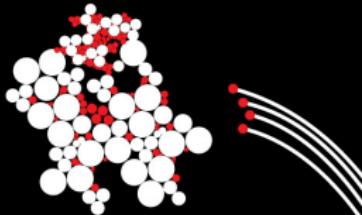


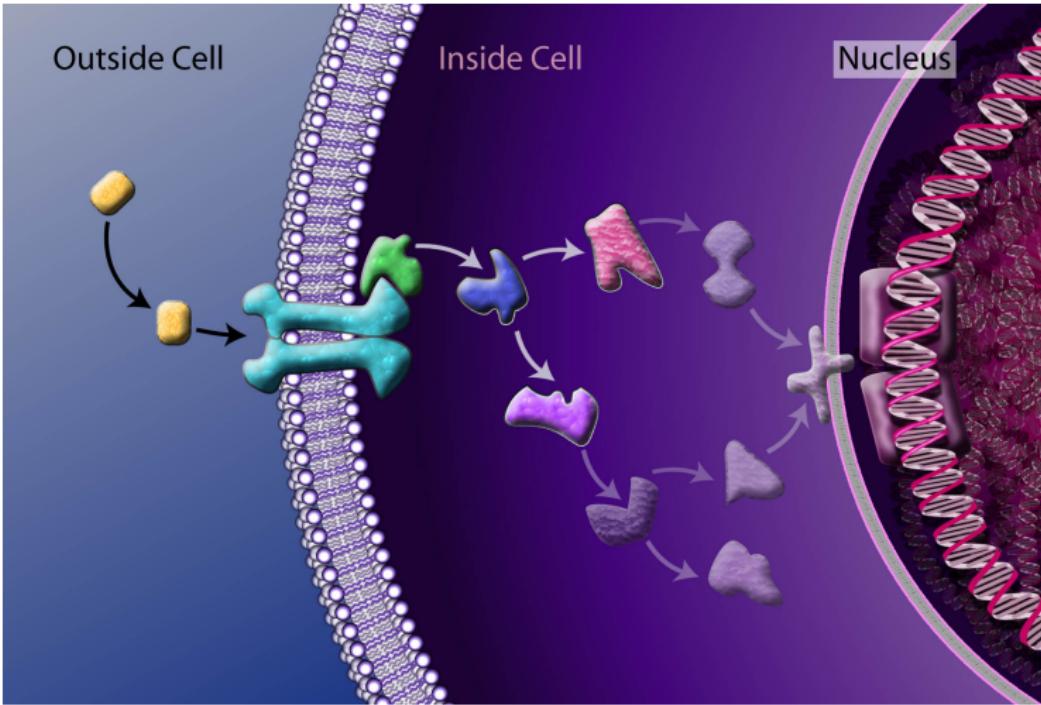
## Setting parameters for biological models with ANIMO

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

University of Twente,  
Enschede, The Netherlands  
SynCoP 2014

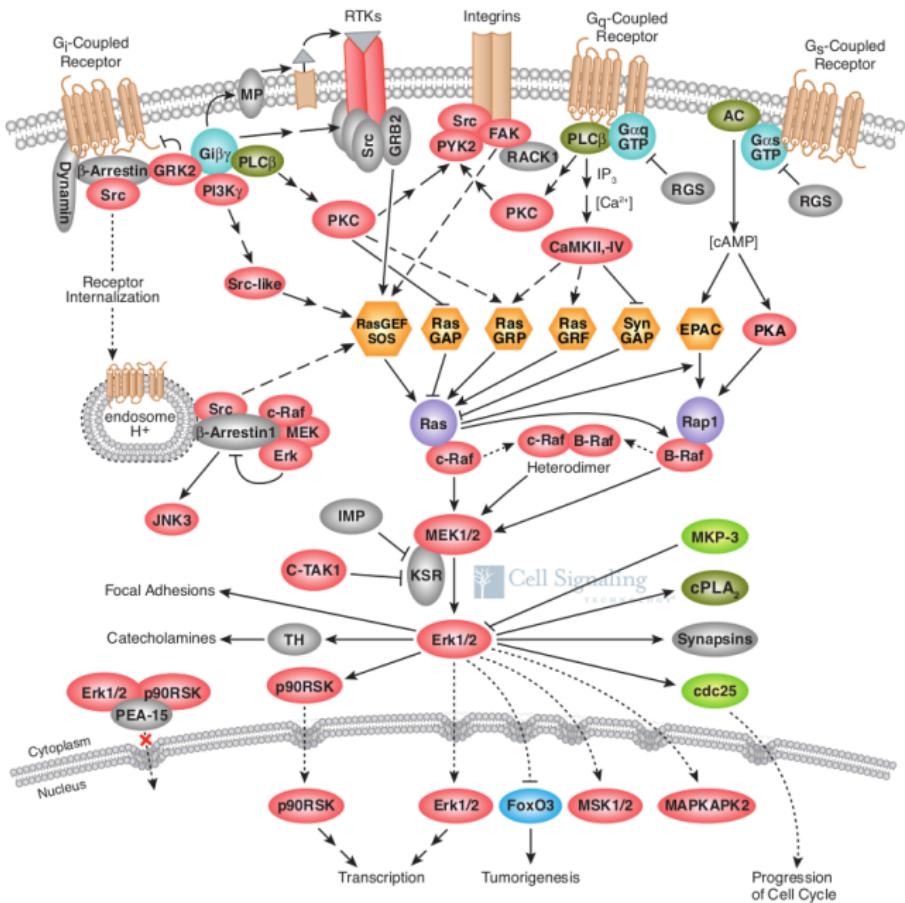


# Signalling Pathways



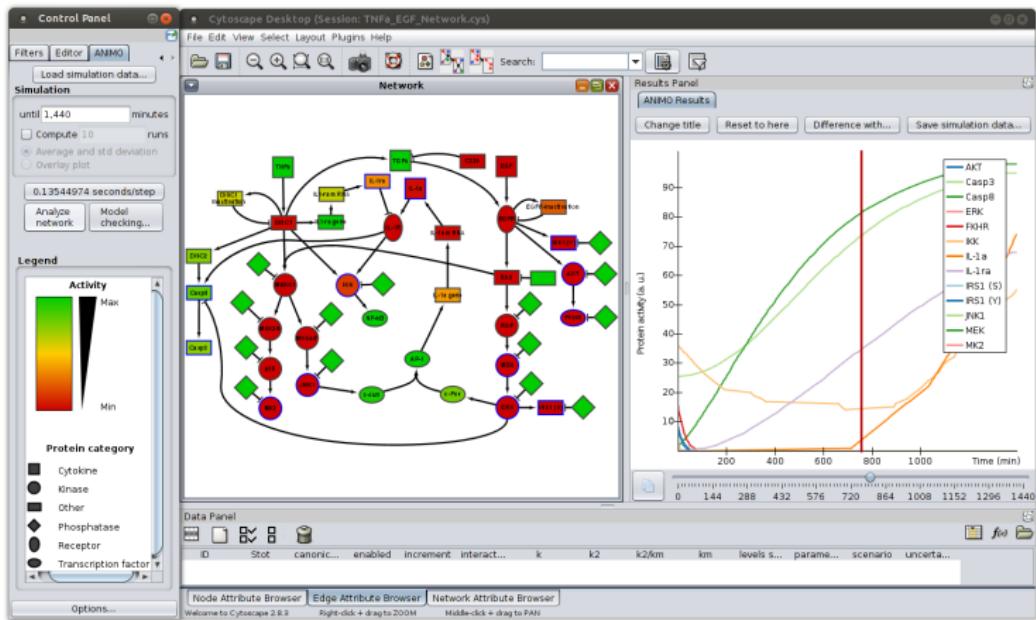
Credit: National Science Foundation

# G-Protein Coupled Receptor Signaling to MAPK/ERK

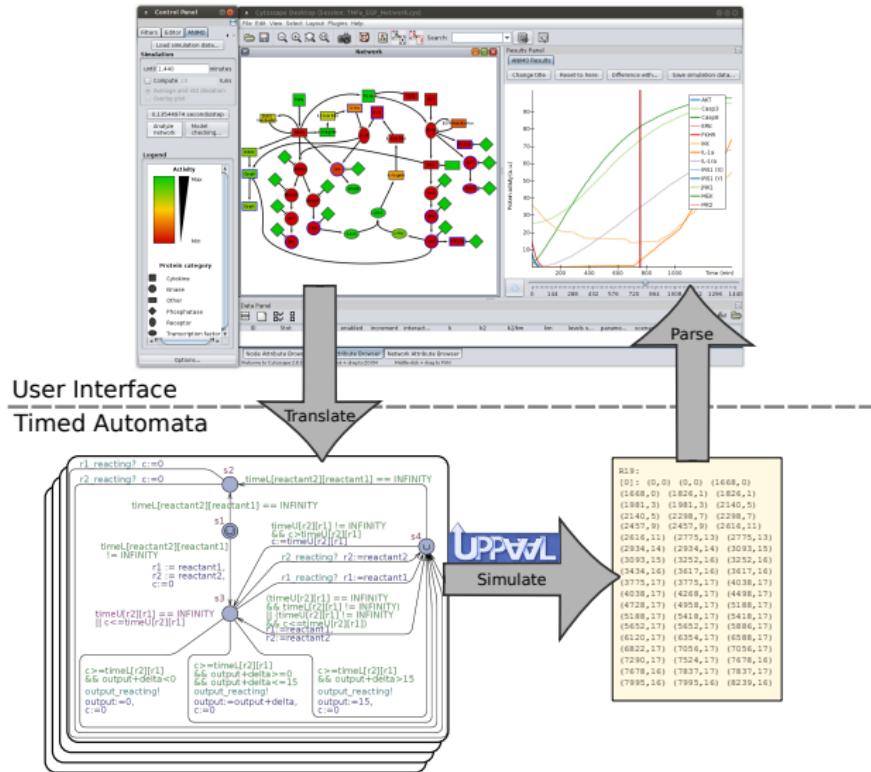


# Analysis of Networks with Interactive MOdelling

## ► Interaction based



# Analysis of Networks with Interactive MOdelling



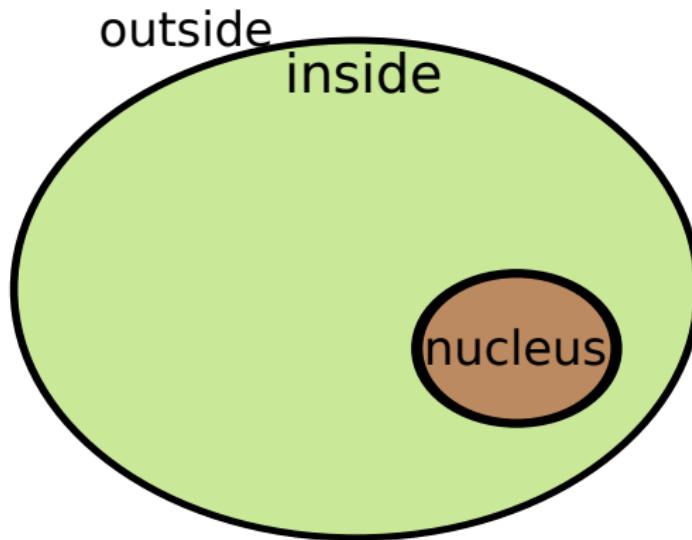
# Analysis of Networks with Interactive MOdelling

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- ▶ Interaction based
- ▶ Discrete concentration/activity levels

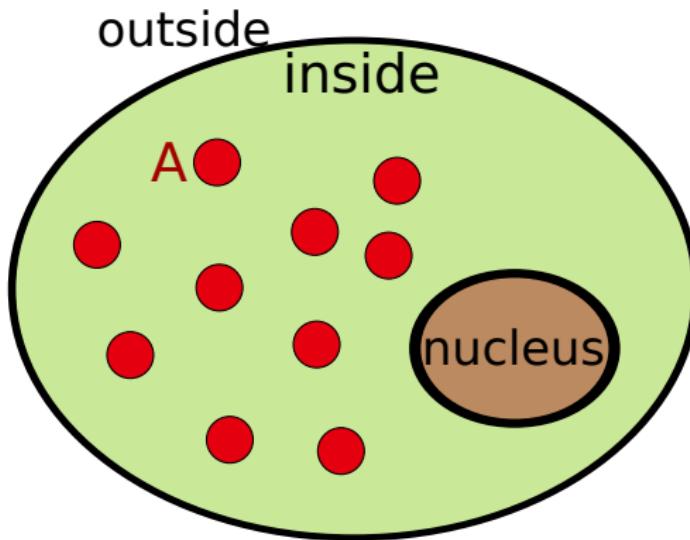
## Discrete activity levels

---



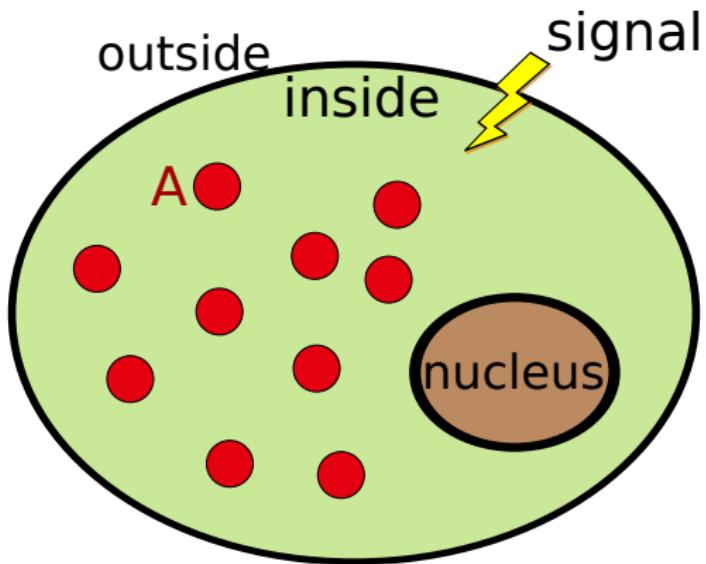
# Discrete activity levels

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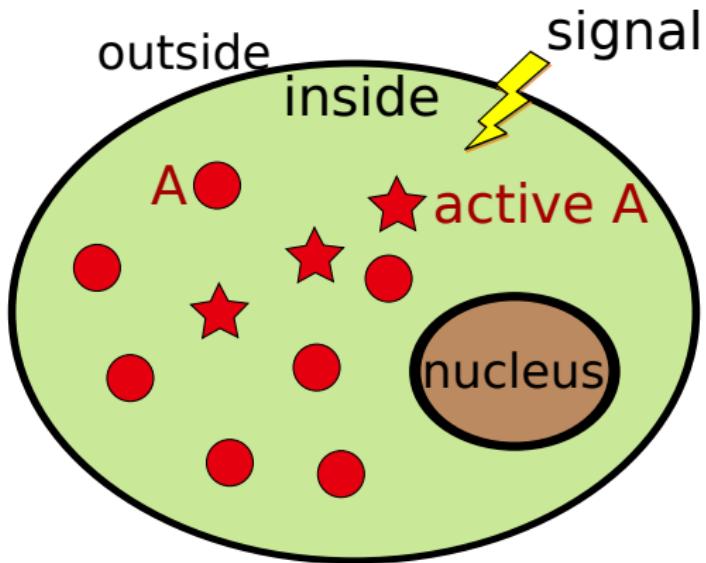
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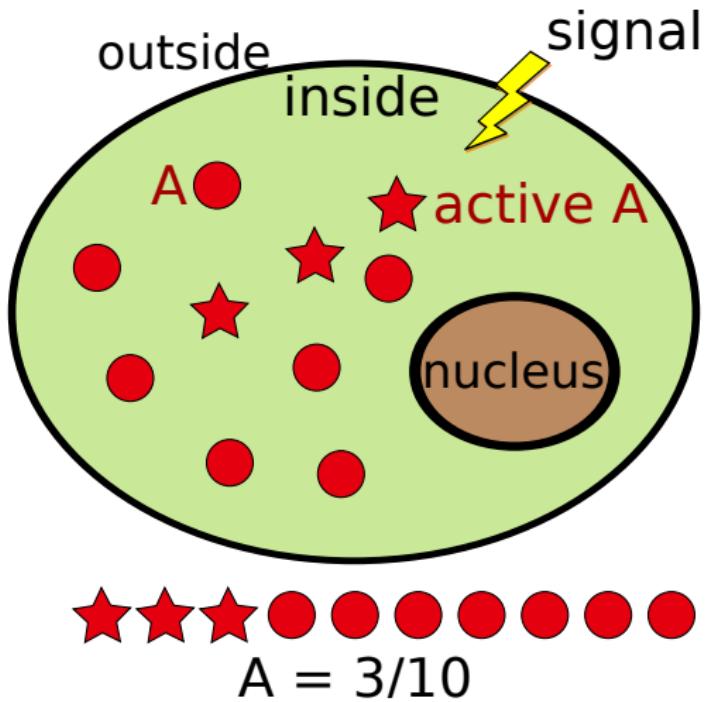


## Discrete activity levels

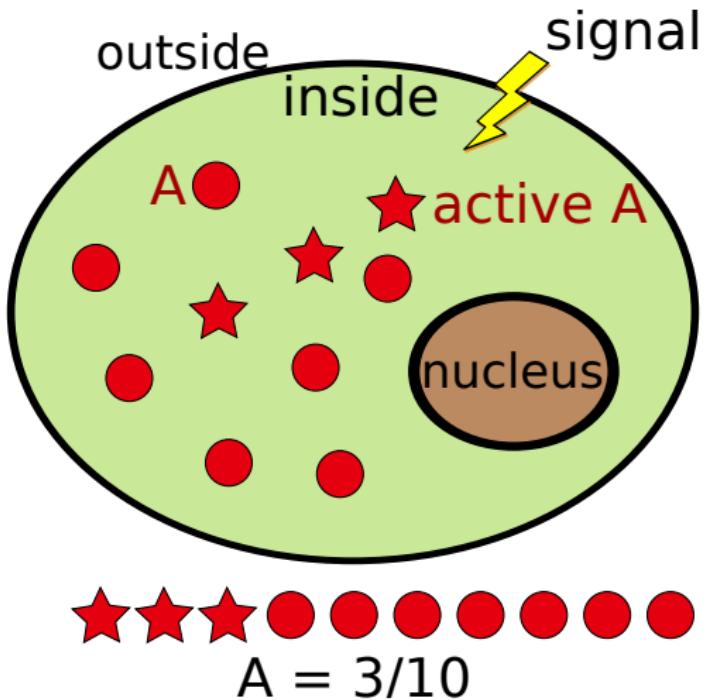
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## Discrete activity levels



## Discrete activity levels



Let the user choose granularity: 2 - 100 discrete levels

# Analysis of Networks with Interactive MOdelling

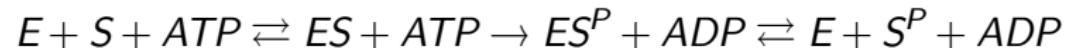
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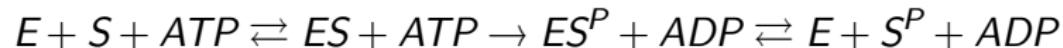


(with  $S + S^P = \text{constant}$  and  $ATP + ADP = \text{constant}$ )

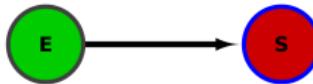
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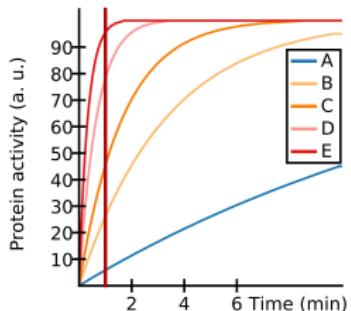
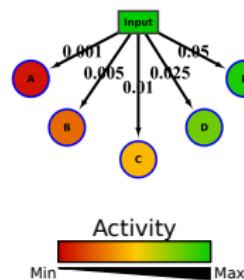
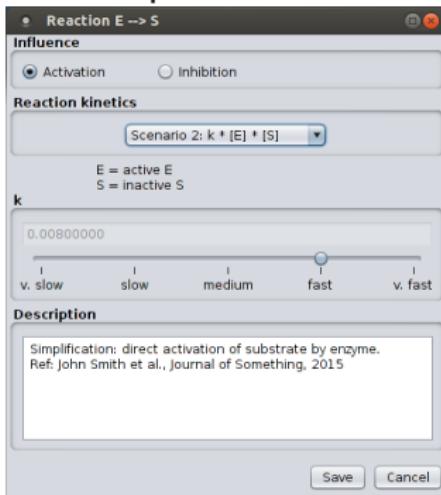


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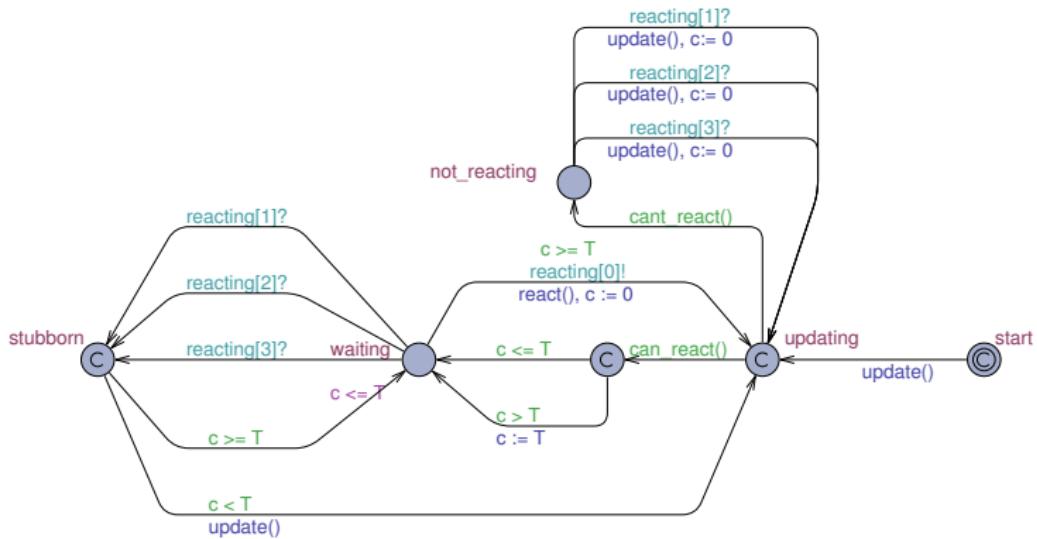


# Analysis of Networks with Interactive MOdelling

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

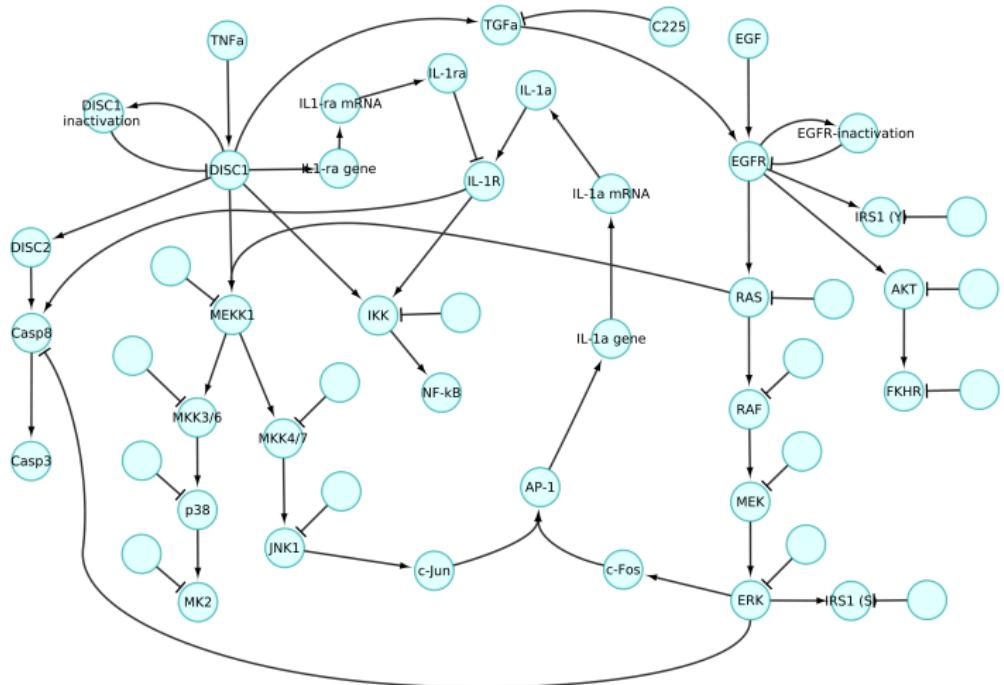


# Timed Automata model



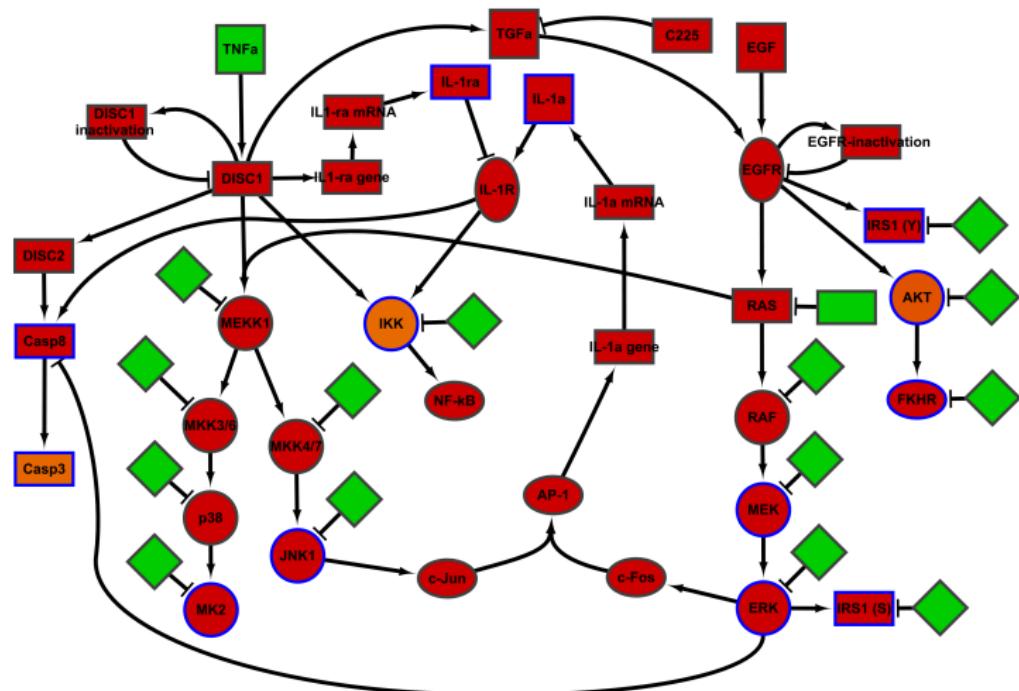
# ANIMO workflow

Start from static network topology



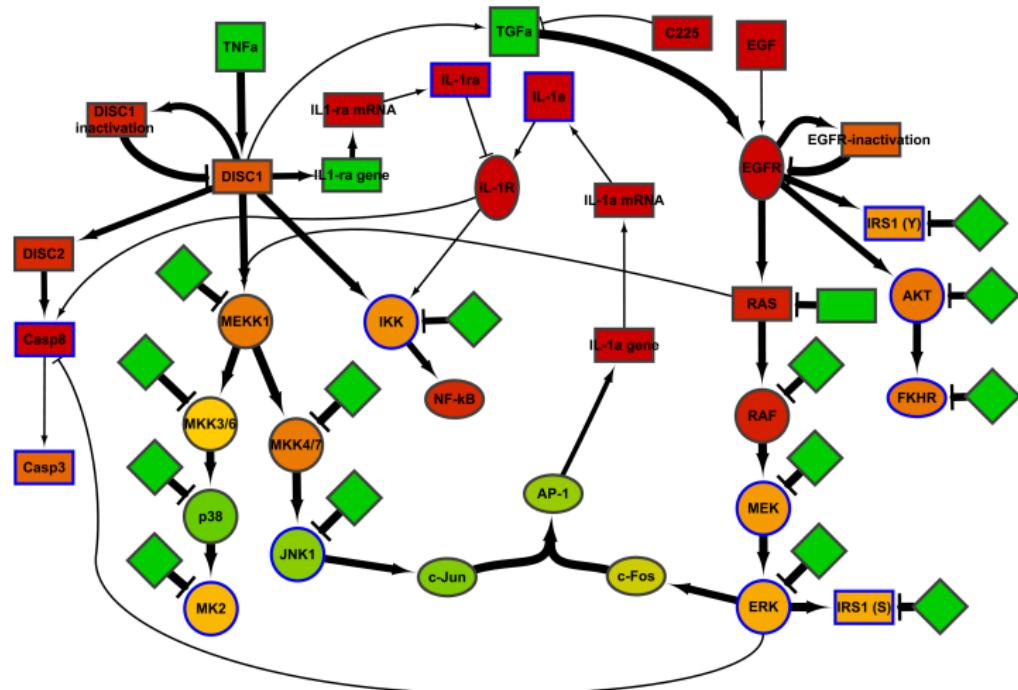
# ANIMO workflow

Add kinetics and choose initial activities



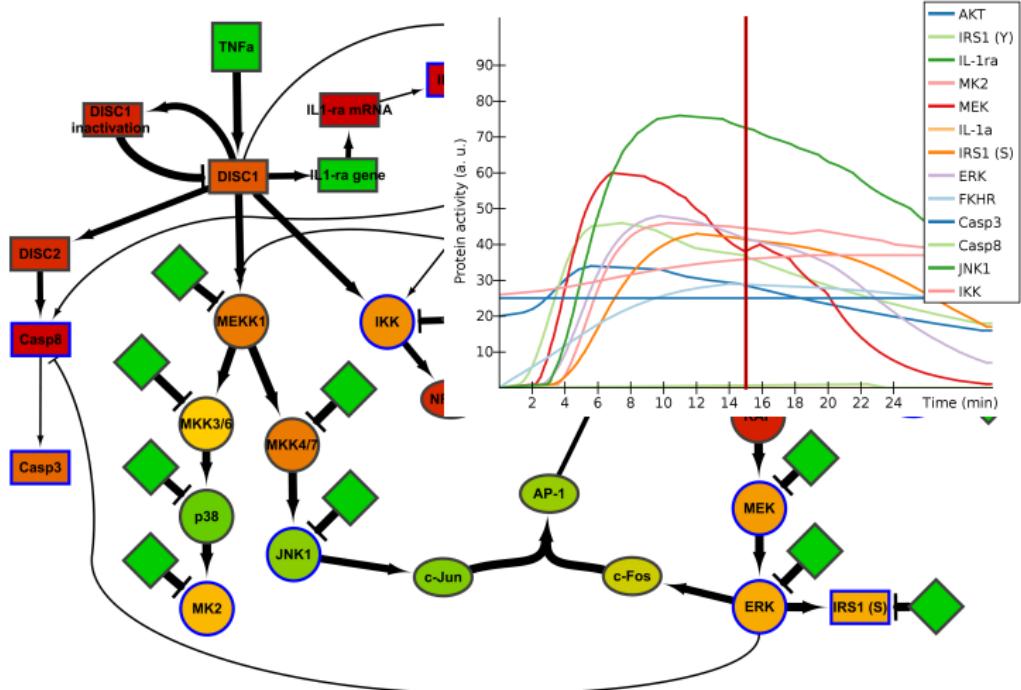
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Inspect system evolution on the fly



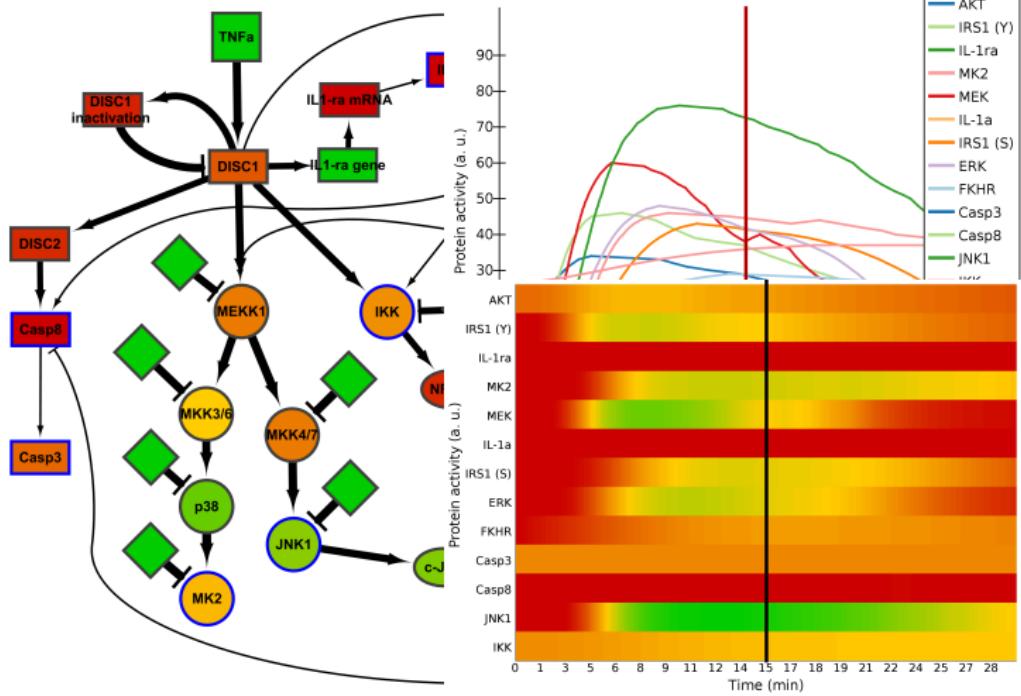
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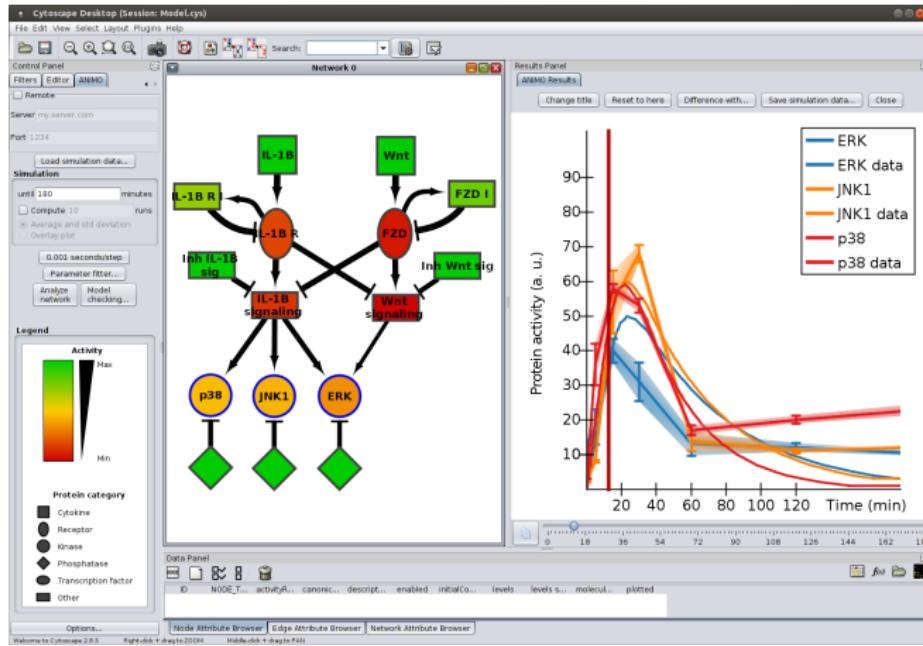


# ANIMO workflow

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?

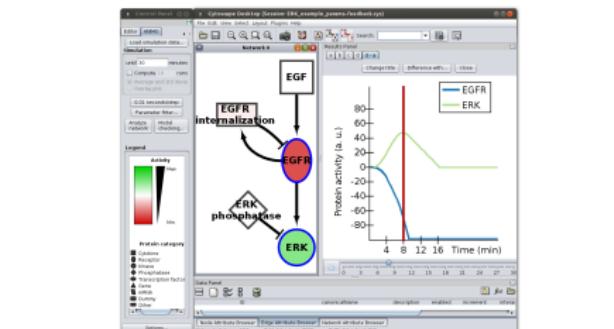
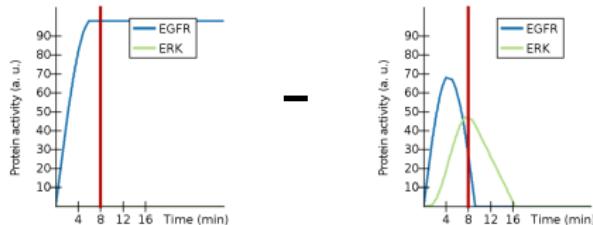
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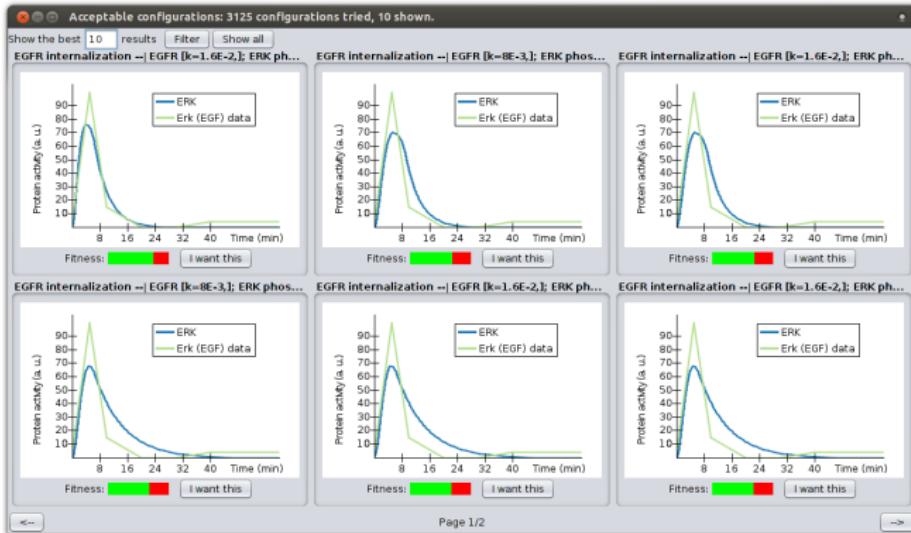
- ▶ Insert parameters manually
- ▶ Compare model versions *subtracting* their activity graphs



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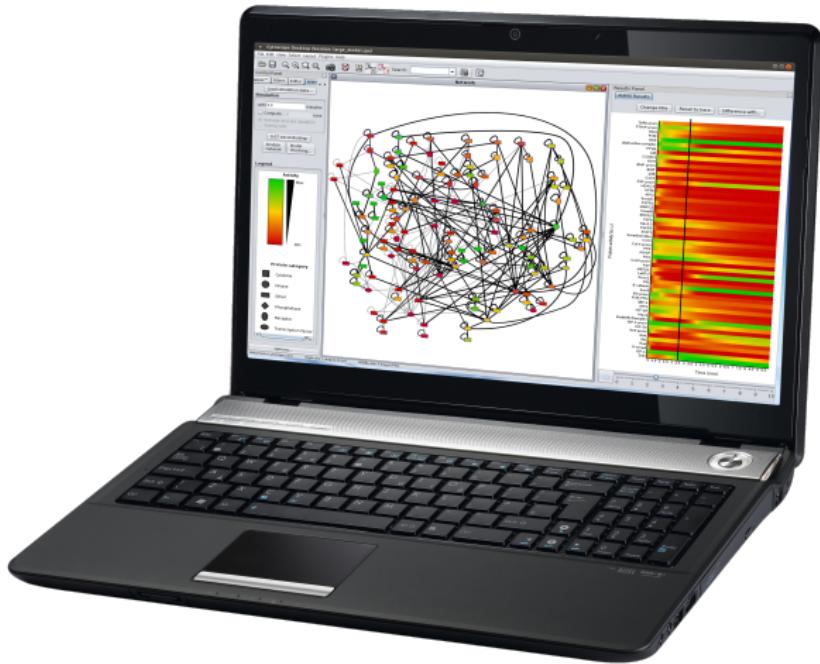
# How to find the parameters?

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



# ANIMO live demo

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# Conclusions

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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

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Typically, biological networks are robust: smaller parameter variations do not change the behavior of the network

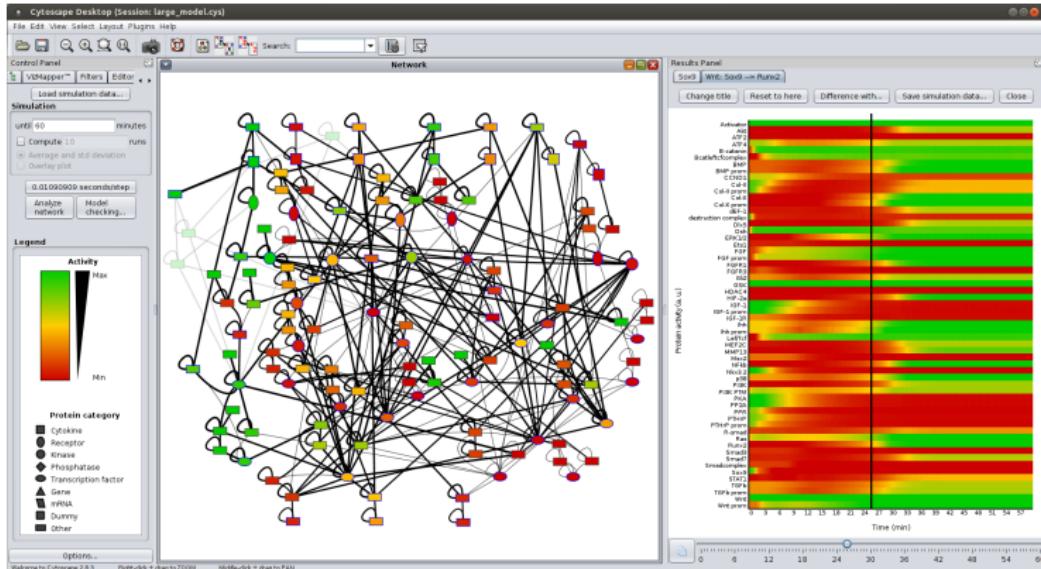
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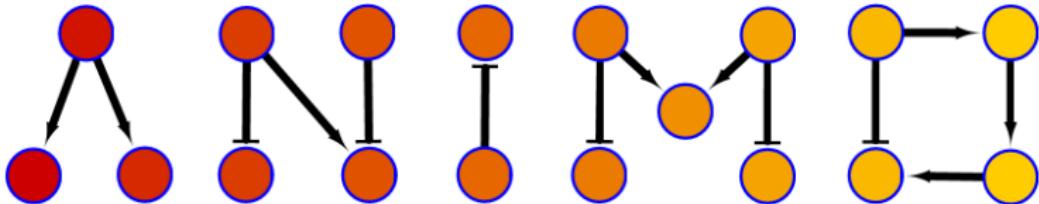
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- ▶ Get a model by feeding data: Automata Learning
- ▶ Use *in-silico experiments* to infer biological hypotheses which can be verified through in-vitro experiments
- ▶ Abstraction techniques to deal with large models

Thank you

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Analysis of Networks with Interactive MOdelling

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

