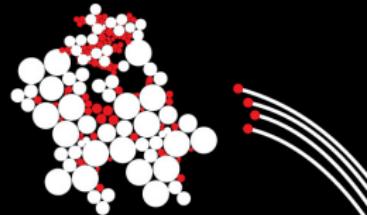


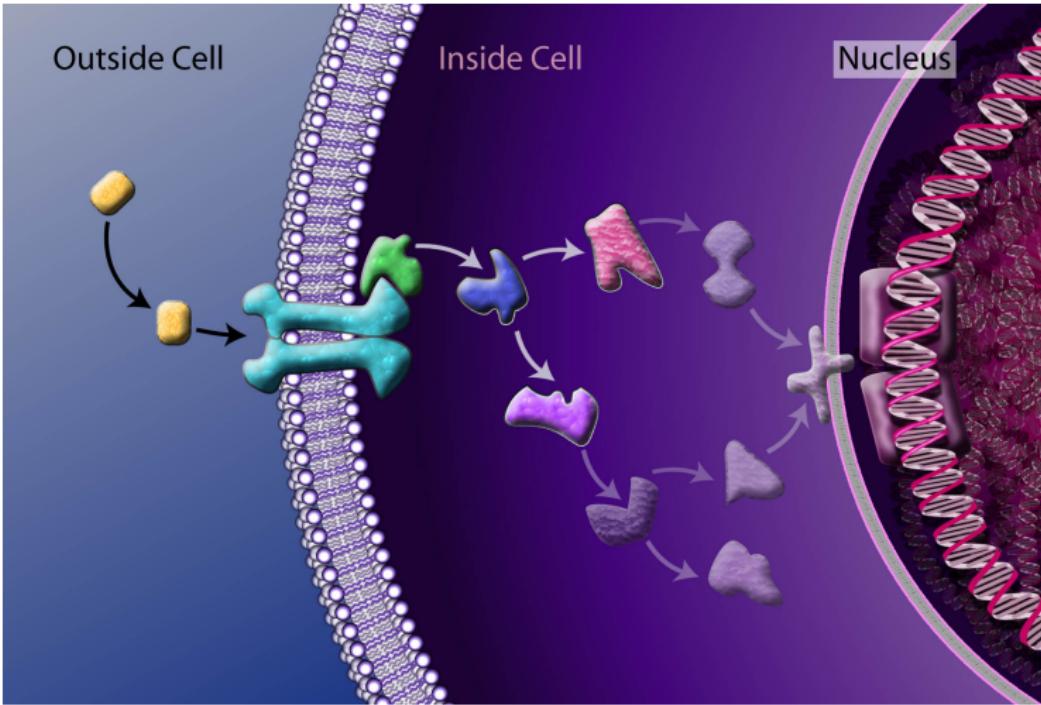
Setting parameters for biological models with ANIMO

Stefano Schivo, Jetse Scholma,
Marcel Karperien, Janine N. Post,
Jaco van de Pol, Rom Langerak

University of Twente,
Enschede, The Netherlands
SynCoP 2014

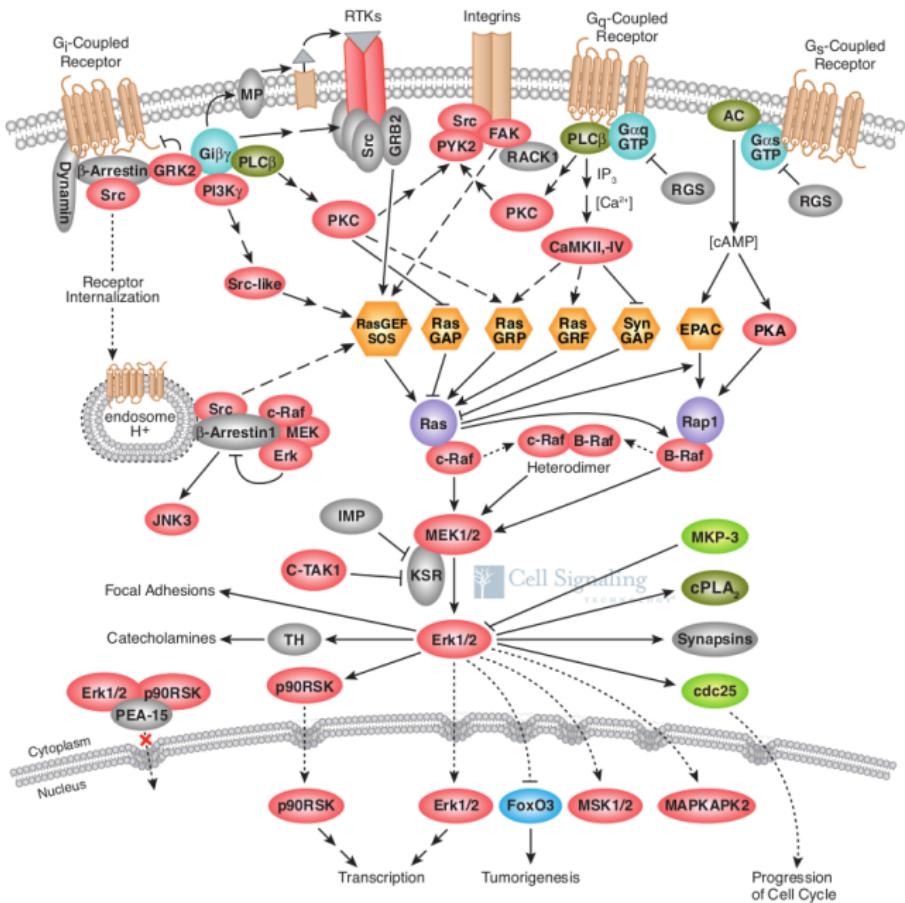


Signalling Pathways



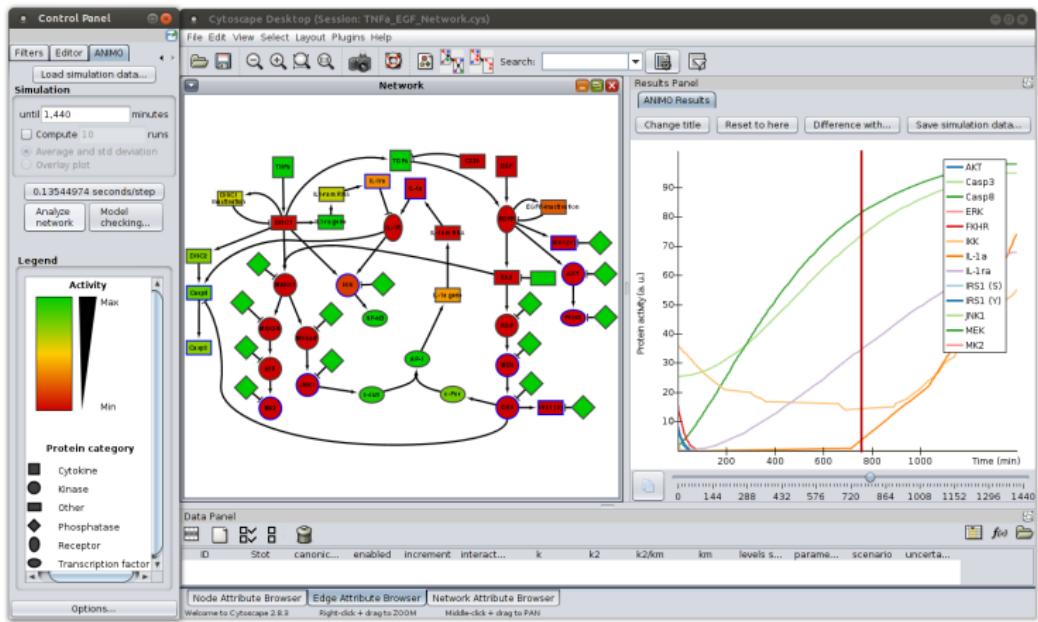
Credit: National Science Foundation

G-Protein Coupled Receptor Signaling to MAPK/ERK

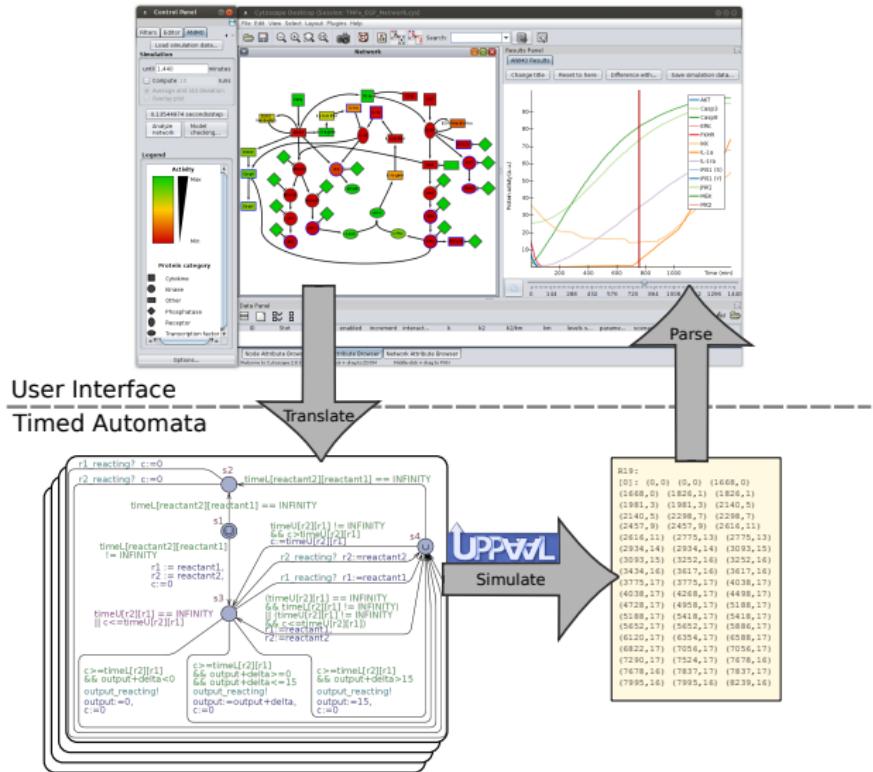


Analysis of Networks with Interactive MOdelling

► Interaction based



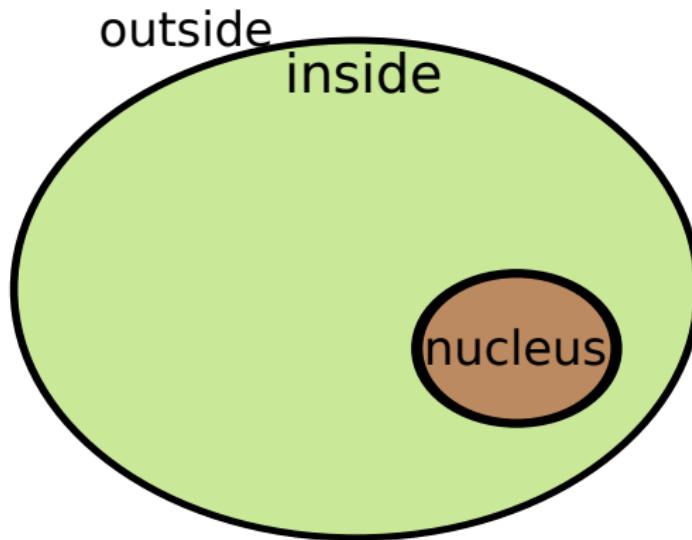
Analysis of Networks with Interactive MOdelling



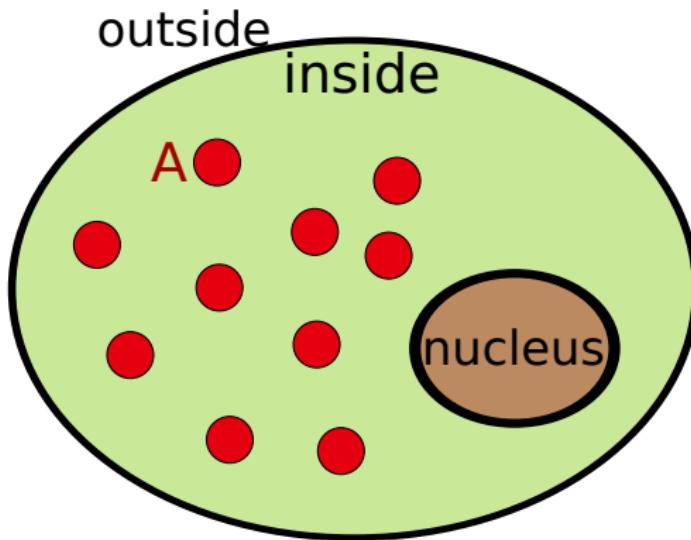
Analysis of Networks with Interactive MOdelling

- ▶ Interaction based
- ▶ Discrete concentration/activity levels

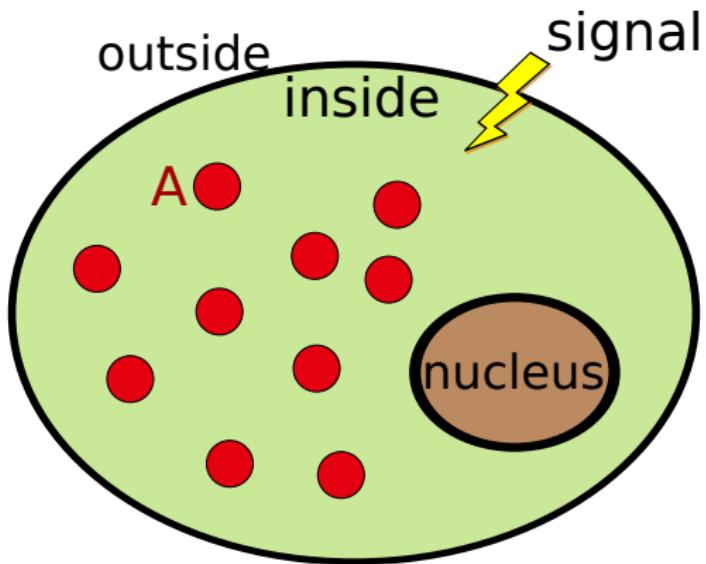
Discrete activity levels



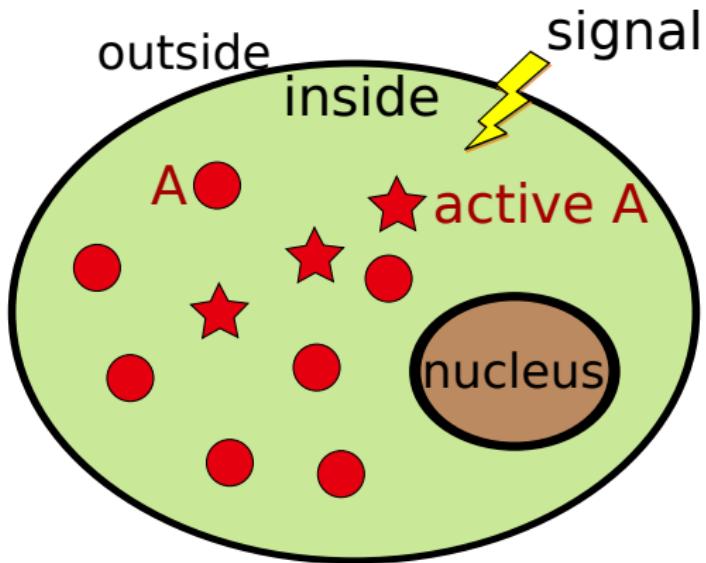
Discrete activity levels



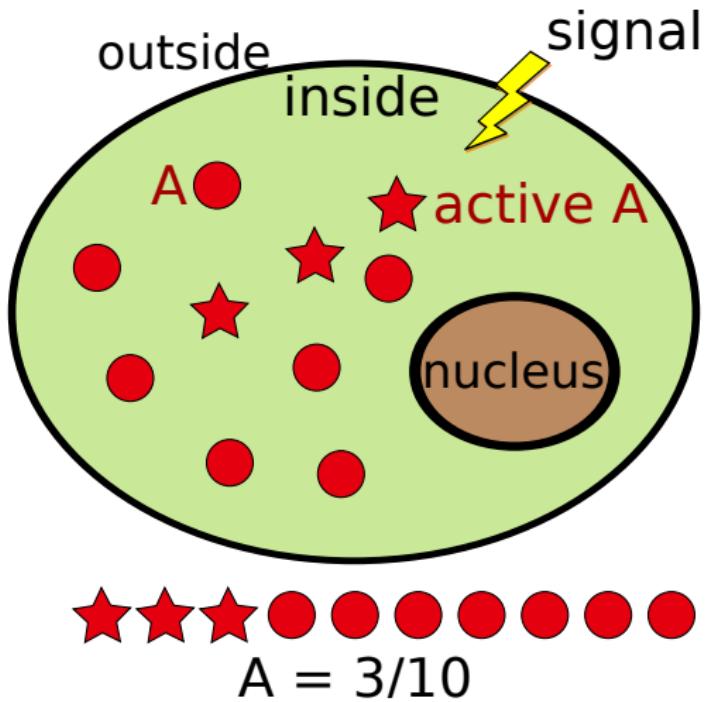
Discrete activity levels



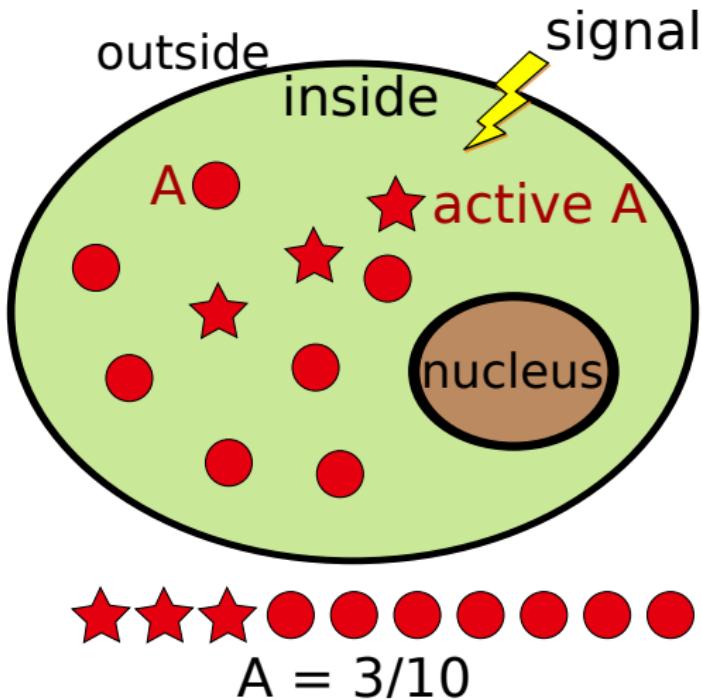
Discrete activity levels



Discrete activity levels



Discrete activity levels



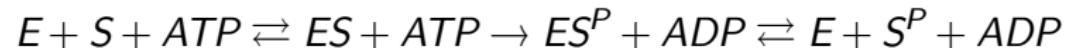
Let the user choose granularity: 2 - 100 discrete levels

Analysis of Networks with Interactive MOdelling

- ▶ Interaction based
- ▶ Discrete concentration/activity levels
- ▶ Precise reactions ⇒ abstract *interactions*

Analysis of Networks with Interactive MOdelling

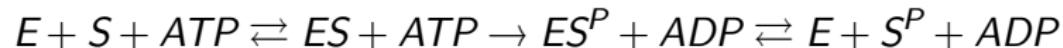
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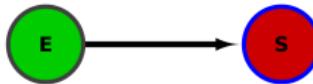
(with $S + S^P = \text{constant}$ and $ATP + ADP = \text{constant}$)

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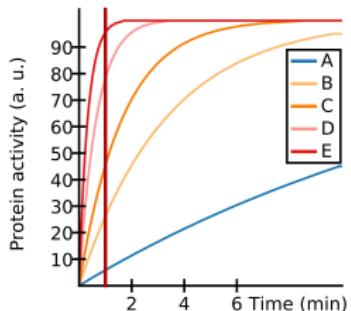
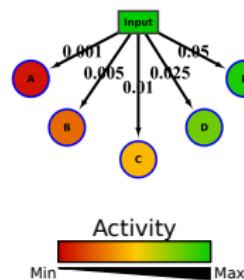
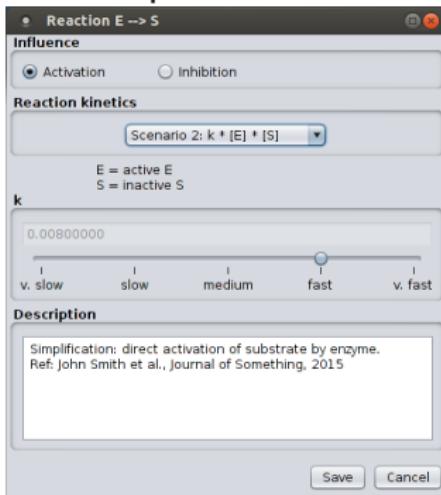


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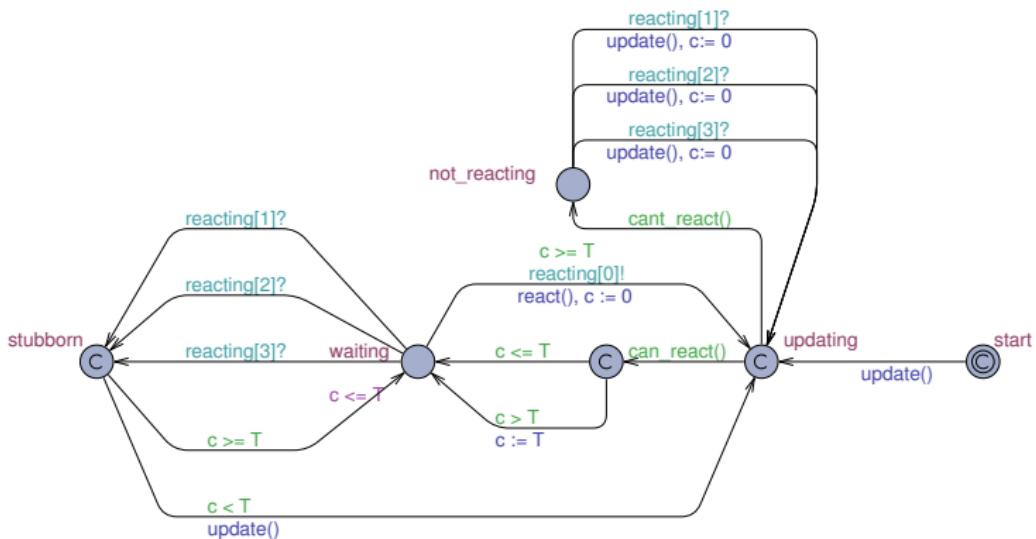


Analysis of Networks with Interactive MOdelling

- ▶ Interaction based
- ▶ Discrete concentration/activity levels
- ▶ Precise reactions ⇒ abstract *interactions*
- ▶ Simplified scenarios for rate computation

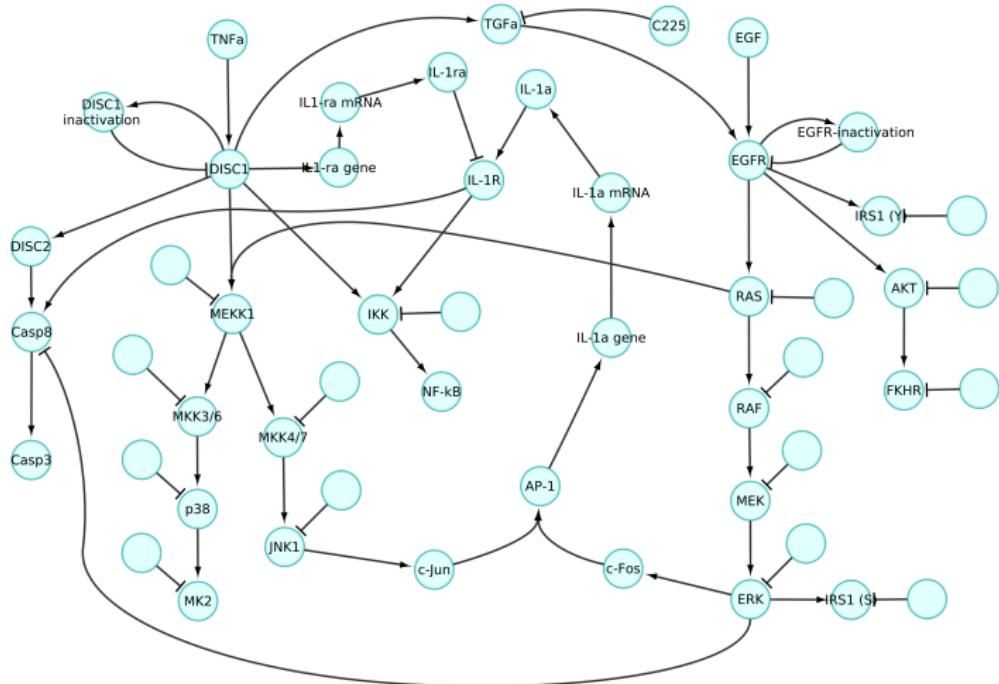


Timed Automata model



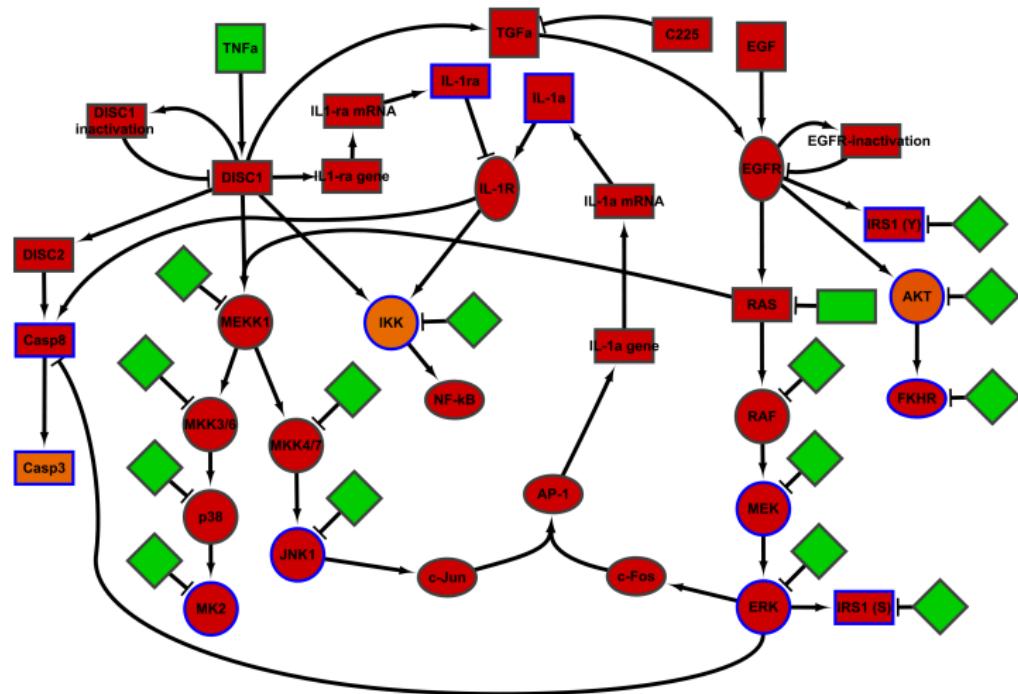
ANIMO workflow

Start from static network topology



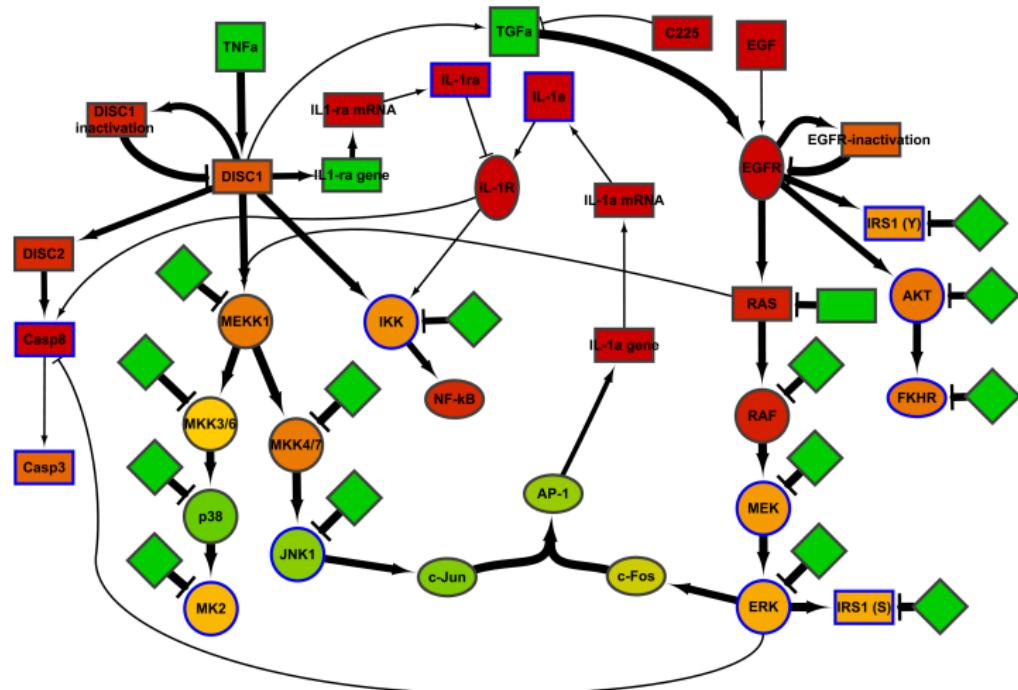
ANIMO workflow

Add kinetics and choose initial activities



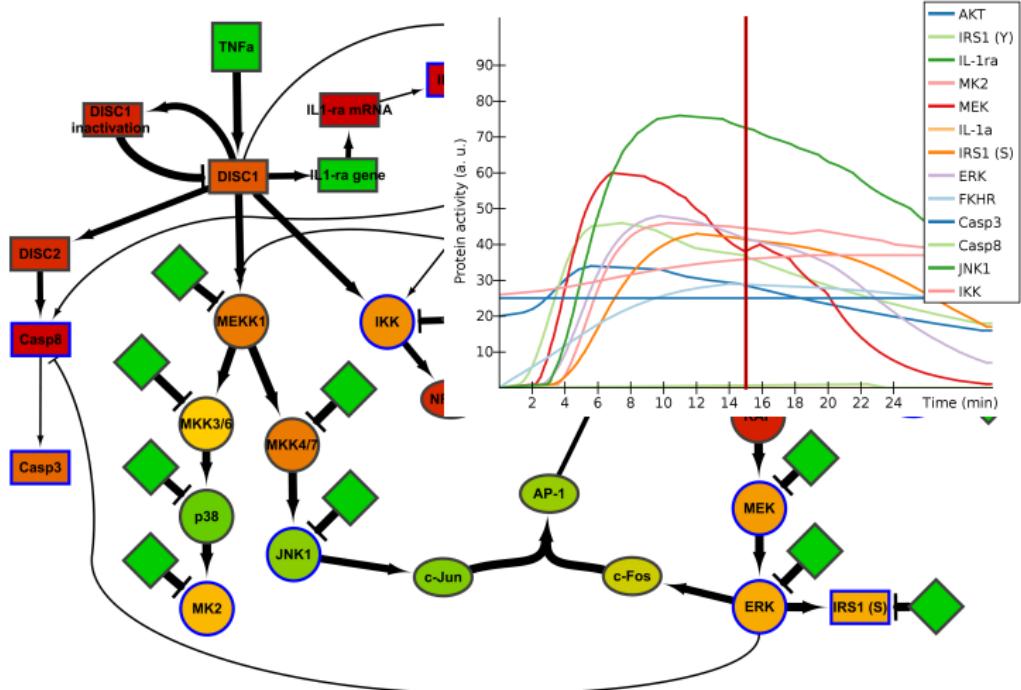
ANIMO workflow

Inspect system evolution on the fly



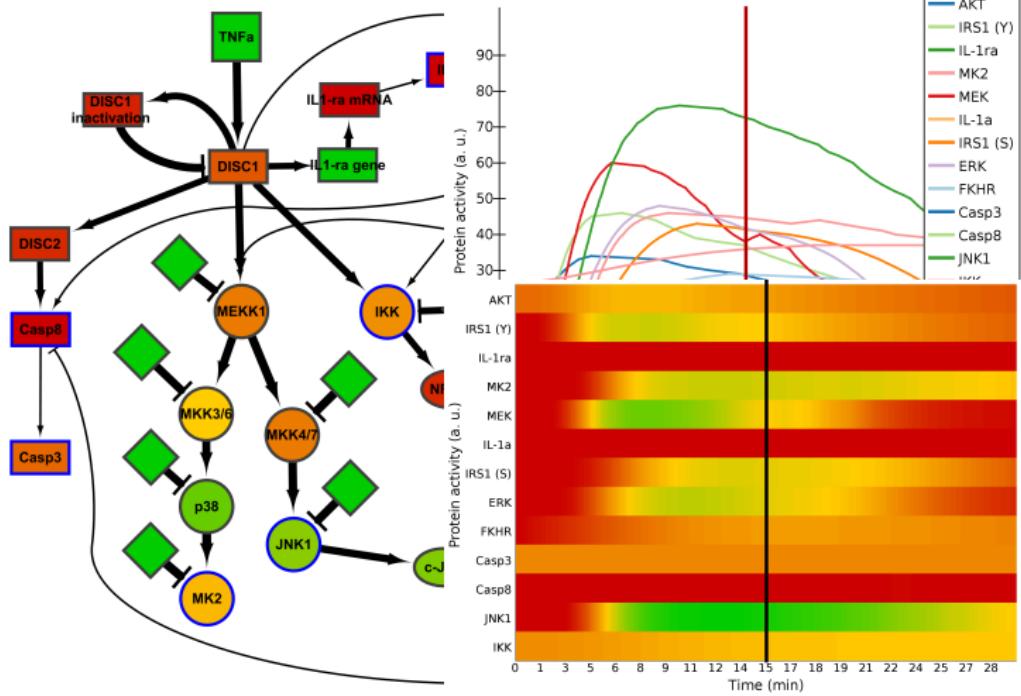
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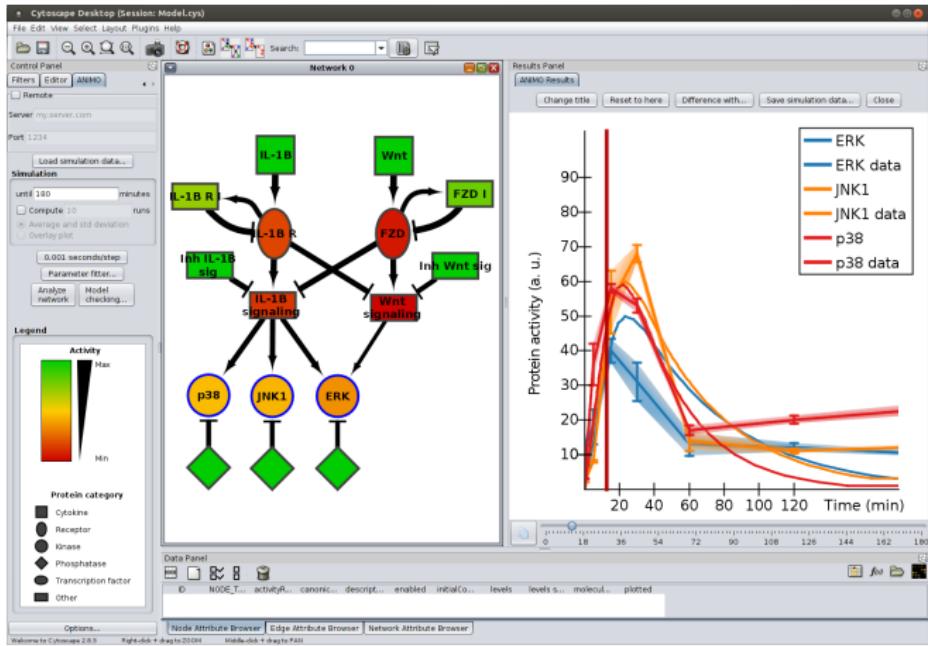


ANIMO workflow

Inspect system evolution on the fly



Experimental data as reference



Use data and model to improve knowledge, generate hypotheses.

All good and nice, but...

How to find the parameters?

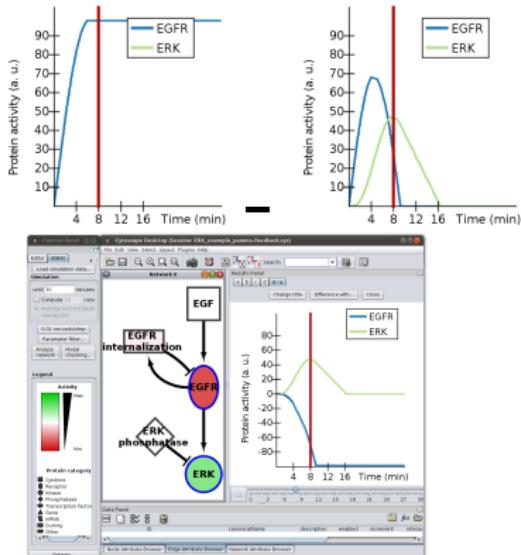
- ▶ Insert parameters manually



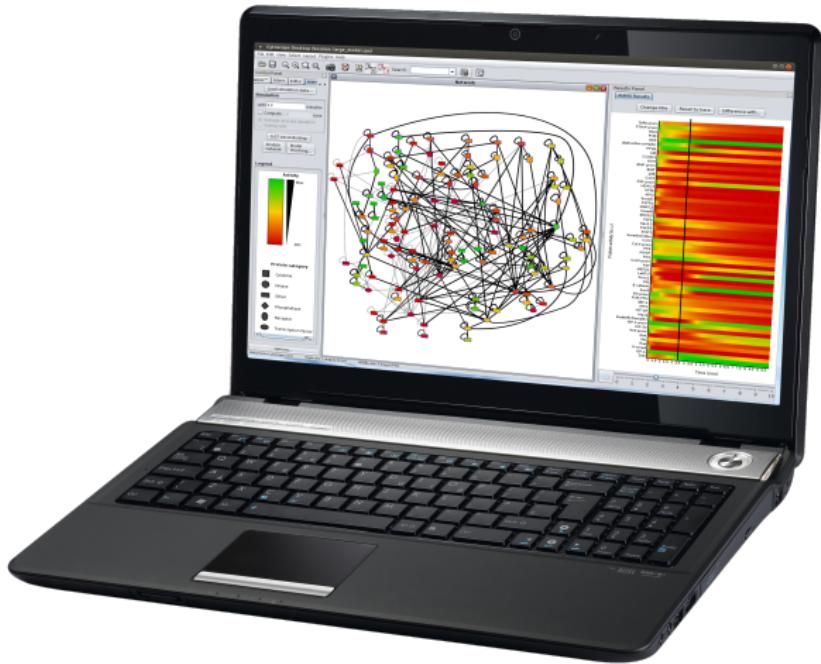
All good and nice, but...

How to find the parameters?

- ▶ Insert parameters manually
- ▶ Compare model versions *subtracting* their activity graphs



ANIMO live demo



Conclusions

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Timed Automata → dynamic behaviour

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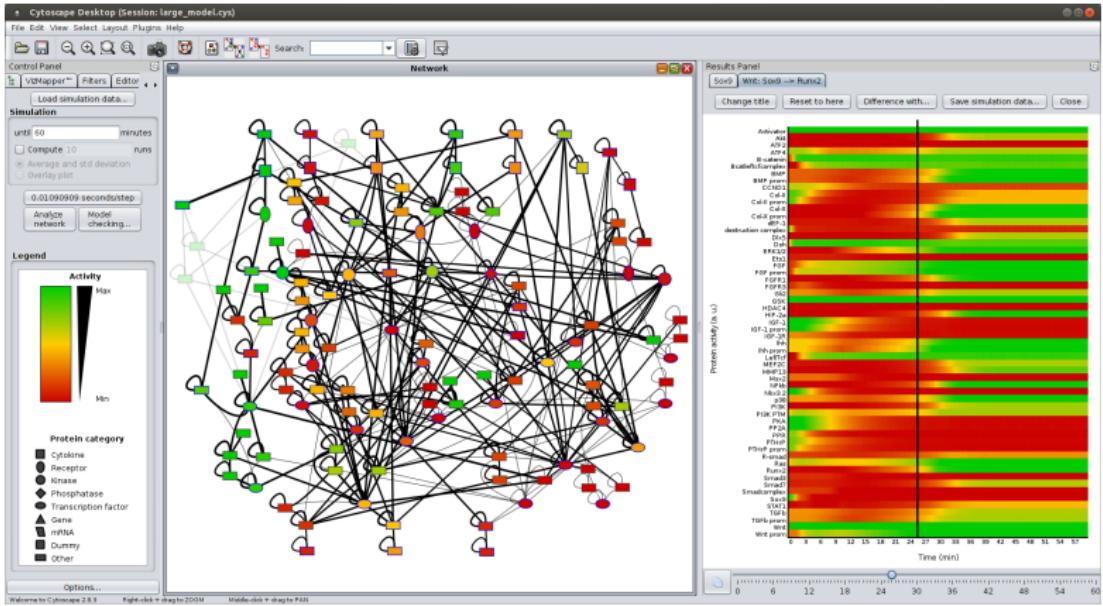
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- ▶ Complex models:
 - ▶ perform *in silico* experiments
 - ▶ use model checking

Future work

- ▶ Use *in-silico experiments* to infer biological hypotheses which can be verified through in-vitro experiments



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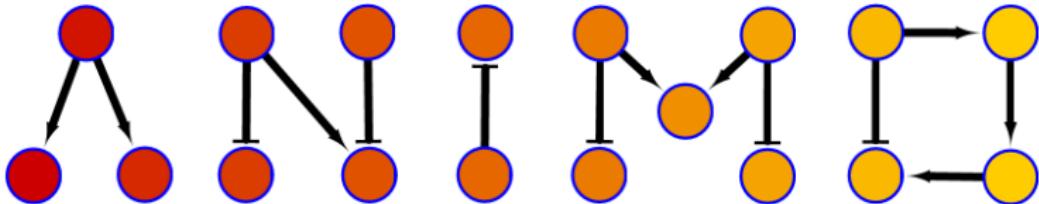
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Thank you



Analysis of Networks with Interactive MOdelling

<http://fmt.cs.utwente.nl/tools/animo>

