

ilsi ...

modeling complex systems in the life sciences

clean and powerful mathematical/computational tools

combinatorial dynamics

multi-level dynamics

model-checking stochastic systems

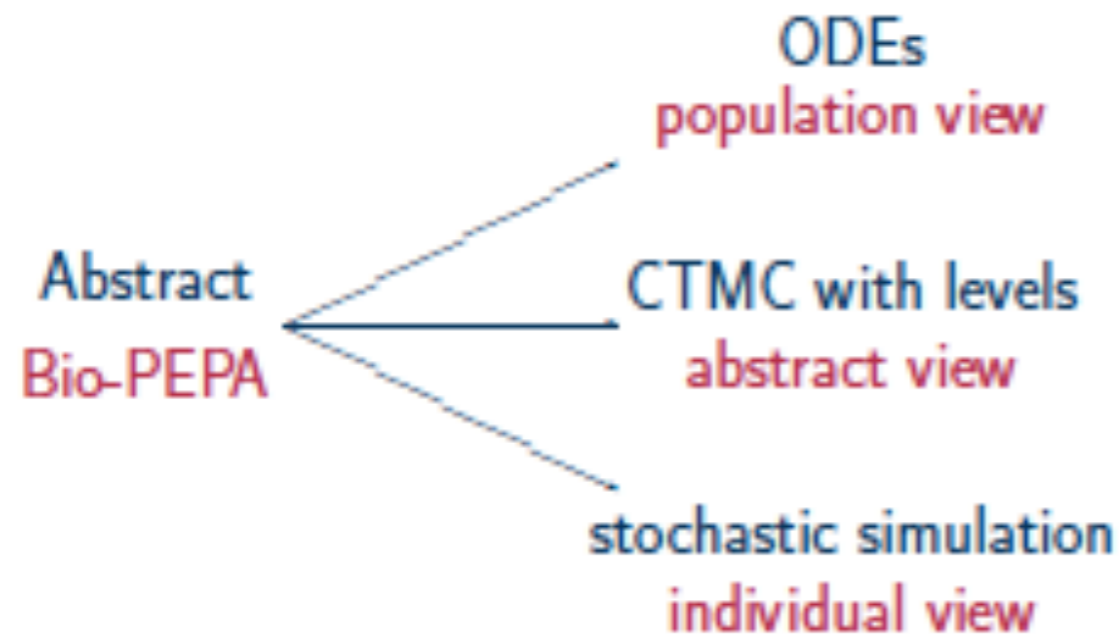
stochastic machine learning

self-organised dynamics

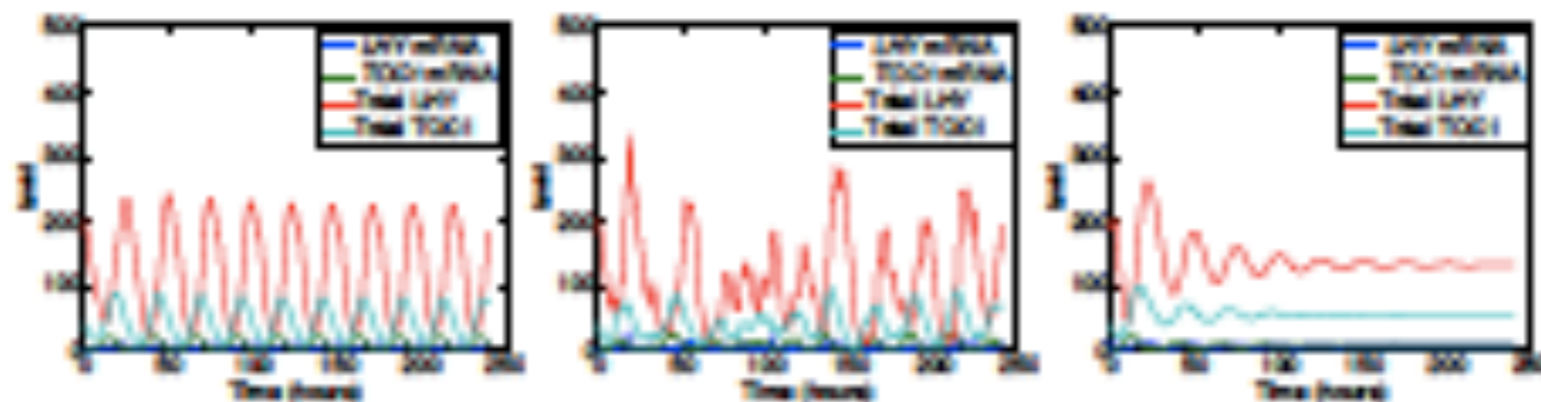
BIO-PEPA

modelling projects on circadian rhythms & tumour development

- ▶ Computational language for dynamic modelling
- ▶ Formal compositional representation of biochemical systems
- ▶ Molecular species \Rightarrow concurrent interacting processes
- ▶ Biochemical reactions \Rightarrow interactions
- ▶ Kinetic laws \Rightarrow functional rates



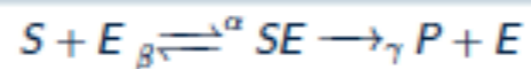
- ▶ Solution of the underlying ordinary differential equations
- ▶ Markovian analysis
- ▶ Verification of system properties via probabilistic model-checking
- ▶ Time-series analysis via stochastic simulation



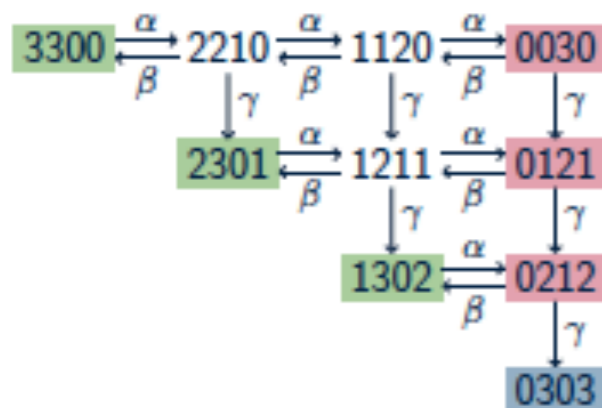
semantic equivalences to model biological behaviour

relate models with same behaviour - for labelled transition systems/CTMC with levels

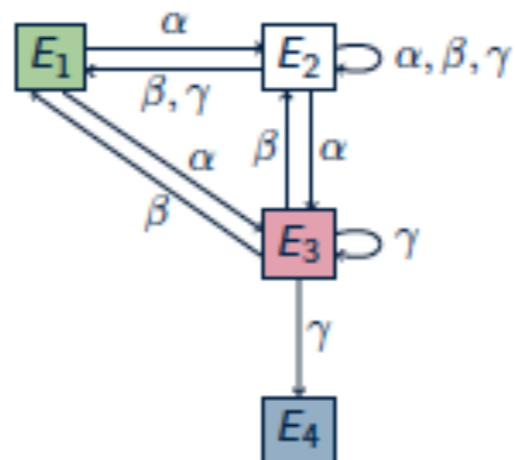
Equivalent behaviour based on two discretisations of same model: compression bisimulation



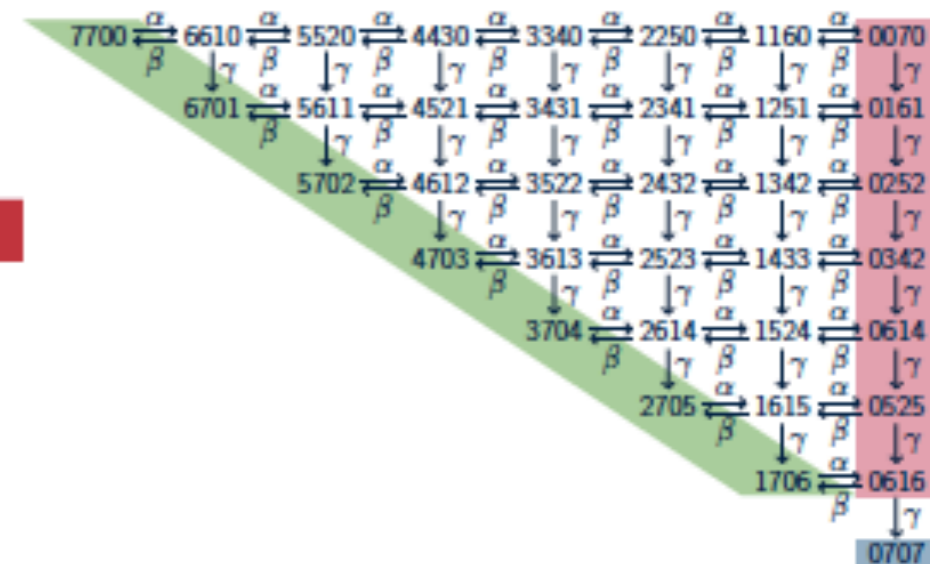
- maximum level for all species is 3
- construct LTS for Bio-PEPA model



- transition system over sets of states with the same reactions



- maximum level for all species is 7



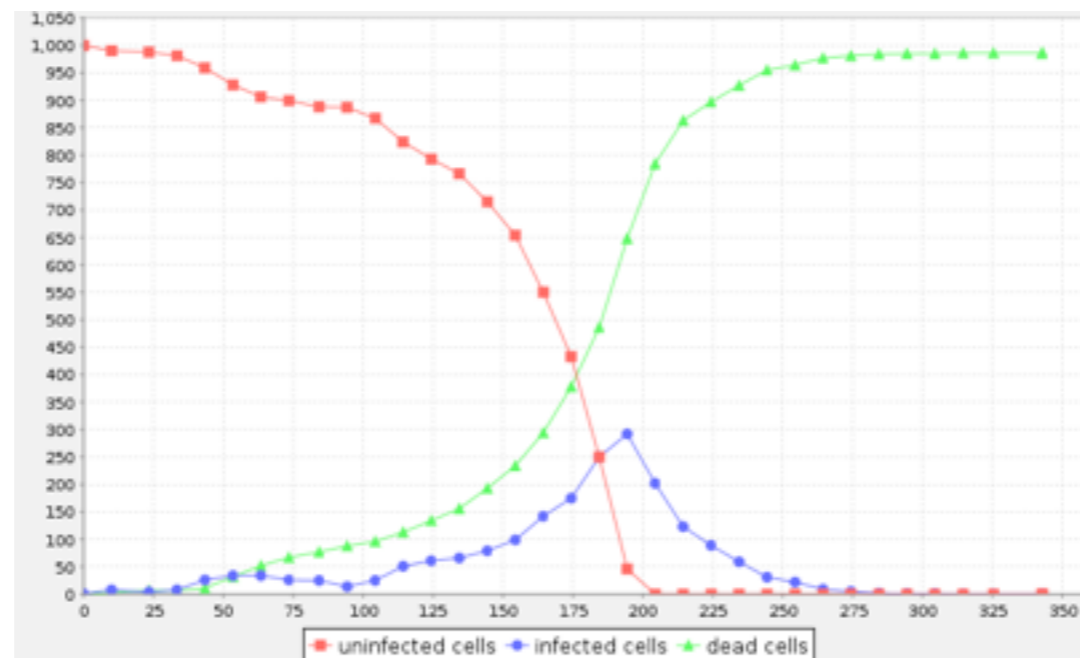
- two models are compression bisimilar when their equivalences classes (based on reactions) and induced labelled transition systems are bisimilar
- in this example, identical equivalence classes and induced transition systems are obtained, hence bisimilar

the Lambda language

stochastic multi-level multiset rewriting

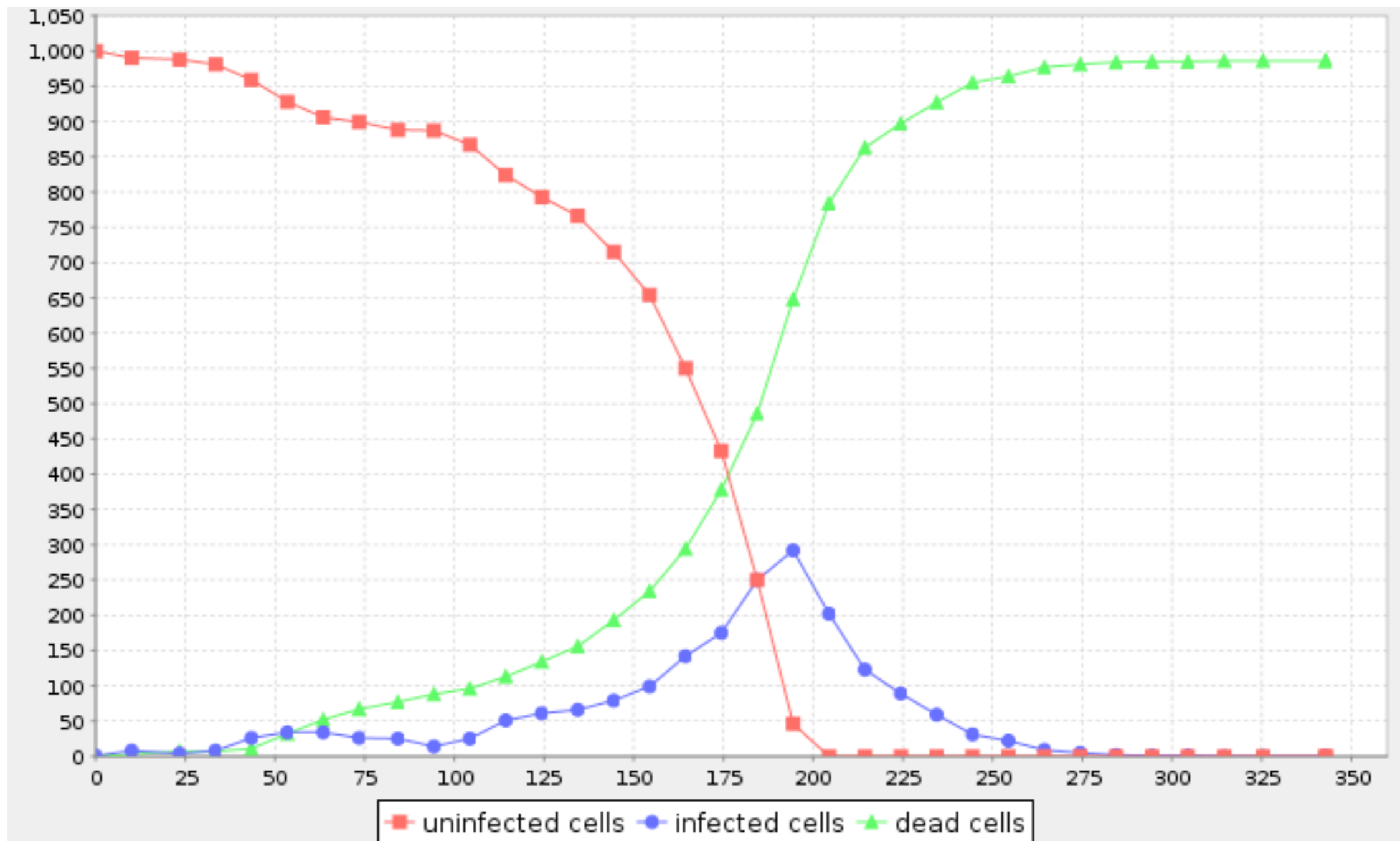
Virus, Cell $\xrightarrow{k_6}$ InfectedCell(gen, 80V₁, 40V₂)

InfectedCell(x, gen, str) $\xrightarrow{k_5}$ InfectedCell(x), Virus



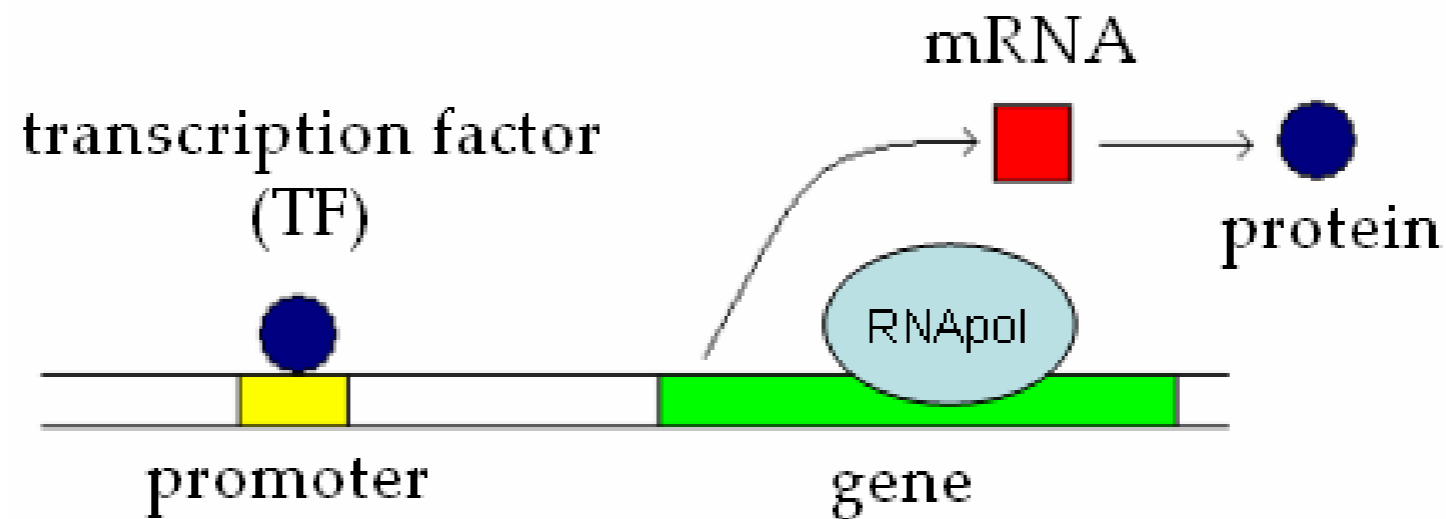
arbitrary multi-level dynamics

Model interacting cells, each with internal biochemistry



Stochastic transcriptional processes

reconstructing TF activities for transcriptional networks

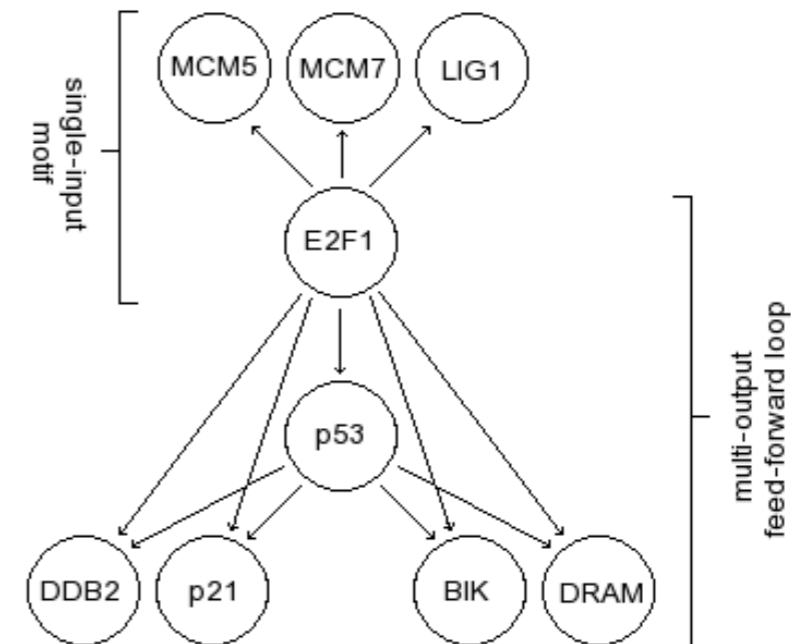
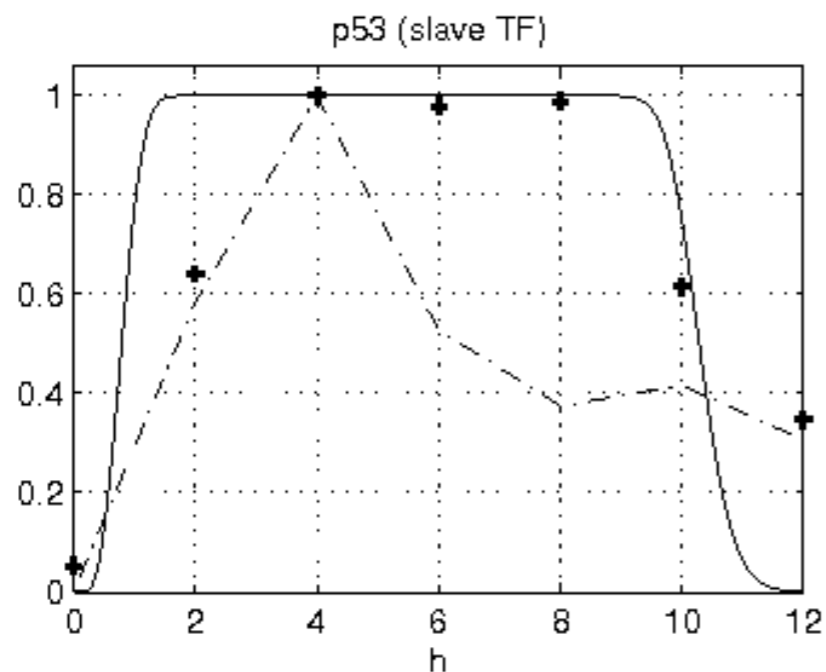


Dynamical model of transcription

$$\frac{dx_i(t)}{dt} = A_i \mu(t) + b_i - \lambda_i x_i(t)$$

p53 a feed-forward loop model

- ▶ p53 is involved in a FFL where it acts as a slave TF (Nature Reviews, 2009)
- ▶ E2F1 represents the master TF which activates p53 and p53 target genes
- ▶ We compute inference on p53 activity using a FFL model and compare our results with prediction of a single-input motif (SIM) model (Barenco et al, Genome Biol 2006)

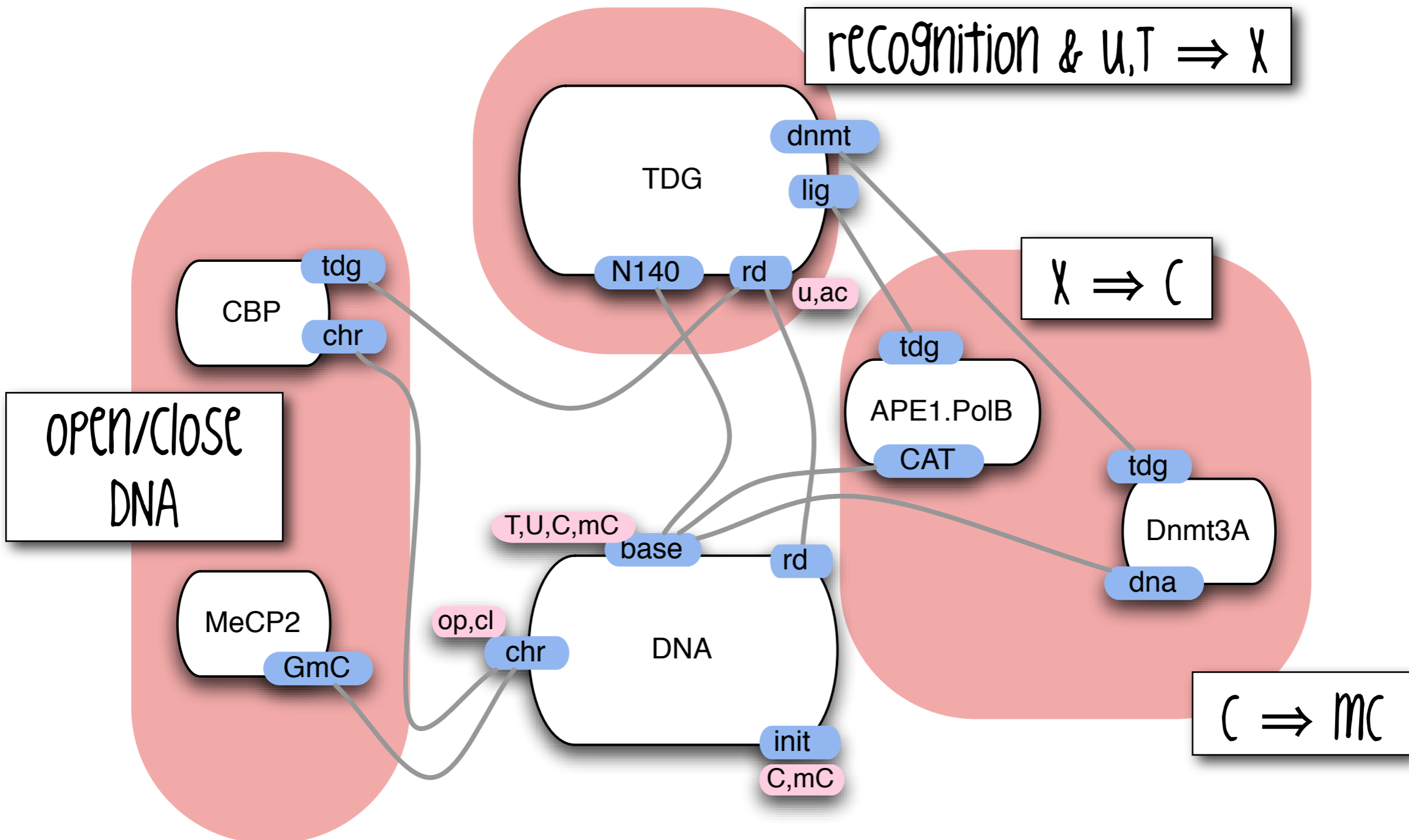


- ▶ p53 activity experimental measure (crosses)
- ▶ SIM prediction (dashed) compared with our FFL prediction (solid)

The Kappa language

Combinatorial dynamics

recognition & u,T \Rightarrow X

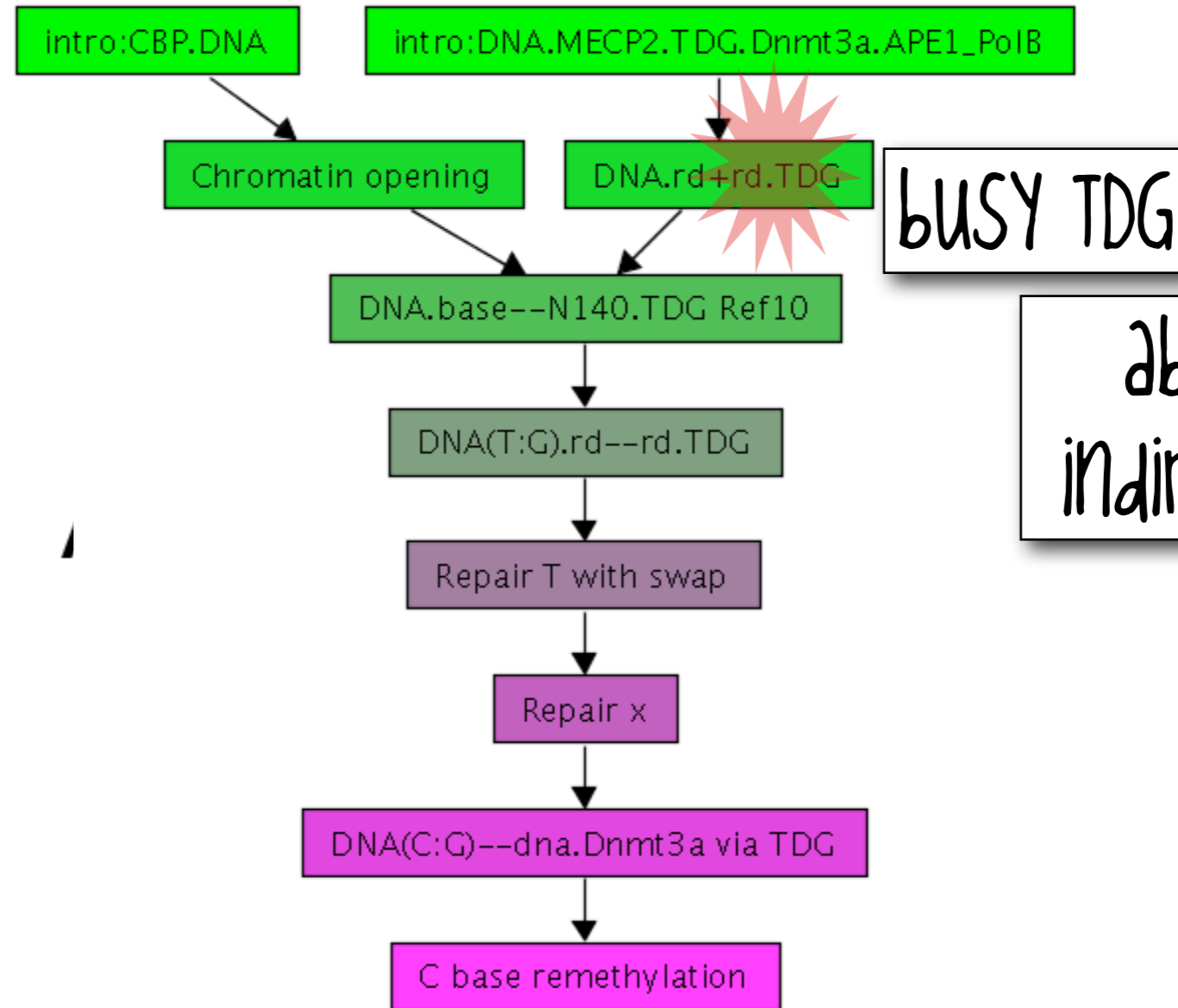


causality - stories

Story :=
incompressible
causal trace

-
"everything
matters"

-
causal debugging
of the model



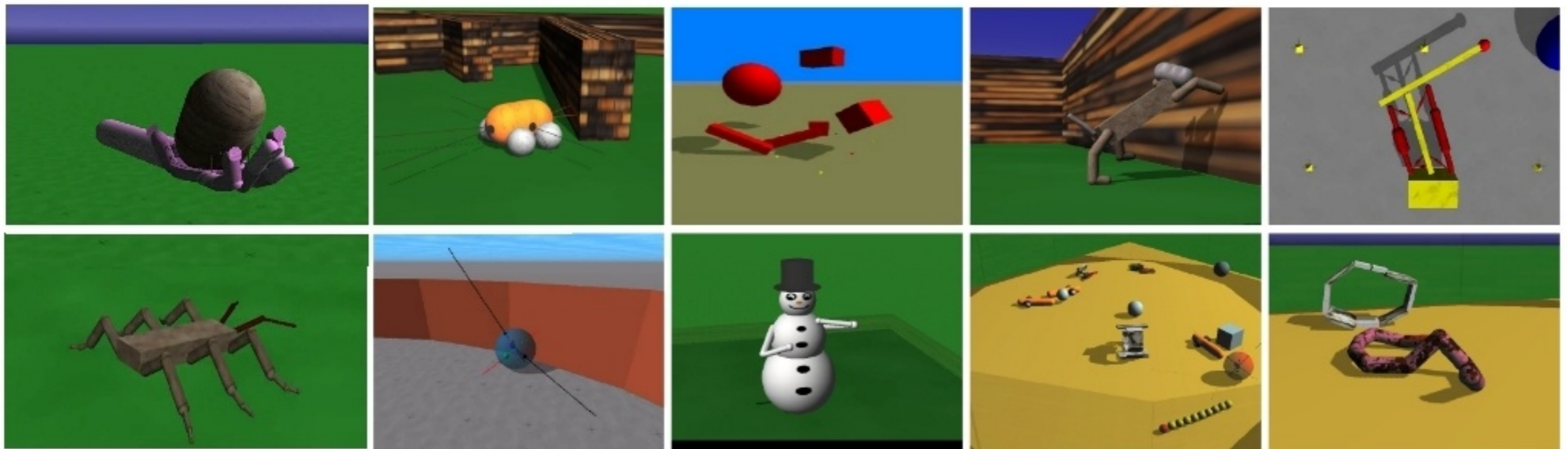
BUSY TDG

about 10%
indirect repair

Robots

self-regulating dynamics

- Self-Organization of adaptive behaviours by simultaneous optimisation of two conflicting goals: Choose actions to
- maximize **predictability** of the on own sensors and to
 - maximize **information** gained by the new sensory inputs.
- + Emergence of agile behaviours in a variety of robots.



Self-organisation

Self-organising control generates mainly exploratory behaviour: Guidance towards **goal-oriented behaviours** by

- distal teaching
- reinforcement learning
- using hints (symmetries)

Applications:

- control of transradial prostheses
- feedback loops in neural systems
- generation of options for decisions
- biological modelling (**neurorobotics**)

