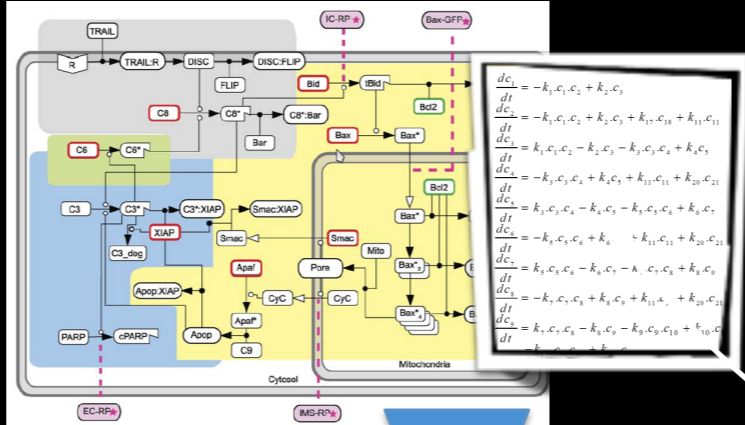


TOWARDS A FRAMEWORK FOR EFFICIENT ANALYSIS OF MACRO-  
SCALE DYNAMICAL SYSTEMS:

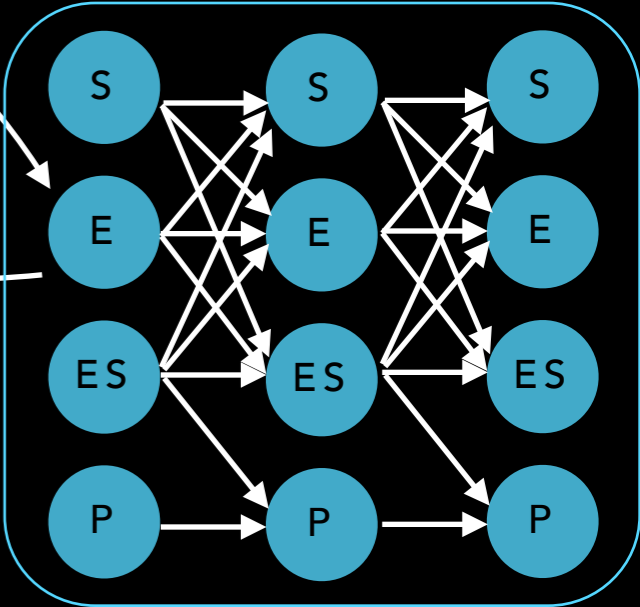
DBNS FOR APPROXIMATING THE  
TEMPORAL DYNAMICS OF APOPTOSIS  
PATHWAY

Sucheendra K. Palaniappan  
SUMO Team, INRIA

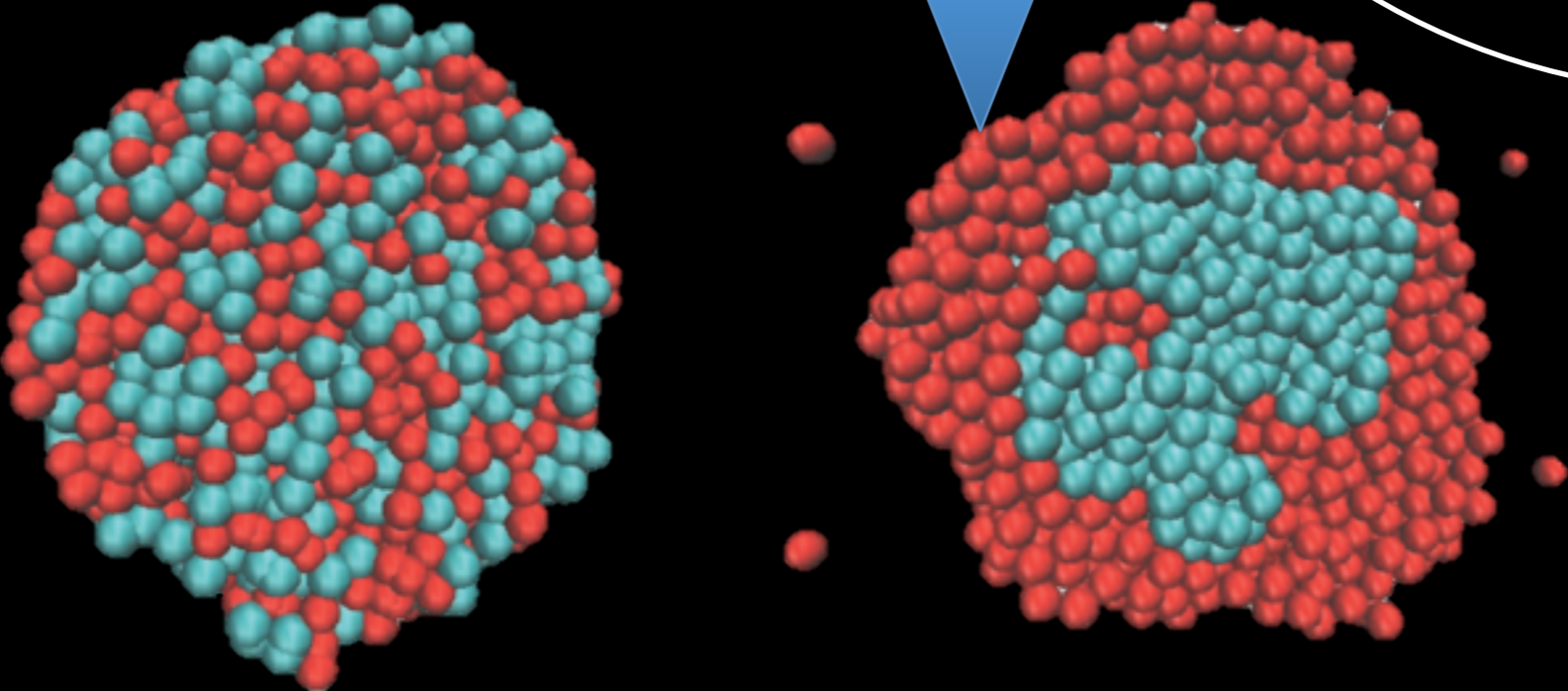
# GOAL : UNDERSTANDING MACROSCALE DYNAMICS OF APOPTOSIS PATHWAY



OUR MOTIVATION



RECAP OF BLAISE'S SLIDES



# ORGANISATION OF THIS TALK

- Dynamic Bayesian network (DBN)  
approximations of ODE Dynamics
  - How to build the DBN (Liu et.al 2011)
- DBN Approximation for the Apoptosis pathway
  - distinguishing features of the pathway
- Plan

# DBN AS EFFICIENT APPROXIMATION OF ODE DYNAMICS

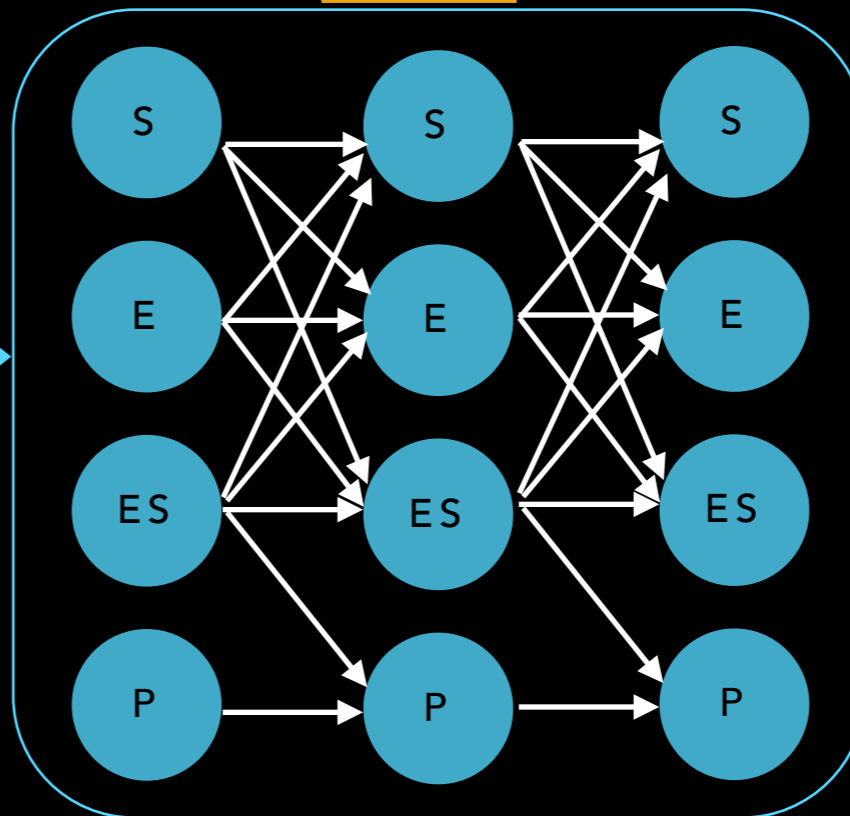


ODE

$$\begin{aligned} \frac{dS}{dt} &= -k_1 \cdot S \cdot E + k_2 \cdot ES \\ \frac{dE}{dt} &= -k_1 \cdot S \cdot E + (k_2 + k_3) \cdot ES \\ \frac{dES}{dt} &= k_1 \cdot S \cdot E - (k_2 + k_3) \cdot ES \\ \frac{dP}{dt} &= k_3 \cdot ES \end{aligned}$$

dynamics

DBN



probabilistic inference

ANALYSIS

MATTHIEU'S TALK

RECAP OF BLAISE'S SLIDES

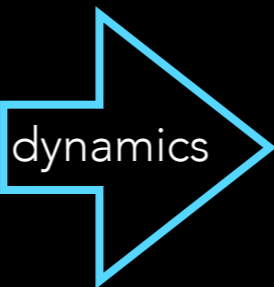
# DBN AS EFFICIENT APPROXIMATION OF ODE DYNAMICS

TOPIC OF THIS TALK

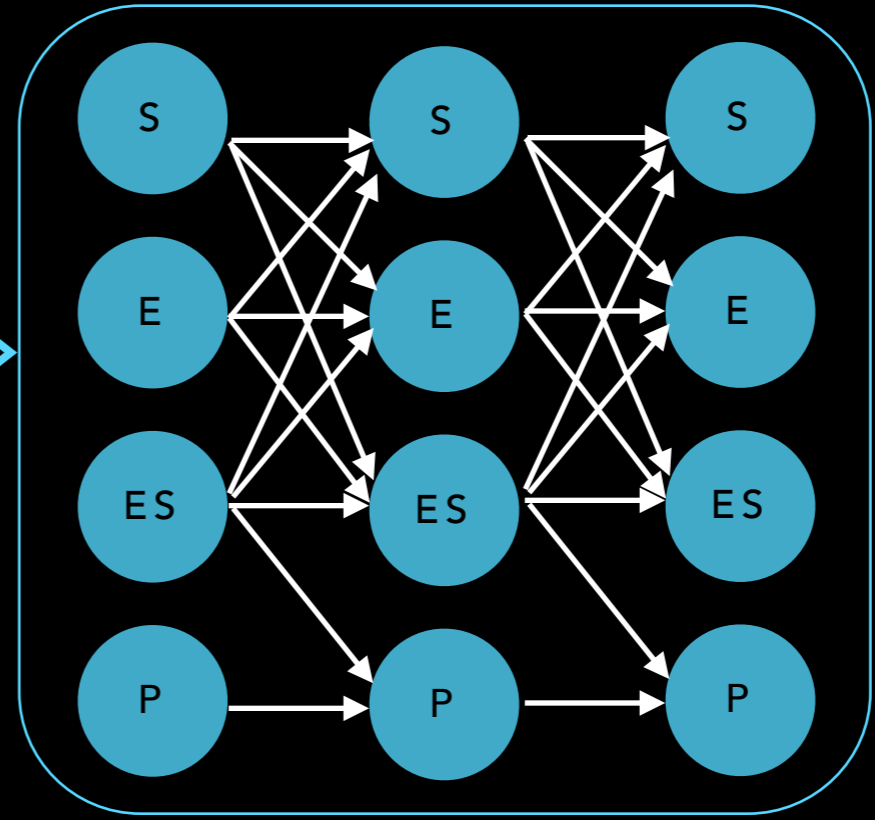


ODE

$$\begin{aligned} \frac{dS}{dt} &= -k_1 \cdot S \cdot E + k_2 \cdot ES \\ \frac{dE}{dt} &= -k_1 \cdot S \cdot E + (k_2 + k_3) \cdot ES \\ \frac{dES}{dt} &= k_1 \cdot S \cdot E - (k_2 + k_3) \cdot ES \\ \frac{dP}{dt} &= k_3 \cdot ES \end{aligned}$$



DBN



probabilistic inference

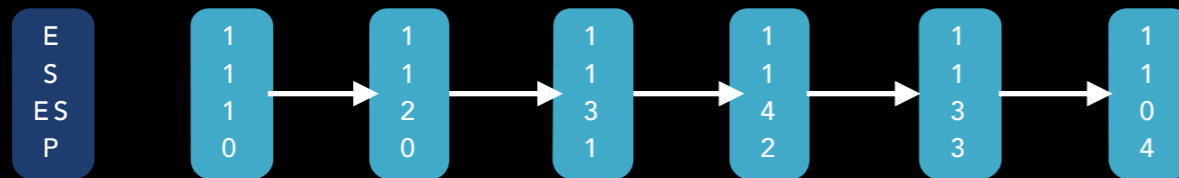
ANALYSIS

MATTHIEU'S TALK

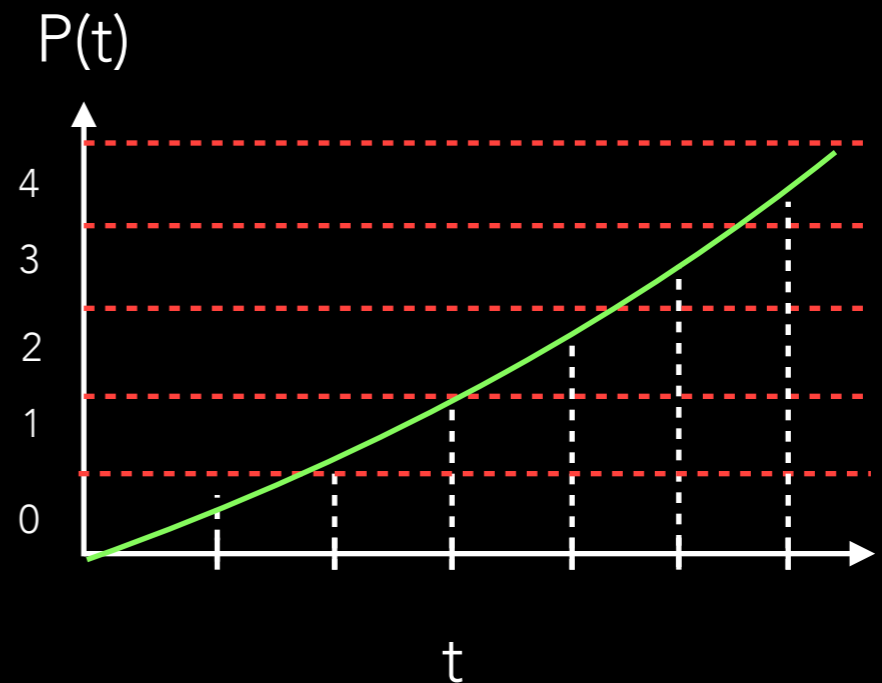
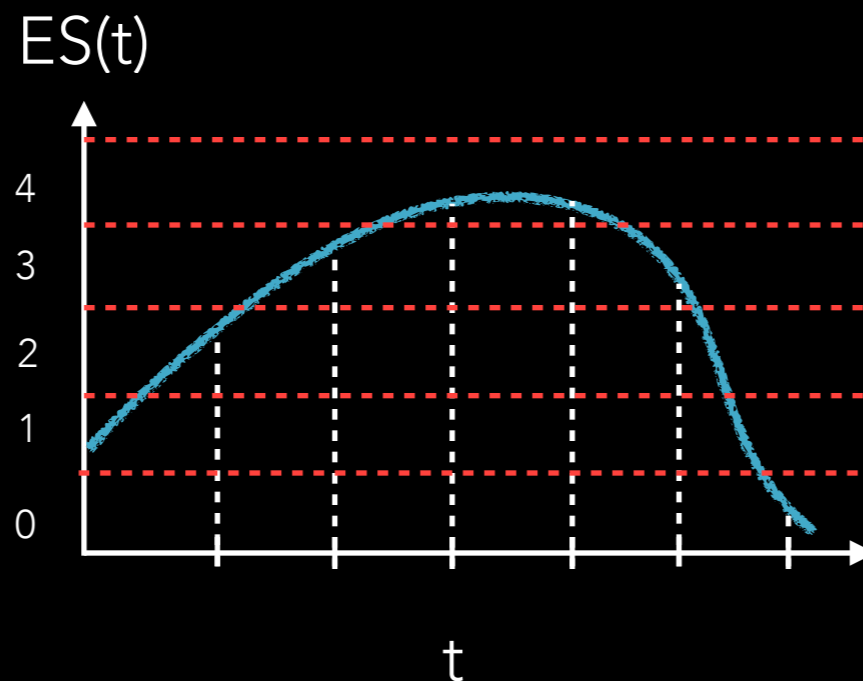
RECAP OF BLAISE'S SLIDES

# HOW TO BUILD THE DBN

## ODE DYNAMICS



## SINGLE TRAJECTORY OF THE SYSTEM



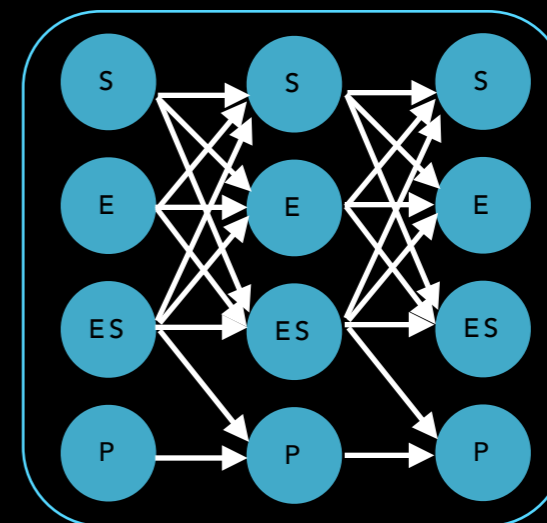
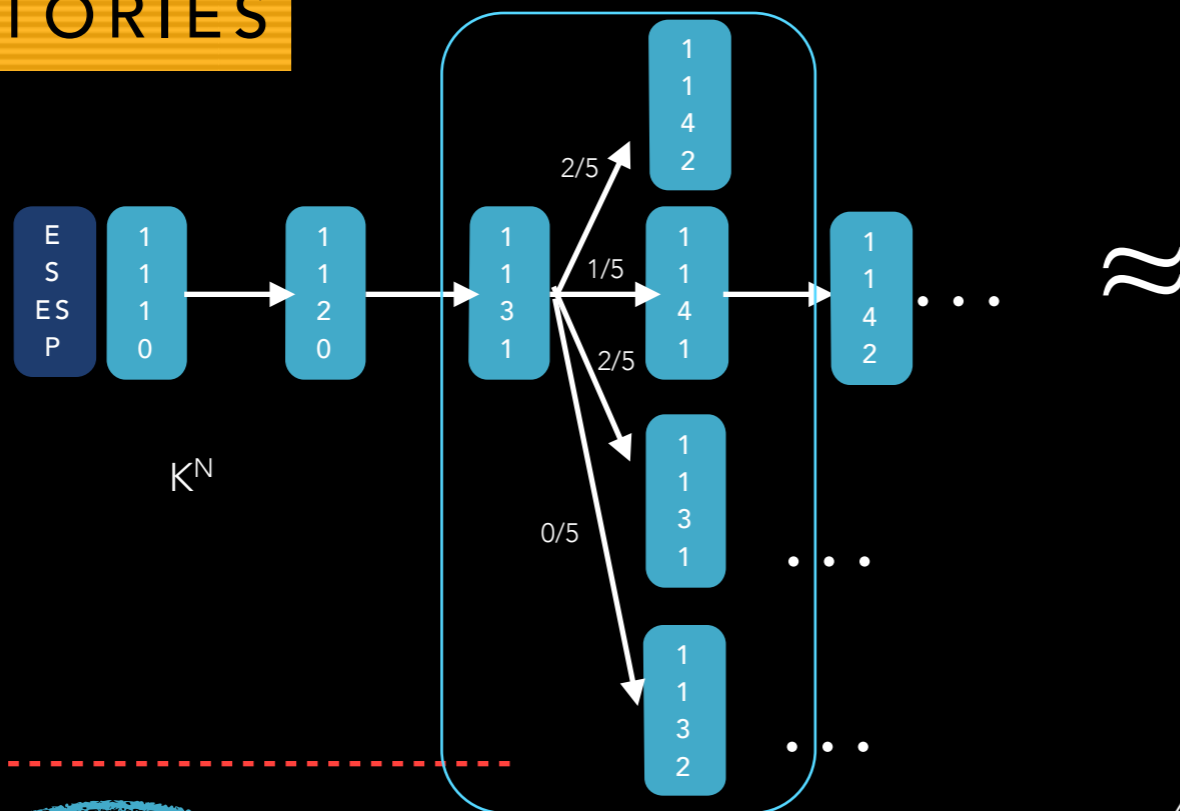
### ASSUMPTIONS

- The value domain of each species is discretized
- It is assumed that dynamics of the system is only observable at certain time points



# HOW TO BUILD THE DBN

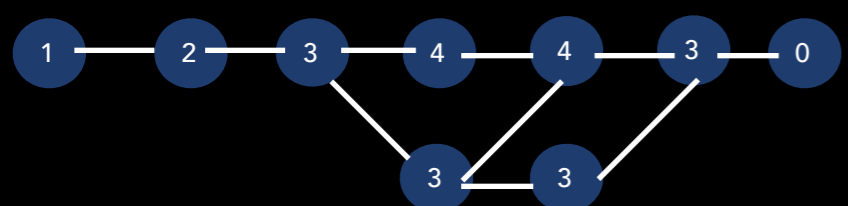
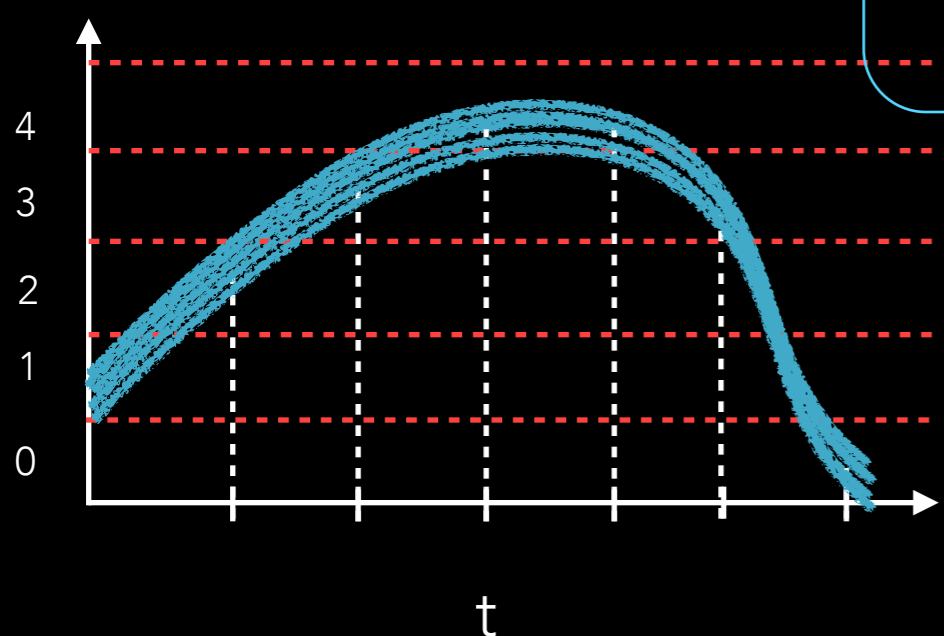
## GROUP OF TRAJECTORIES



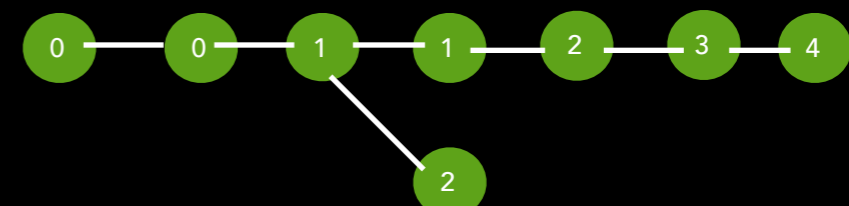
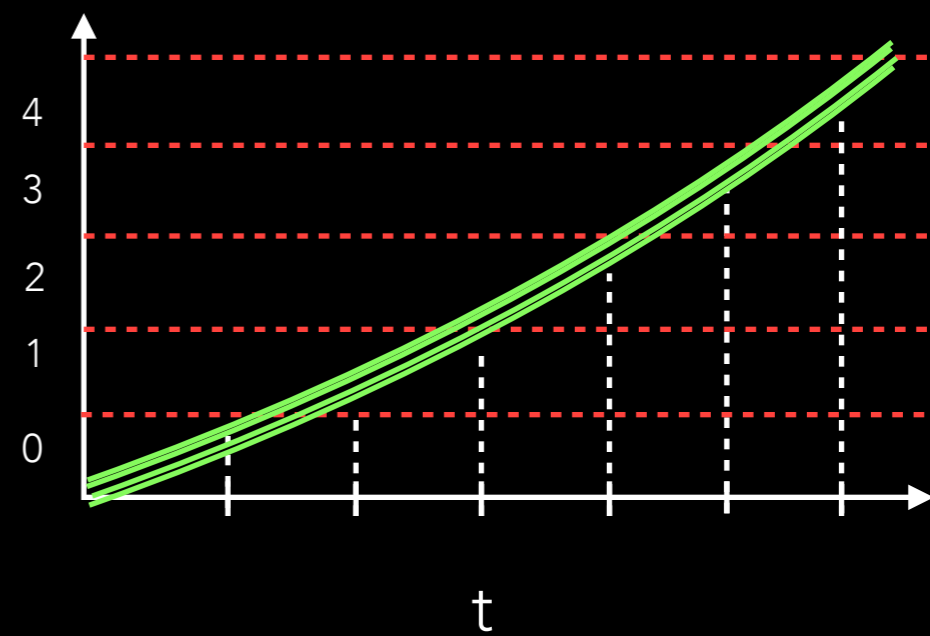
**CPT**  
conditional probability table

**DBN**  
 $N * K^p$

ES(t)



P(t)

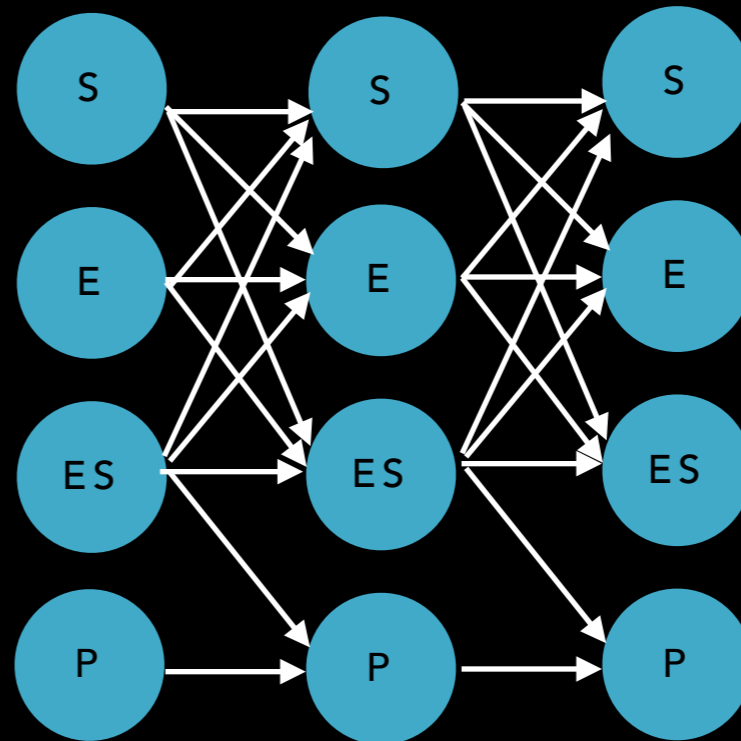


# HOW TO BUILD THE DBN

## STRUCTURE

- nodes -> Every variable of the mathematical model
- edges -> Dictated by the corresponding equation for each variable

$$\begin{aligned}\frac{dS}{dt} &= -k_1.S.E + k_2.ES \\ \frac{dE}{dt} &= -k_1.S.E + (k_2 + k_3).ES \\ \frac{dES}{dt} &= k_1.S.E - (k_2 + k_3).ES \\ \frac{dP}{dt} &= k_3.ES\end{aligned}$$





# HOW TO BUILD THE DBN

## STRUCTURE

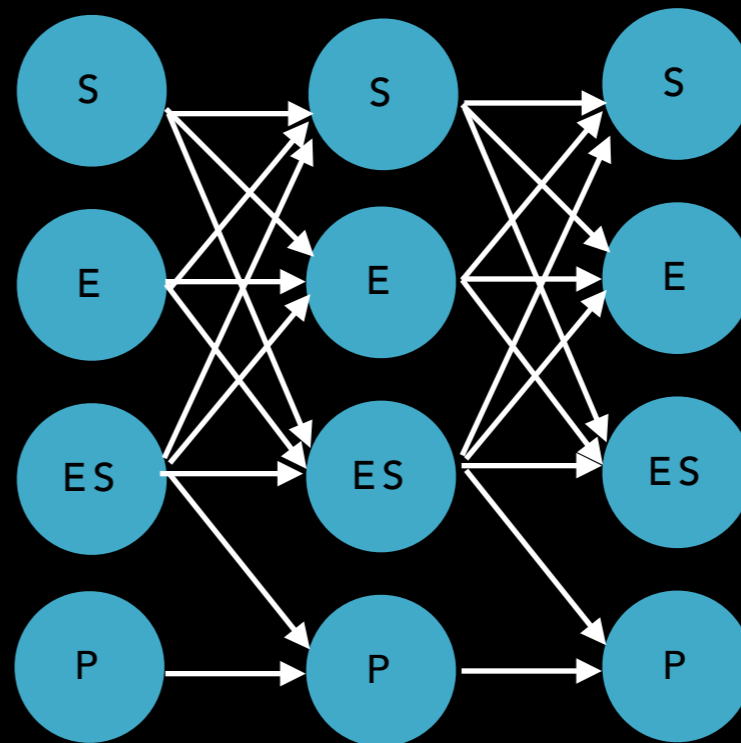
- nodes -> Every variable of the mathematical model
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$$\frac{dS}{dt} = -k_1 \cdot S \cdot E + k_2 \cdot ES$$

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$$\frac{dES}{dt} = k_1 \cdot S \cdot E - (k_2 + k_3) \cdot ES$$

$$\frac{dP}{dt} = k_3 \cdot ES$$



# HOW TO BUILD THE DBN

## STRUCTURE

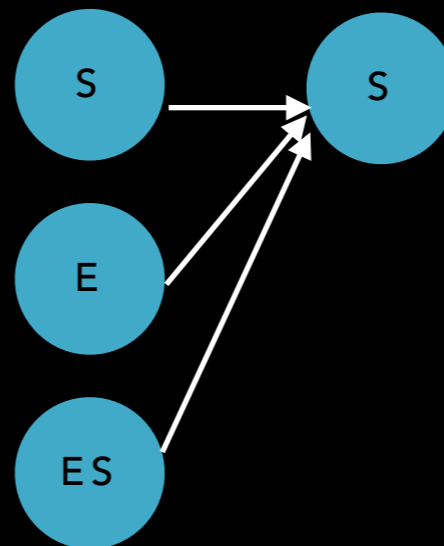
- nodes -> Every variable of the mathematical model
- edges -> Dictated by the corresponding equation for each variable

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$$\frac{dE}{dt} = -k_1 \cdot S \cdot E + (k_2 + k_3) \cdot ES$$

$$\frac{dES}{dt} = k_1 \cdot S \cdot E - (k_2 + k_3) \cdot ES$$

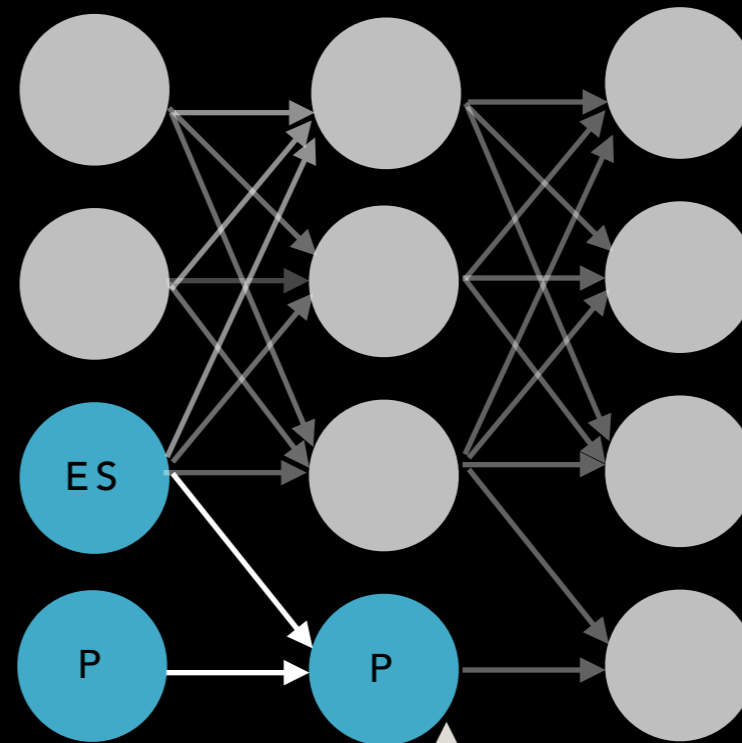
$$\frac{dP}{dt} = k_3 \cdot ES$$



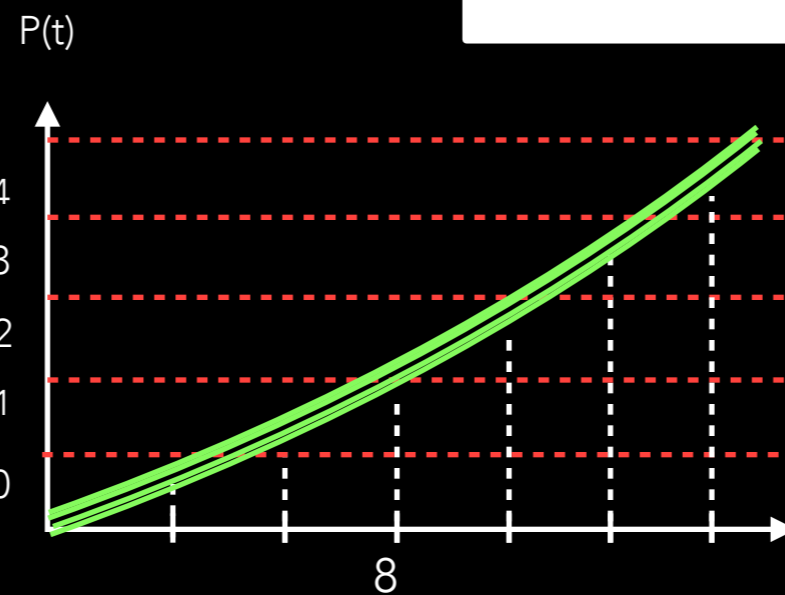
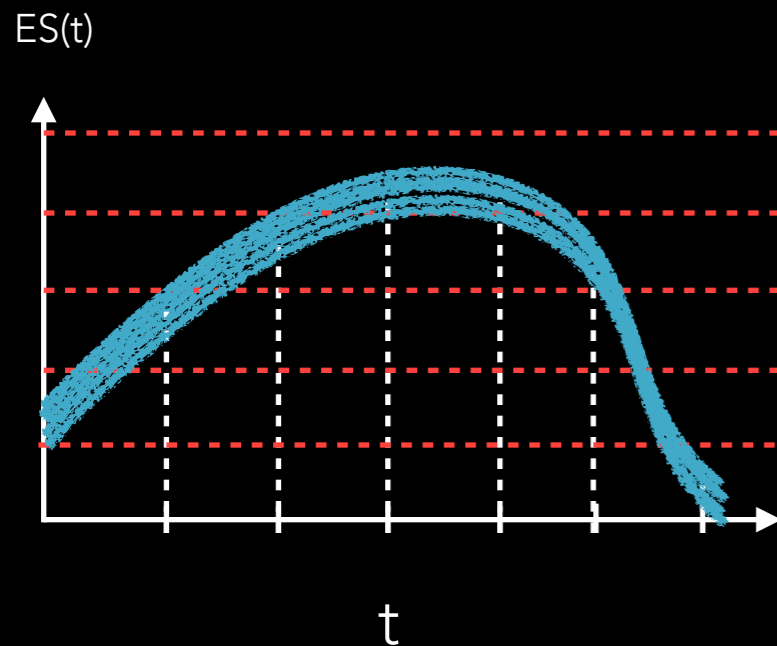
# HOW TO BUILD THE DBN

CPT

$$\frac{dP}{dt} = k_3 \cdot ES$$



$P(p^{t+1}=0 | ES^t=1, p^t=0) = 0.9$   
 $P(p^{t+1}=1 | ES^t=1, p^t=0) = 0.1$   
 $P(p^{t+1}=2 | ES^t=1, p^t=0) = 0.0$   
 .....



Fill by simple counting

ODE ANALYSIS = DBN INFERENCE

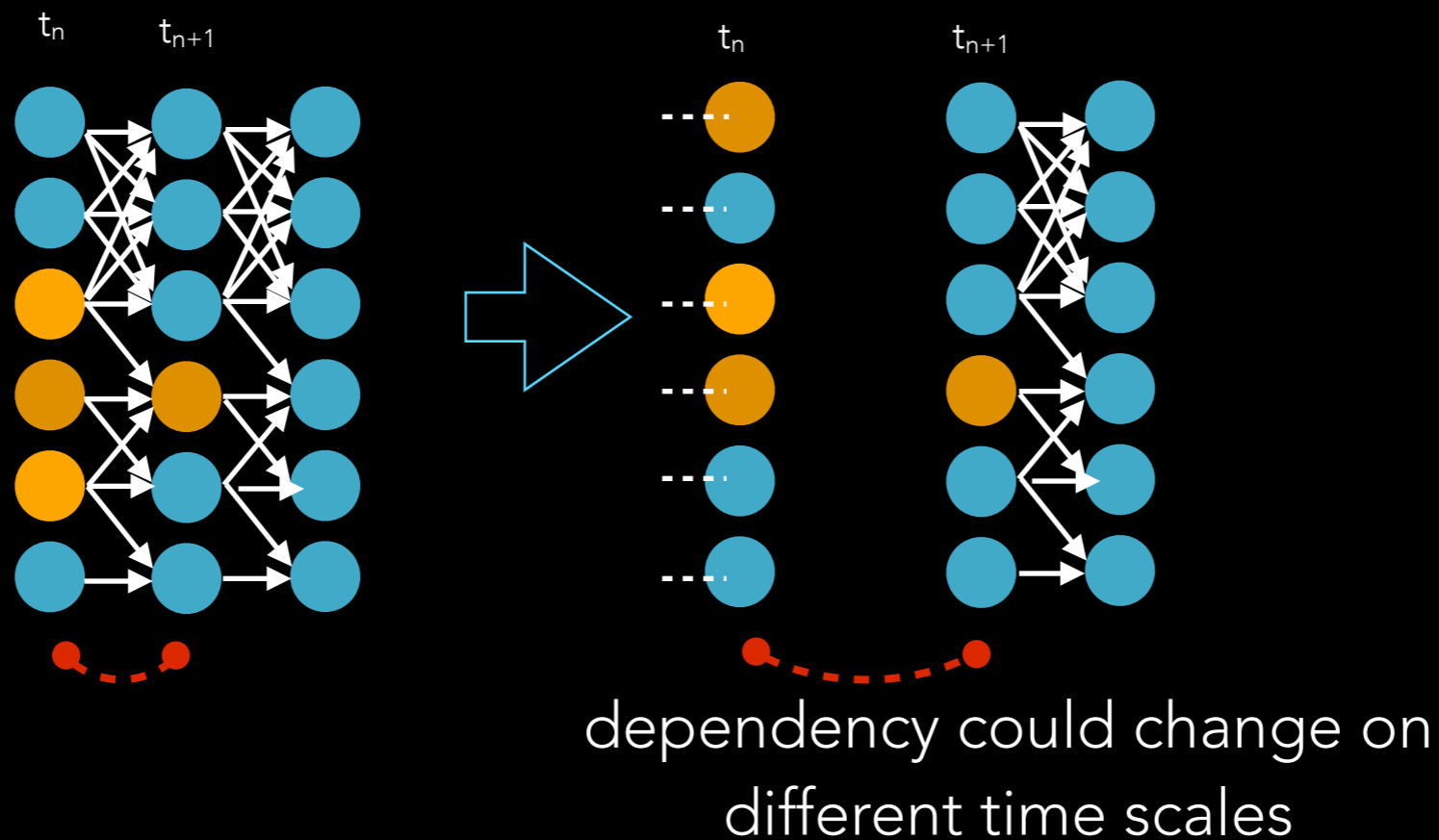
# DBN OF APOPTOSIS PATHWAY : DISTINGUISHING FEATURES

- The pathway model is a hybrid model of both deterministic (ODE) and Stochastic components
- 58 Protein species + mRNA species (governed by stochastic equations)



# DISTINGUISHING FEATURES:

- Separation of timescales
  - The structure of the DBN is based on the assumption that between the time steps the dependency of variables is dictated by their mathematical formalism
  - But, when considering larger time windows this may not be true the dependency between variables can be different



# FINAL THOUGHTS

- Final goal is to have a minimalist and sufficient structure that captures all the interesting dynamics of the Apoptosis pathway
- First Steps - ongoing
  - Building the DBN with only the protein's as DBN variables
  - For nodes with larger nodes, using mutual information to minimise the number of parents