SVS-BBC

Formal methods for discrete modelling

24 Sept. 2024

Tutorial n^o 1 : CTL

The aim of this tutorial is to familiarize you with the use of temporal logic CTL to formalize the dynamic properties of a biological system.

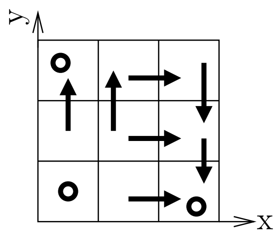
Exercice 1 : (**Transcription of properties expressed in natural language into CTL.**)

Propose a formalization using the temporal logic CTL of each of the following properties.

1. Let α be a formula characterizing a state. From this state, it is possible to reach one of the states characterized by the formula β.
2. Characterize the set of states from which the system can reach a state satisfying the property γ.
3. A state characterized by can be reached by passing through a state characterized by α.
4. The system can reach a state characterized by β without ever violating certain c constraints.
5. To reach a state that satisfies the property β, it is necessary to reach a state that satisfies α first.
6. From an initial state characterised by the property *init*, it is always possible to reach a state that satisfies the property β without ever passing through a state that satisfies α.
7. The φ property (possibly specifying a unique state) of the system is stable, in other words, starting from a state that satisfies φ, the system can only reach states that satisfy φ.
8. From a state in which the φ property is satisfied, the system can remain indefinitely in states all satisfying φ.
9. The system can reach a stable property φ from an initial state *init*.
10. The system must reach a stable state s from an initial state *init*.
11. There are two basins of attraction : either x is below its first threshold and will remain so, or it's above and will remain so.

Exercice 2 : (**Manual verification of CTL formulas**)

The following model is given, with genes labelled x and y respectively. Transcribe each of the following CTL formulae into natural language, then say whether they are satisfied in the transition graph on the right or not, and justify your answers.

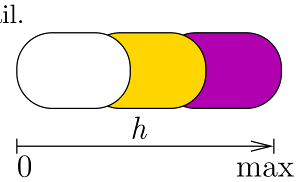


1. $(x{=}0 \wedge y{=}0) \Rightarrow AG(x{=}0 \wedge y{=}0)$
2. $x{=}0 \Rightarrow AG(x{=}0)$
3. $x{>}0 \Rightarrow AG(x{=}2)$
4. $x{>}0 \Rightarrow AF\ AG(x{=}2)$
5. $AF\ AG(x{>}0)$
6. $\neg\ AF\ AG(x{>}0)$
7. $(x{=}1 \wedge y{=}1) \Rightarrow EX(A[y{=}2\ U\ x{=}2])$
8. $(x{=}1 \wedge y{=}1) \Rightarrow EX(y{=}2 \wedge EX(x{=}2 \wedge EX(y{=}1 \wedge EX(y{=}0))))$

Exercice 3 : (**Simplified model of insect embryo development**)

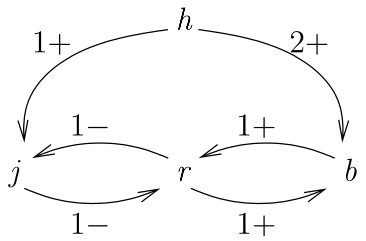
In this exercise we will study the formation of transverse rings during the development of an insect embryo. We assume that this imaginary insect has only 3 rings : a first white ring at the top of the abdomen, then a yellow ring and finally a third and final purple ring on the tail.

We also know that the gradient of a protein h present in the original oocyte is responsible for these colours, and that during proliferation the embryo maintains this gradient globally along the abdomen. However, this protein is colourless and its gradient increases linearly and continuously along the anterior-posterior axis, while the coloured rings are clearly separated.



A study of the genetic network involved in colouration reveals 3 genes that produce proteins responsible for colouration : the gene j is a precursor of a yellow pigment, the gene r is a precursor of a red pigment and the gene b is a precursor of a blue pigment.

This study is based on René Thomas's discrete theory of genetic networks. The concentration of the protein h can be 0, 1 or 2, but the colouring genes j, r and b are all Boolean. The three rings correspond to the three possible values of h : when $h = 0$ the network expresses none of the three genes (since the ring is white), when $h = 1$ only j is expressed and finally when $h = 2$ only the genes r and b are expressed to produce purple.



1. Write the three CTL formulas that express that :
   (a) when $h = 0$ is constant, the ≪ white ≫ state is stable
   (b) when $h = 1$ is constant, the ≪ yellow ≫ state is stable
   (c) and when $h = 2$ is constant, the ≪ purple ≫ state is stable
2. For each of the 3 genes j, r and b, list the Thomas K_{cdots} parameters associated with them. [Since h is imposed by the gradient, we don't consider the $K_{h,\ldots}$ but h must be considered among the possible resources of the 3 genes according to its value].
3. What are the parameters whose values can be deduced from the three stable states, white, yellow and violet ? State these values.
4. Finally, applying Snoussi's conditions, what do we deduce ?
5. In an experiment where h and b are artificially saturated in the cell, the $j \leftrightarrow r$ cycle is found to be functional. What does this mean ? What parameter value can be achieved ?
6. When the egg is formed, the cell still expresses the genes r and b, but not j. When $h = 0$, the cell reaches the stable state $(j, r, b) = (0, 0, 0)$ as follows : b goes out, then r. Write the corresponding Hoare triplet and deduce one of the two missing parameters.
7. What experiment would you suggest to find the value of the missing parameter ?