function against internal and external perturbations.

Kitano, 2004a

What is robustness…

Robustness is a property that allows a system to maintain its function against internal and external perturbations.

Kitano, 2004a

function ~ behavior ~ property

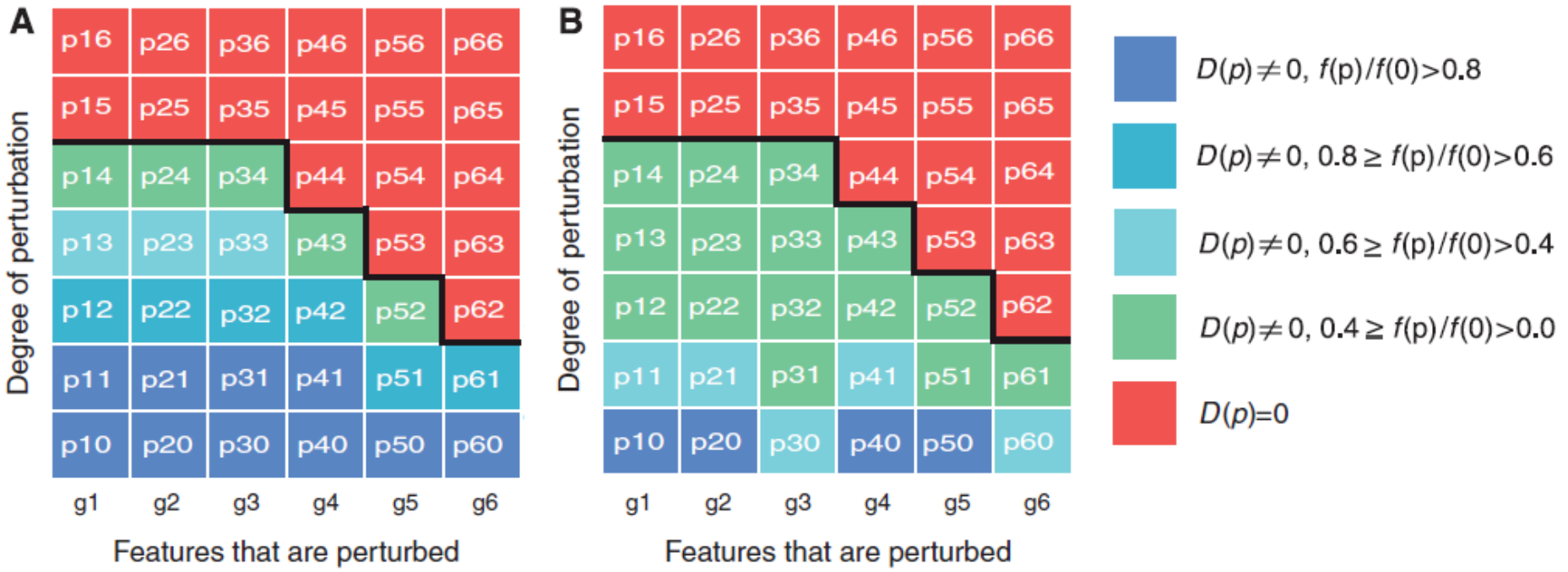
$$R^{S}_{a,P} = \int_{P} \psi(p) D^{S}_{a}(p) dp$$

Robustness is a property that allows a system to maintain its property against internal and external perturbations.

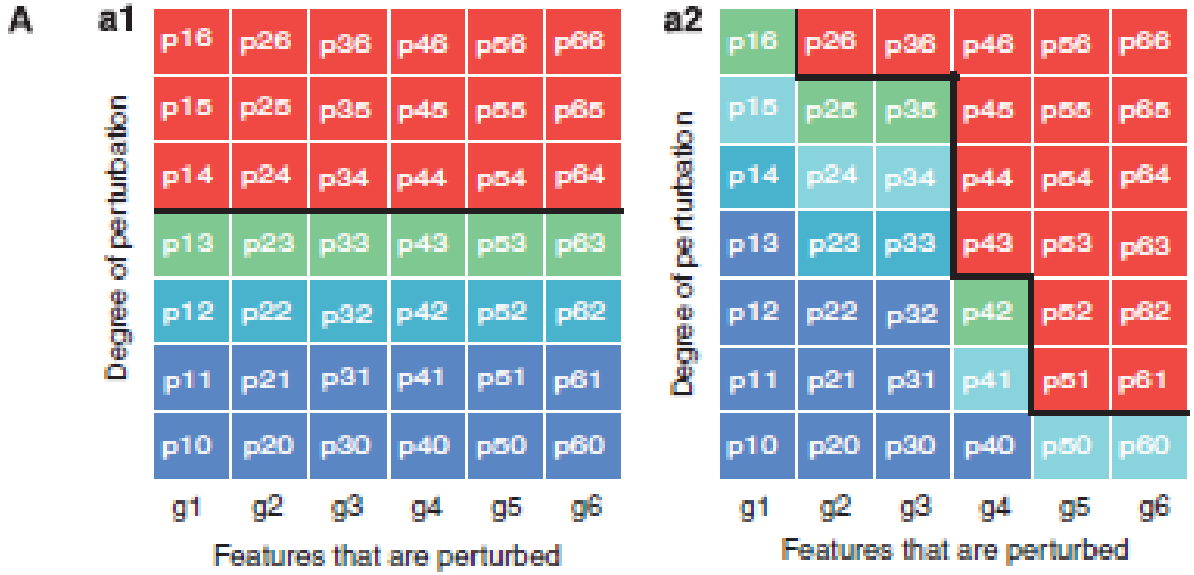
Kitano, 2004a

$$R^{S}_{a,P} = \int_{P} \psi(p) D^{S}_{a}(p) dp$$

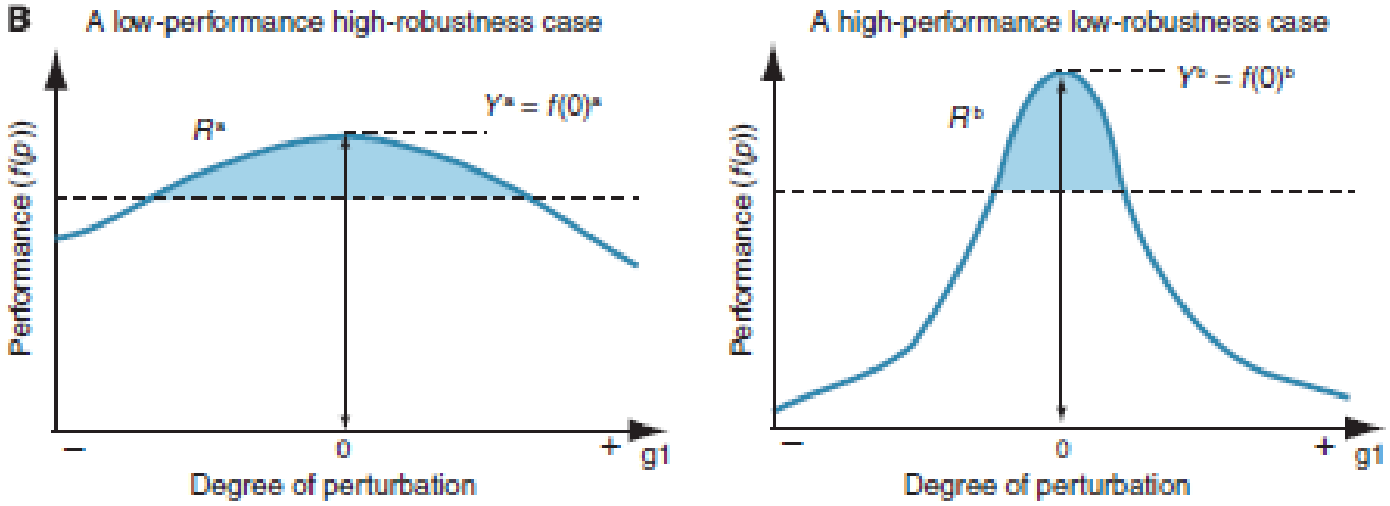
What is robustness



Robustness and tradeoffs



Robustness–fragility trade-off



What is a dynamic reaction system

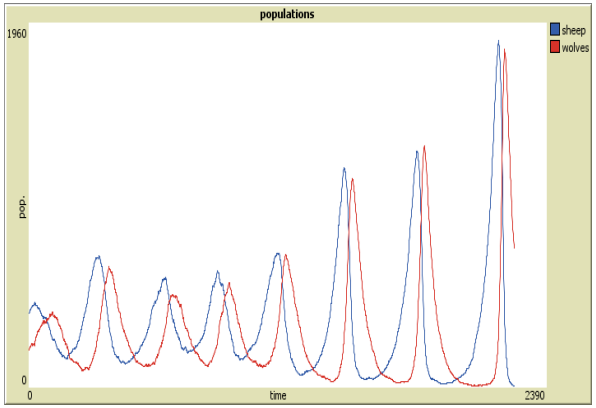
Demo

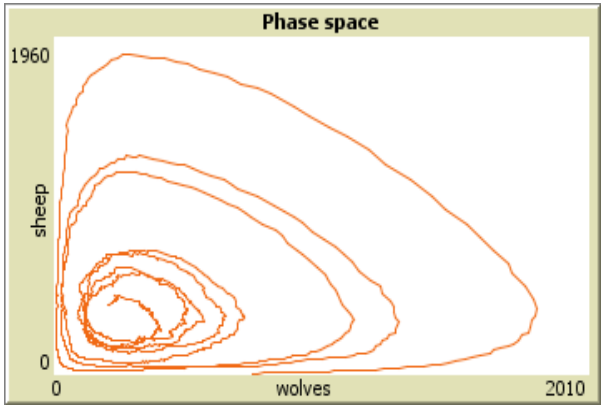
Dynamic reaction systems – Example

$$S \xrightarrow{k1} 2\,S$$

$$W + S \xrightarrow{k2} 2\,W$$

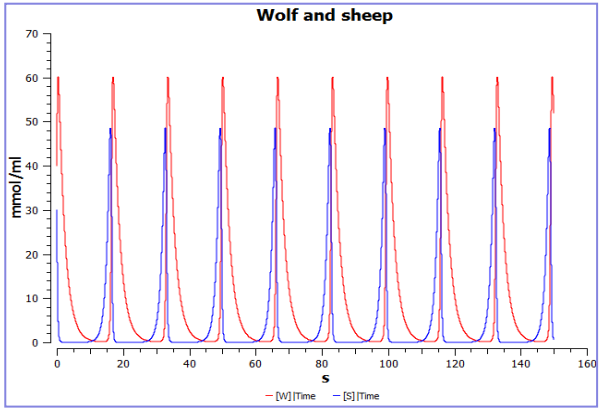
$$W \xrightarrow{k3}$$

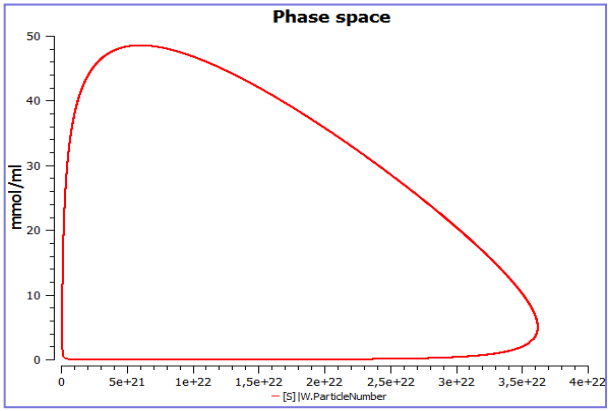




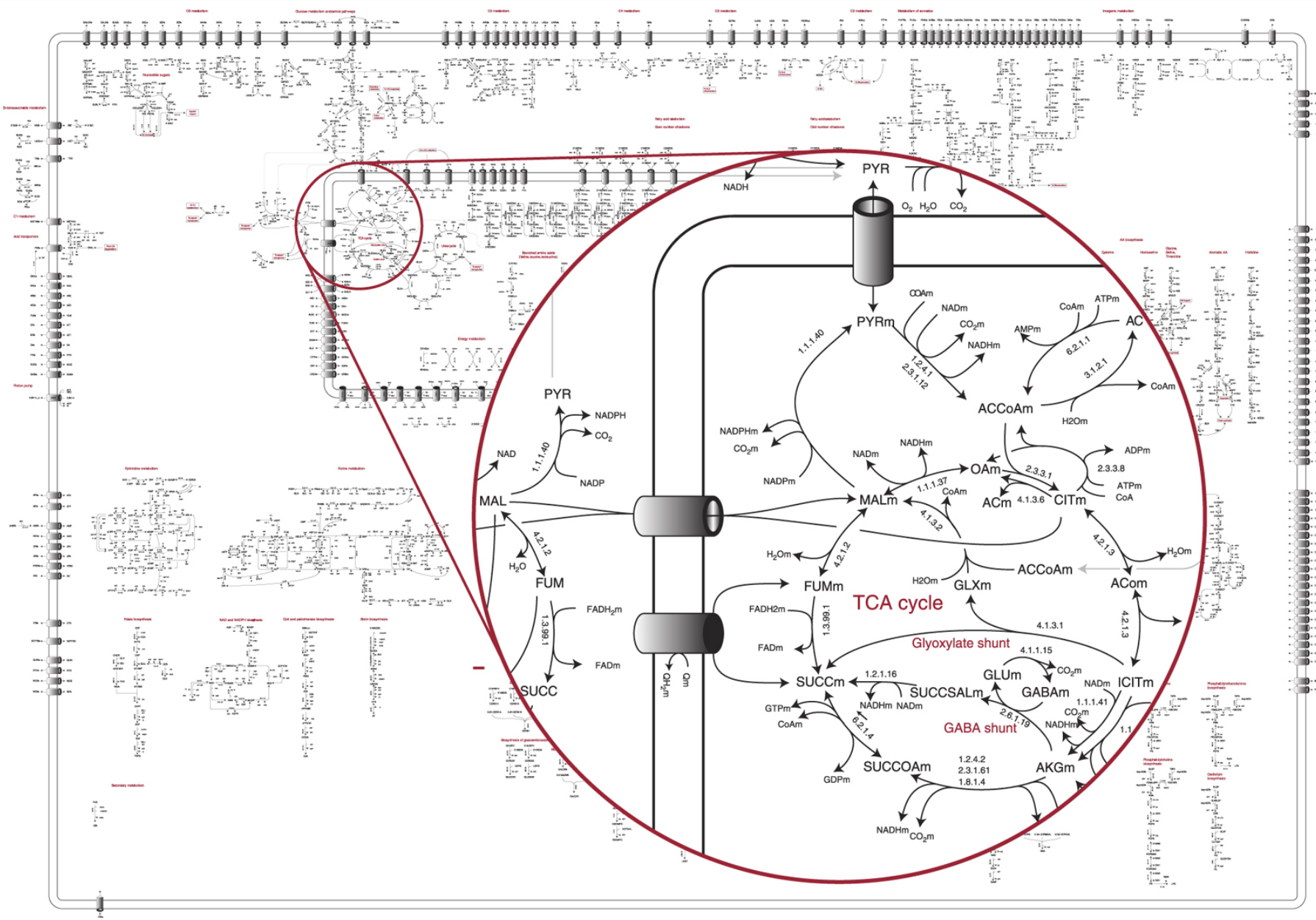
$$\frac{dS}{dt} = k_1 \cdot [S] - k_2 \cdot [W] \cdot [S]$$

$$\frac{dW}{dt} = k_2 \cdot [W] \cdot [S] - k_3 \cdot [W]$$





Dynamic reaction systems – Bigger example



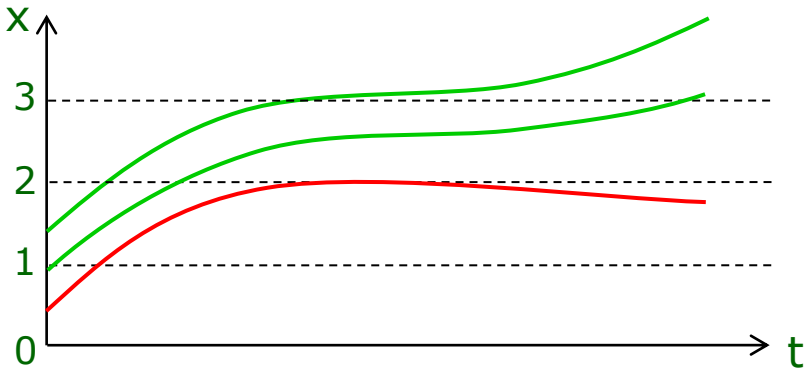
What is a behavior?

98.8% common DNA

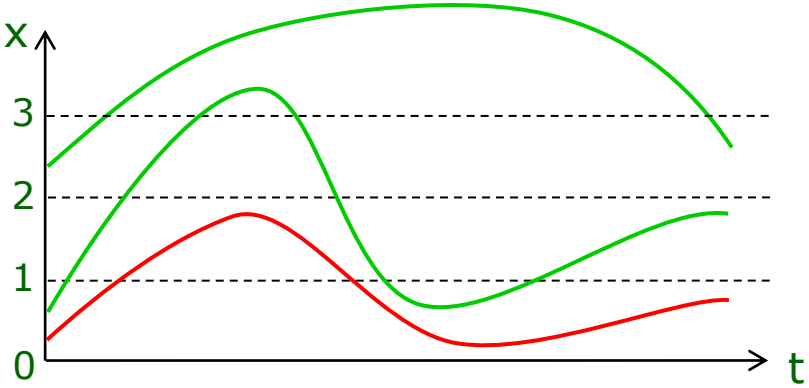
Any difference in behavior?

What is a behavior ~ property

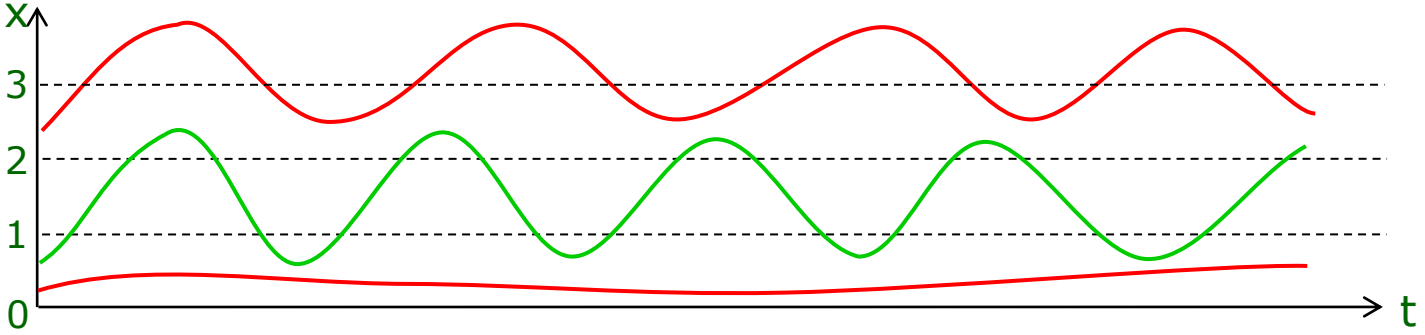
Reachability - F(x>3)



Response - G((x<1) ⇒ F(x>3))

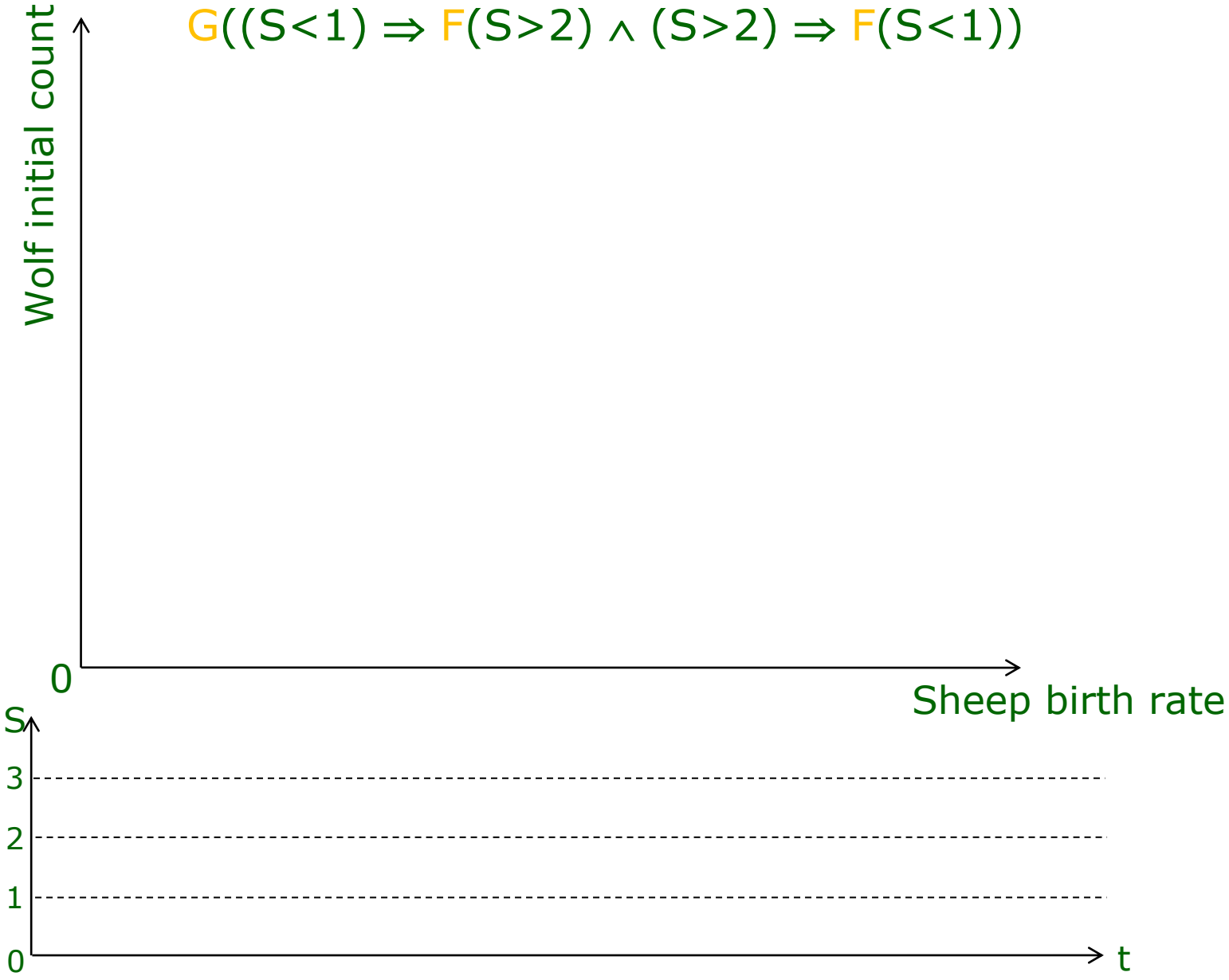


Oscillation - G((x<1) ⇒ F(x>2) ∧ (x>2) ⇒ F(x<1))



Computing robustness

$$G((S<1) \Rightarrow F(S>2) \wedge (S>2) \Rightarrow F(S<1))$$



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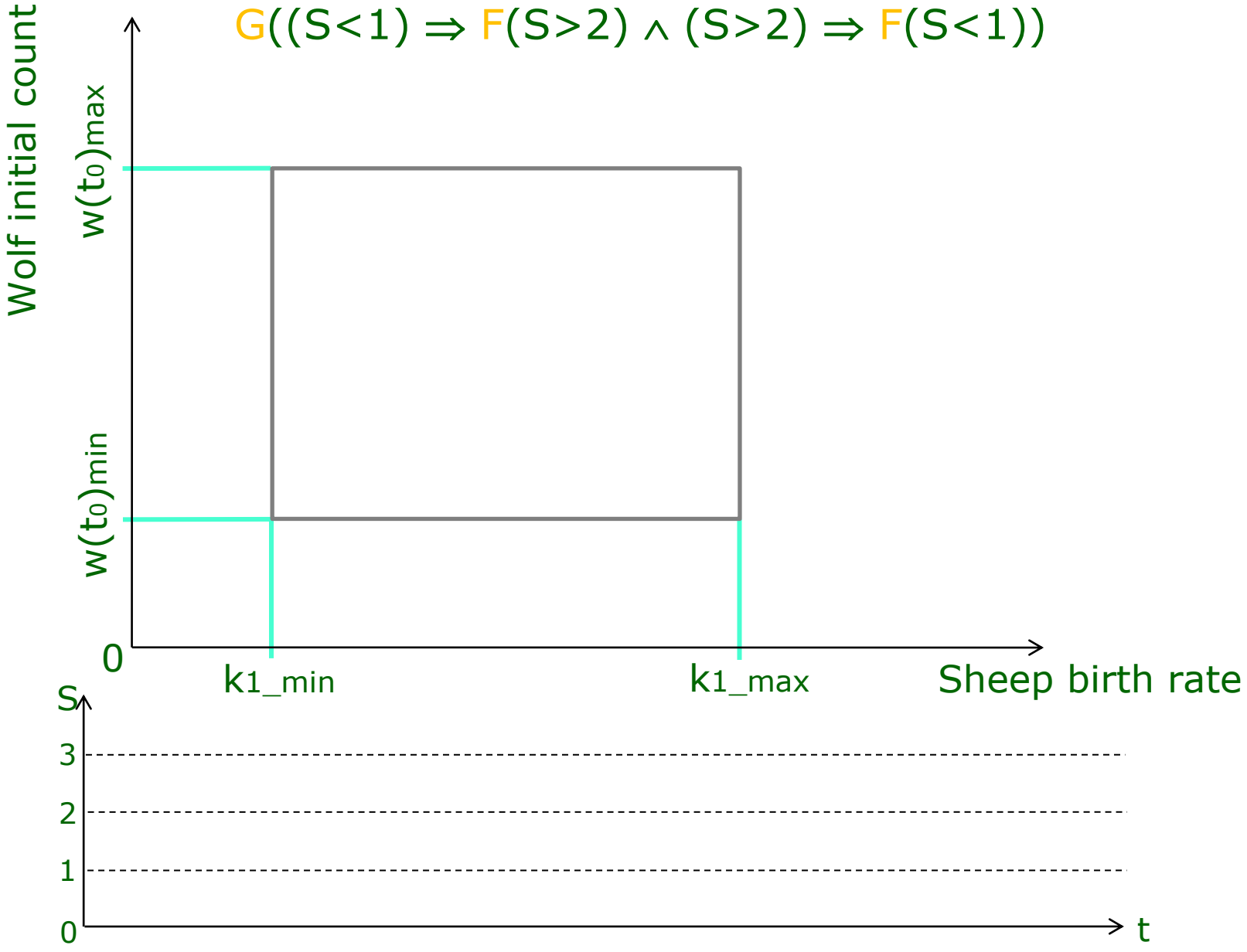

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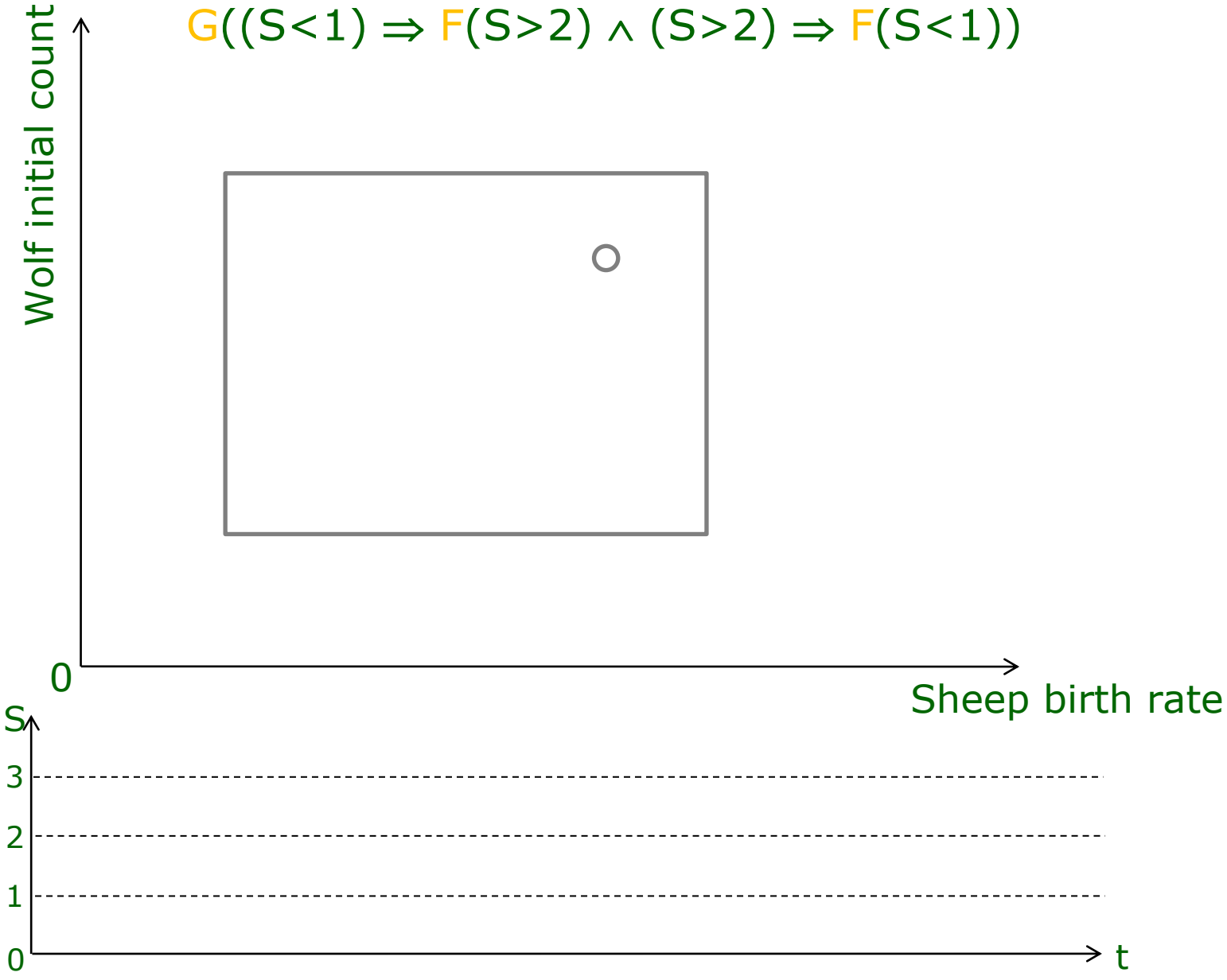

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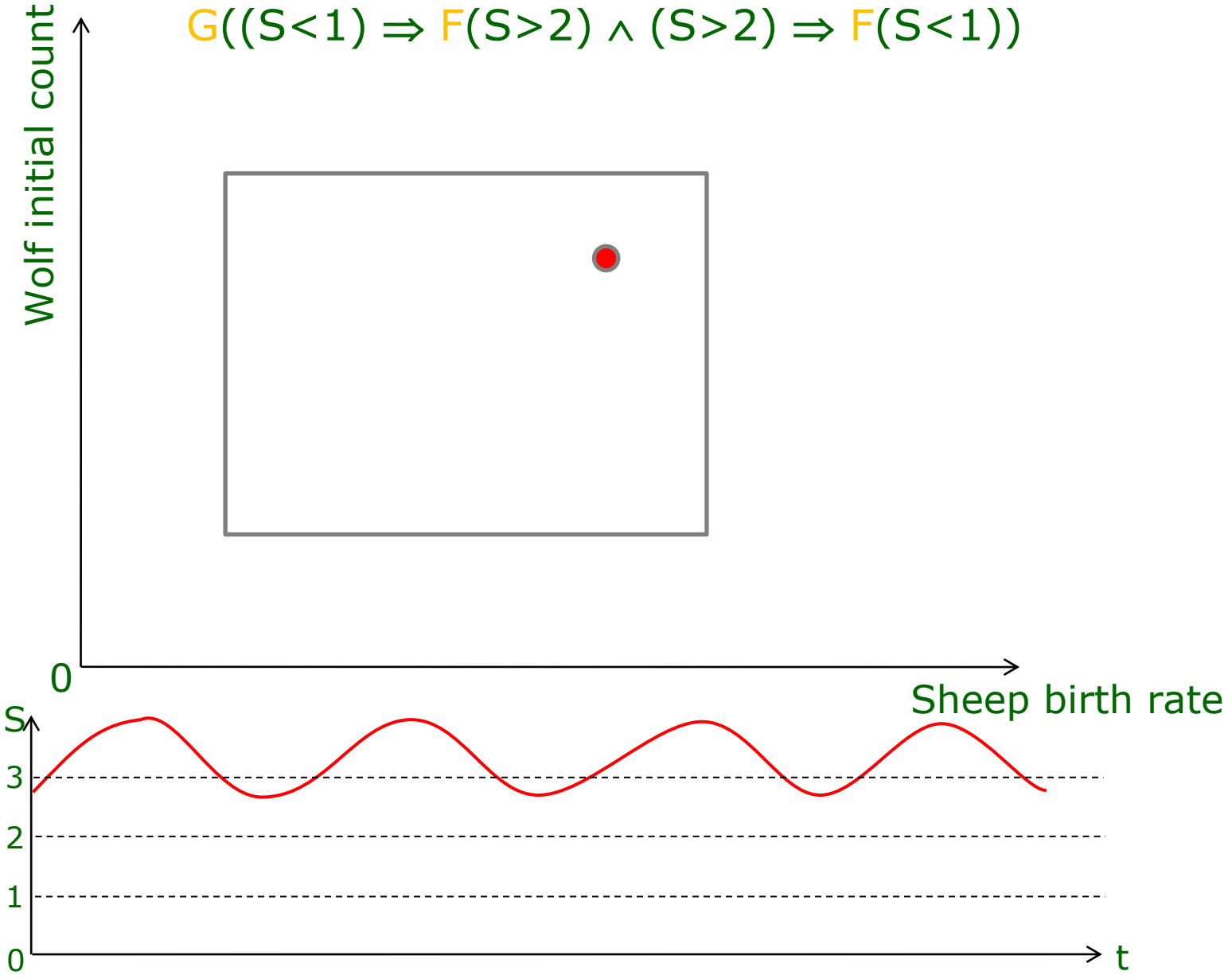

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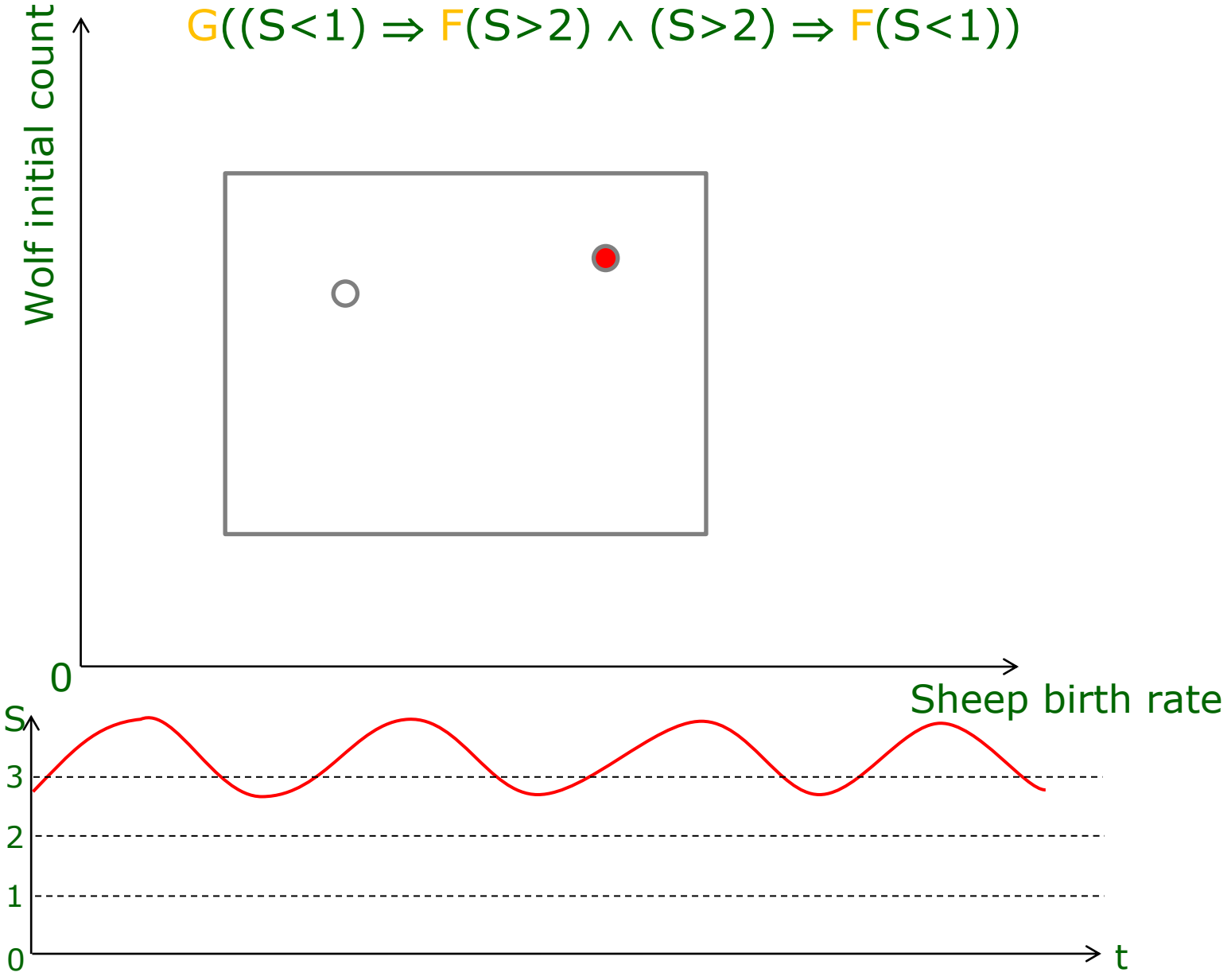

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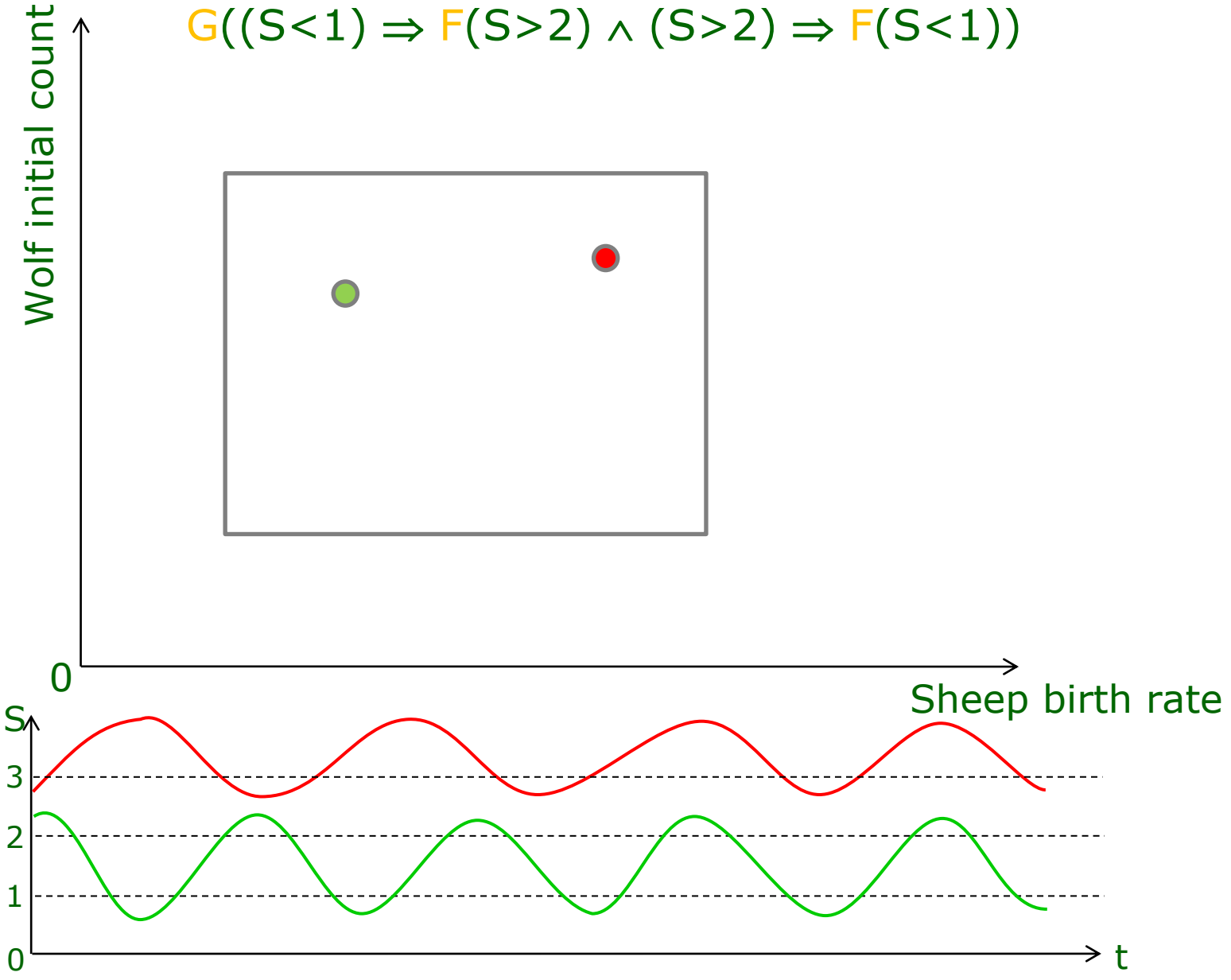

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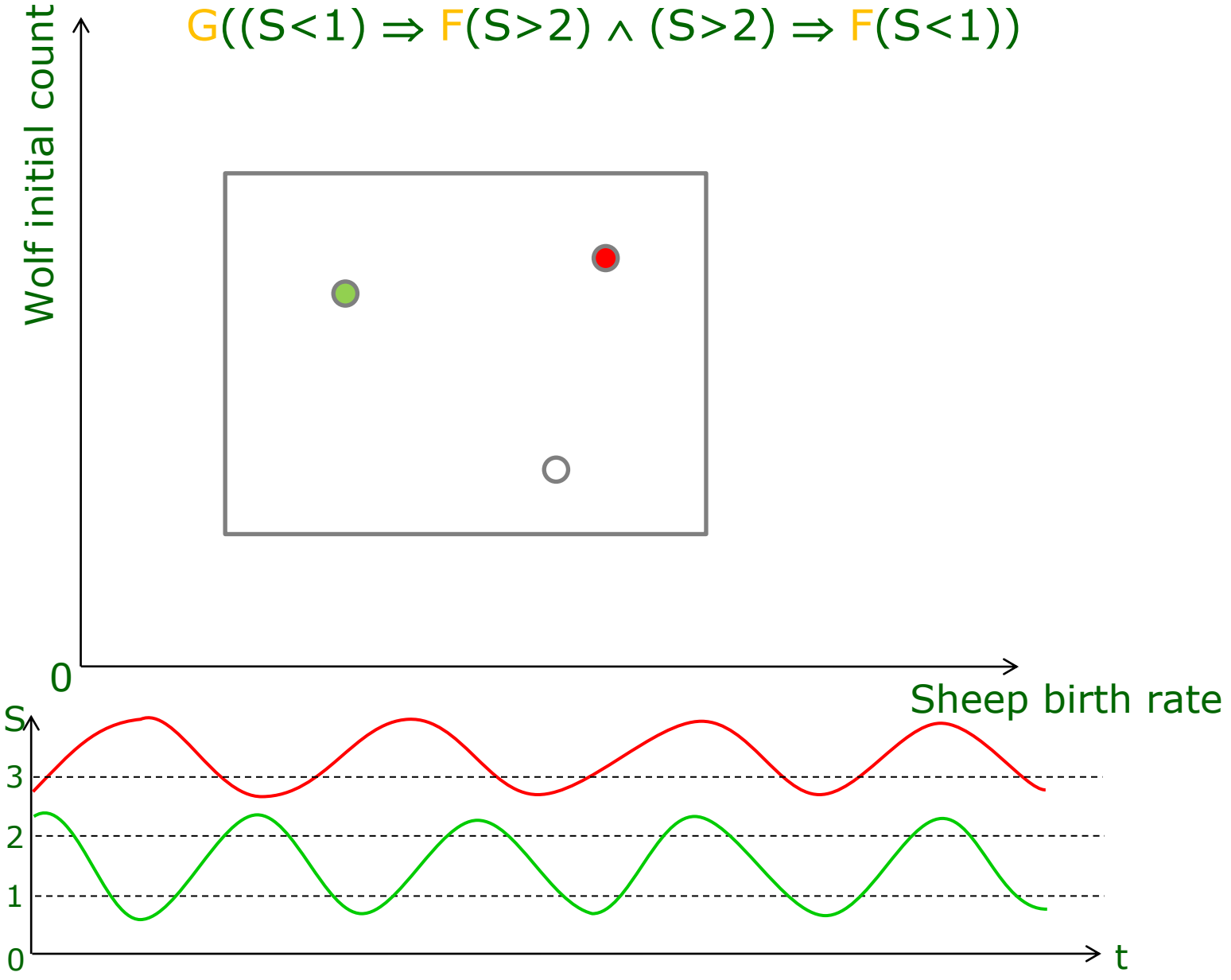

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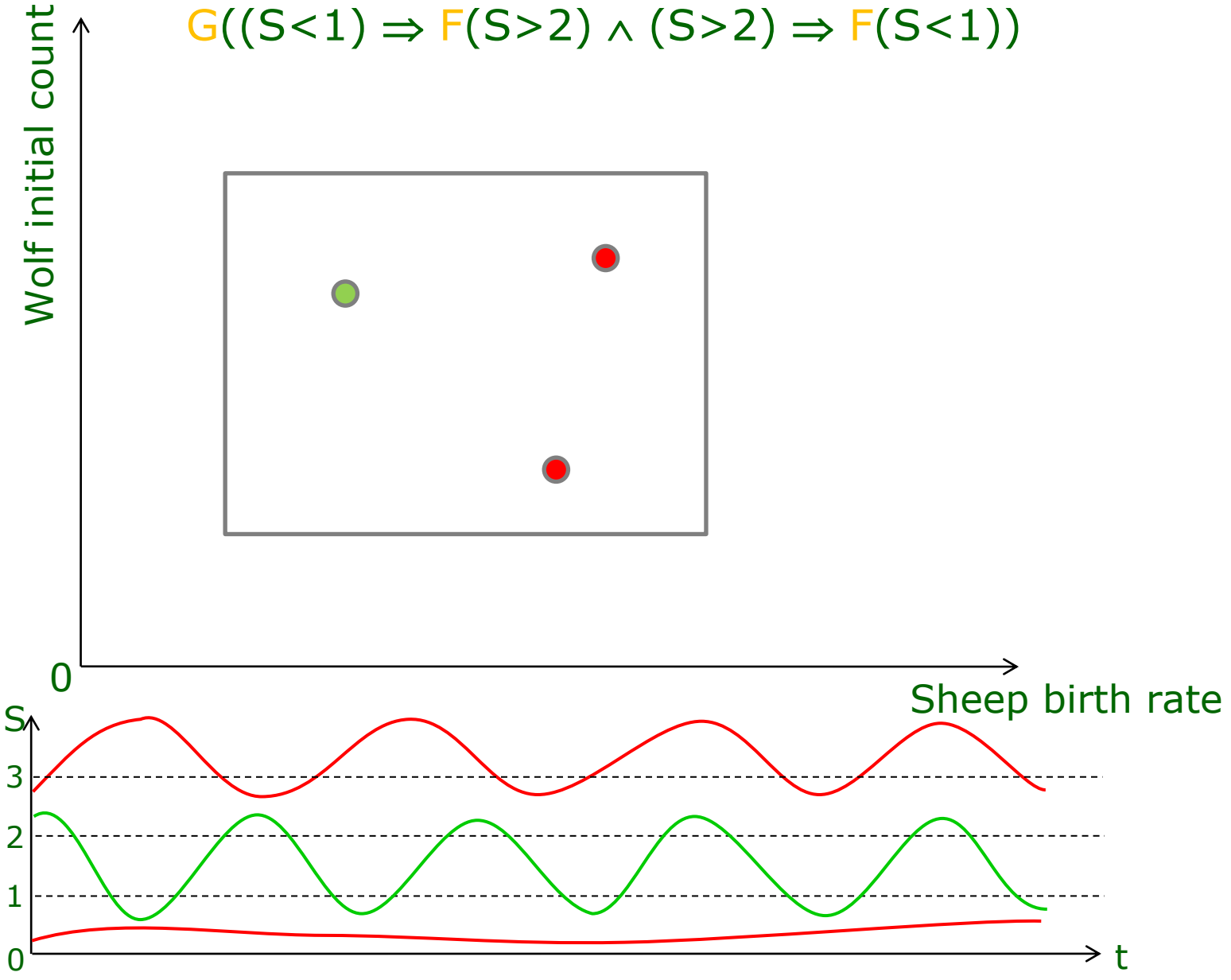
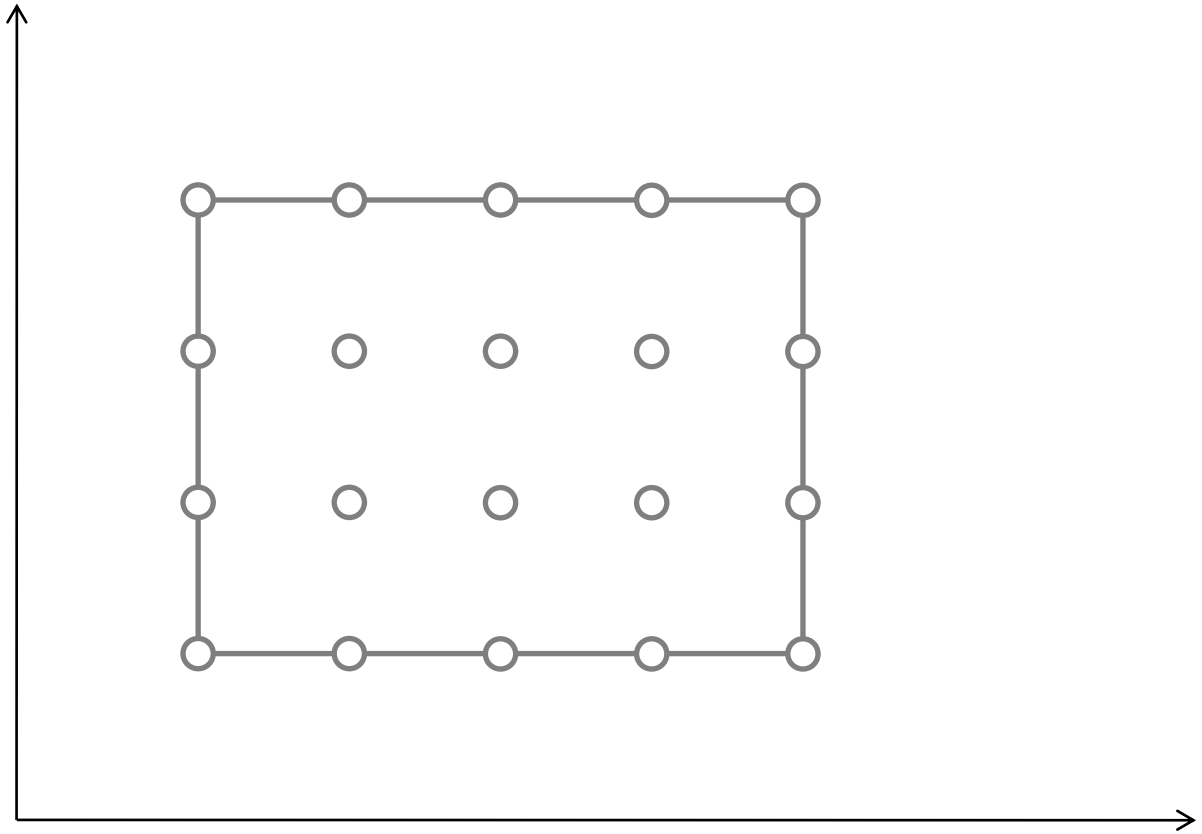


Computing robustness – continuity problem



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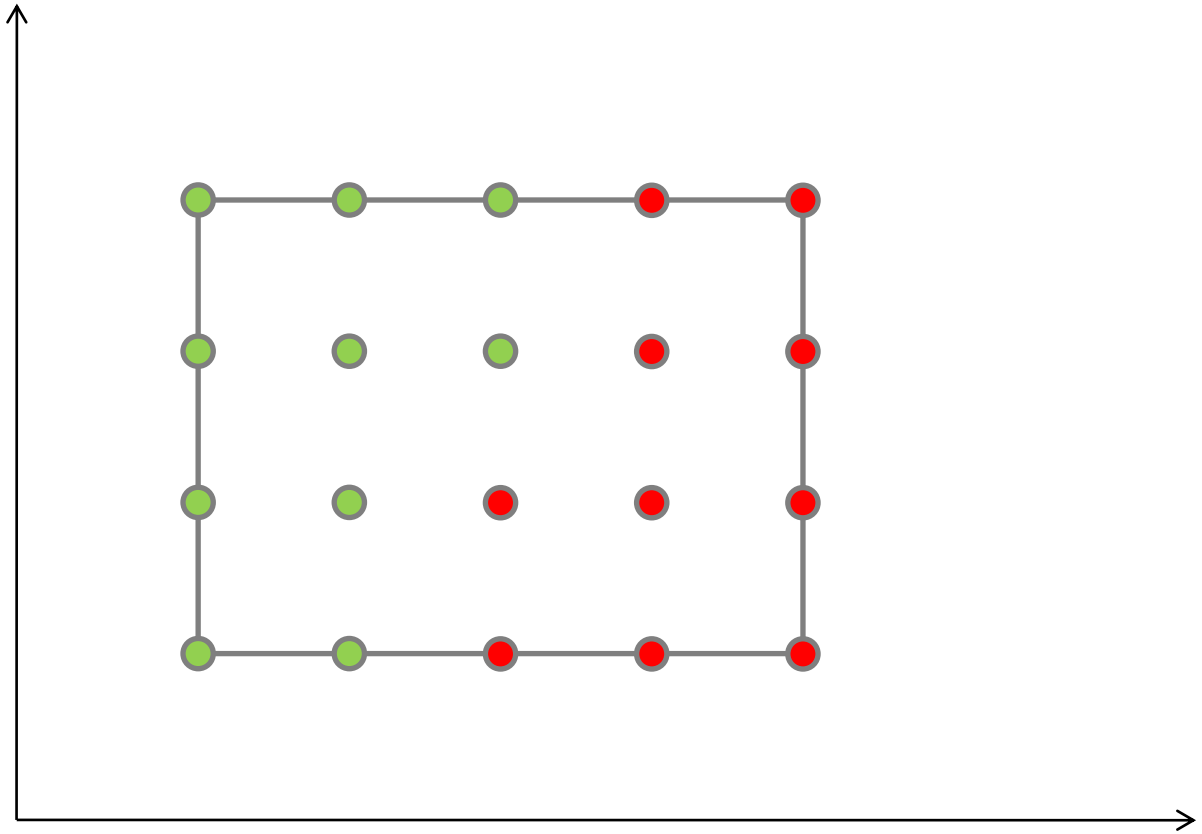
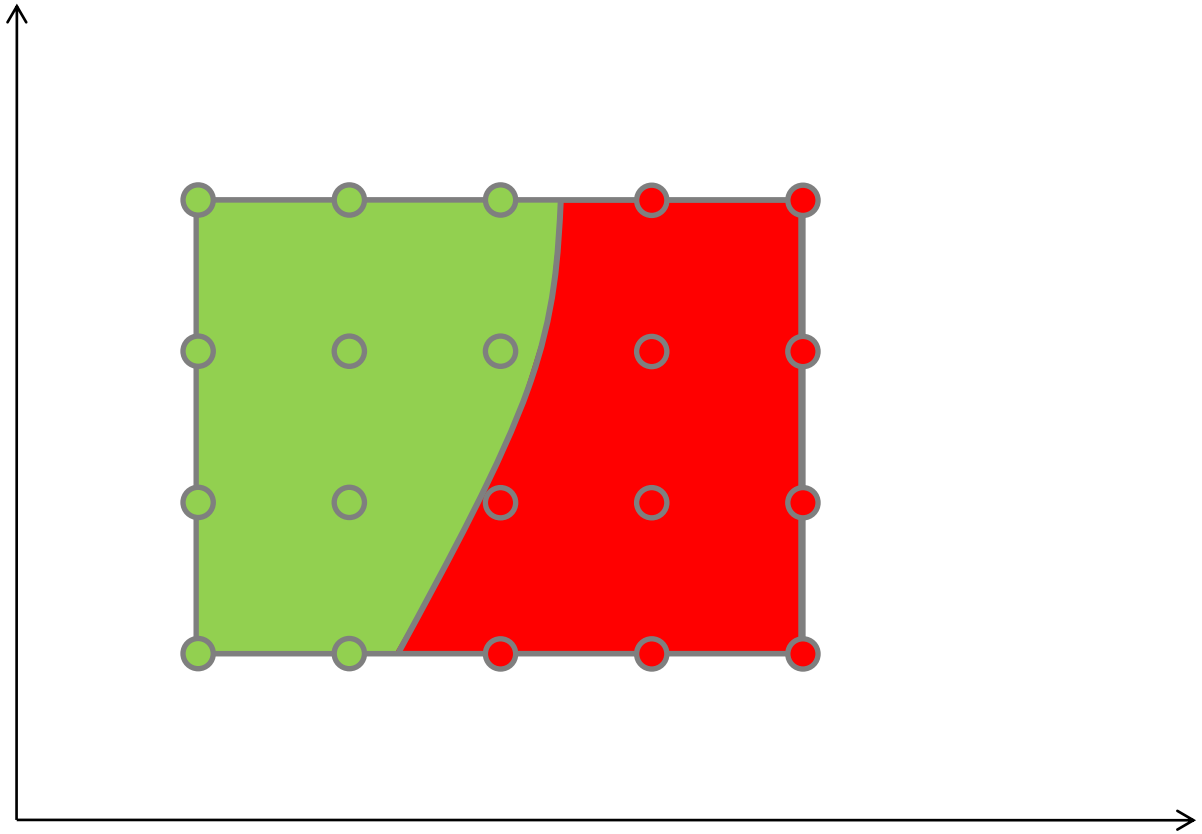
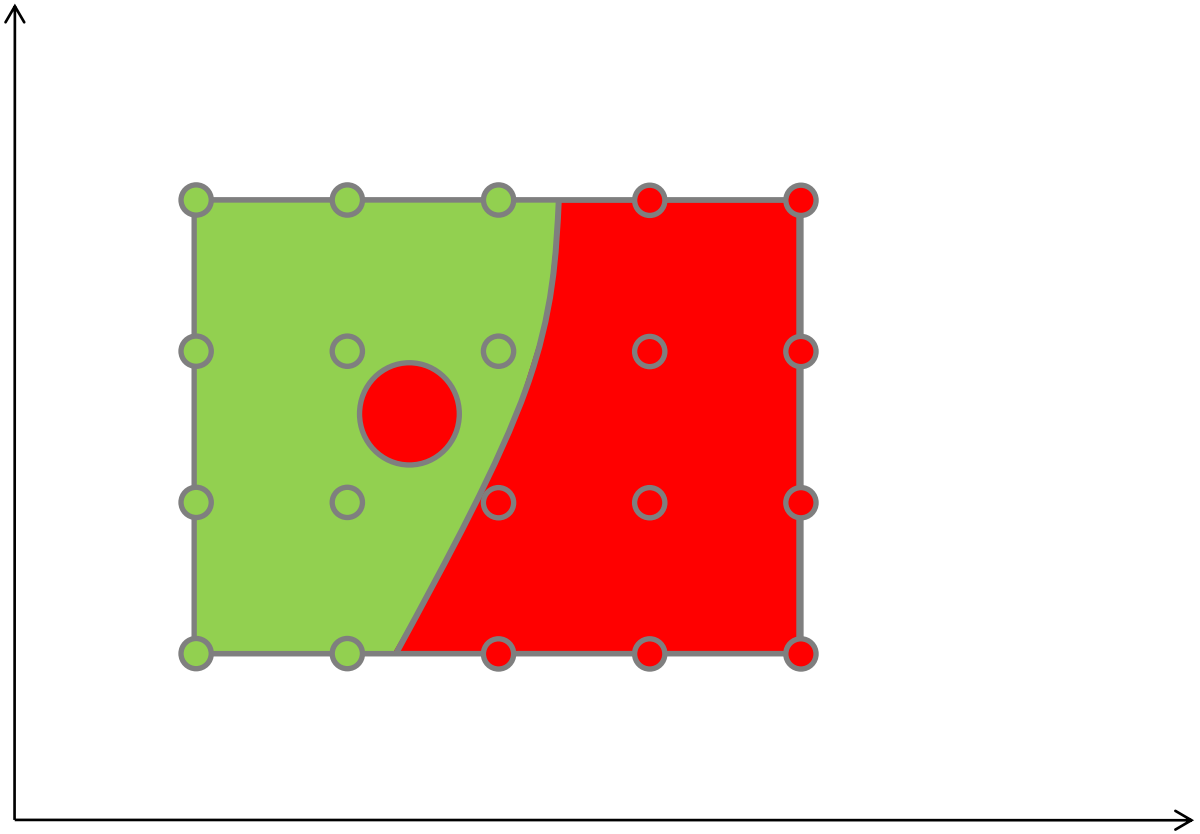


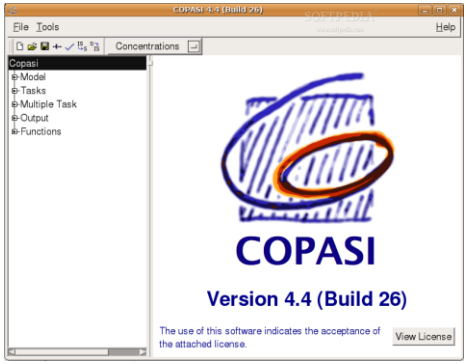
Computing robustness – continuity problem

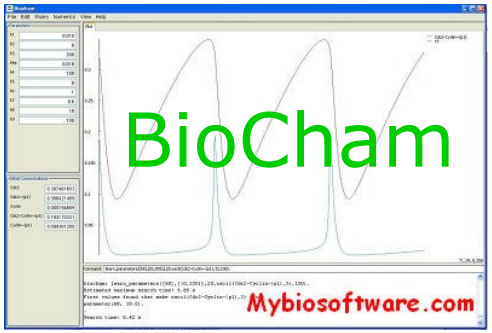


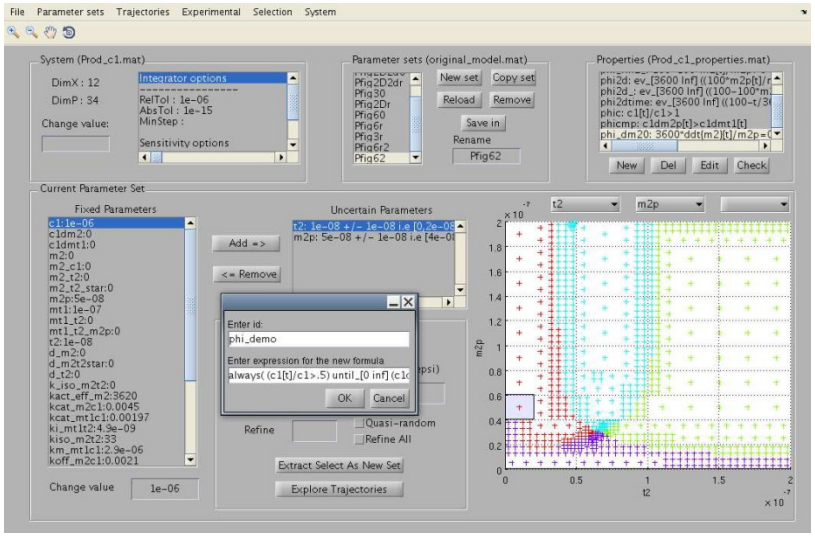
Computing robustness – continuity problem



Current approaches

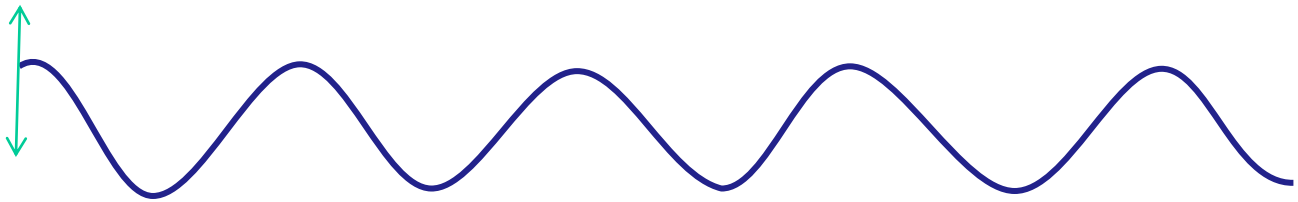






Breach (Donzé A. and Maler O. 2010)

How does a neighborhood behave?



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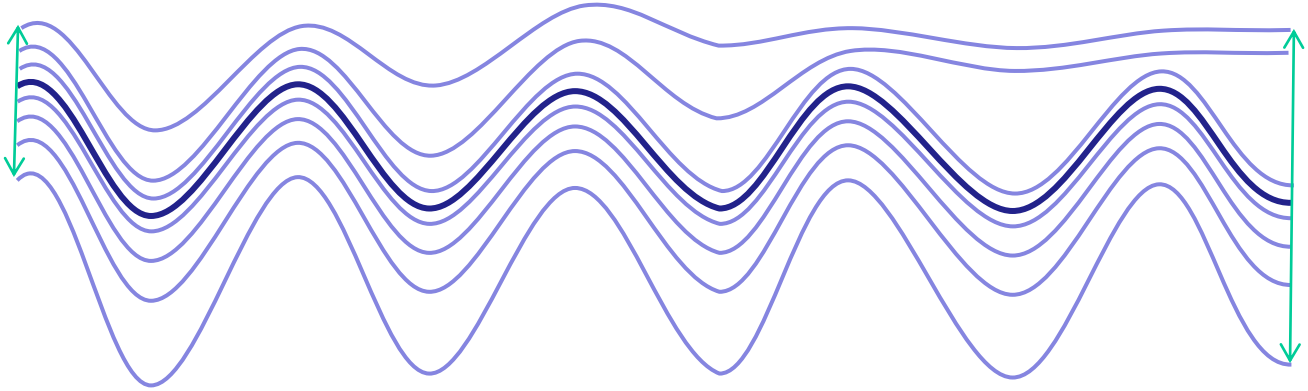

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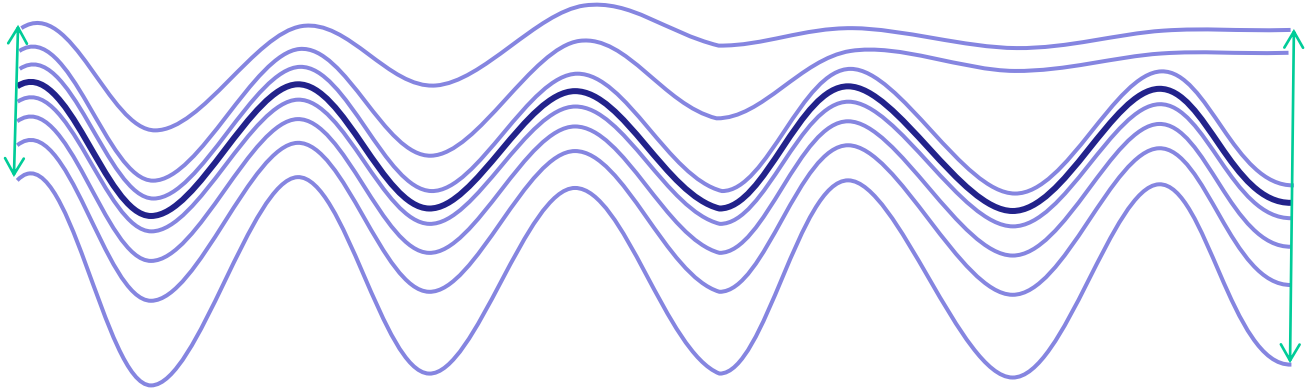
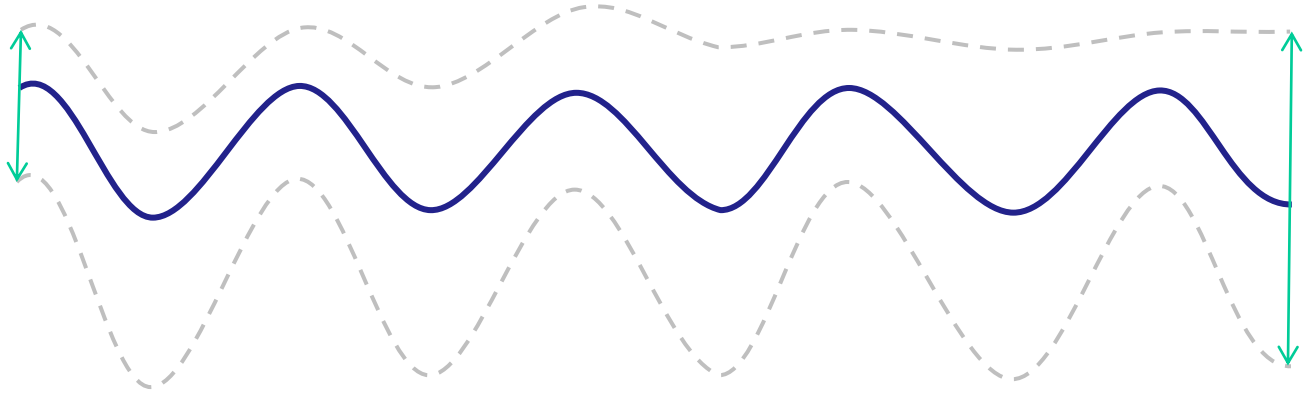
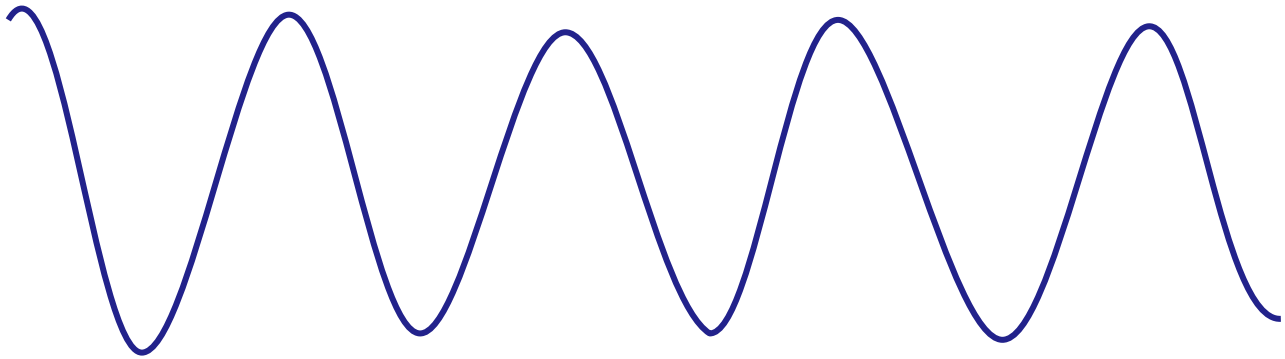


Sensitivity analysis

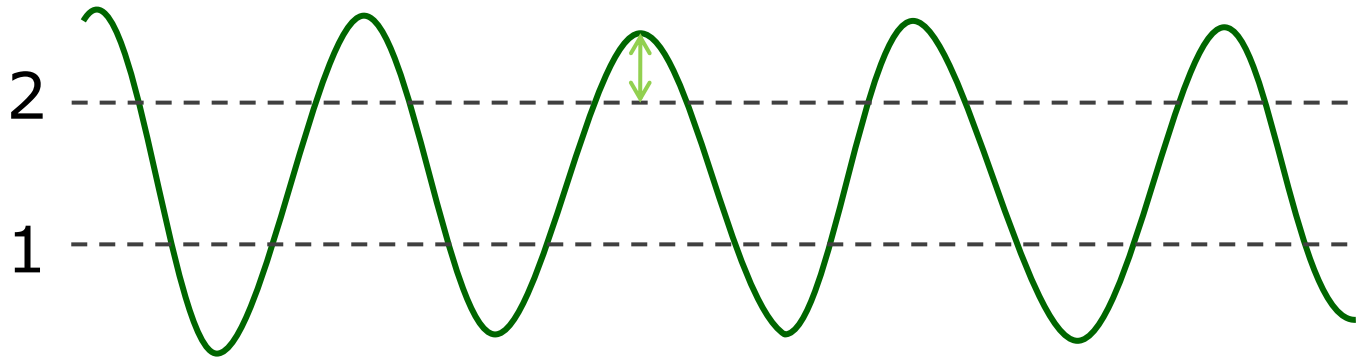


Local property robustness



$$G((S<1) \Rightarrow F(S>2) \wedge (S>2) \Rightarrow F(S<1))$$

Local property robustness



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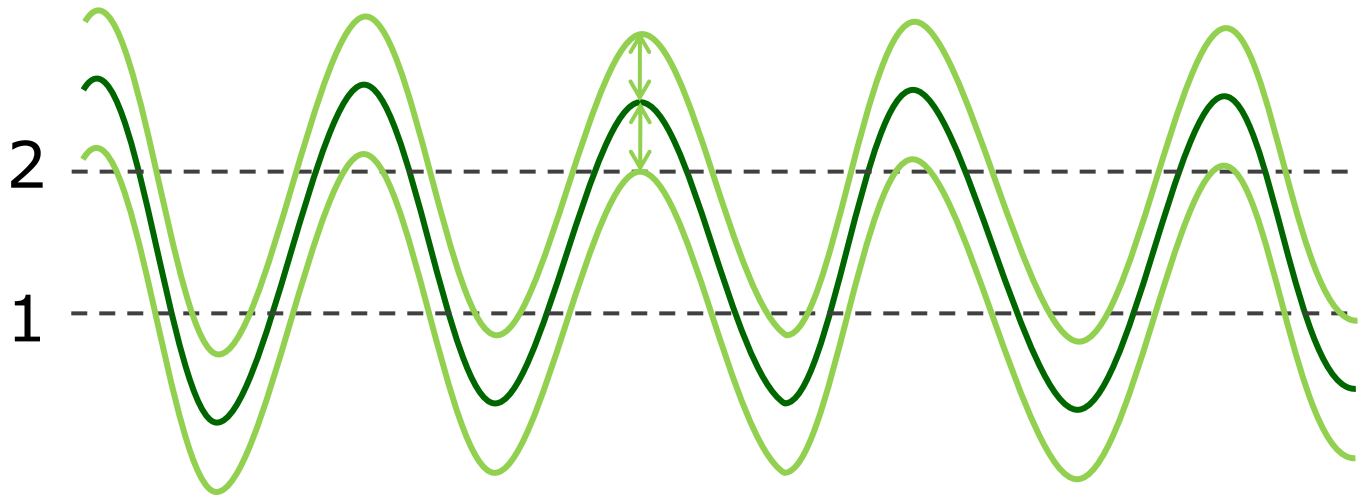
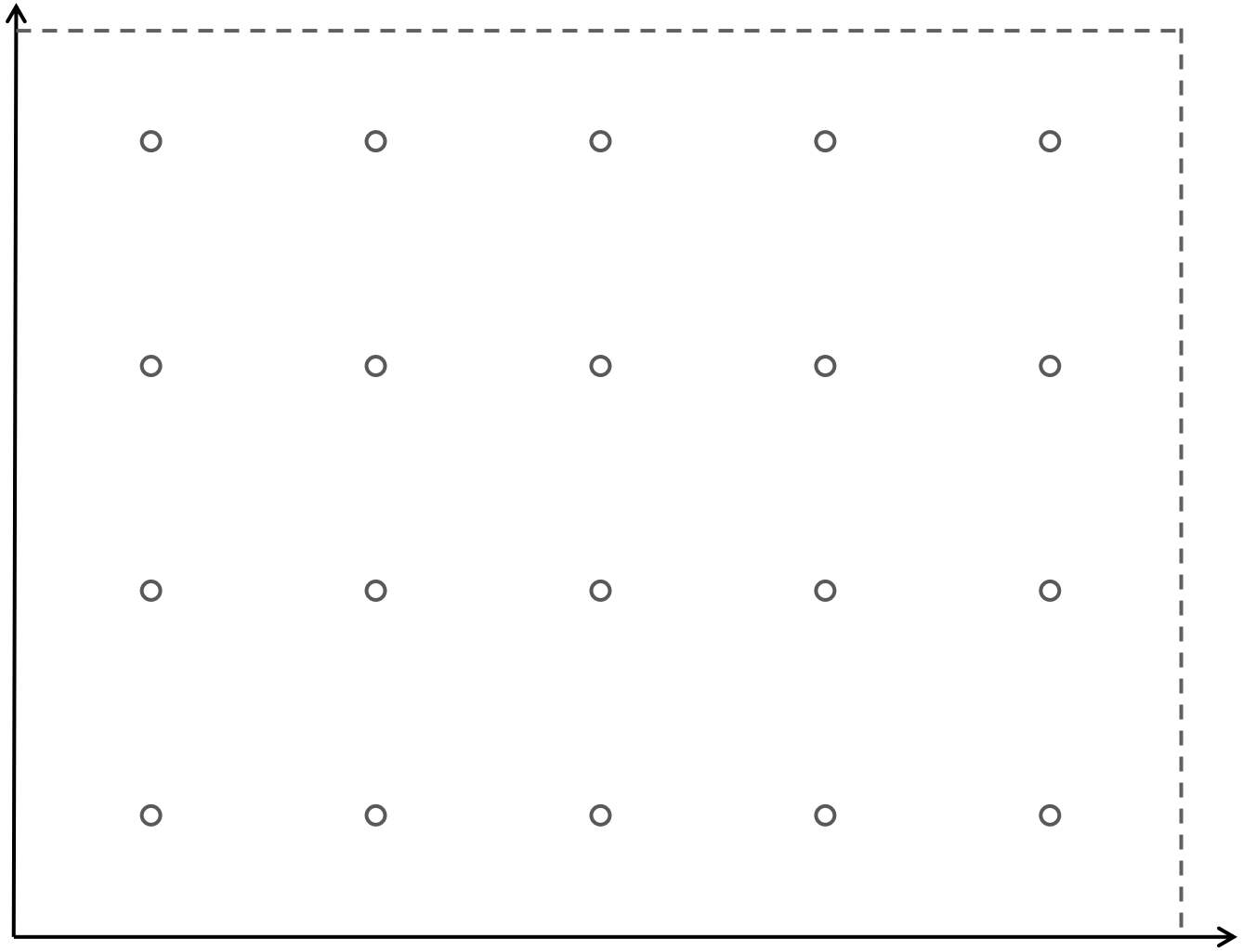


$$G((S<1) \Rightarrow F(S>2) \wedge (S>2) \Rightarrow F(S<1))$$

Hierarchical refinement



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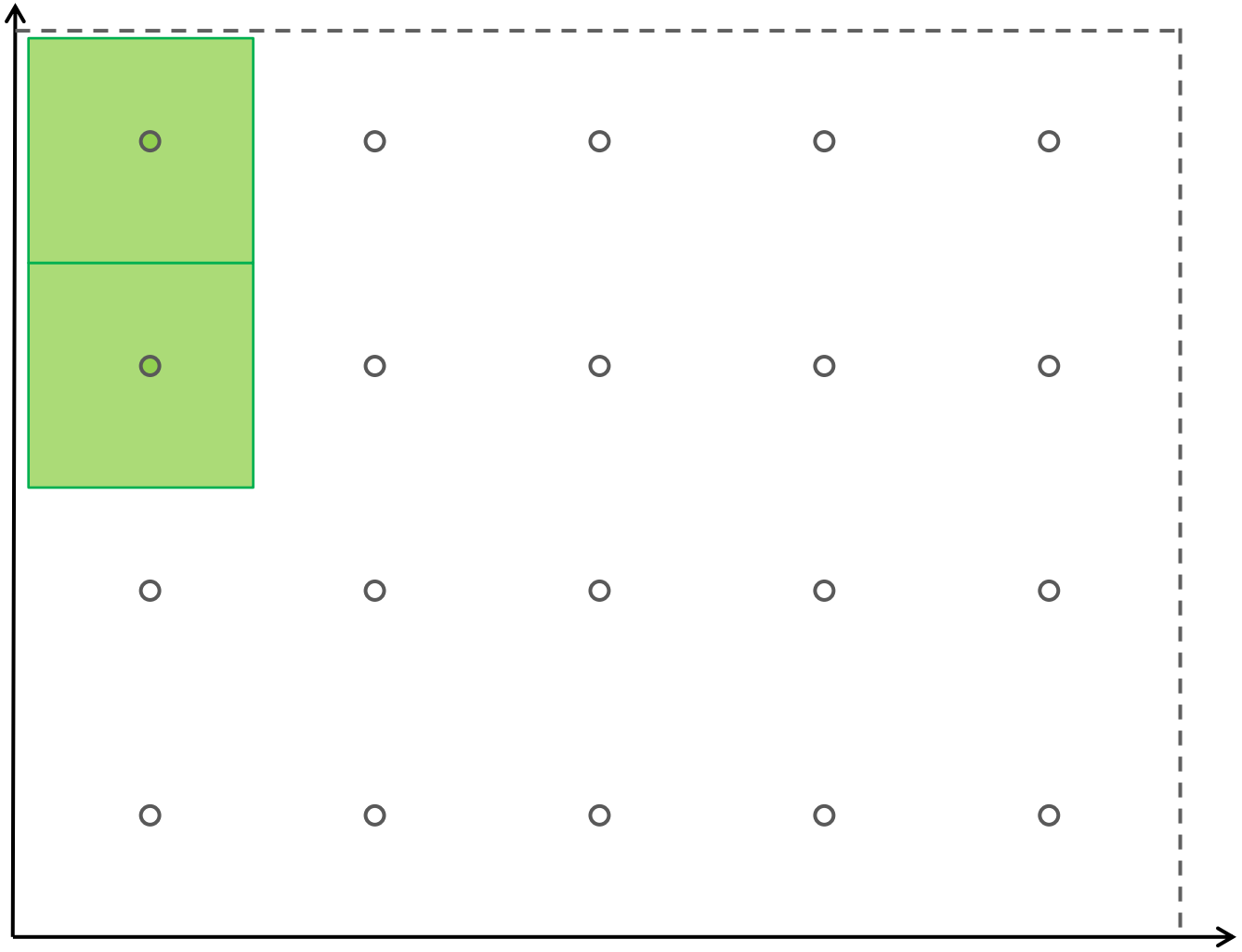

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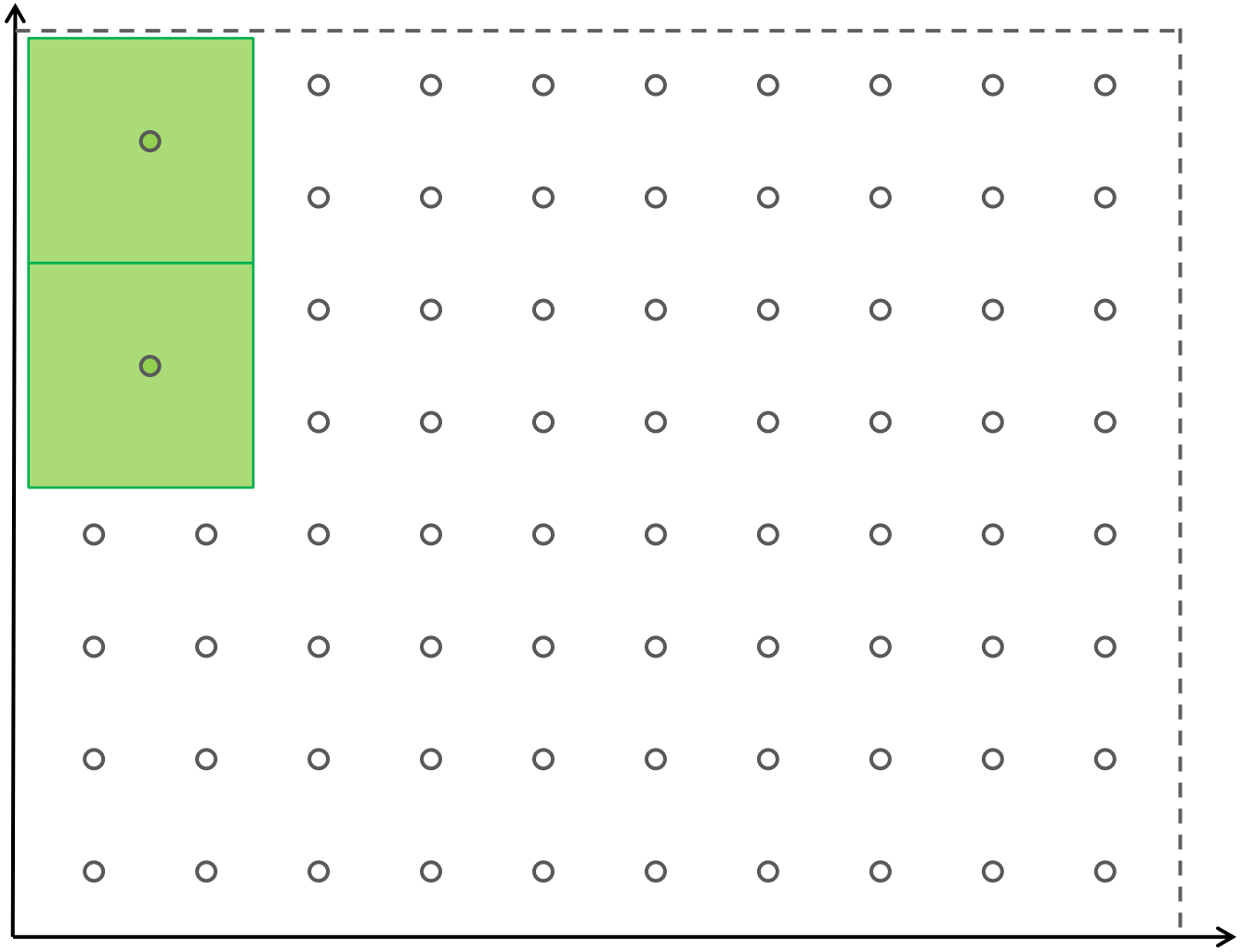

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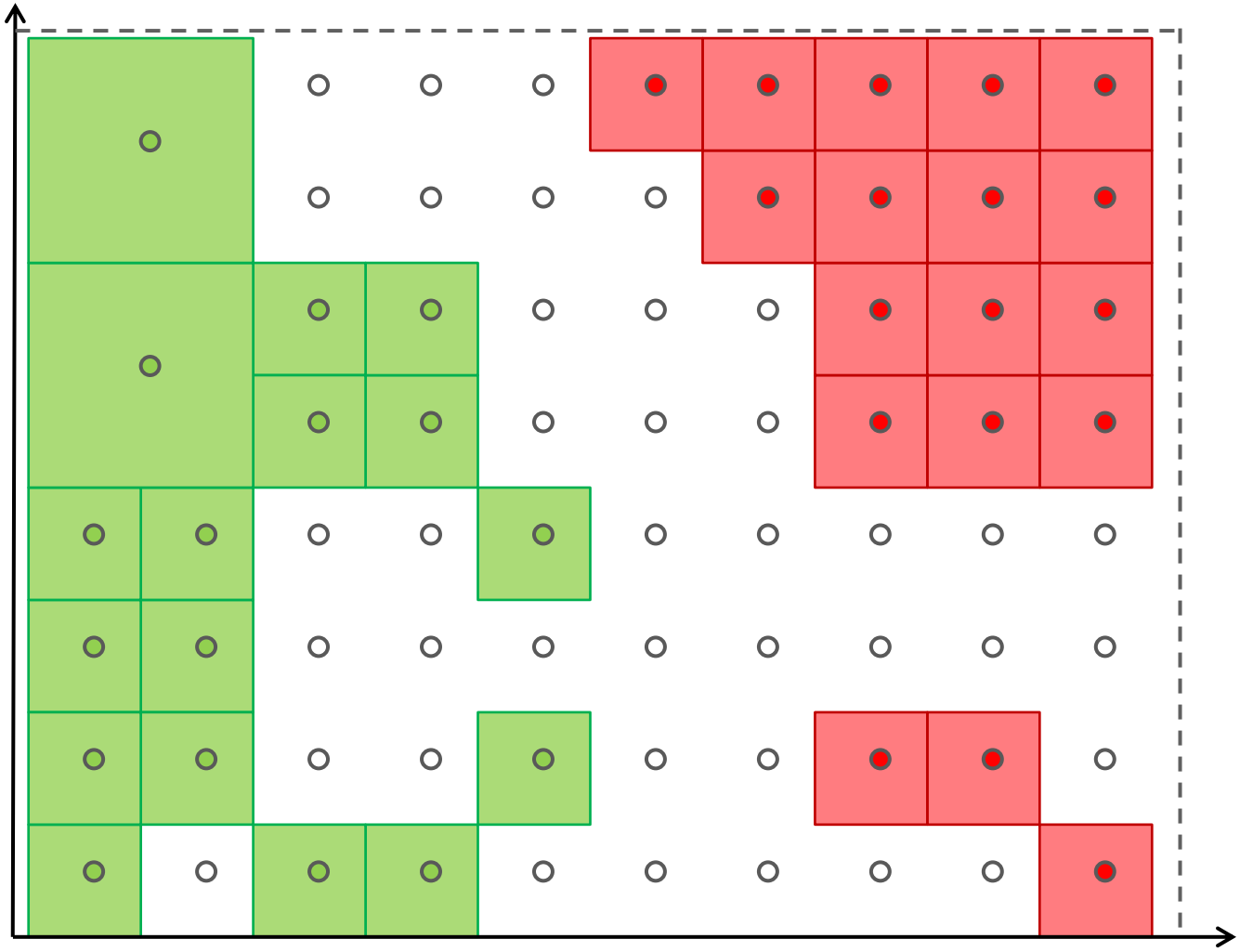

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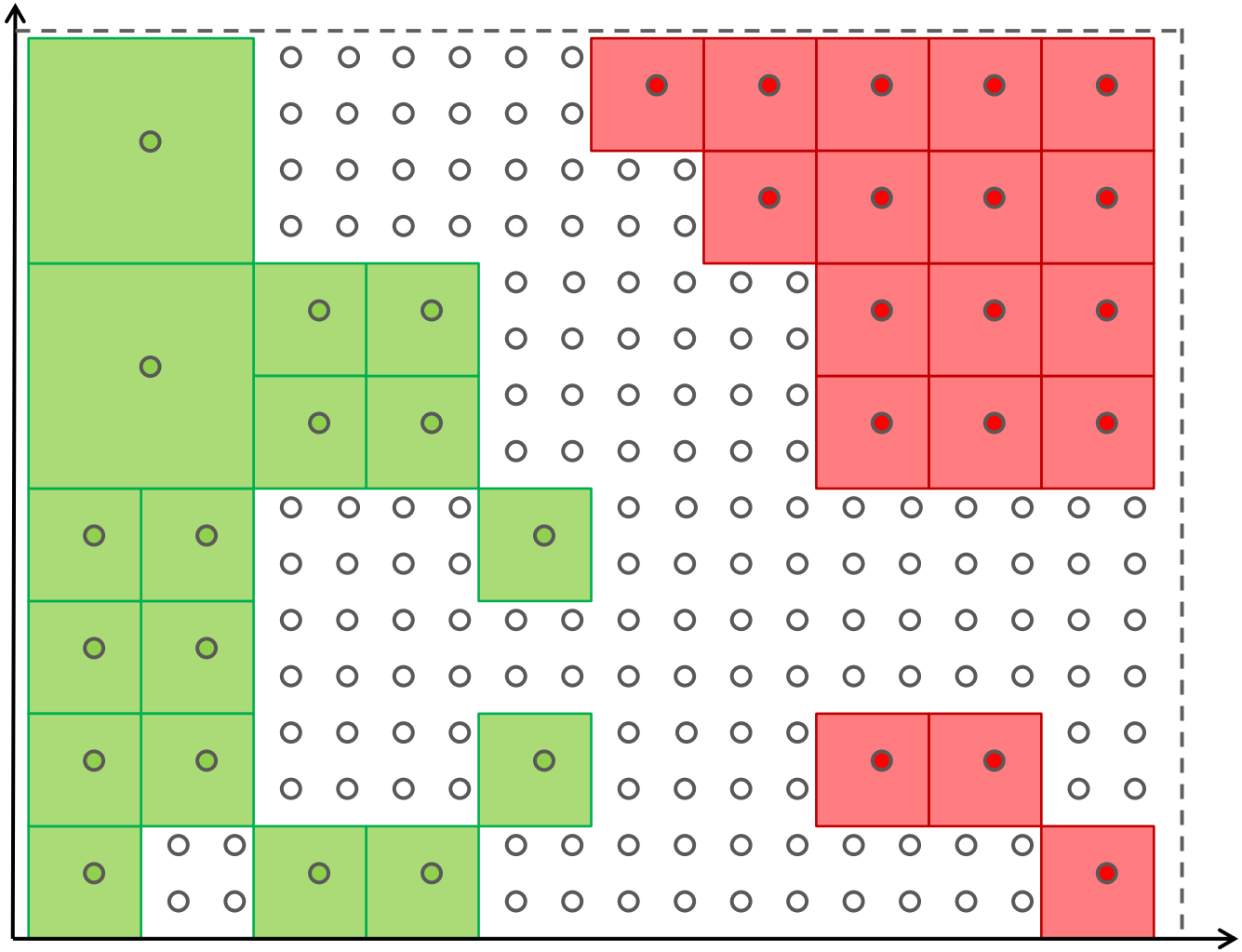

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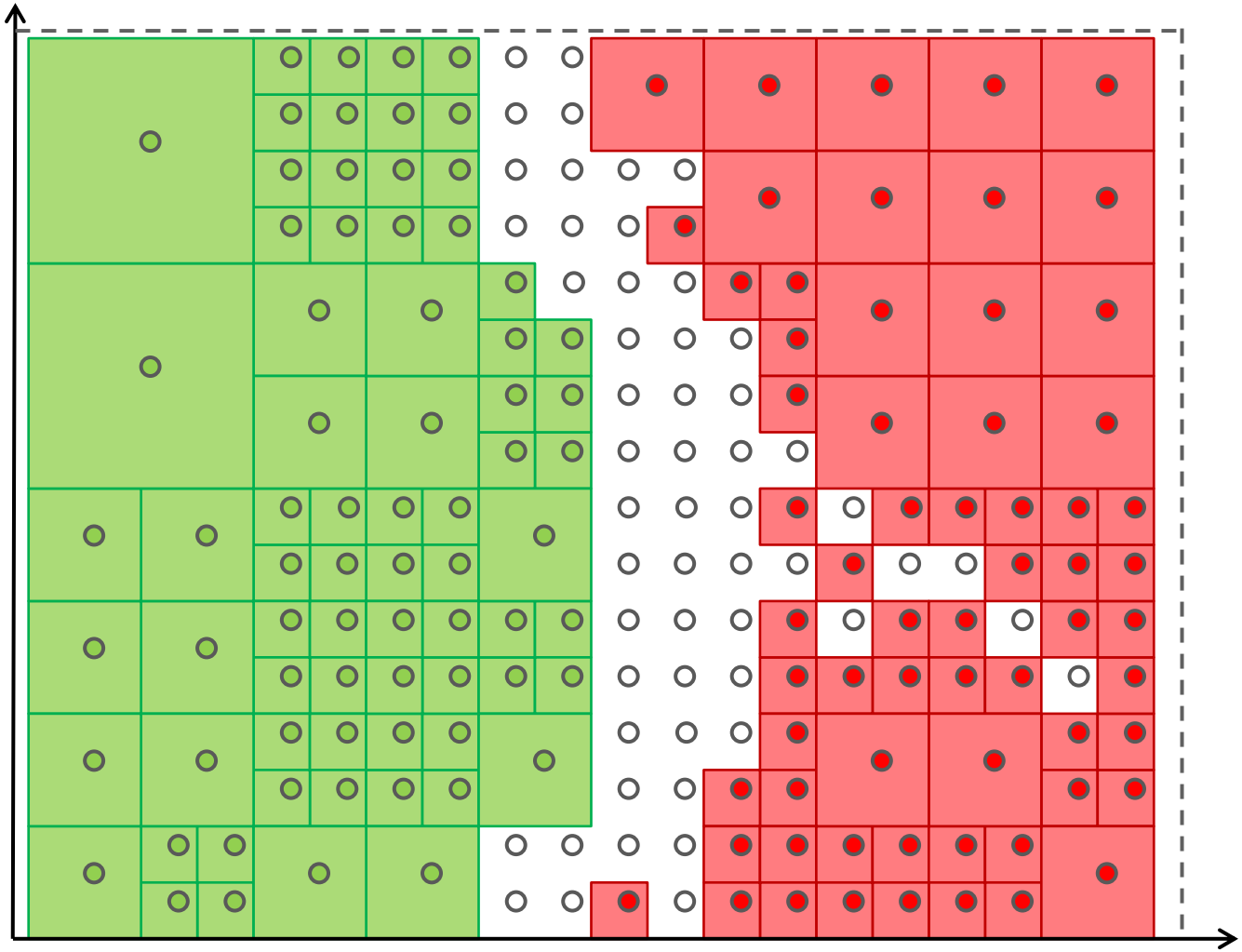

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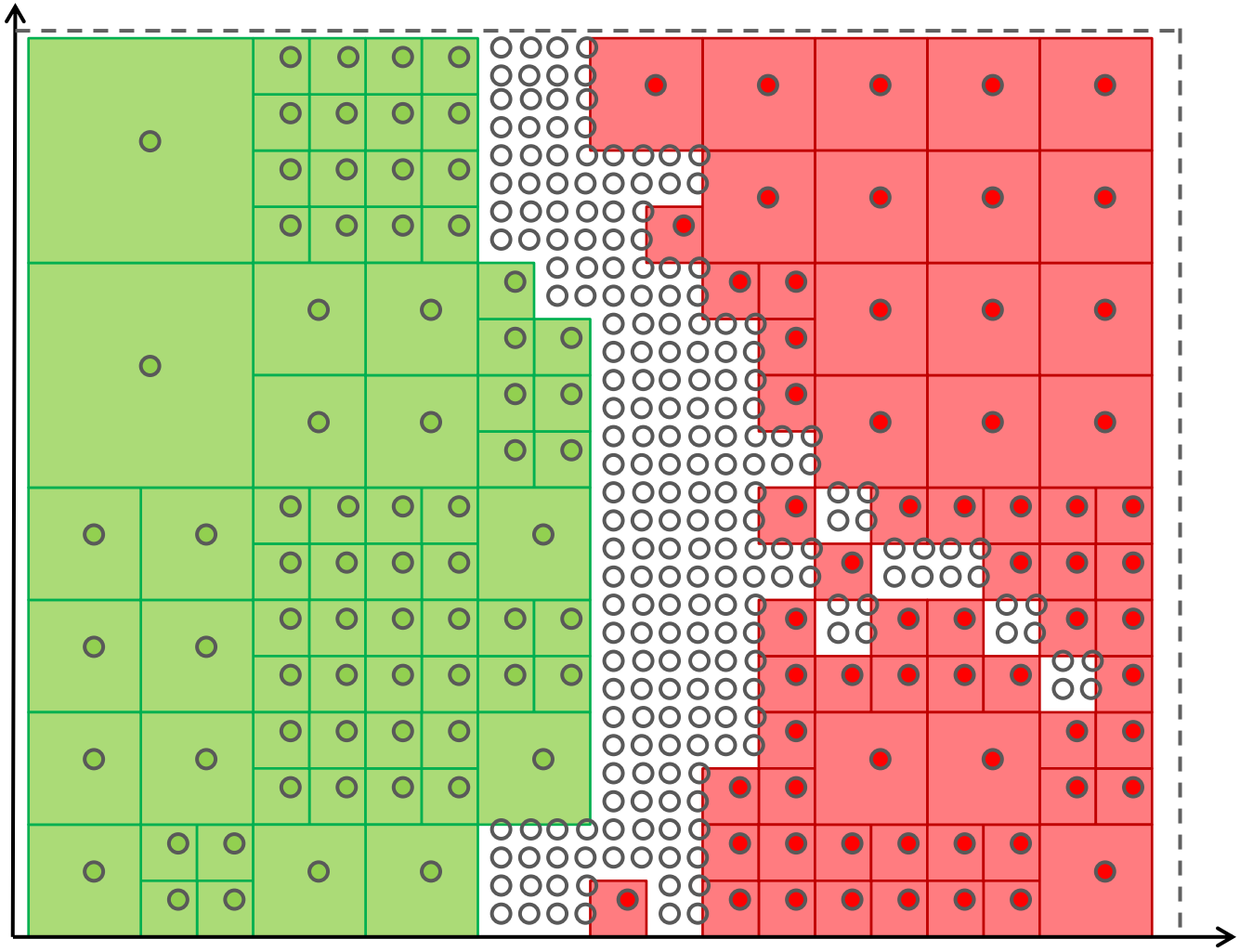
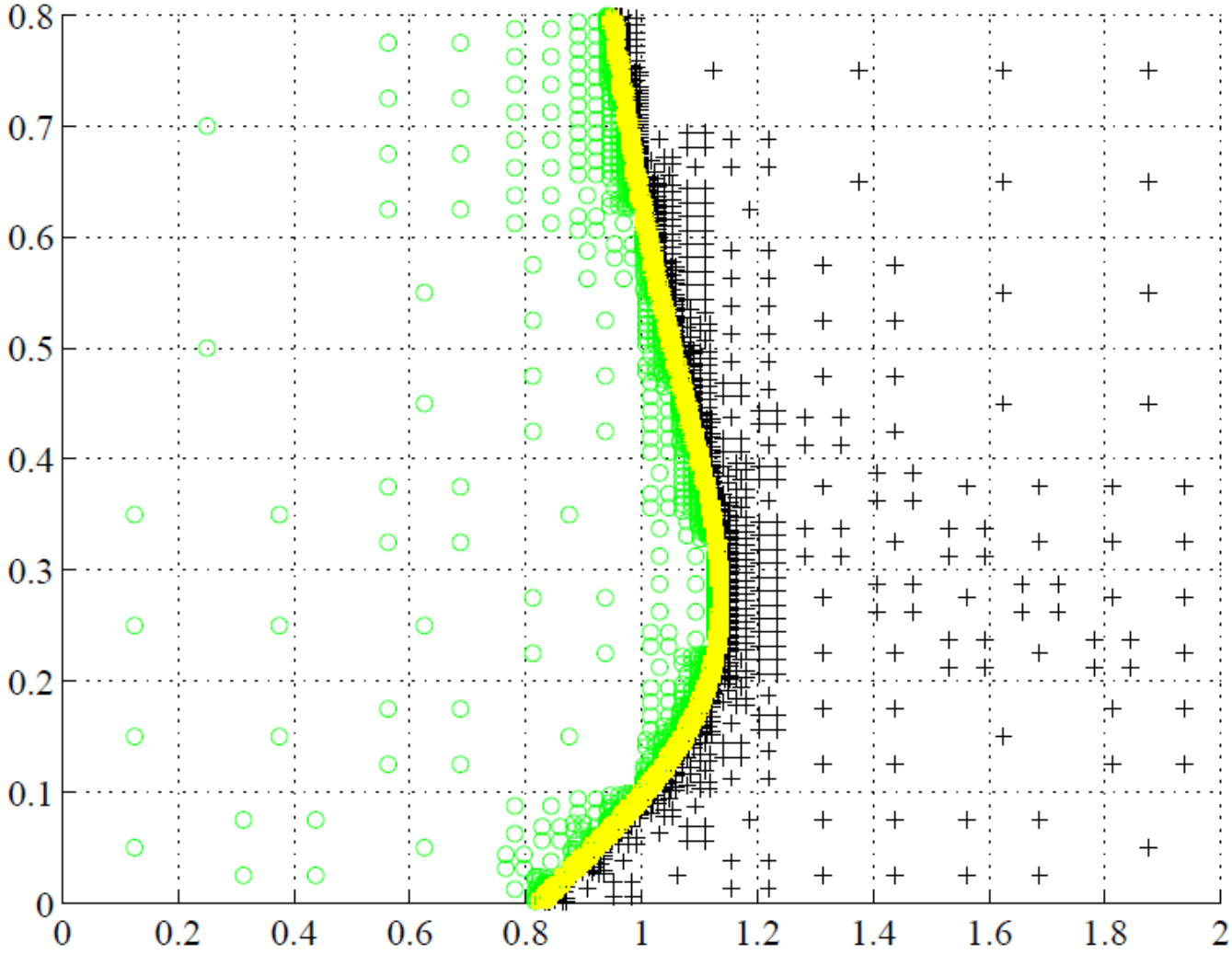
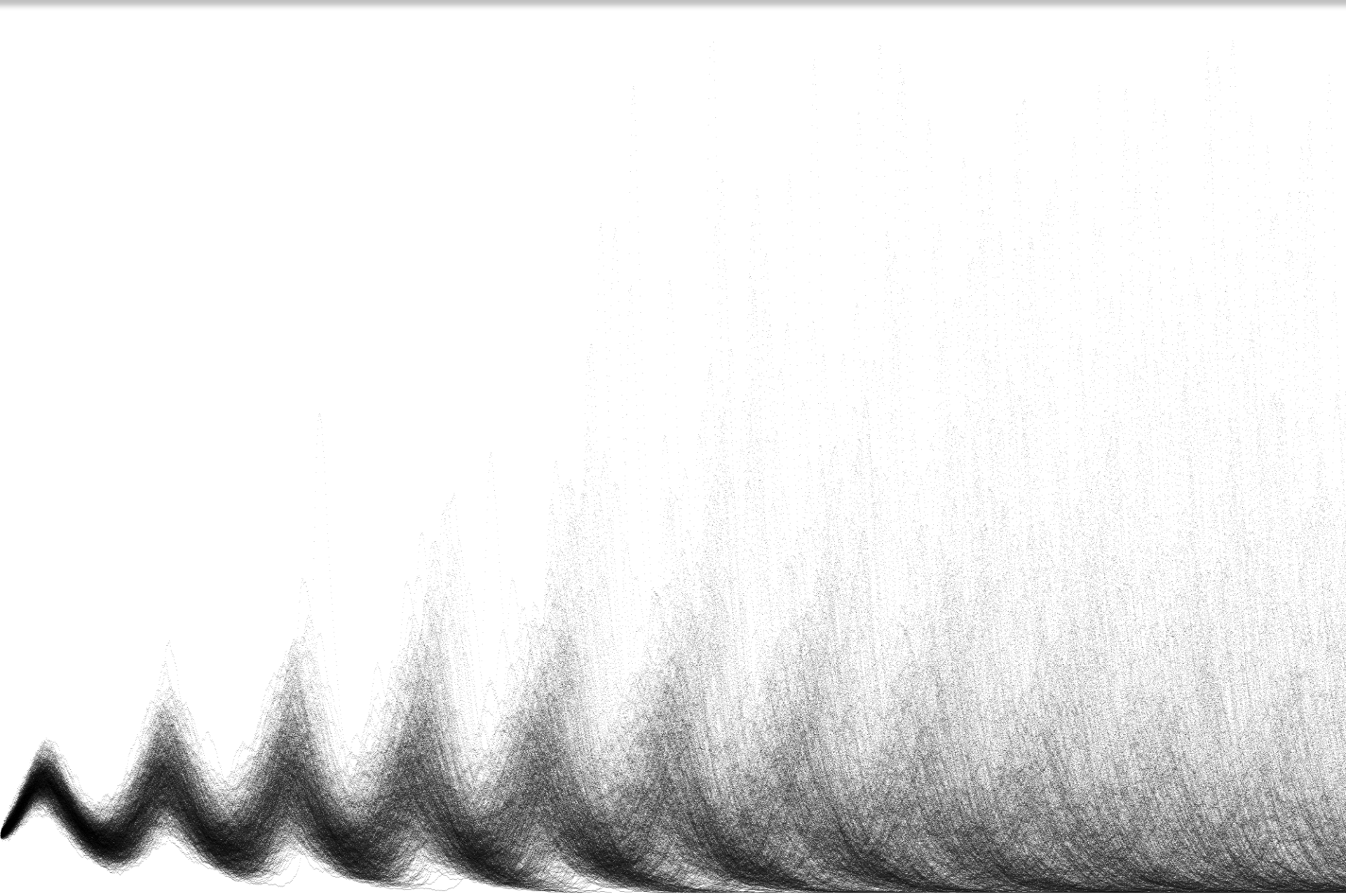


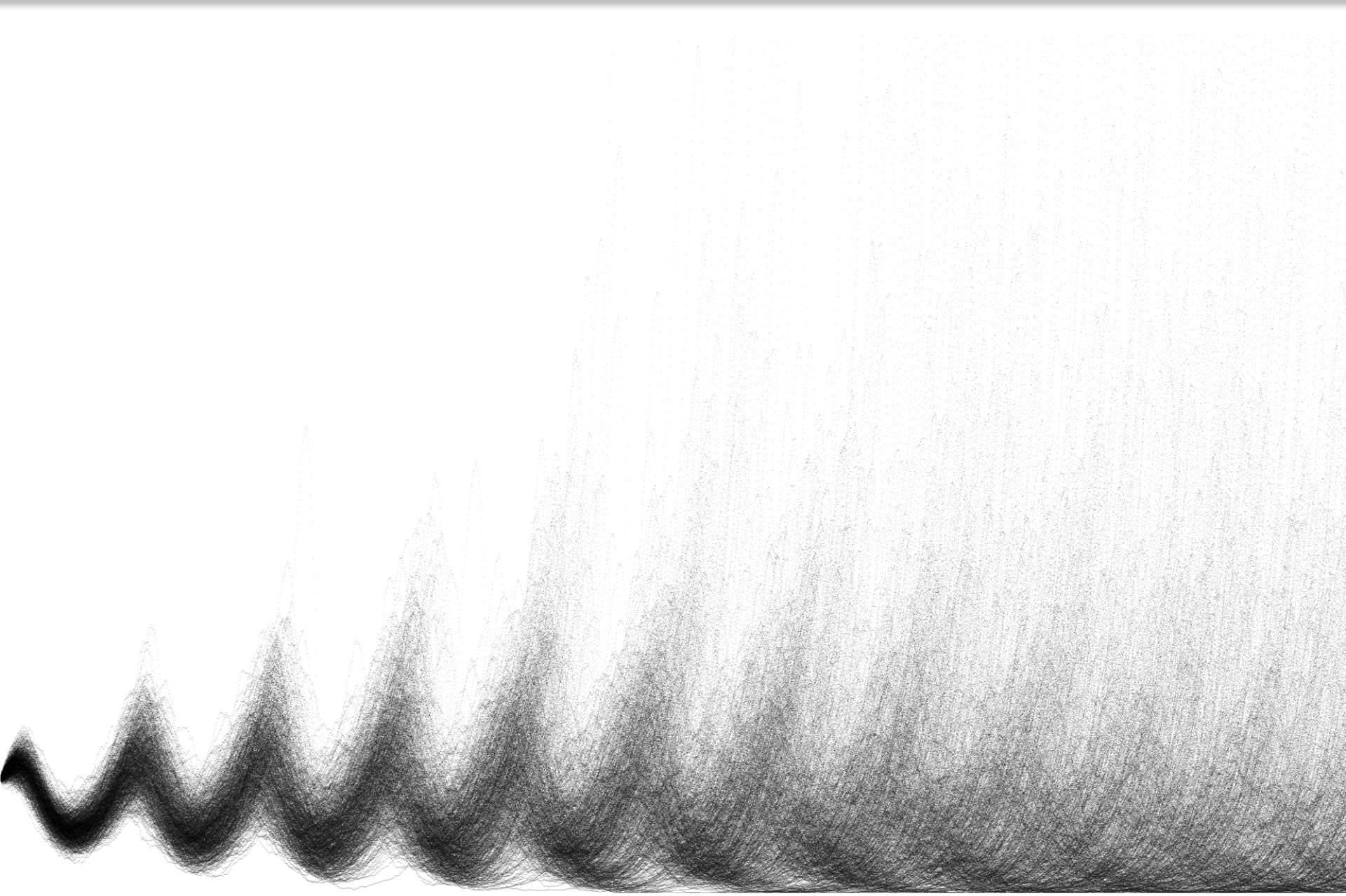
Hierarchical refinement



Robustness of Stochastic systems



Robustness of Stochastic systems



Summary and Conclusion

What have you seen

- What is robustness
- Models of biological systems
- Expressing properties
- Current approaches to robustness of continuous systems
- Robustness of Stochastic systems

Questions and comments are welcome

Thank you for your attention.

Sources

- LTL – Linear Temporal Logic
  - Amir Pnueli. The temporal logic of programs. In Proc. 18th Annual Symposium on Foundations of Computer Science (FOCS), pages 46–57, 1977.
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