

Most Permissive Semantics of Boolean Networks: Beyond Generalized Asynchronicity

Thomas Chatain¹, Stefan Haar¹, *Loïc Paulevé*²

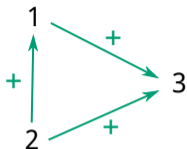
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² CNRS, LRI, Univ Paris-Sud, Univ Paris-Saclay, France

ECCB W6 2018, Athens, Greece



Qualitative vs abstract modelling



Boolean network

- logic of activity w.r.t. regulators
- *update mode* (sync, async, etc.)

Multilevel network

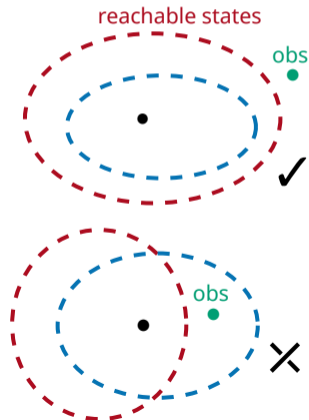
- + define activation thresholds

Quantitative model

information



Consistency
analysis at Boolean level
transposable to multilevel?



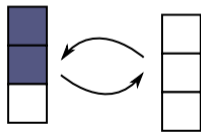
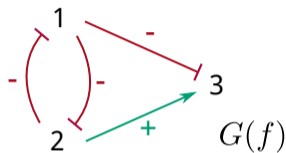
Update modes
of Boolean networks:
a **bug...**

Motivating example (embedded in many actual biological networks)

$$f_1(x) \triangleq \neg x_2$$

$$f_2(x) \triangleq \neg x_1$$

$$f_3(x) \triangleq \neg x_1 \wedge x_2$$

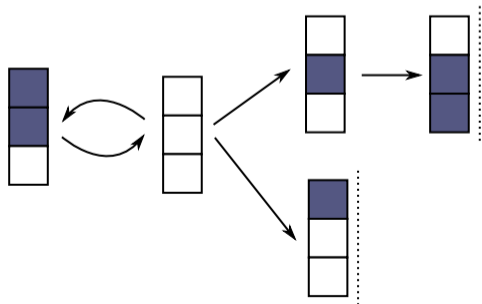
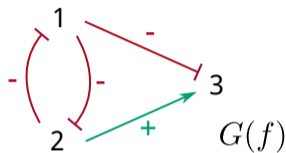


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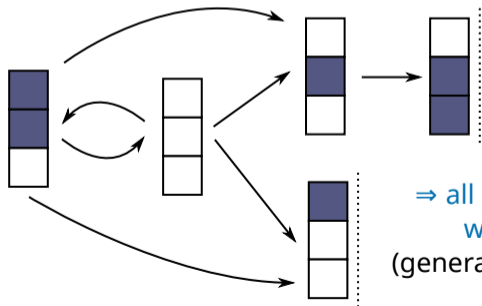
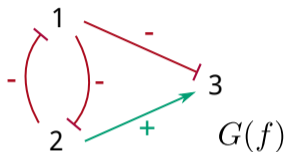


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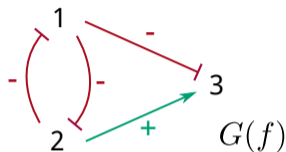
⇒ all configurations reachable
with any update mode
(generalized) asynchronous mode

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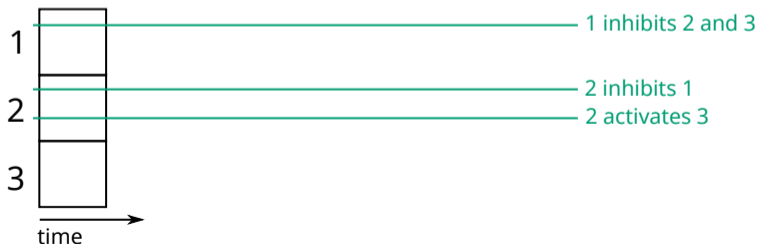
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Compatible **continuous/multilevel** dynamics:

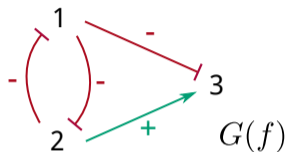


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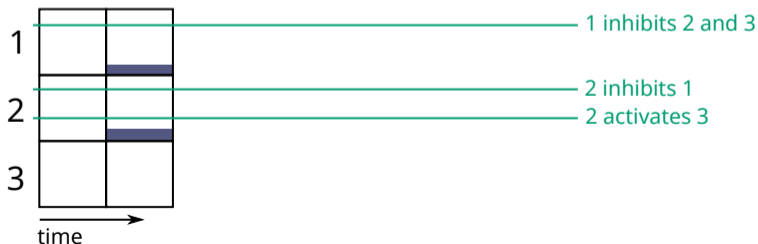
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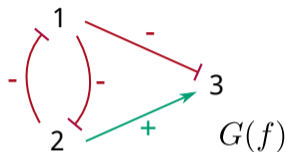
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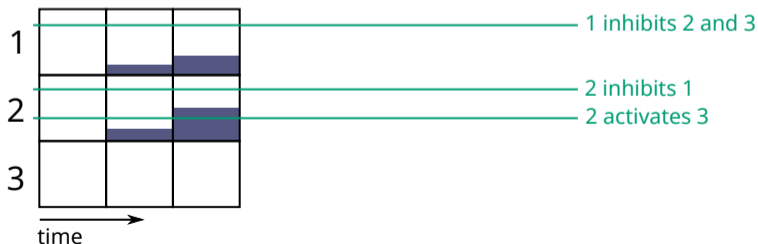
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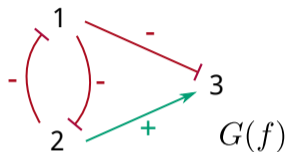


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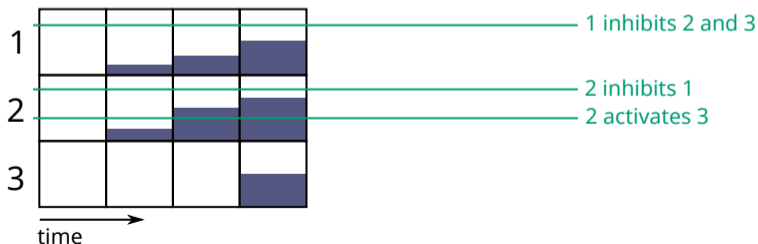
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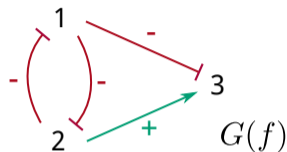


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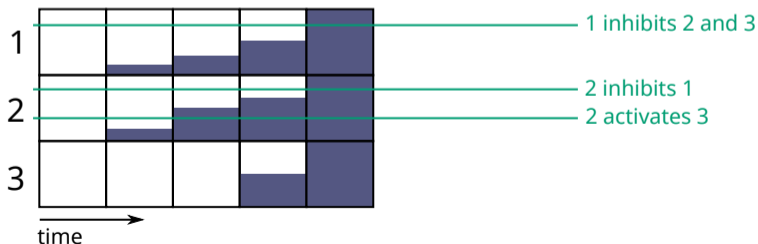
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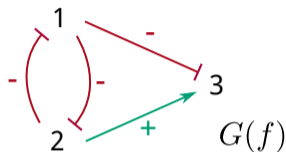
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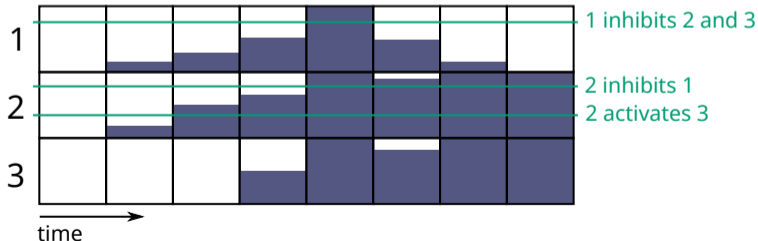
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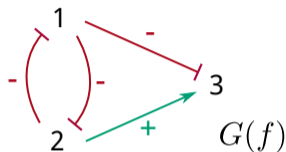


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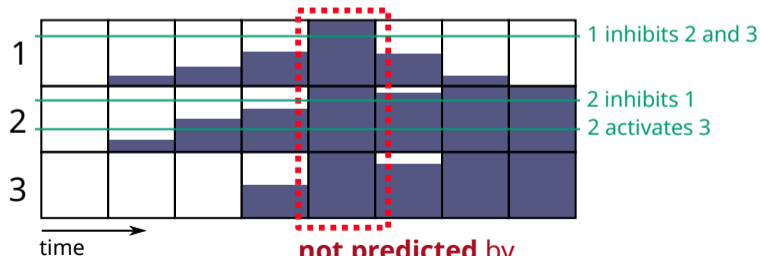
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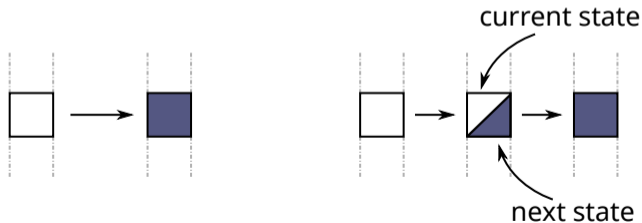
Compatible **continuous/multilevel** dynamics:



**Most permissive semantics
of Boolean networks**
enabling new behaviours

Most permissive semantics

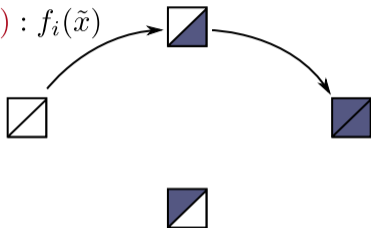
- **delay between firing and application** of state change
⇒ allow interleaving other state changes
- in "intermediate" states 
- **other components choose what they see**



Most permissive semantics

Rules for state of component i :

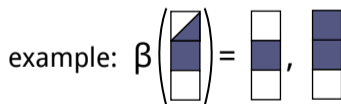
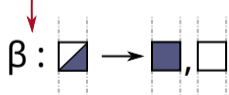
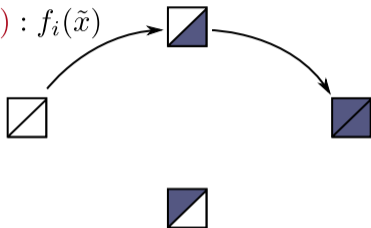
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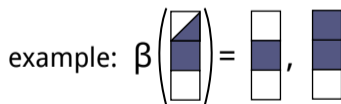
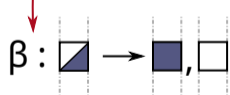
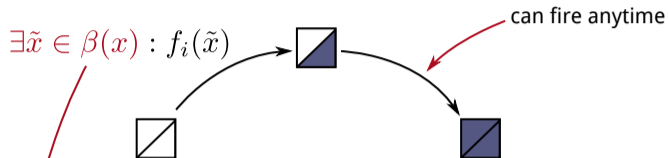
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Choose value of "changing" components
(act as choosing an activation threshold)

Most permissive semantics

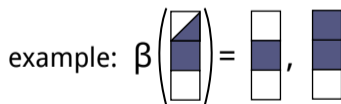
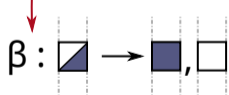
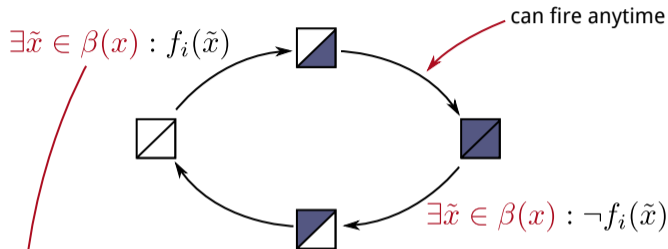
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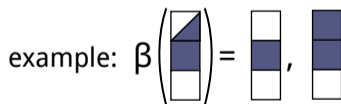
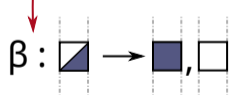
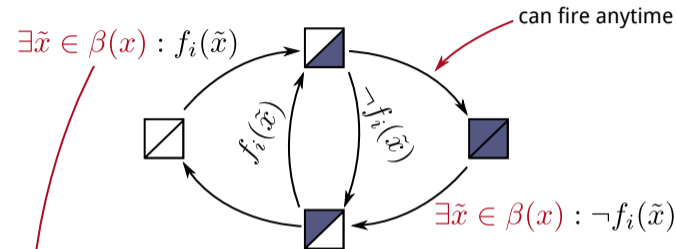
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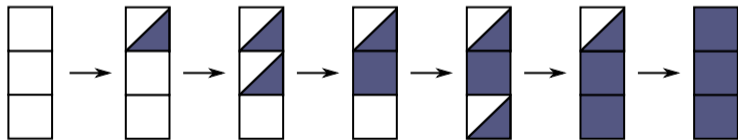
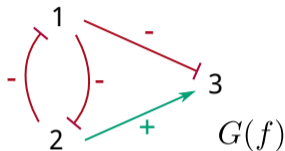
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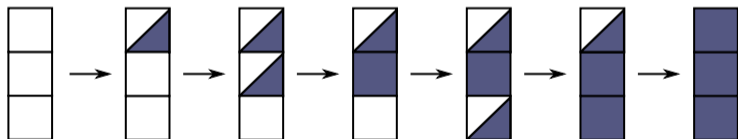
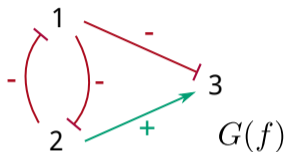


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\Rightarrow valid with respect to multivalued refinements

Properties of the most permissive semantics

Correct abstraction of multilevel/quantitative systems:

- includes all the **transitions of every update mode**
- multilevel **refinements only remove behaviours**

- **Reachability** (configuration y is reachable from x):
 - ⇒ comput. in **quadratic time** (instead of PSPACE-complete)
 - ⇒ **no need for simulations / model-checking / ...**
 - ⇒ should be scalable to thousands of components

- **Attractors are hypercubes** (minimal trap spaces)
 - ⇒ finding **attractors is in NP** (instead of PSPACE-complete)

Conclusion

Update modes of Boolean networks (sync, async, etc.):

- can **miss important behaviours** [CHP at AUTOMATA'18]
- ⇒ lead to **reject valid models** of biological systems...
- have limited tractability (model-checking, ...)

Most permissive semantics:

- **correct abstraction**: guarantees that adding information (multilevel, thresholds) will only remove behaviours
- **simpler complexity**: reachability PTIME, attractors NP
- ⇒ higher tractability

Future work: software tool, paper (report available)