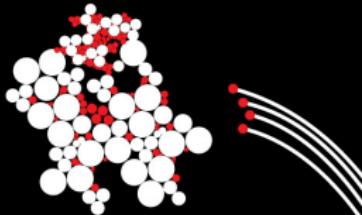


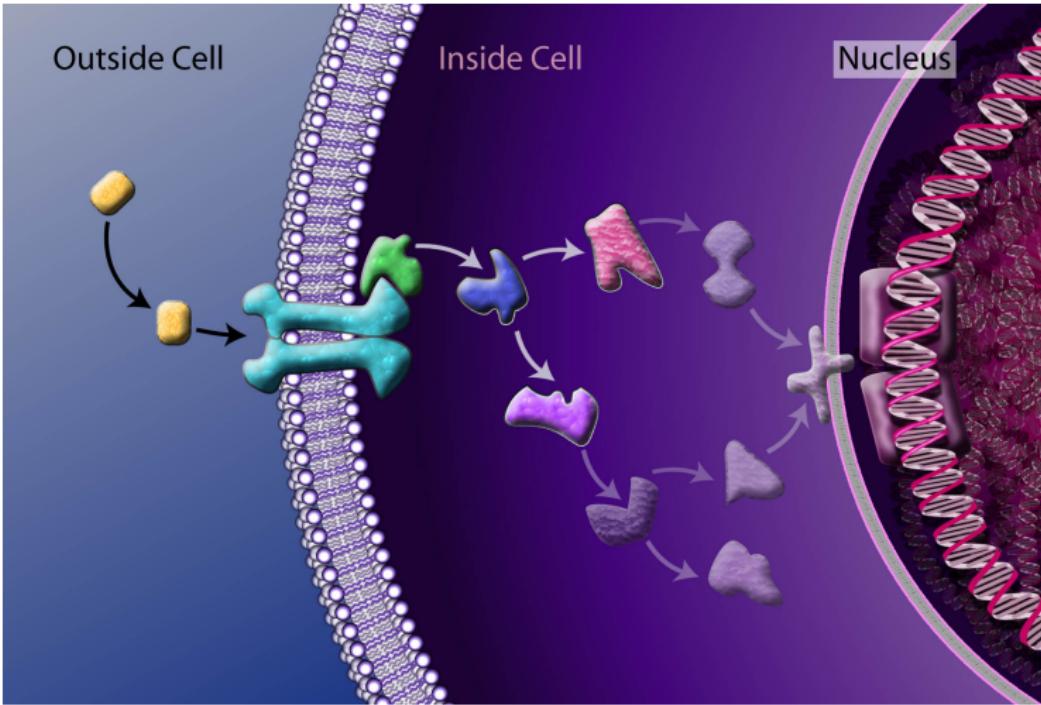
Setting parameters for biological models with ANIMO

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

University of Twente,
Enschede, The Netherlands
SynCoP 2014

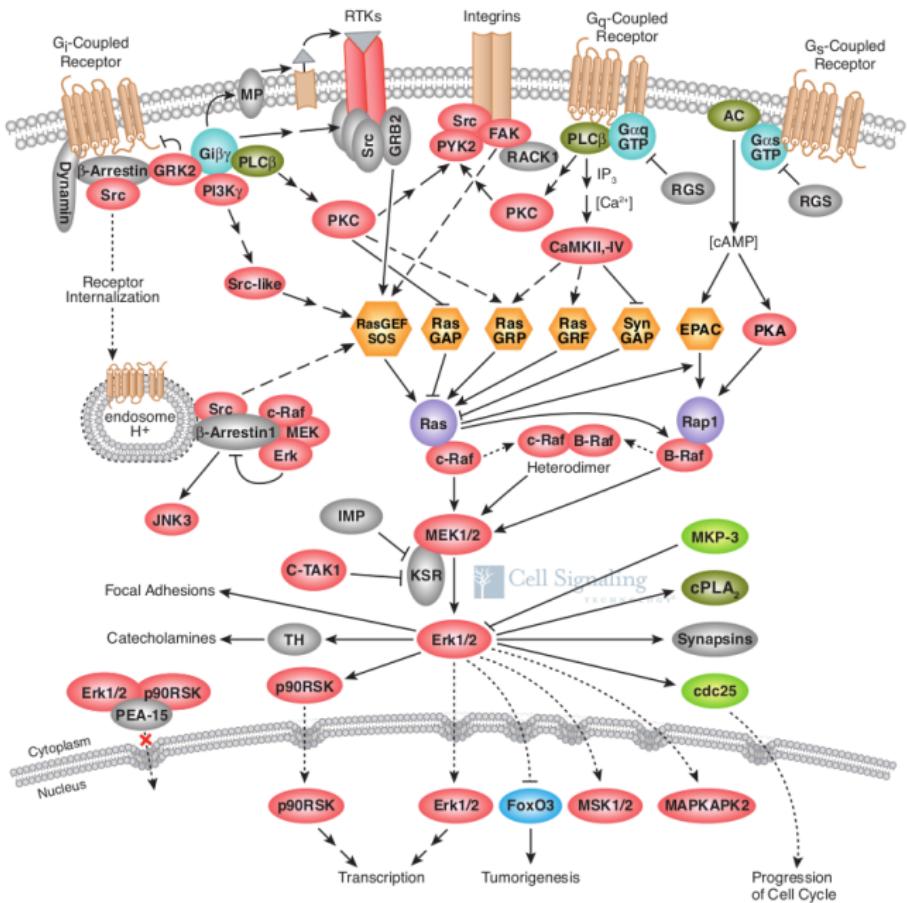


Signalling Pathways



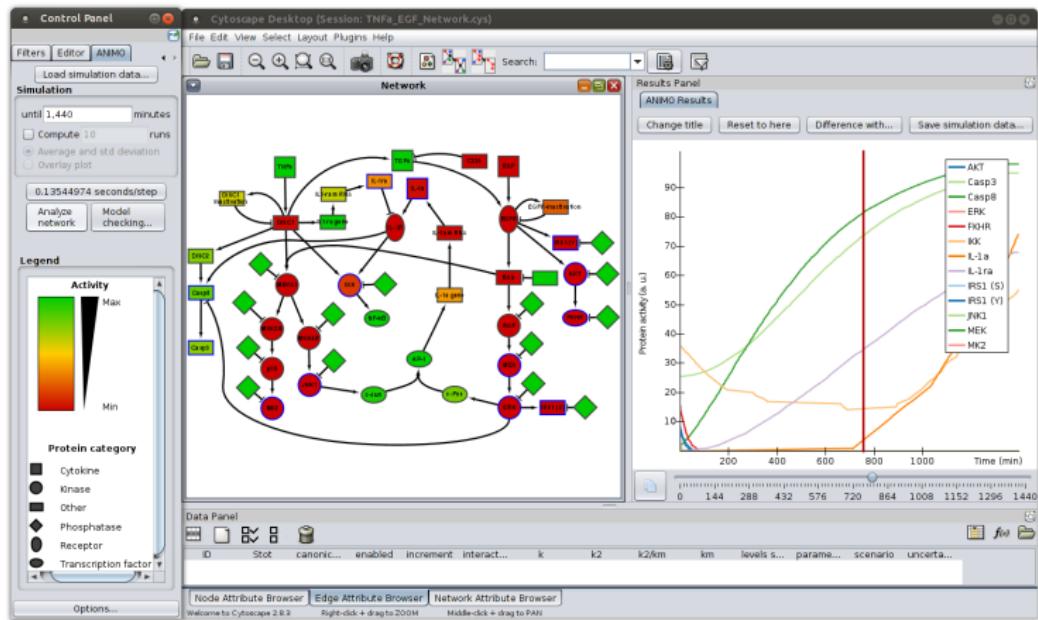
Credit: National Science Foundation

G-Protein Coupled Receptor Signaling to MAPK/ERK

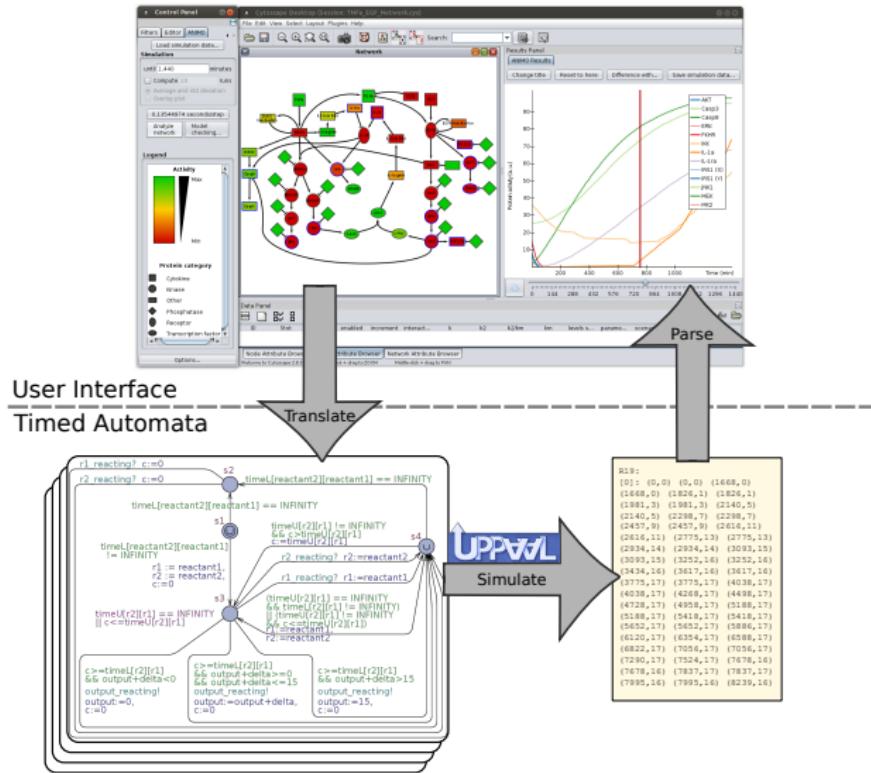


Analysis of Networks with Interactive MOdelling

► Interaction based



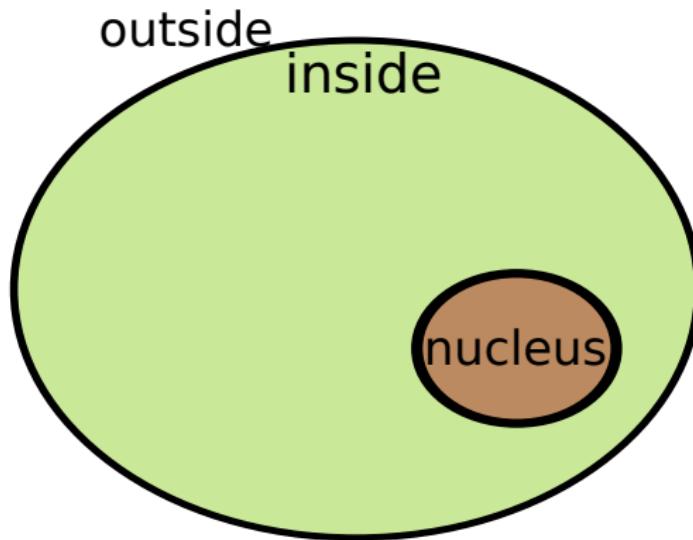
Analysis of Networks with Interactive MOdelling



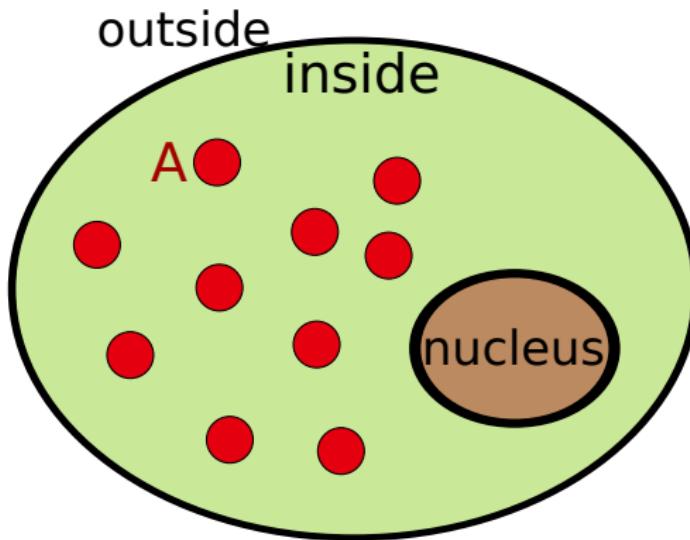
Analysis of Networks with Interactive MOdelling

- ▶ Interaction based
- ▶ Discrete concentration/activity levels

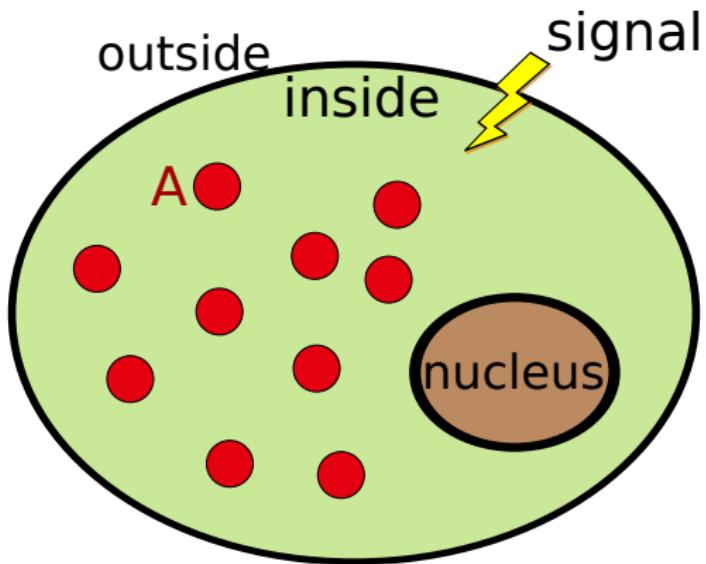
Discrete activity levels



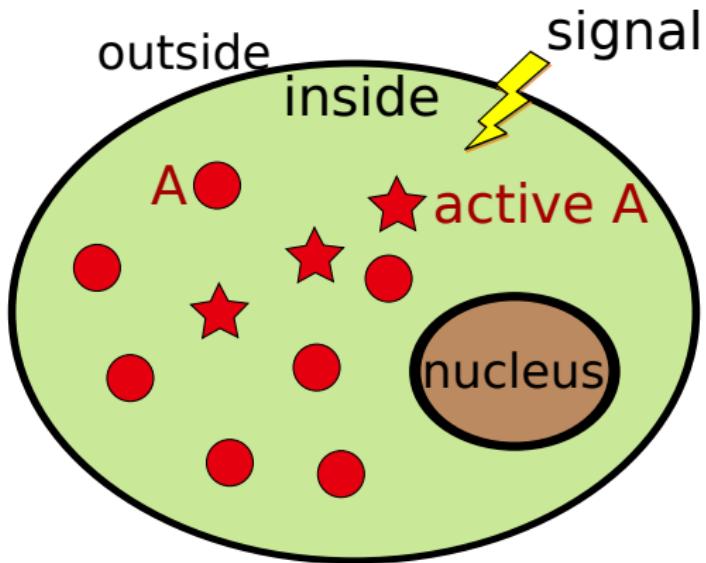
Discrete activity levels



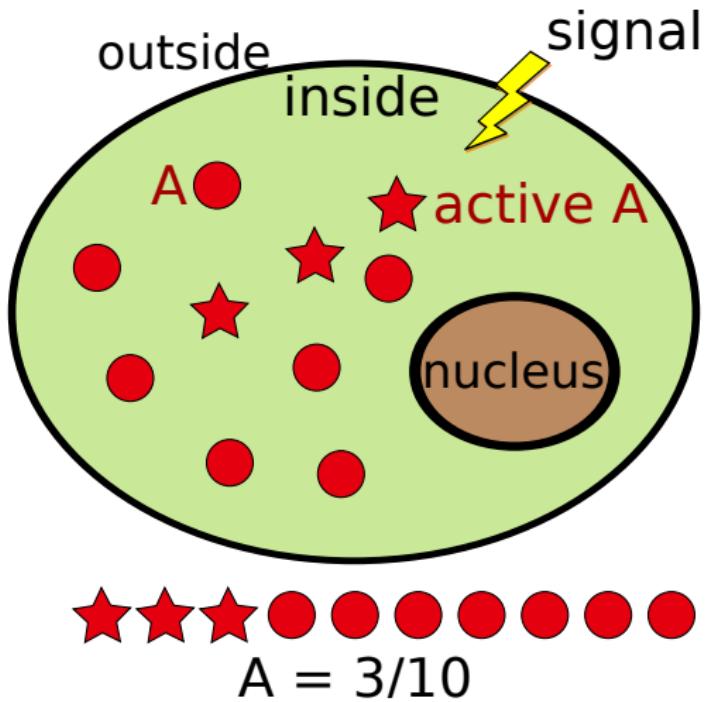
Discrete activity levels



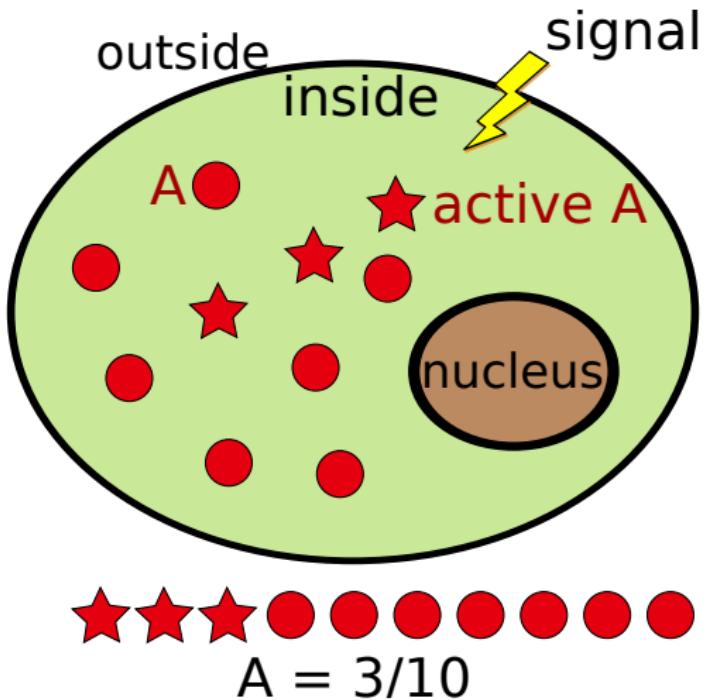
Discrete activity levels



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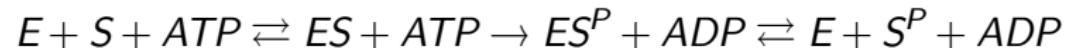
Let the user choose granularity: 2 - 100 discrete levels

Analysis of Networks with Interactive MOdelling

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

Analysis of Networks with Interactive MOdelling

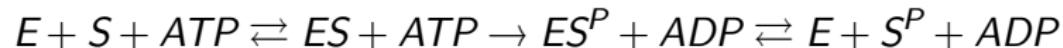
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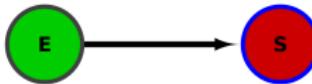
(with $S + S^P = \text{constant}$ and $ATP + ADP = \text{constant}$)

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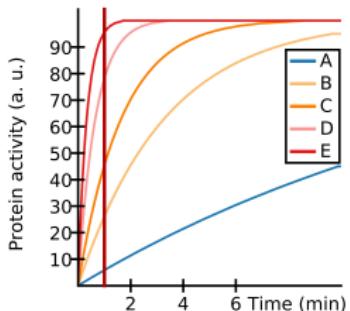
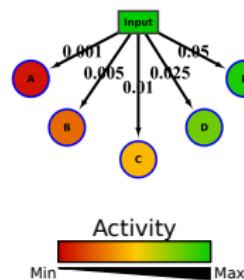
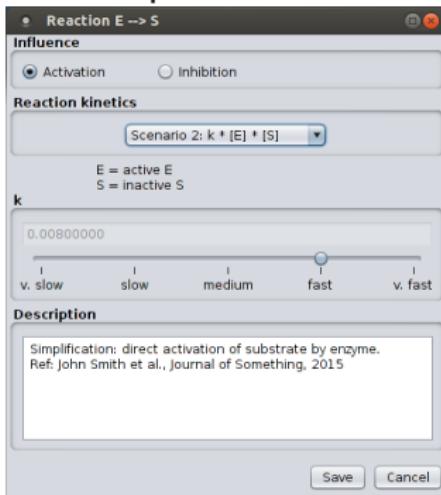


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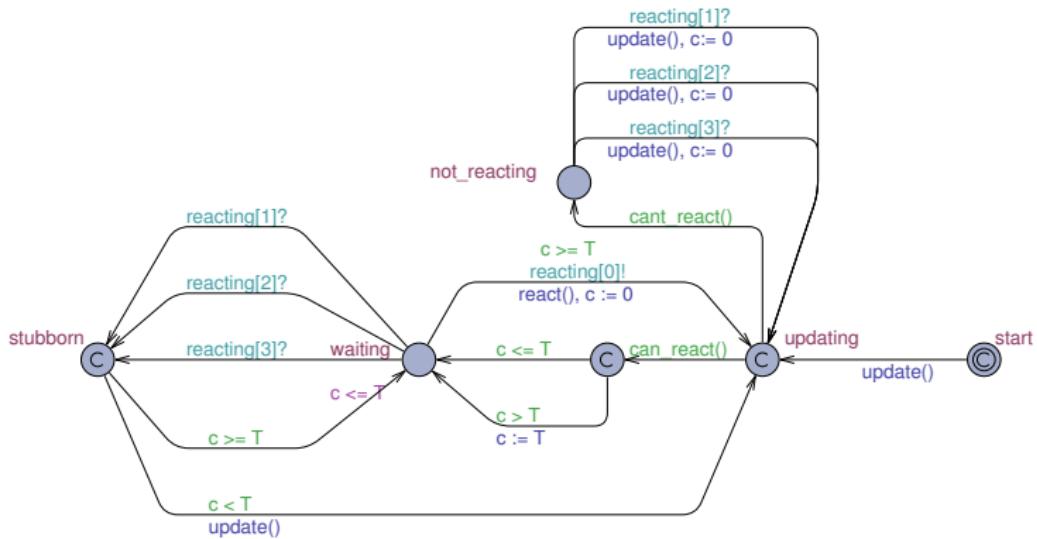


Analysis of Networks with Interactive MOdelling

- ▶ Interaction based
- ▶ Discrete concentration/activity levels
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- ▶ Simplified scenarios for rate computation

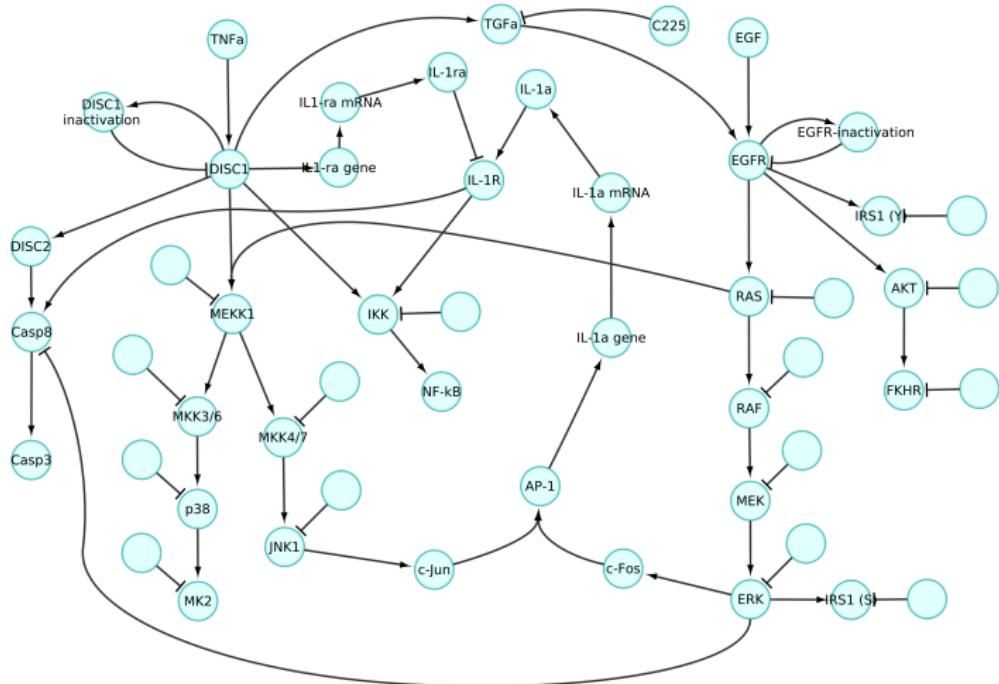


Timed Automata model



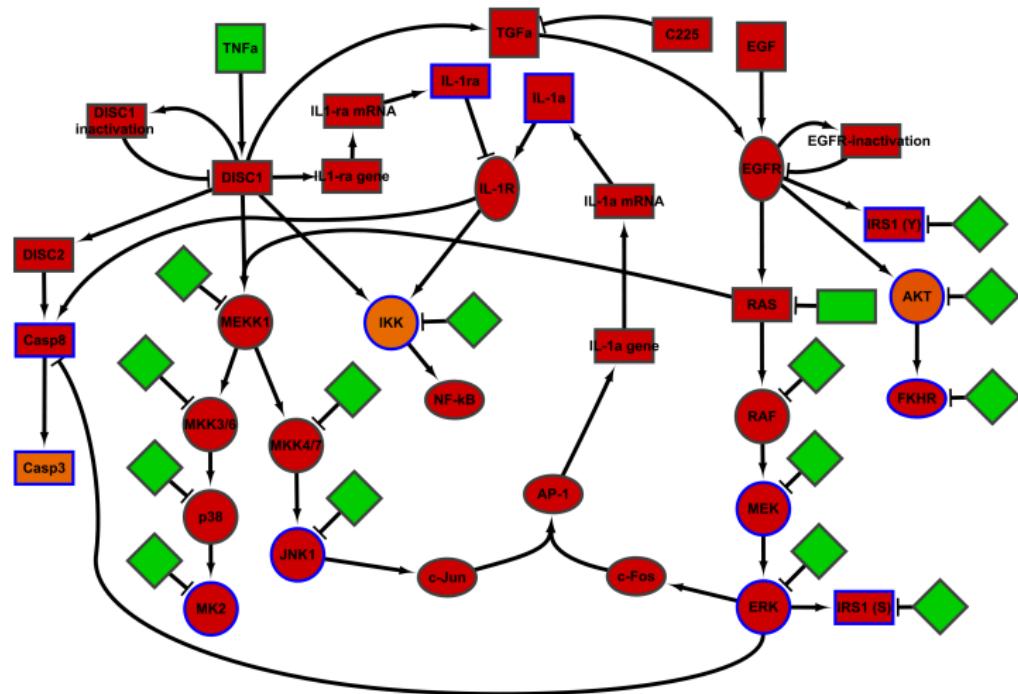
ANIMO workflow

Start from static network topology



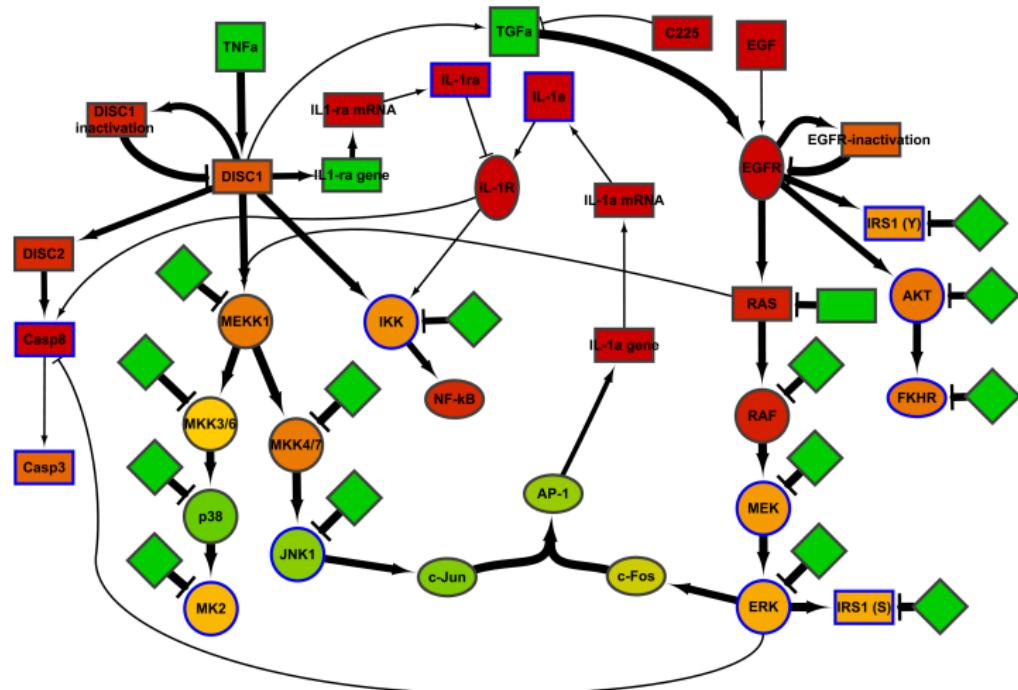
ANIMO workflow

Add kinetics and choose initial activities



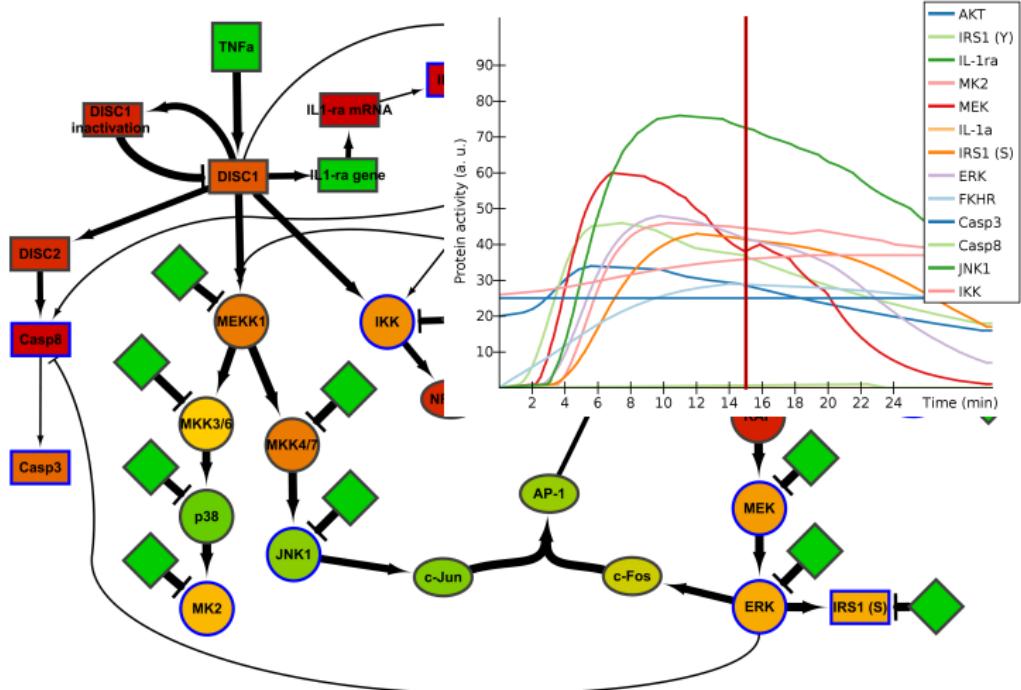
ANIMO workflow

Inspect system evolution on the fly



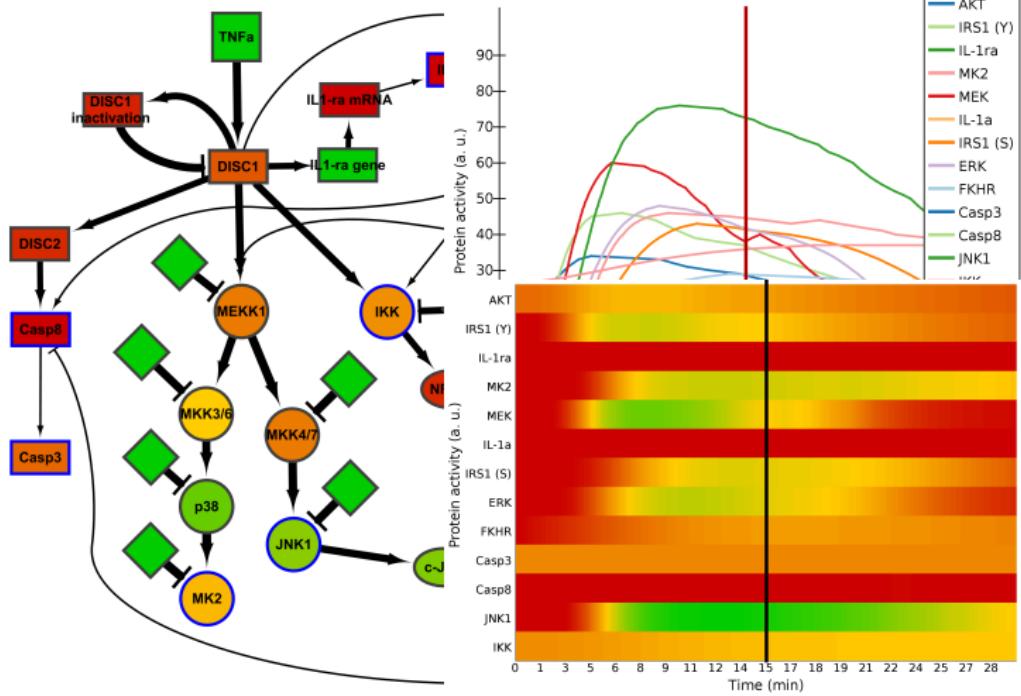
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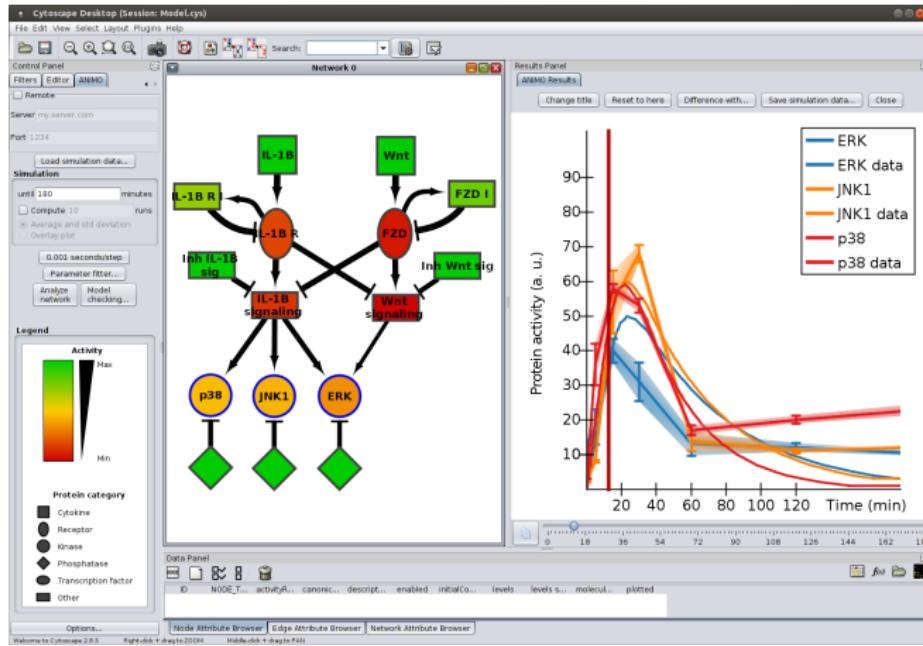


ANIMO workflow

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?

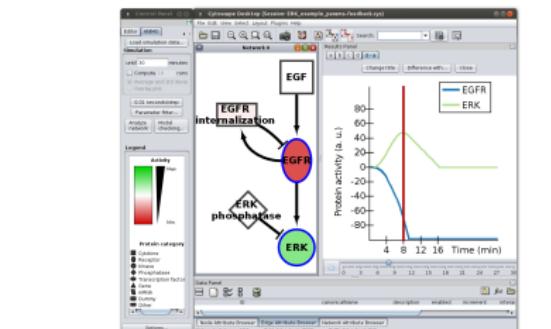
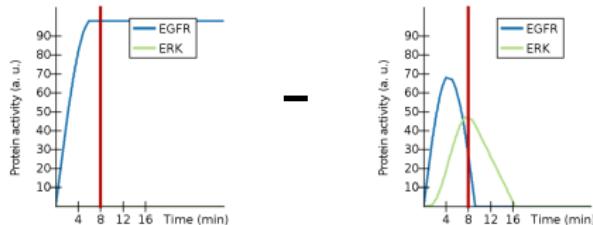
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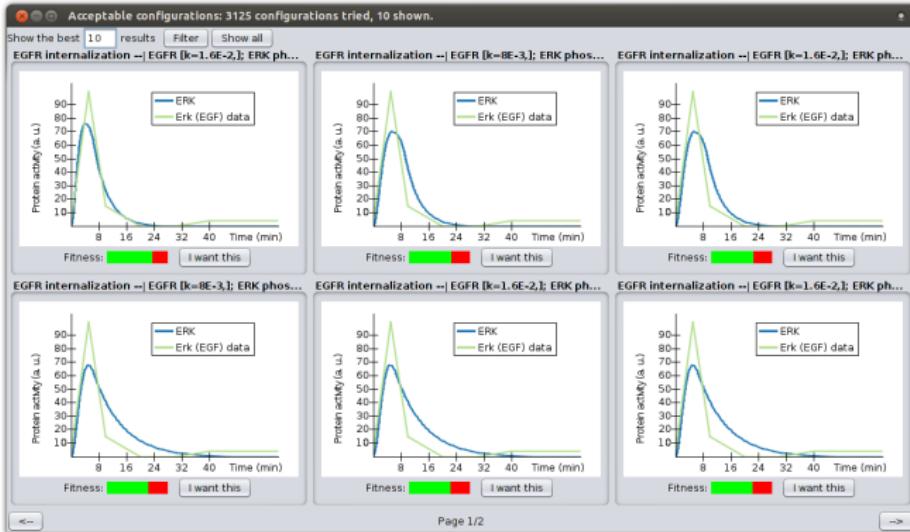
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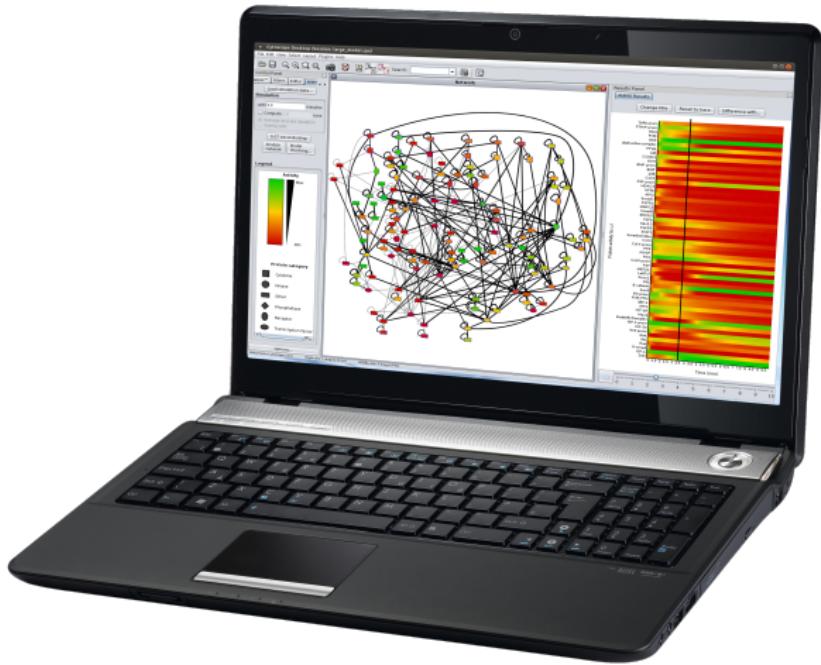
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How to find the parameters?

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- ▶ Compare model versions *subtracting* their activity graphs
- ▶ Perform automatic parameter scans



ANIMO live demo



Conclusions

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Timed Automata → dynamic behaviour

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- ▶ ANIMO allows biologists to draw network “sketches”
- ▶ Parameter choice:
 - ▶ manual settings, choice of qualitative parameters
 - ▶ comparison of different model versions
 - ▶ parameter sweeps

Future work

- ▶ Deal with parameter sensitivity and model *robustness*

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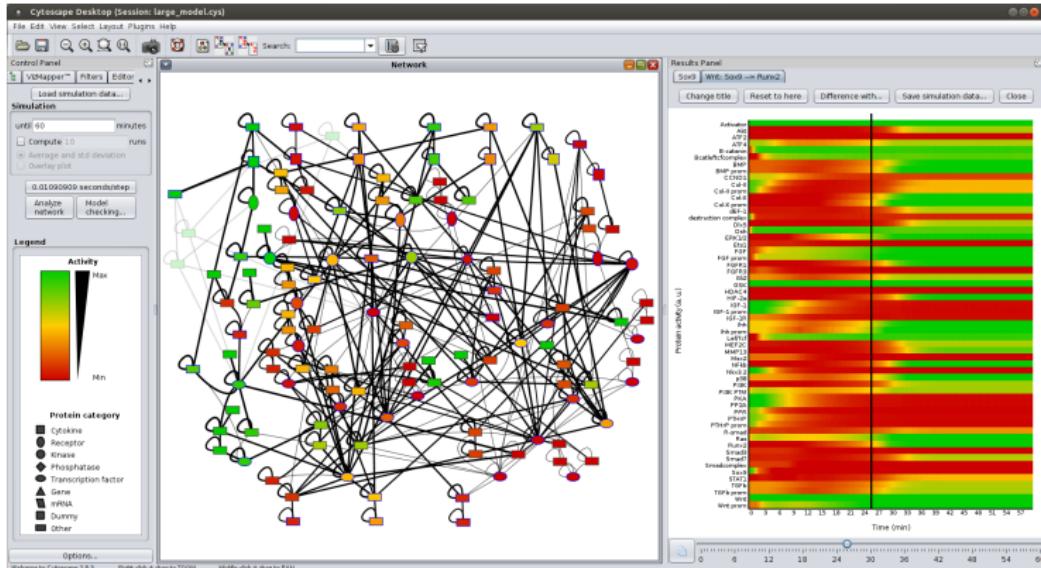
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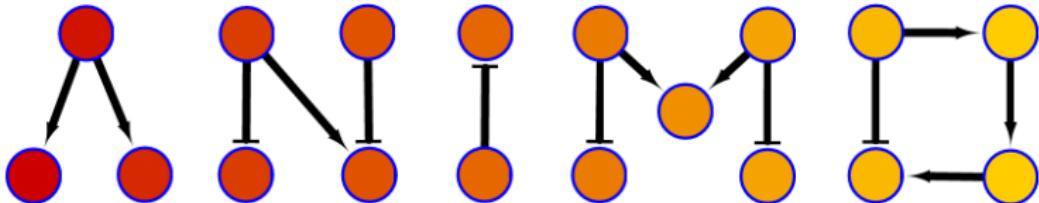
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- ▶ Get a model by feeding data: Automata Learning
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- ▶ Abstraction techniques to deal with large models

Thank you



Analysis of Networks with Interactive MOdelling

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

