



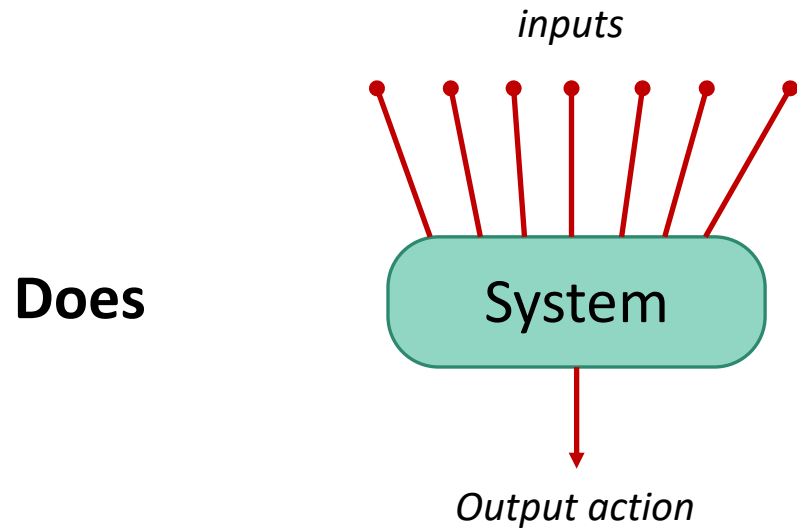
Heart modeling: Timed automata

Lecture 12

Principles of Modeling for Cyber-Physical Systems

Instructor: Madhur Behl

Why model checking ?

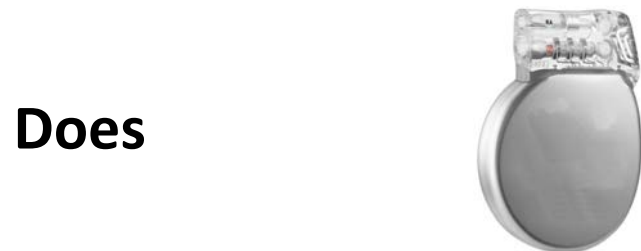


satisfy



?

Requirements



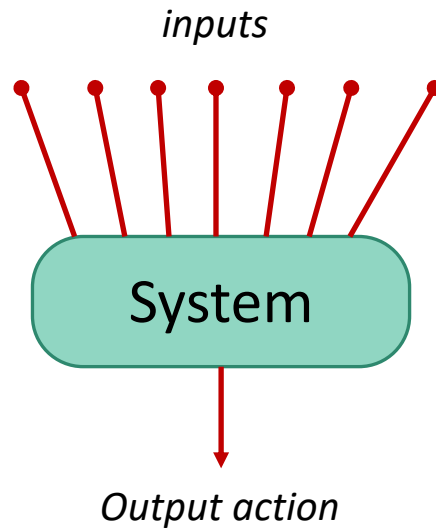
satisfy

Maintain at least LRI ventricle rate
Do not pace beyond maximum rate (URI)

...

?

Does



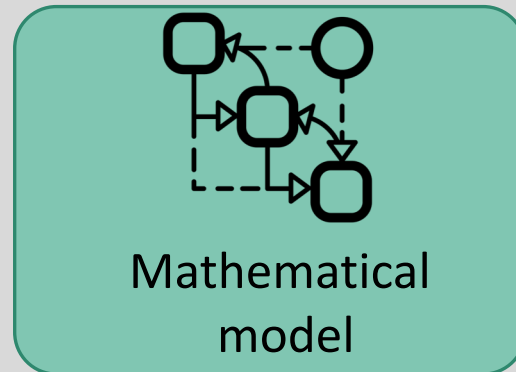
satisfy



?

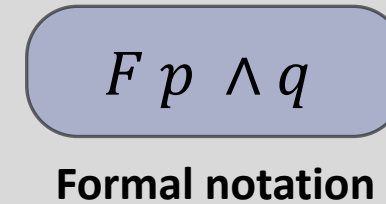
Model Checking UPPAAL Model Checker

Does



Timed automata

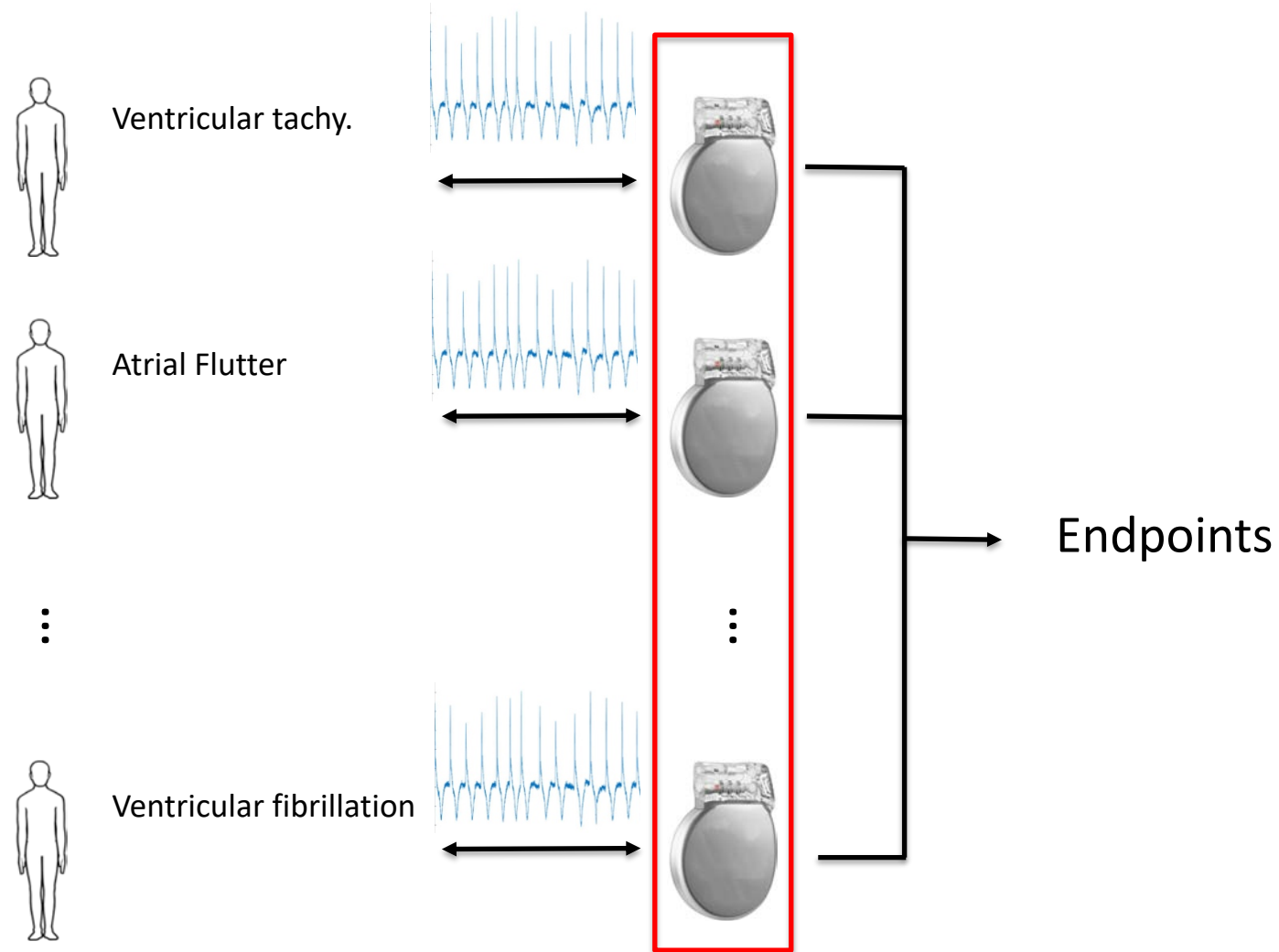
satisfy

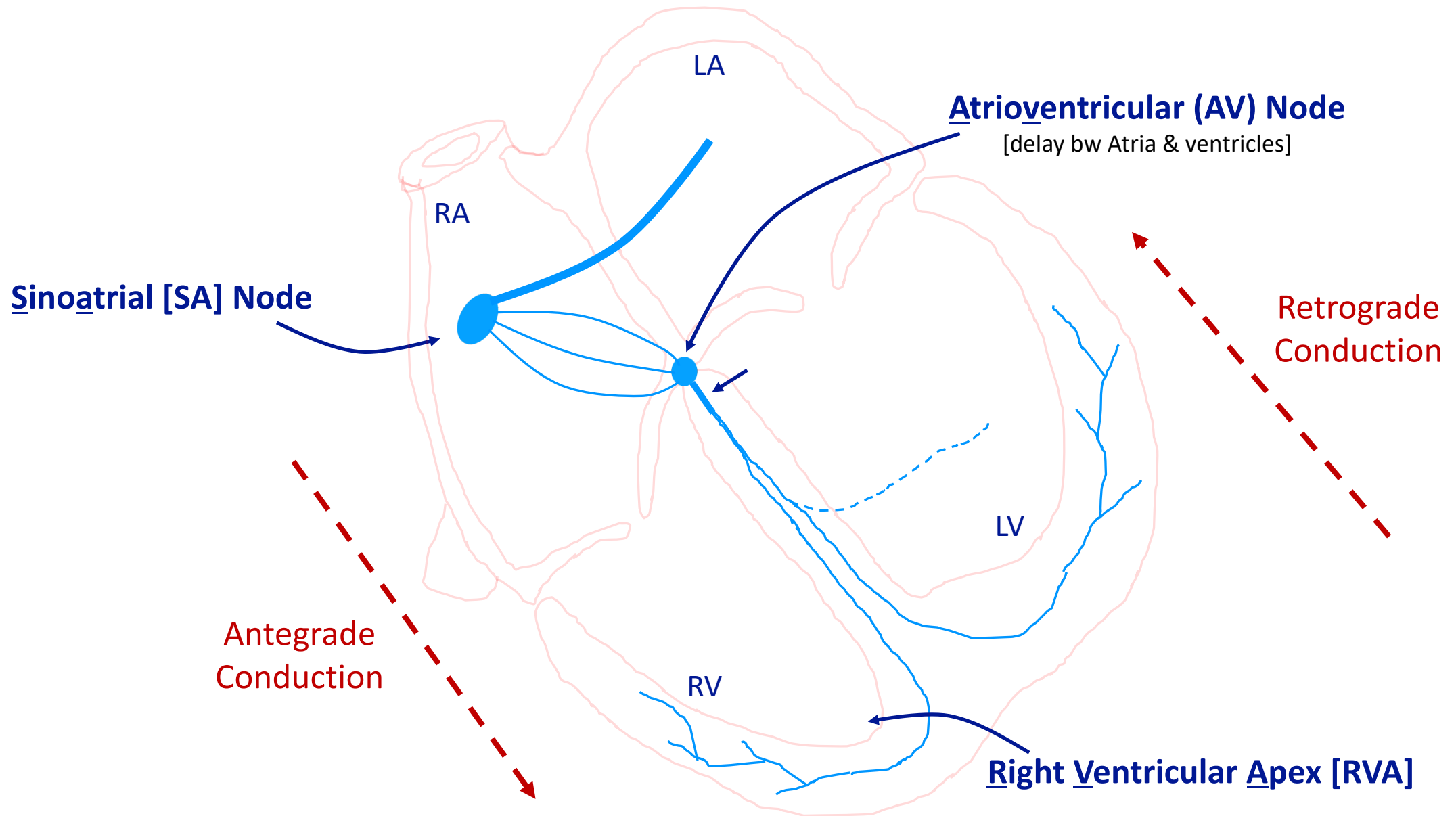


Linear Temporal Logic

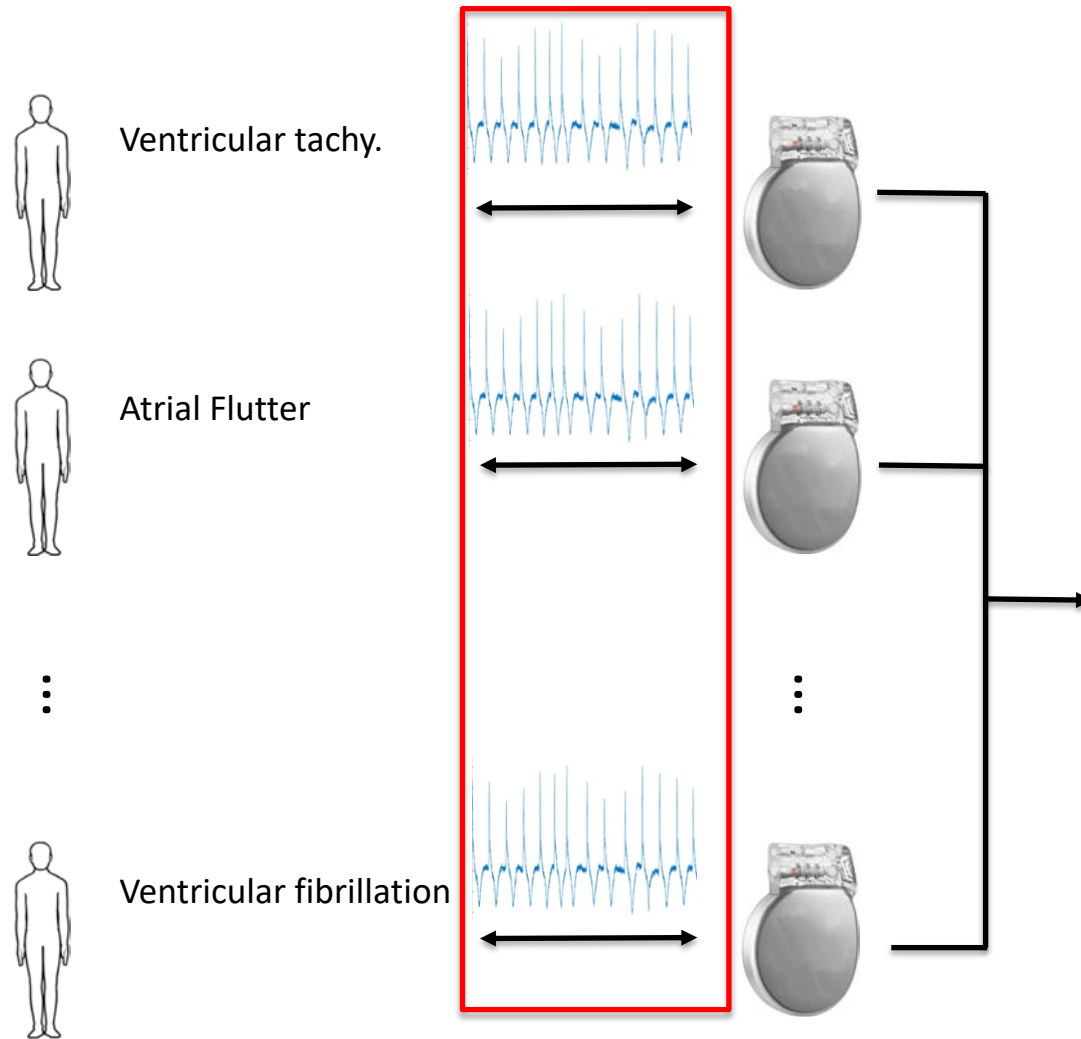
?

So far: Looked at a device algorithm



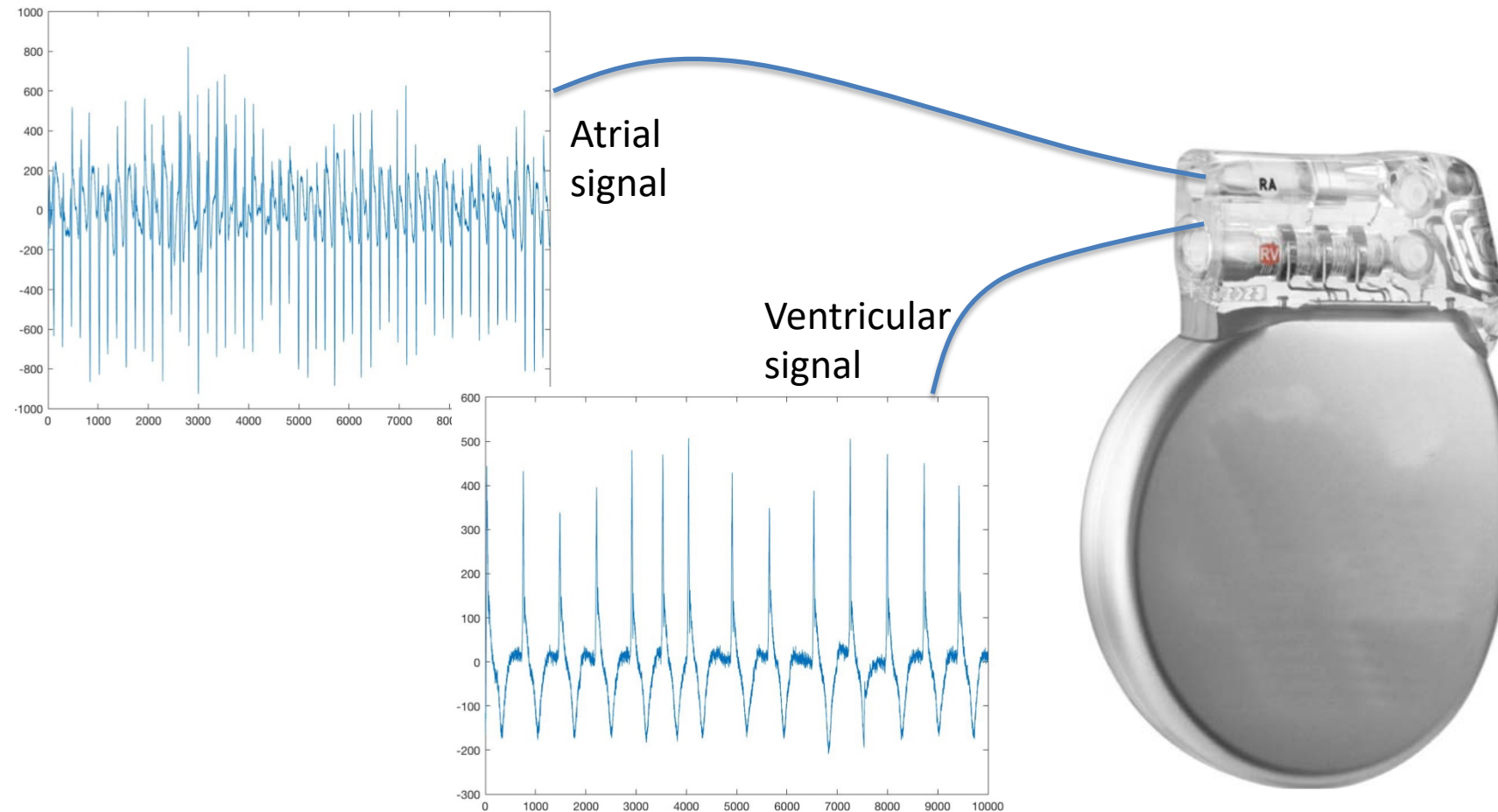


Need: a model of device inputs



Need: a model of device inputs

Inputs to pacemaker are intra-cardiac electrograms



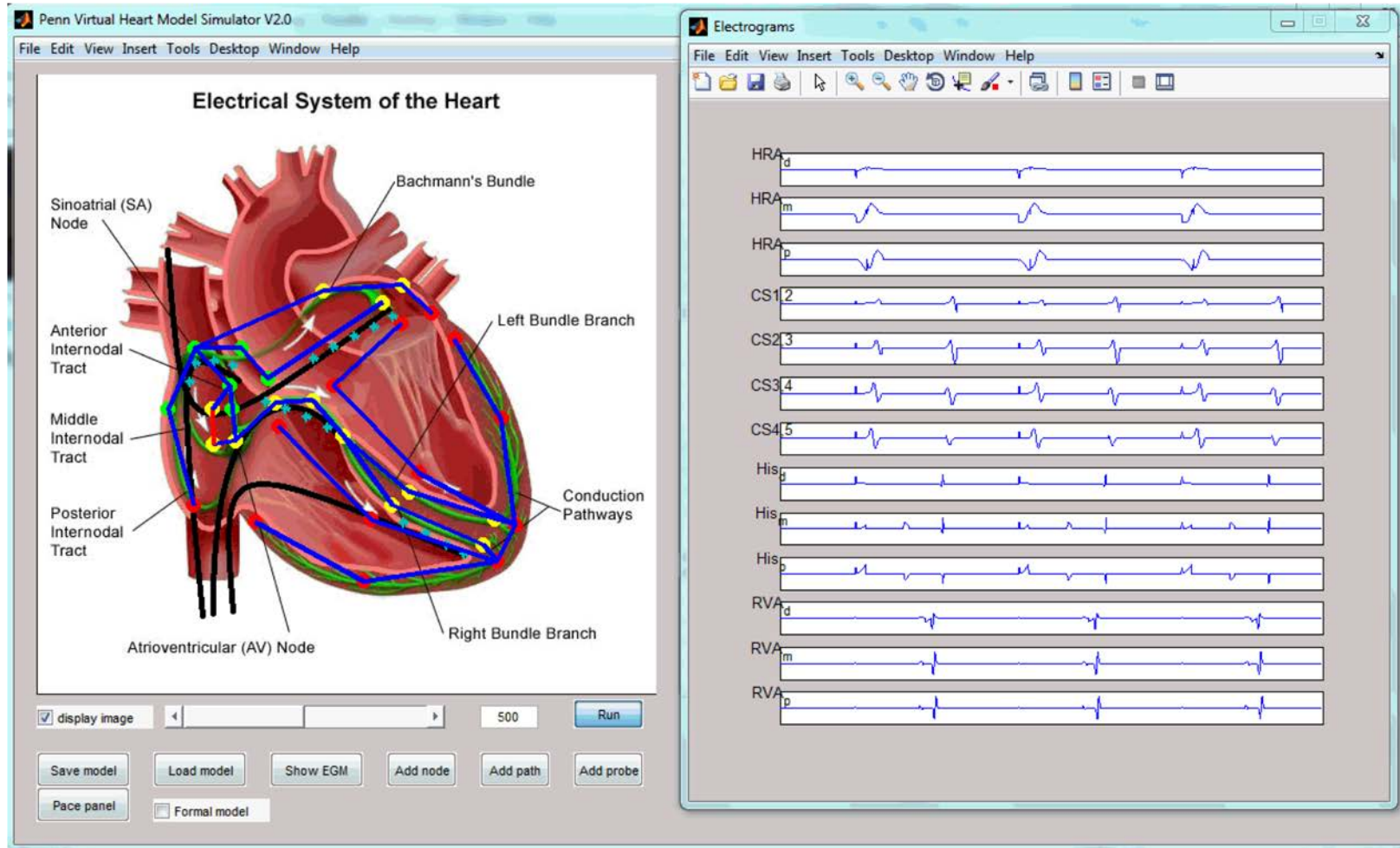
Lets model the heart as a timed automaton

Its about time!

Modeling choices

- Molecular
 - Cellular
 - Tissue
 - Whole organ
-
- Mechanical
 - Electrical

What do we want from the heart model?

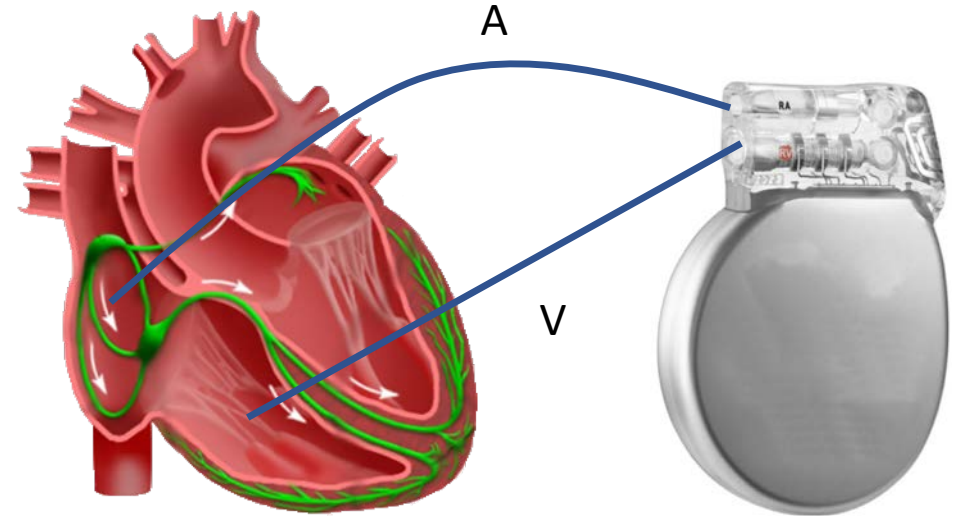
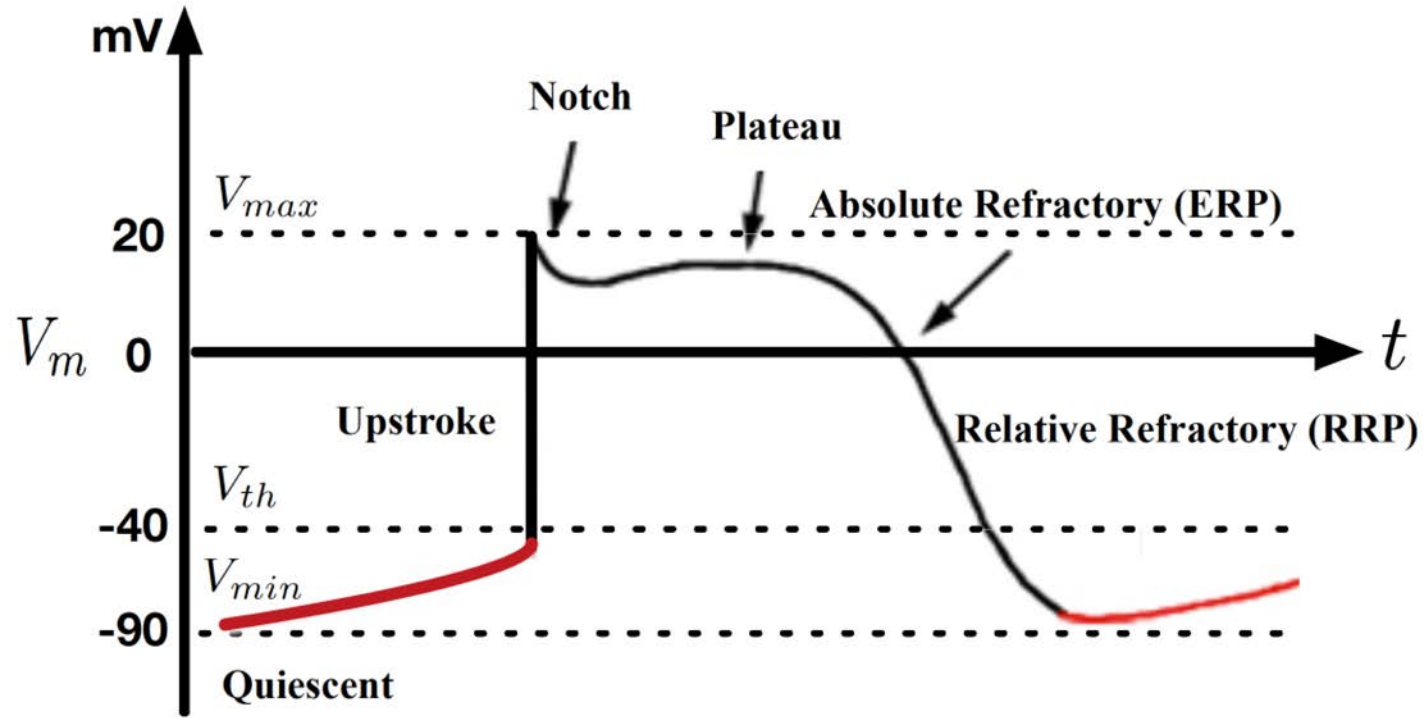


- Predict when it misses beats → model outputs are events in A and V.
- Receive pacing from device → inputs are *pacing* events.

Modeling choices

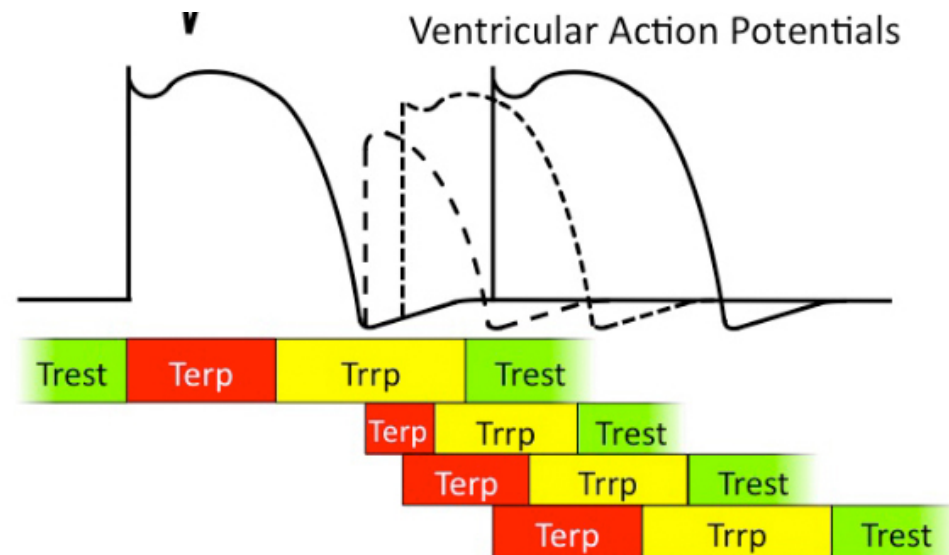
- Molecular
 - Cellular
 - Tissue
 - Whole organ
-
- Mechanical
 - Electrical

Action potential



Refractory periods

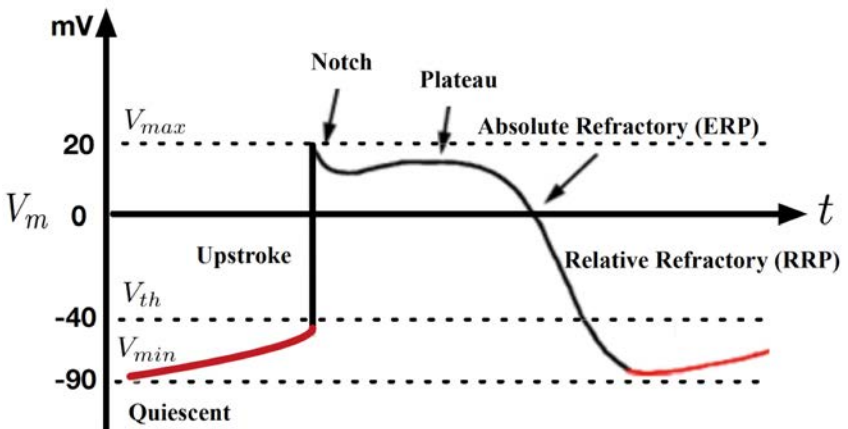
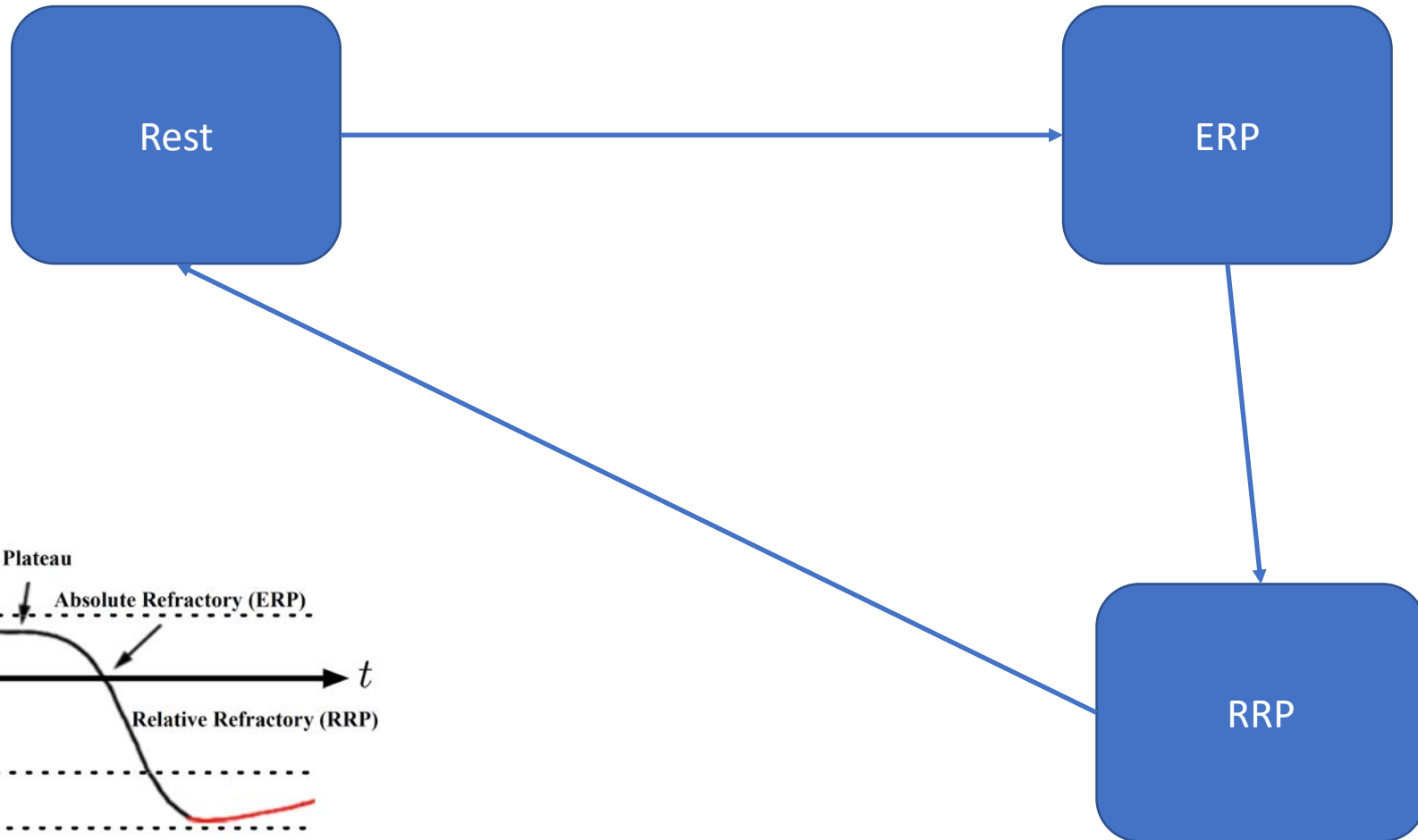
- Divide refractory period into time periods – Rest, ERP, and RRP
- Model refractory properties as timers.
- These time periods can be measured during EP study



Excitable Cardiac cells

- A piece of heart tissue (myocardium) is made of many *excitable* cells
- Each cell has (roughly speaking) three phases: Rest, Effective Refractory Period (ERP), and the Relative Refractory Period (RRP).
- In Rest, the cell can be excited by electricity. It can also self-excite if enough time elapses
- After being excited (*depolarized*), it enters a refractory phase during which it cannot be excited a second time. This is the Effective Refractory Period
- After the ERP, it enters a second refractory phase during which it can be excited, but with greater difficulty and with a smaller reaction. This is the Relative Refractory Period
- After the RRP, it returns to Rest and cycle repeats.

One cell



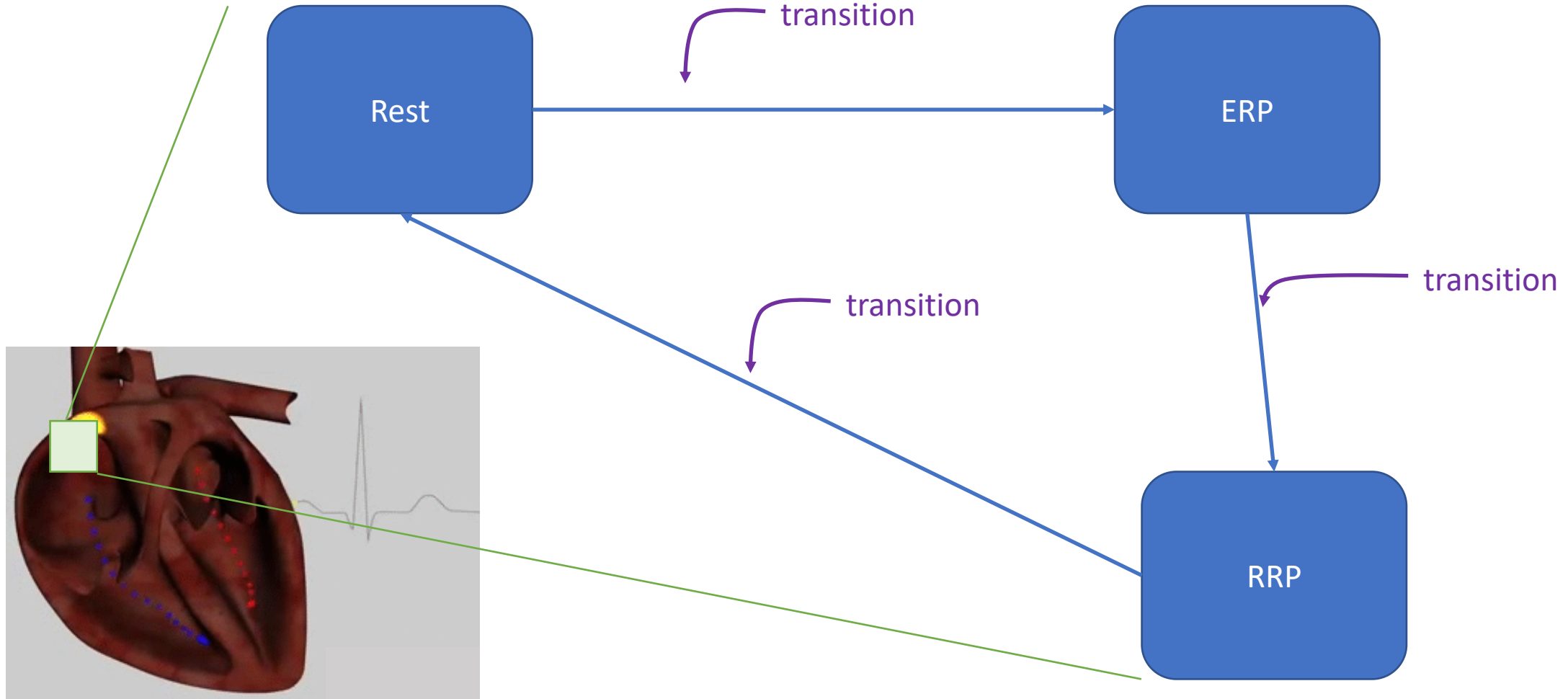
Cardiac tissue : Functional Syncytium

We can model **an entire piece of cardiac tissue** as having the same three phases as the cells that make it up: Rest, ERP and RRP.

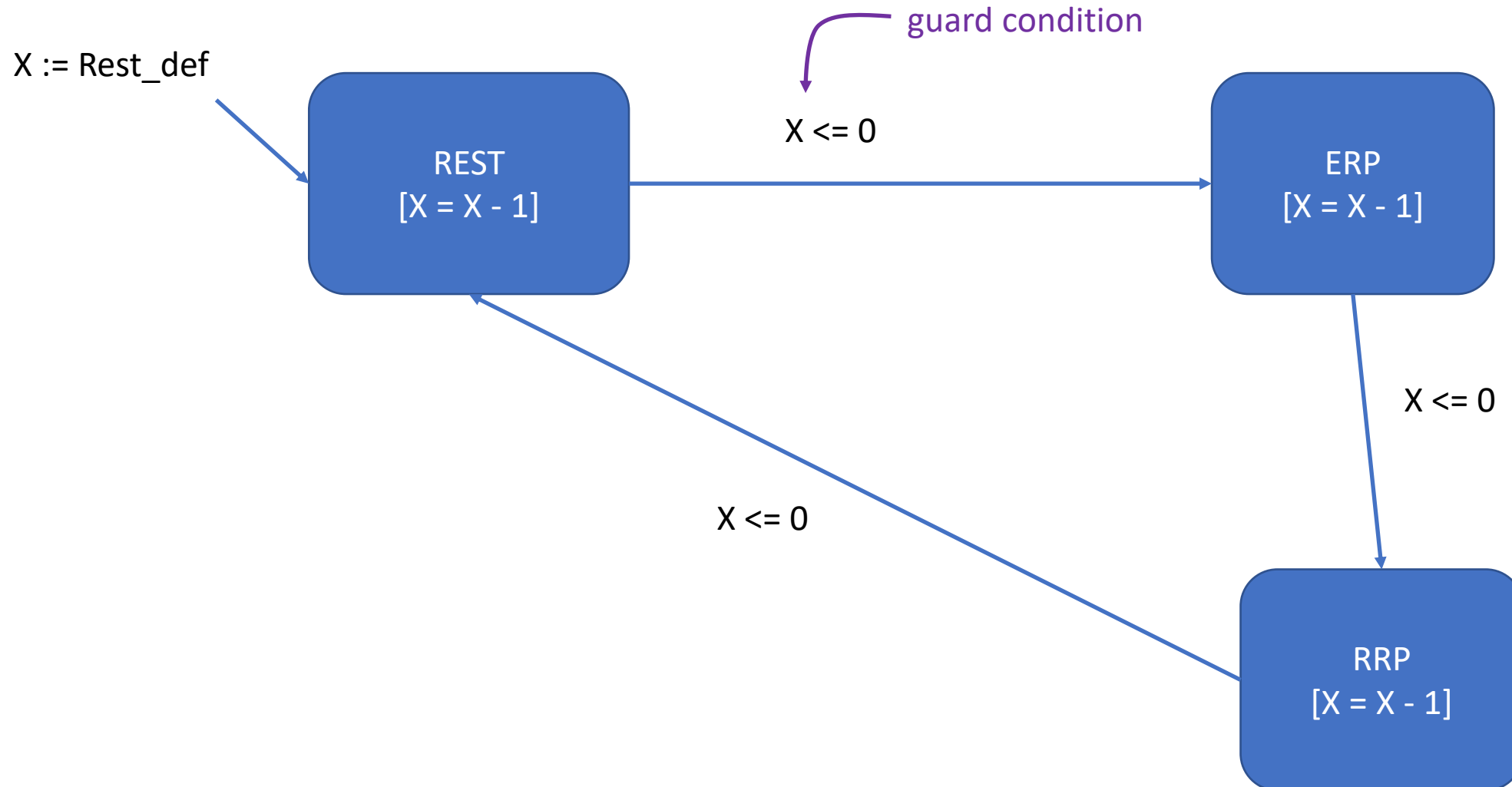
Homegenization:

even though some quantities are time- or space-varying, it might be OK, to first order, to model them as constants across time (and space)

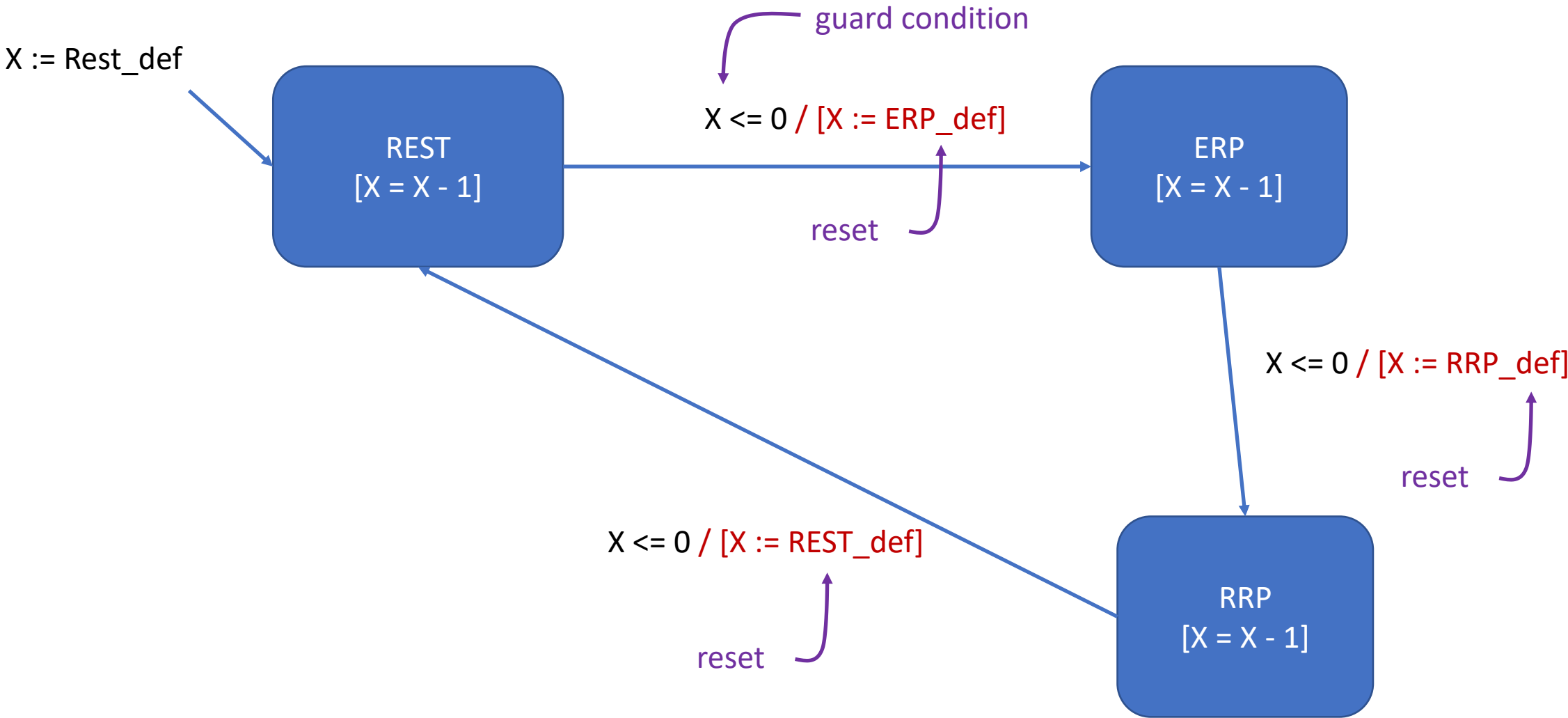
Cardiac tissue: one *node automaton*



Node automaton with **clocks**

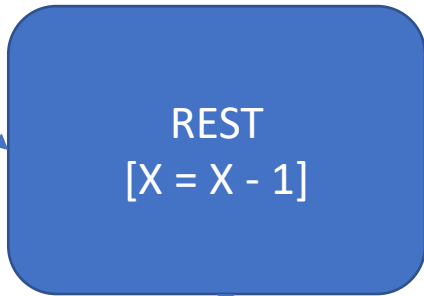


Node automaton with **clocks** and **resets**

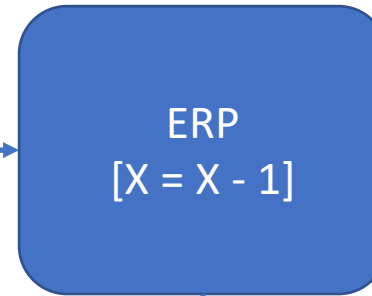


Node automaton with **clocks**, **resets** and **actions**

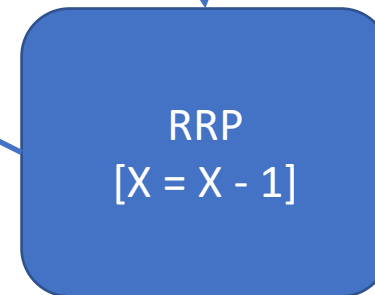
$X := \text{Rest_def}$



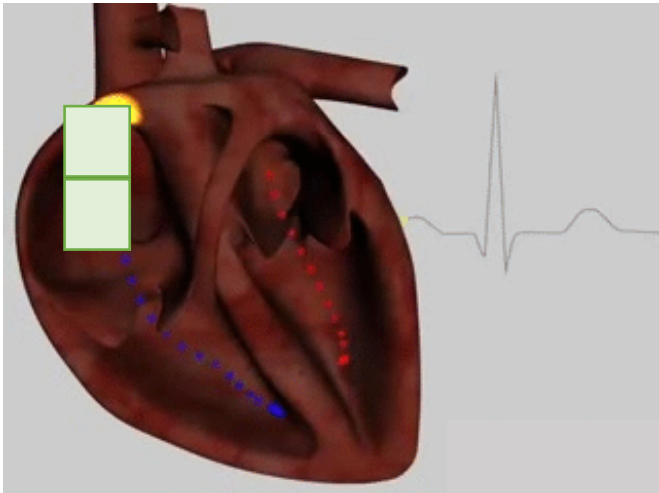
$X \leq 0 / [X := \text{ERP_def}]$



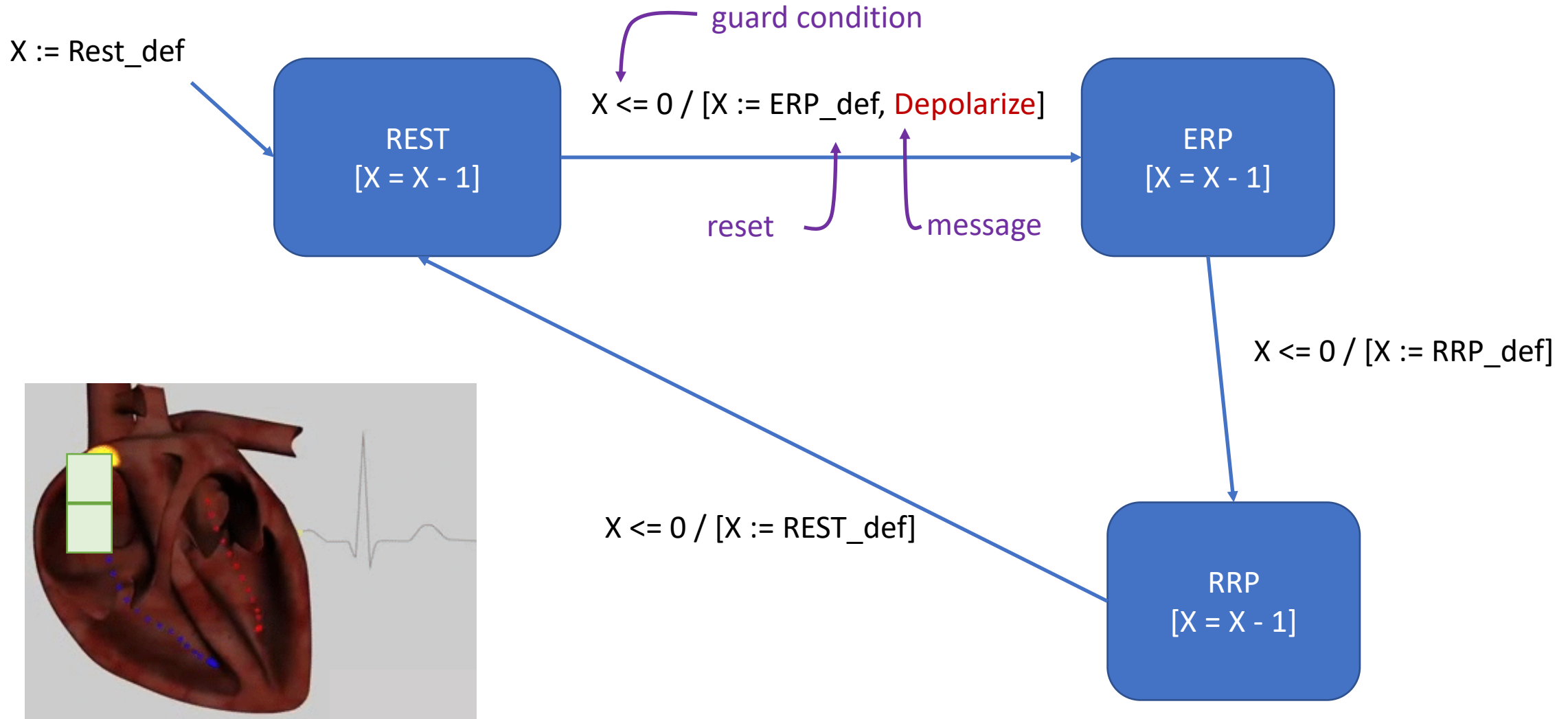
$X \leq 0 / [X := \text{RRP_def}]$



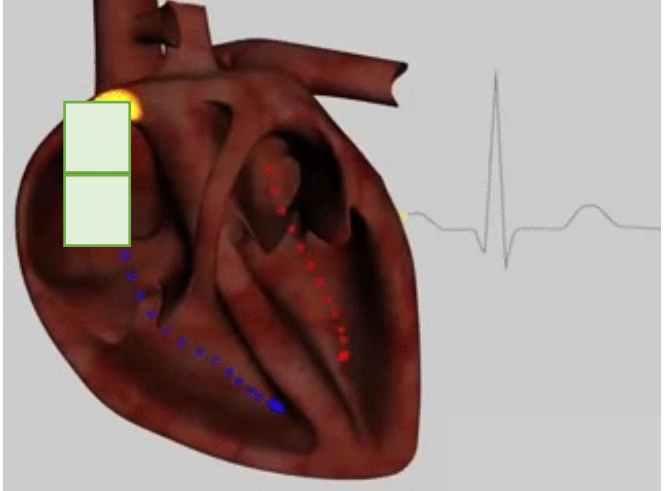
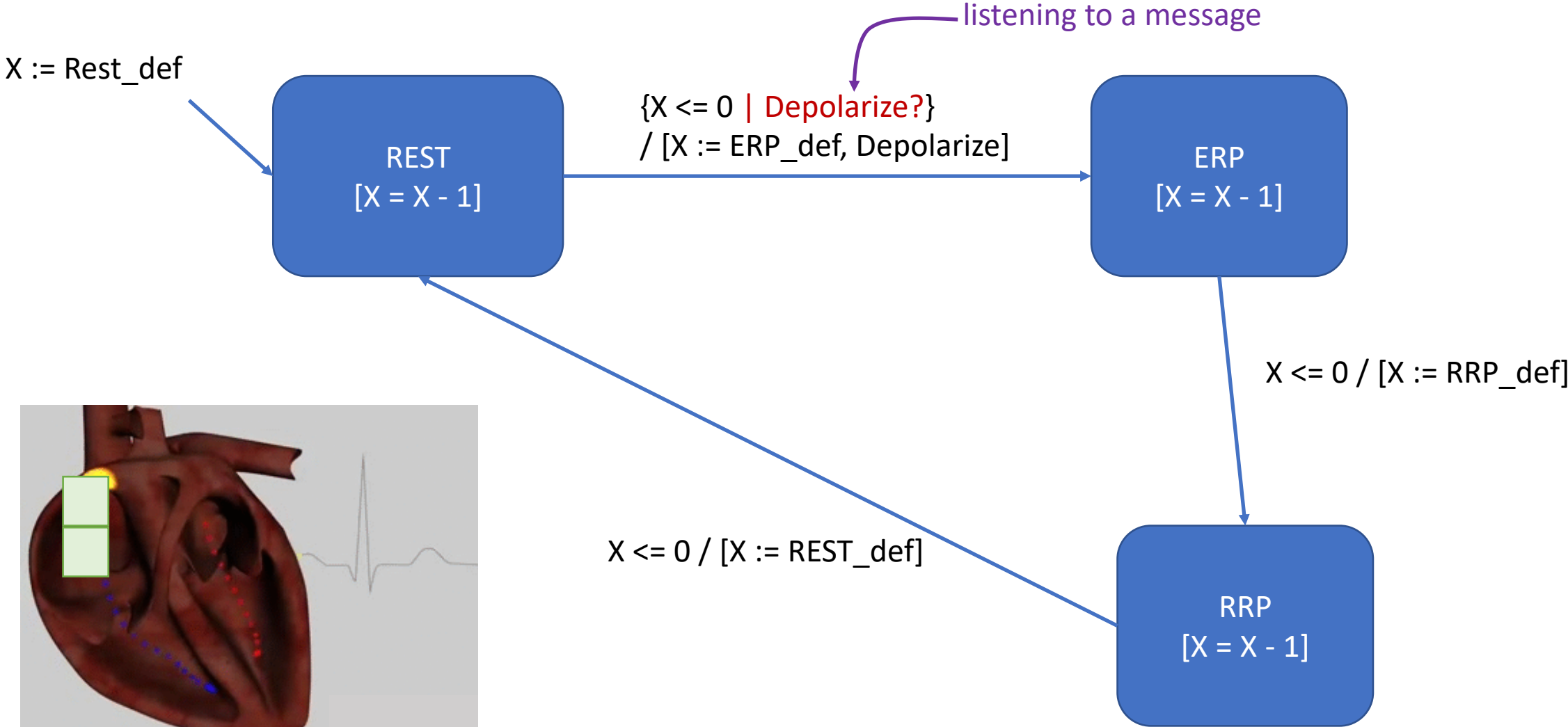
$X \leq 0 / [X := \text{REST_def}]$



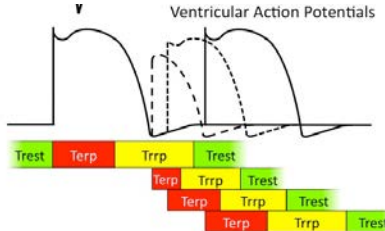
Node automaton with **clocks**, **resets** and **actions**



Node automaton with **clocks**, **resets** and **actions** receiving an action (message)



Node automaton with **clocks**, **resets** and **actions** receiving an action (message)



$X := \text{Rest_def}$



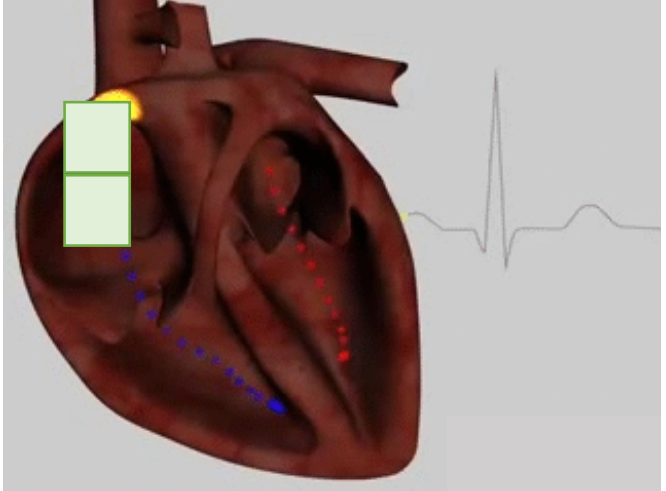
$\{X \leq 0 \mid \text{Depolarize?}\}$
/ [X := ERP_def, Depolarize]



$\{\text{Depolarize?}\}$
/ [X := ERP_def, Depolarize]

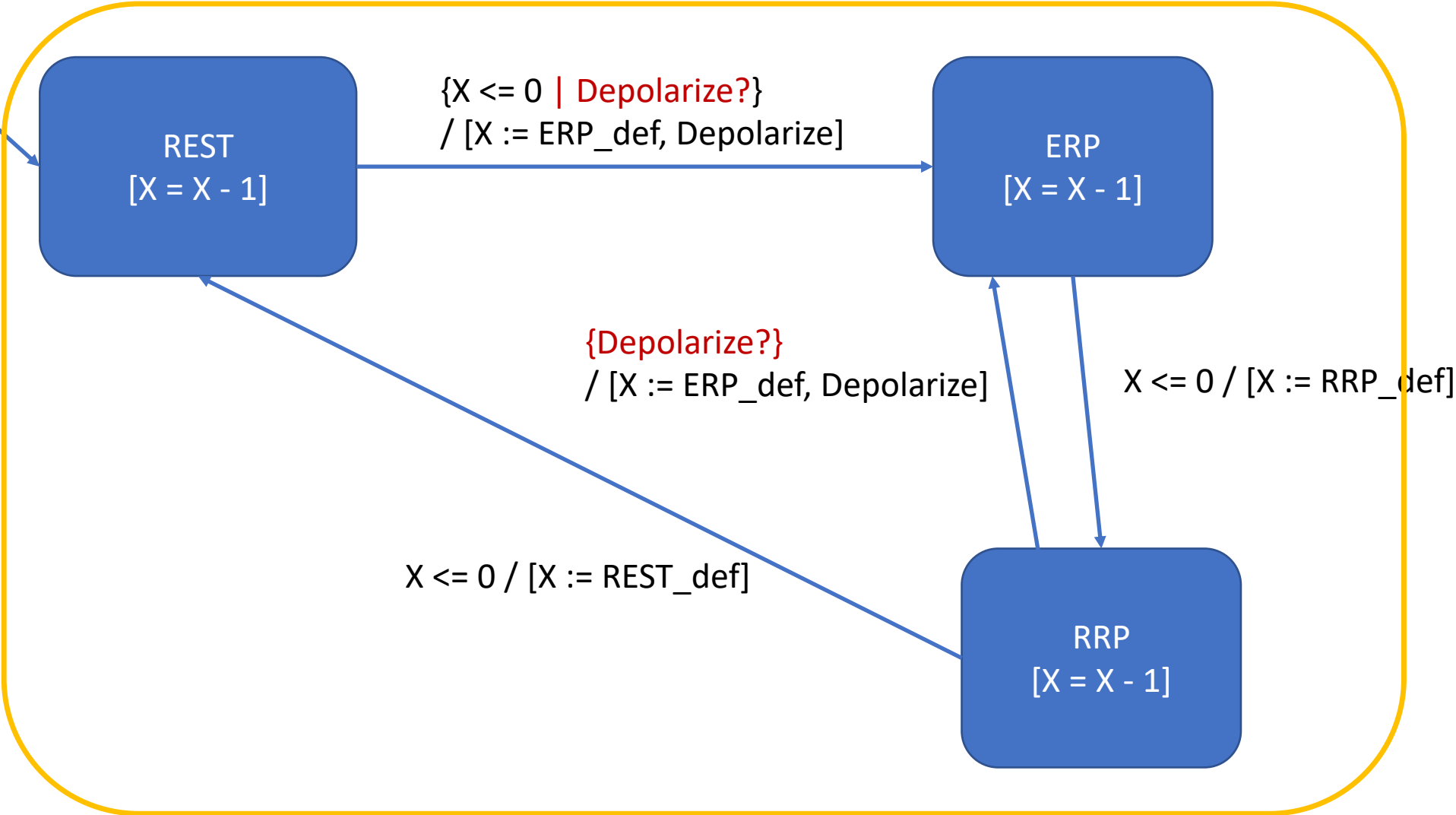
$X \leq 0 \mid [X := \text{RRP_def}]$

$X \leq 0 \mid [X := \text{REST_def}]$



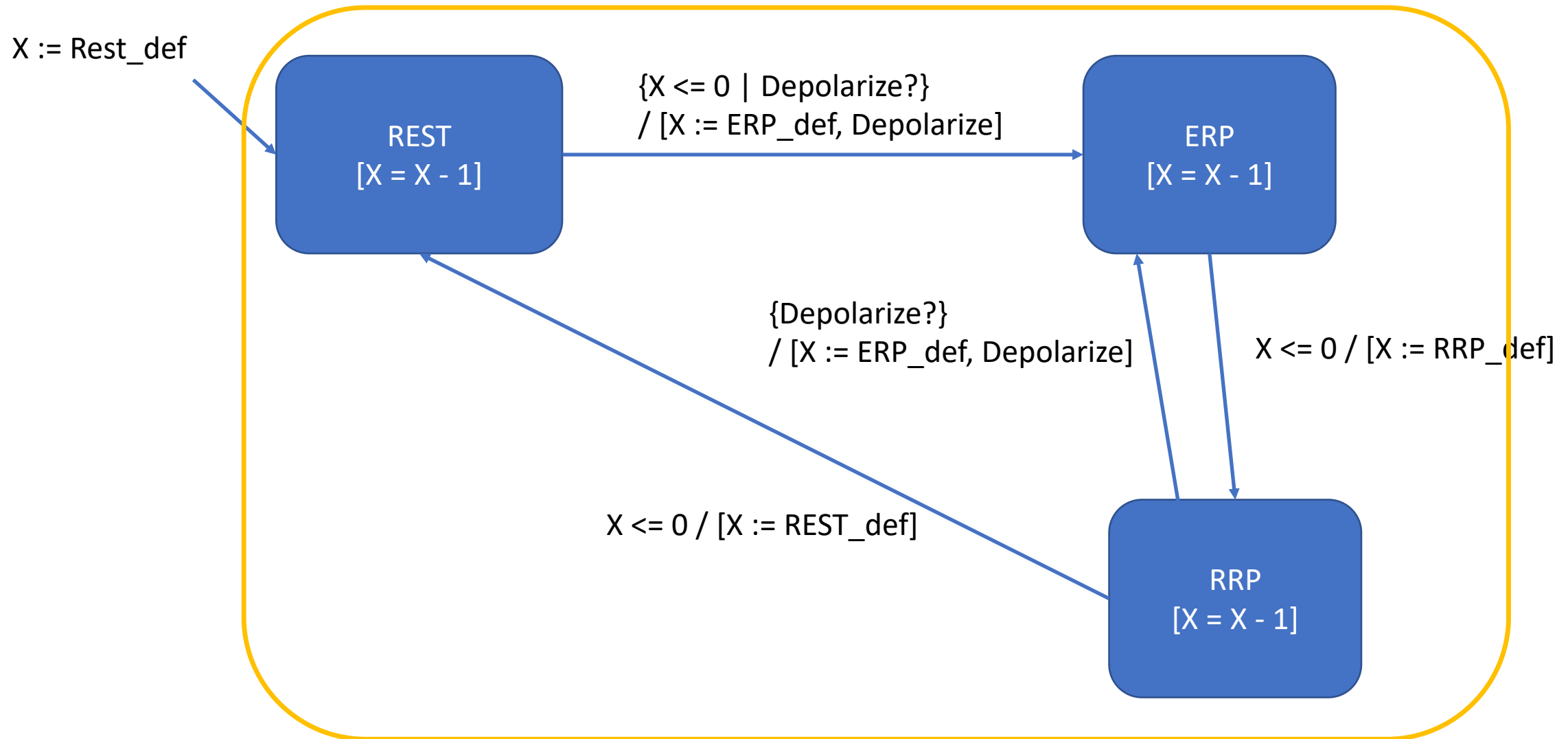
Node automaton with **clocks**, **resets** and **actions**

$X := \text{Rest_def}$

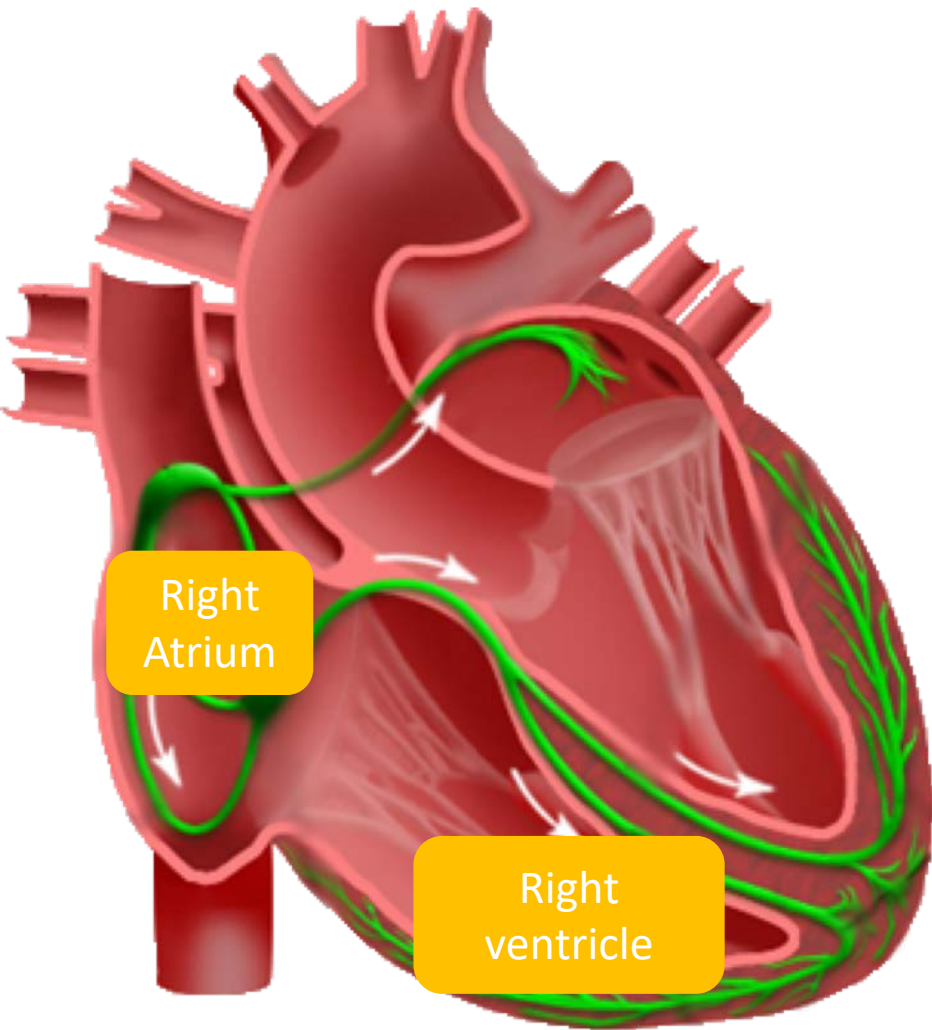


Node automaton with **clocks**, **resets** and **actions**

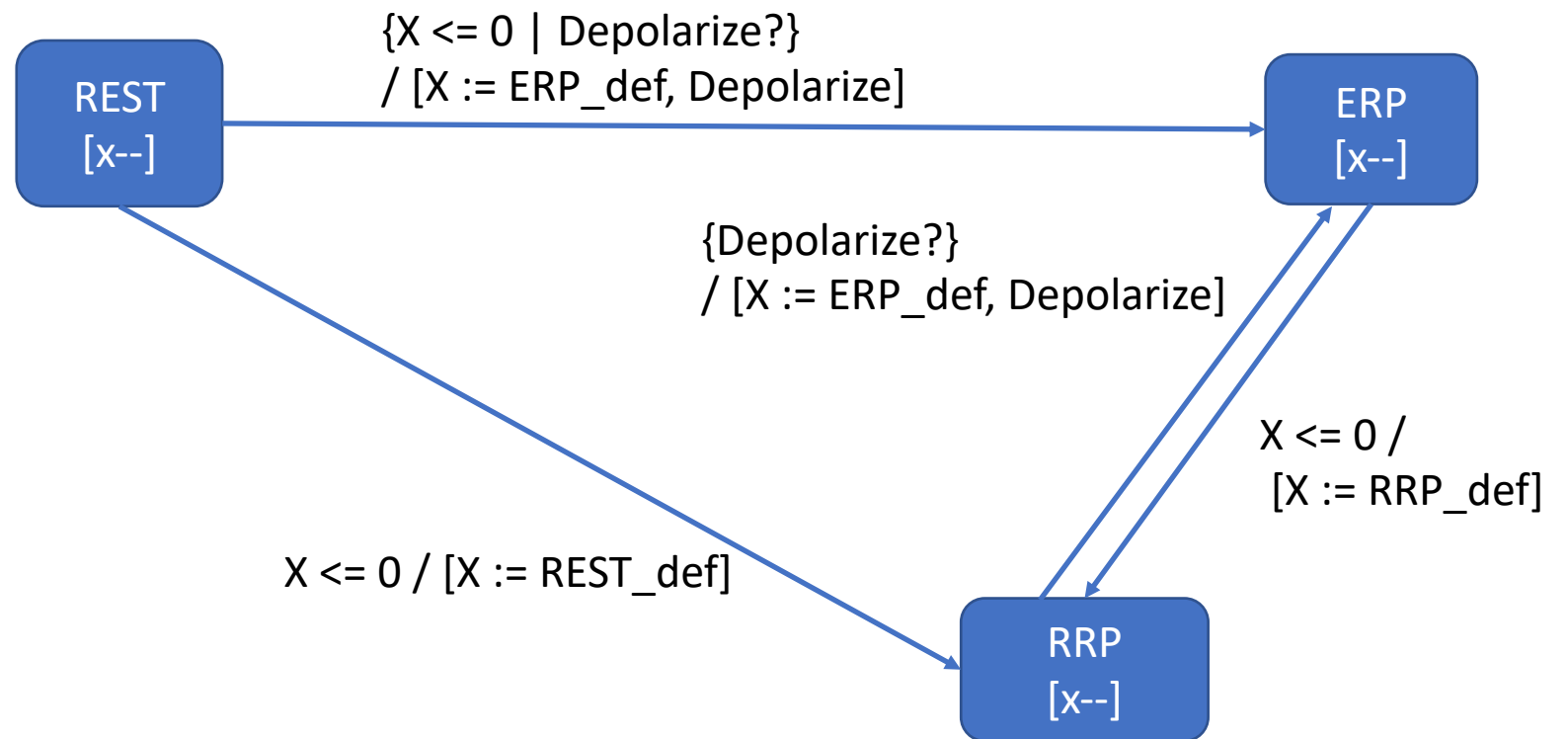
Timed Automaton



Different tissues with different properties = nodes with different parameters



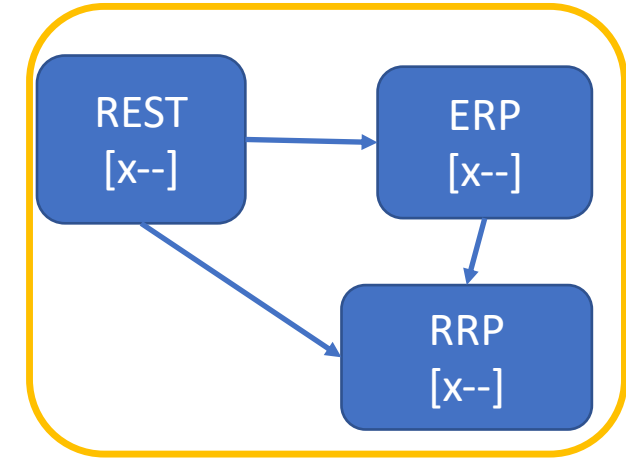
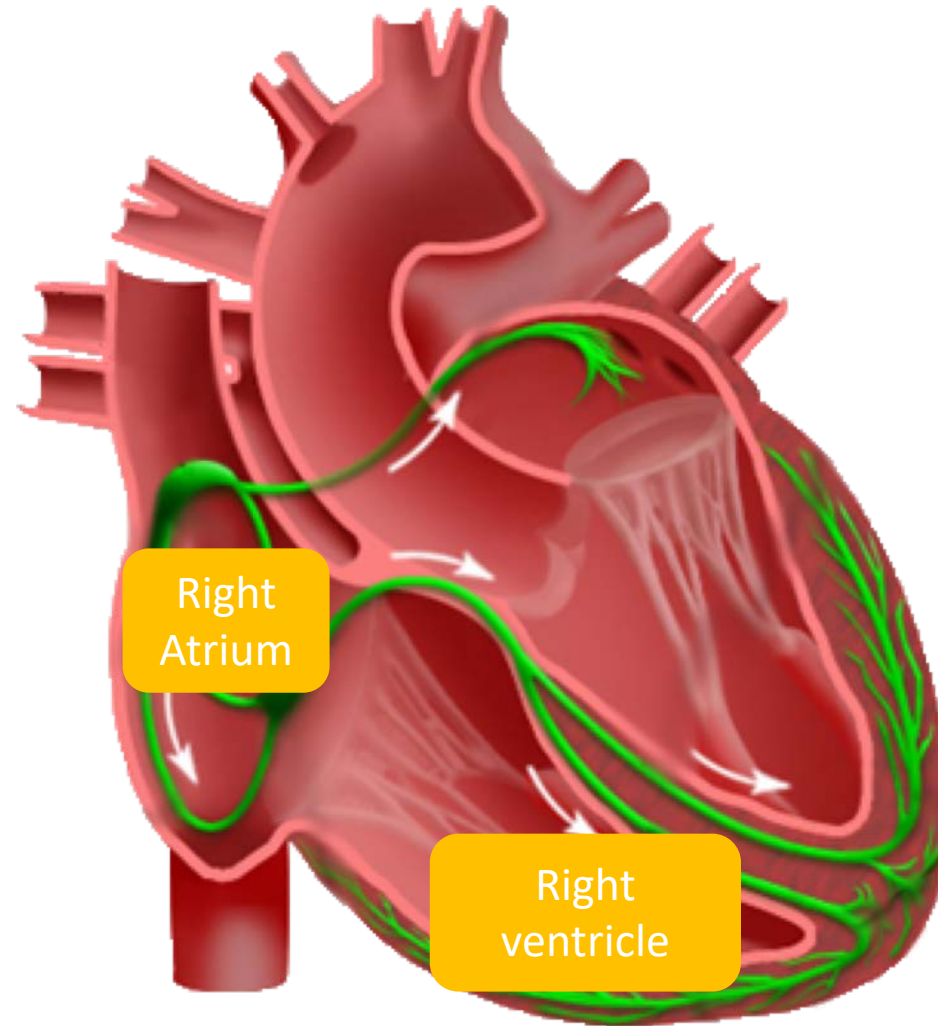
What parameters might be different between High Right Atrium (HRA) and Right Ventricular Apex (RVA)?



Different tissues with different properties = nodes with different parameters

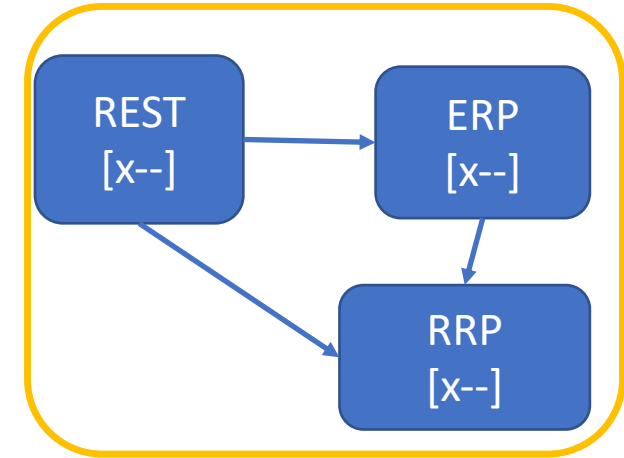
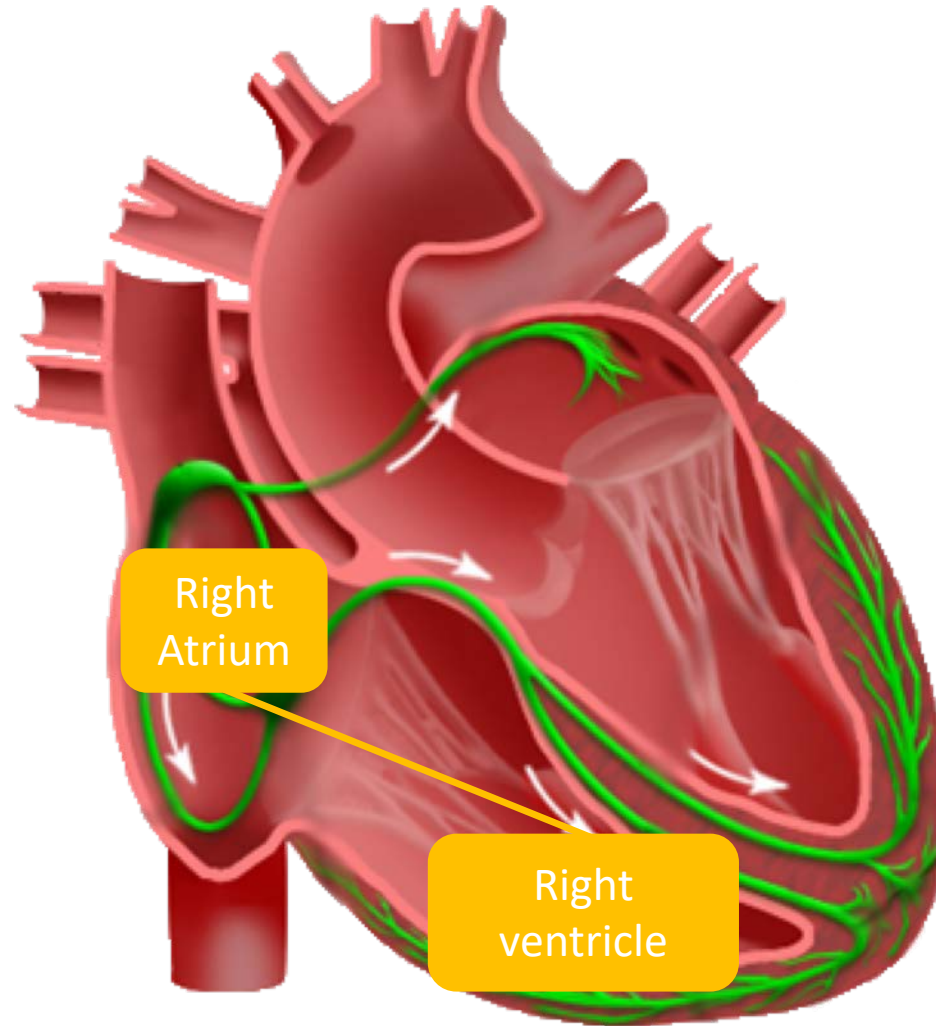
Atrium must depolarize faster than everybody →
 $\text{Atrium.Rest_def} <$
 $\text{Ventricle.Rest_def}$

E.g. if the modeled heart rate is 60 beats per minute (bpm), atrium fires every 1 sec →
 $\text{Atrium.Rest_def} = 1\text{sec.}$
Can choose
 $\text{Ventricle.Rest_def} = 10\text{secs, say.}$

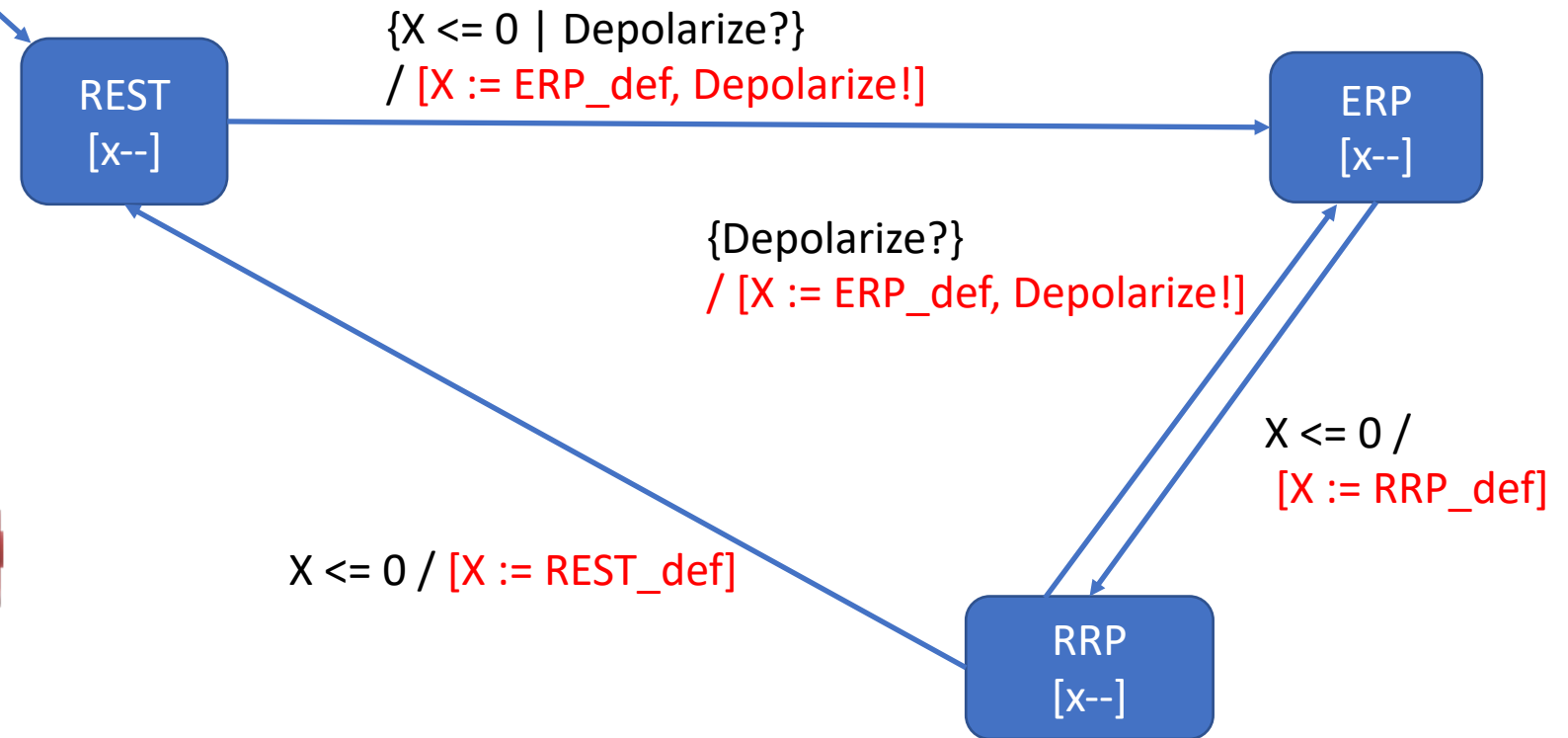
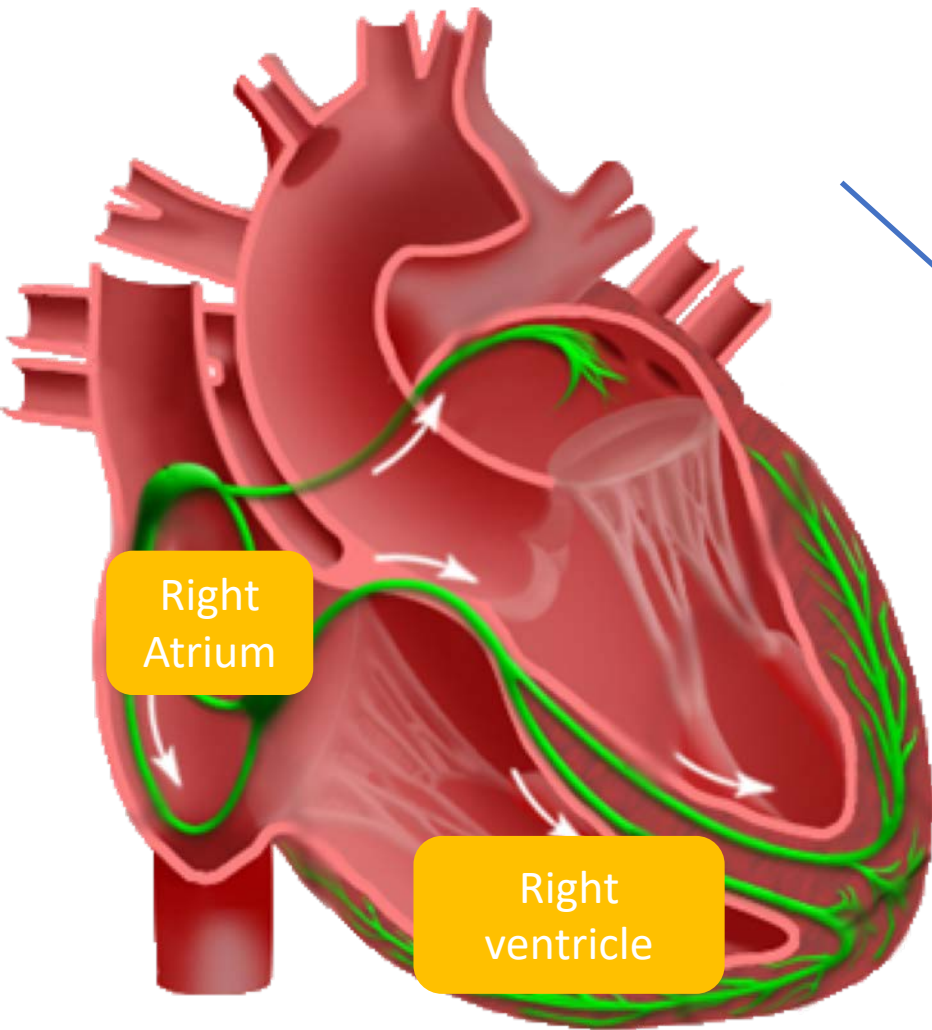


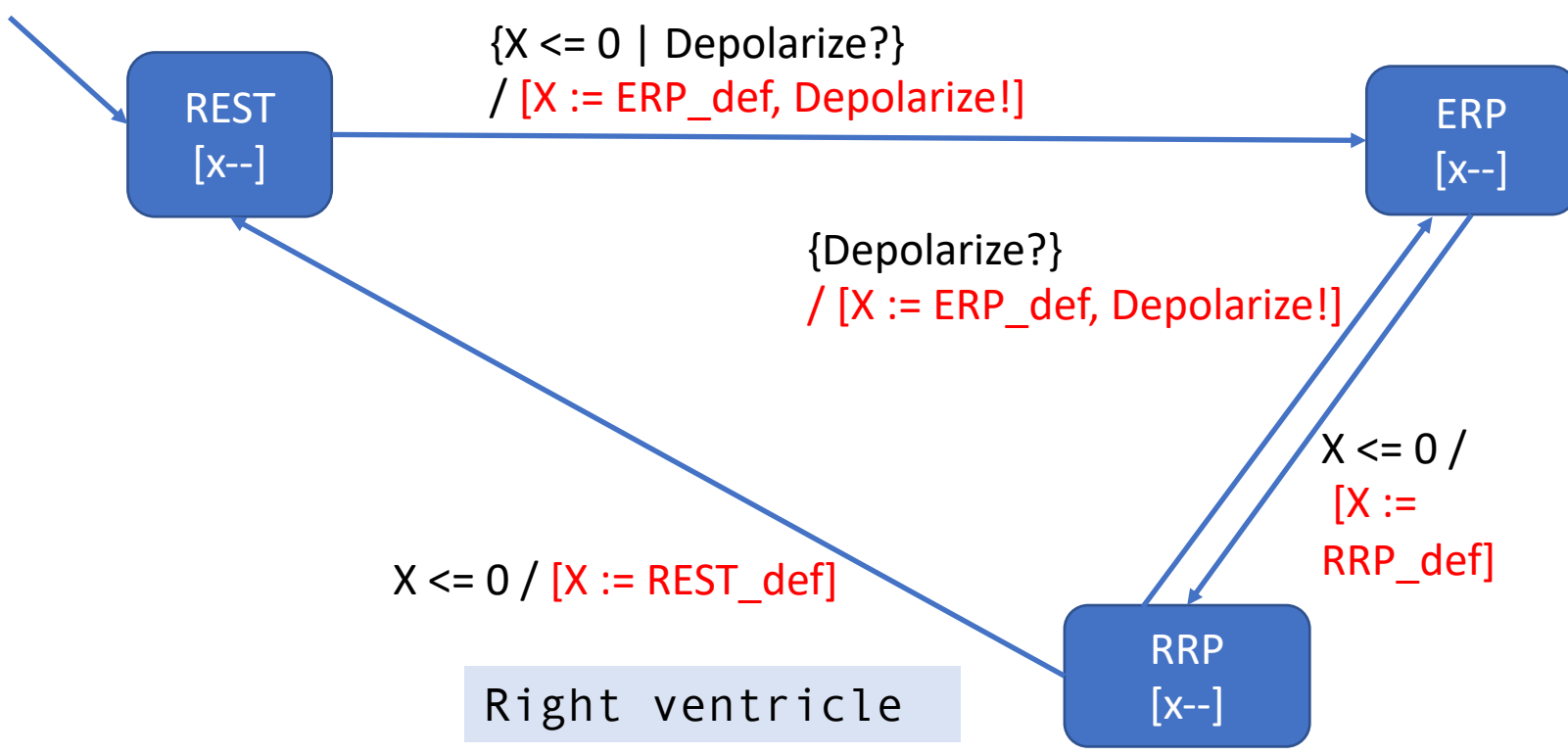
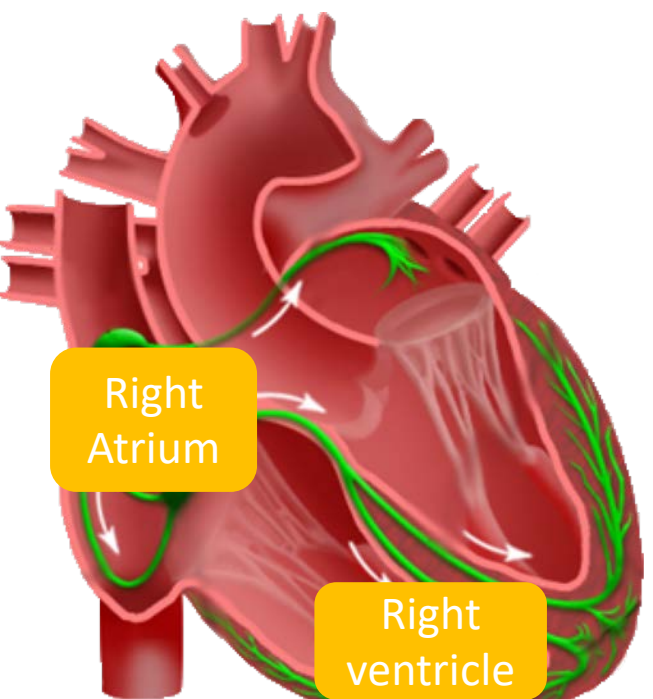
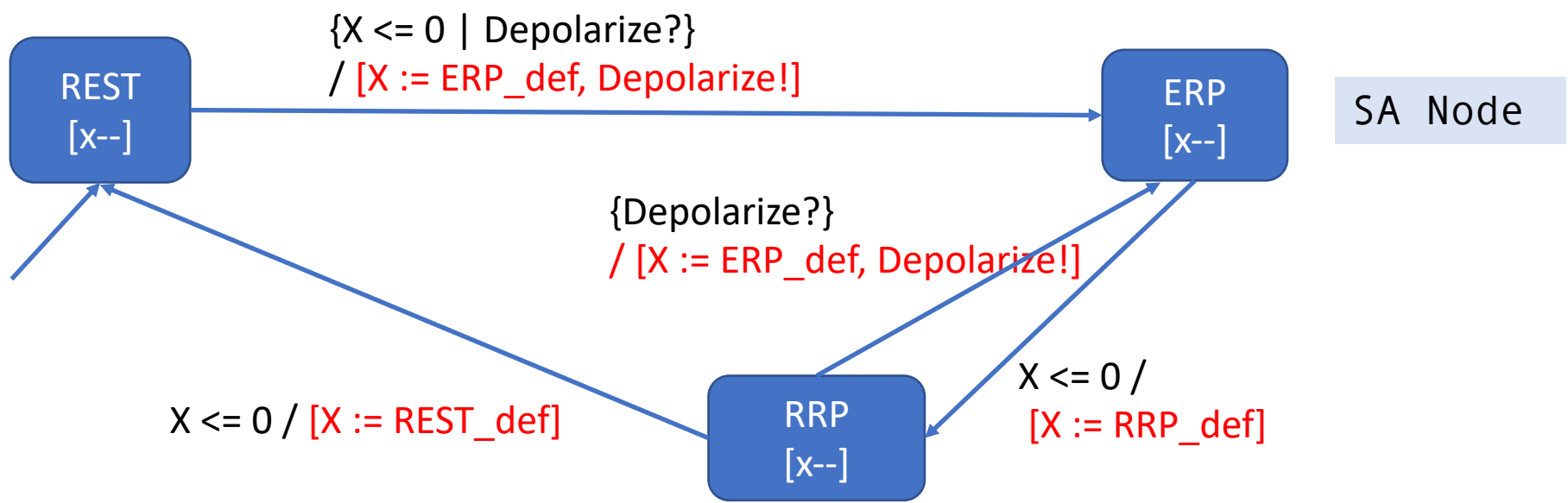
Connecting two tissues = connecting two nodes

How do we model the propagation of activity, i.e. of event [Depolarize], from Atrium to Ventricle?



Communicating between timed automata

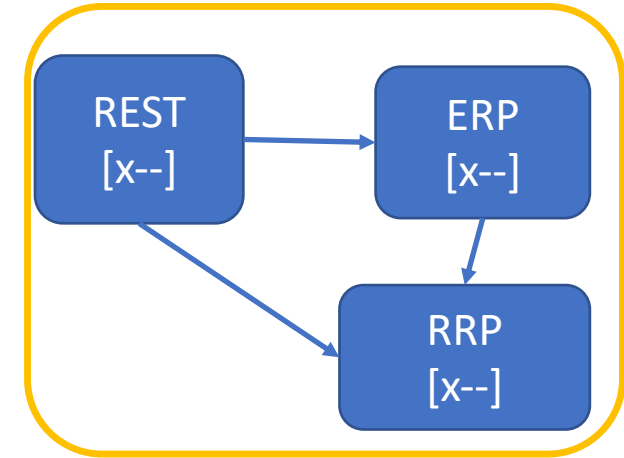
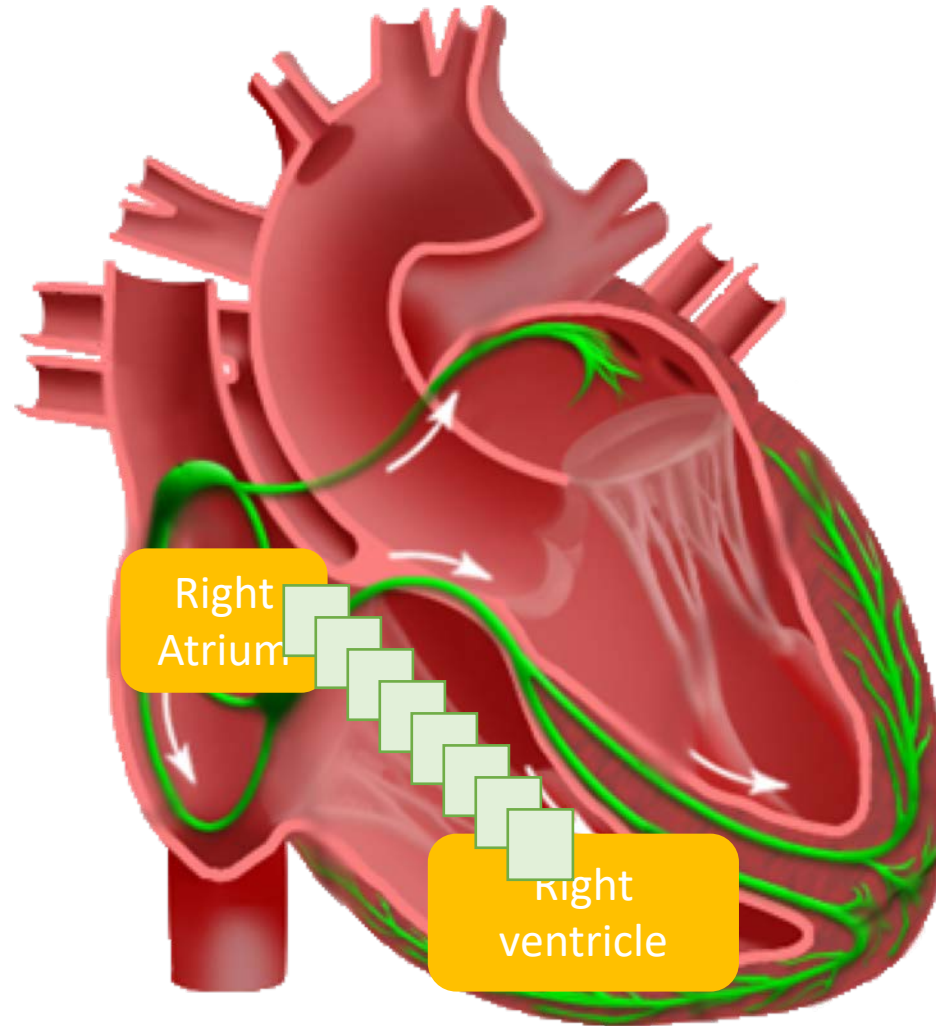




Connecting two tissues = connecting two nodes

How do we model the propagation of activity, i.e. of event [Depolarize], from Atrium to Ventricle?

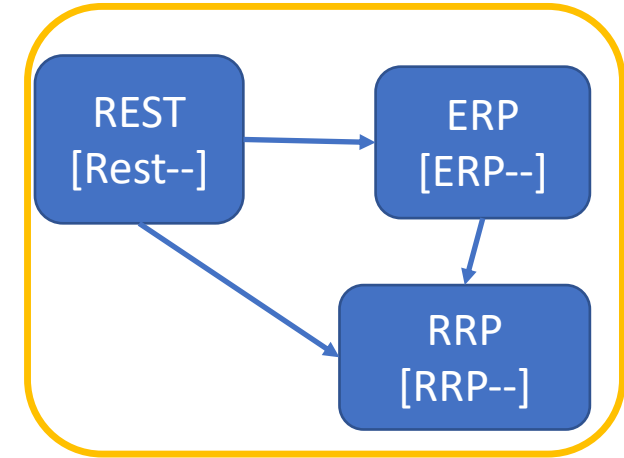
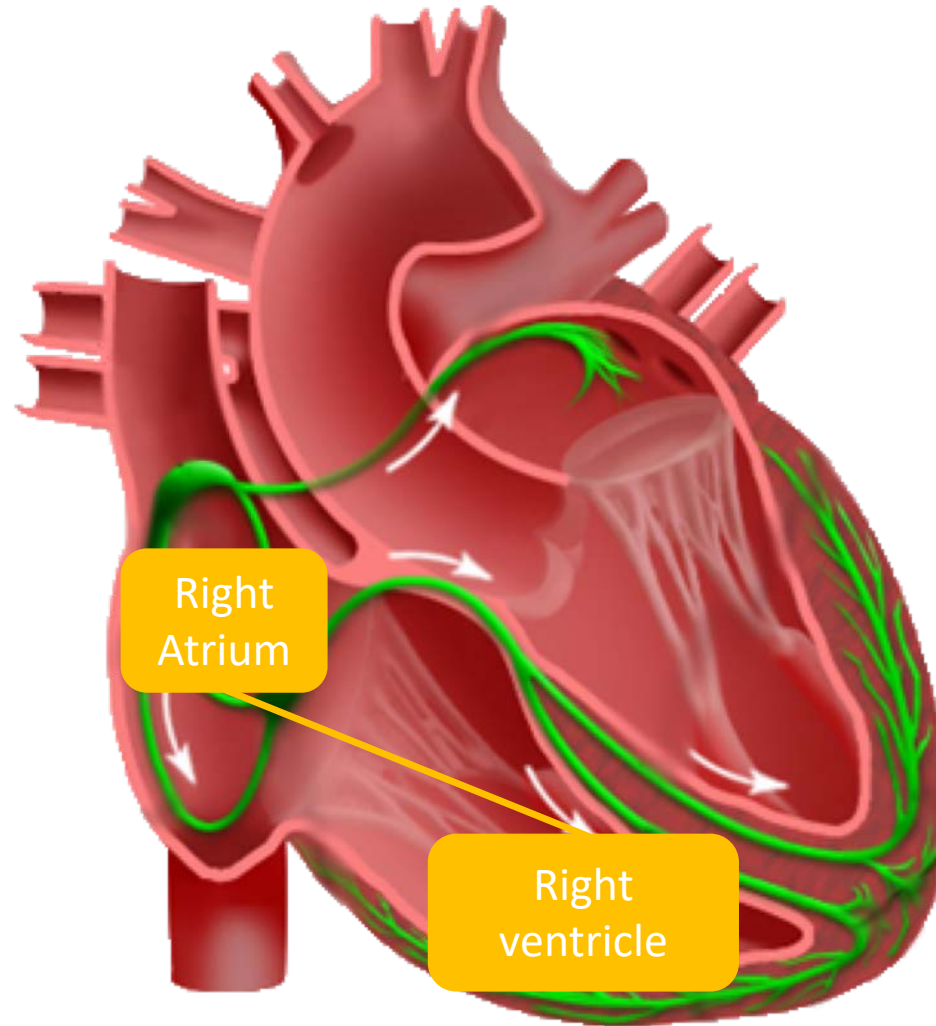
A large # of cells between the two...

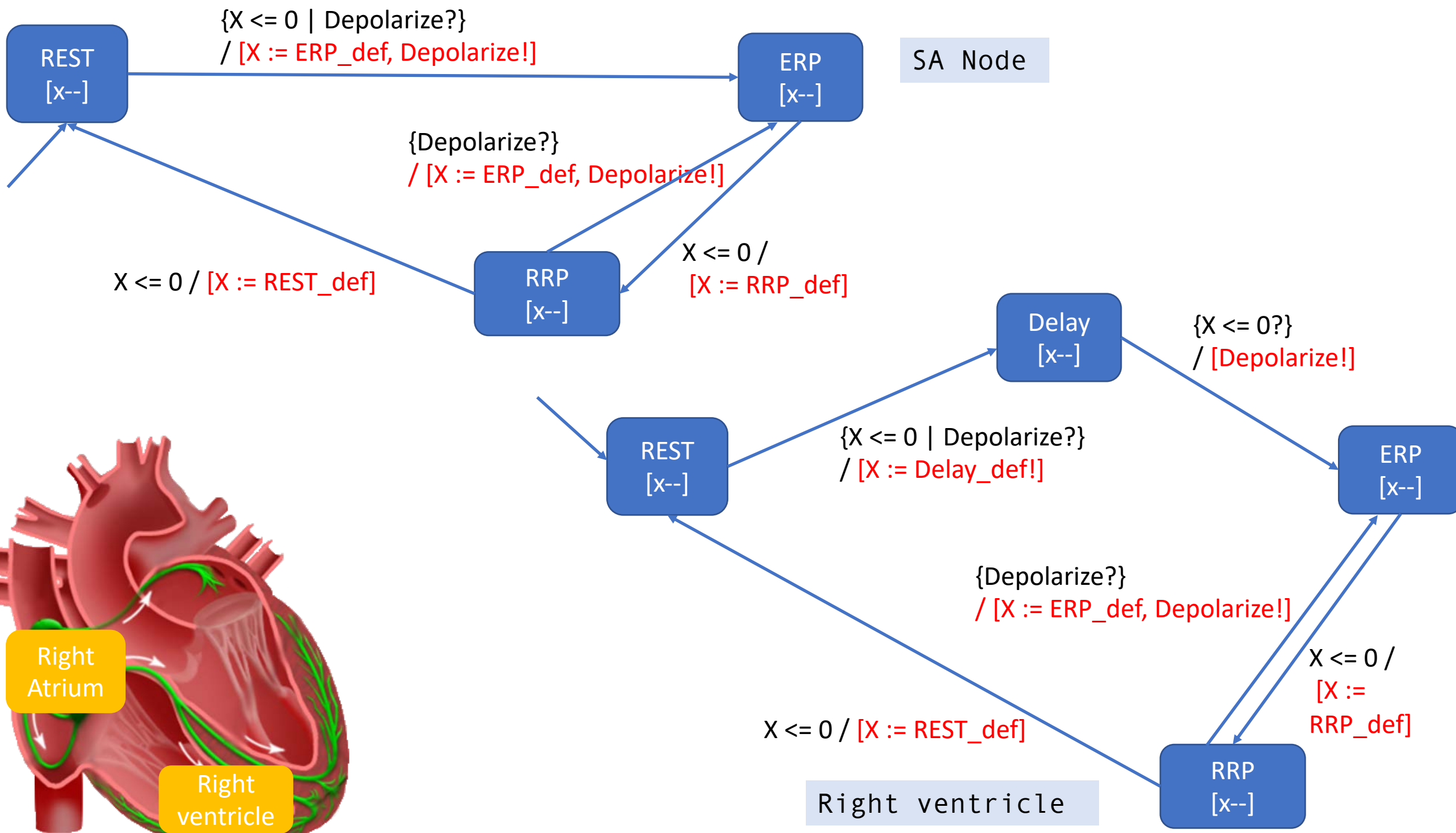


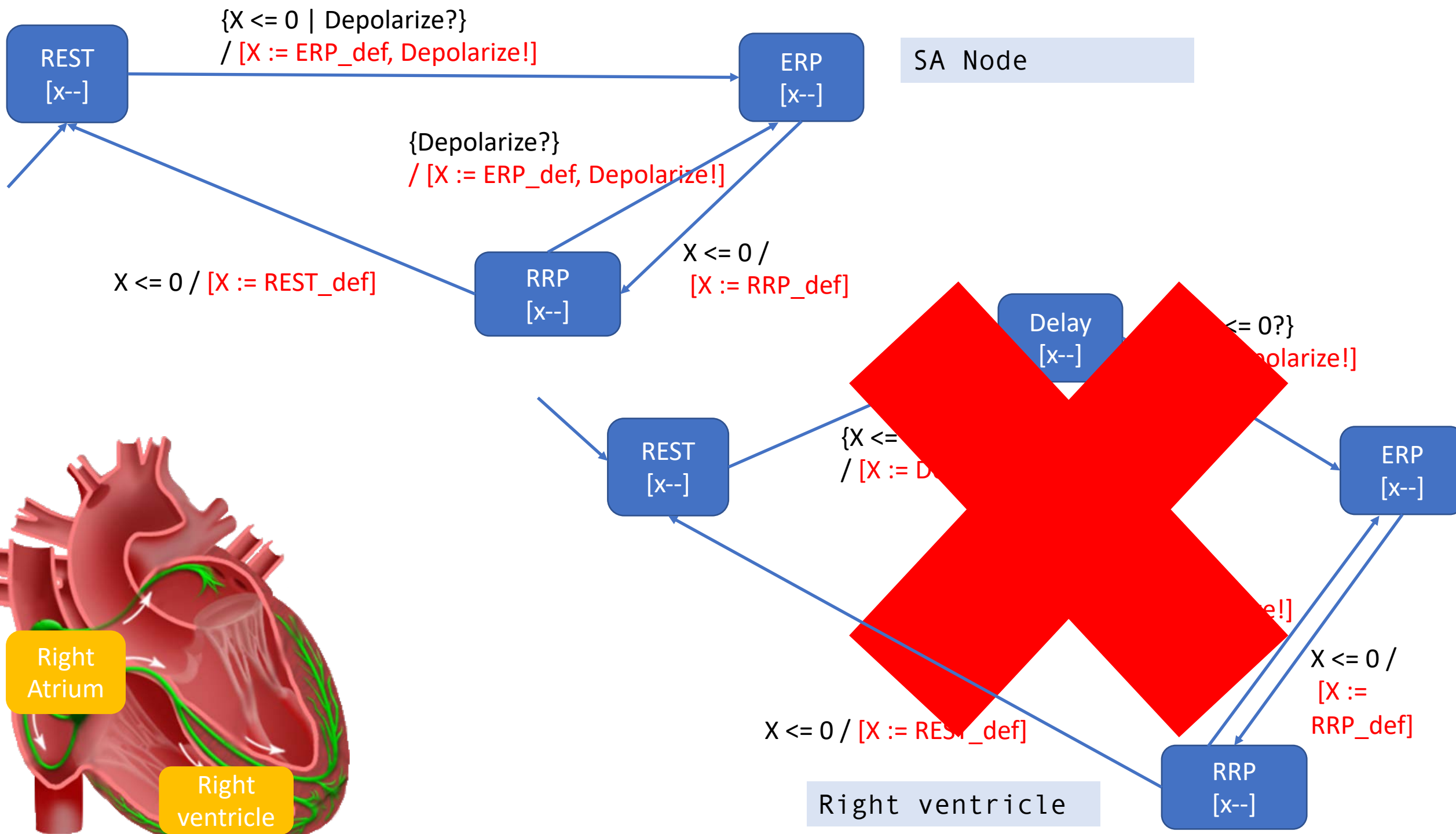
Connecting two tissues = connecting two nodes

How do we model the propagation of activity, i.e. of event **[Depolarize]**, from Atrium to Ventricle *as a timed automaton*?

Stick to same formalism as much as possible: Different formalisms add complexity to the analysis as you try to make two mathematical languages talk to each other.

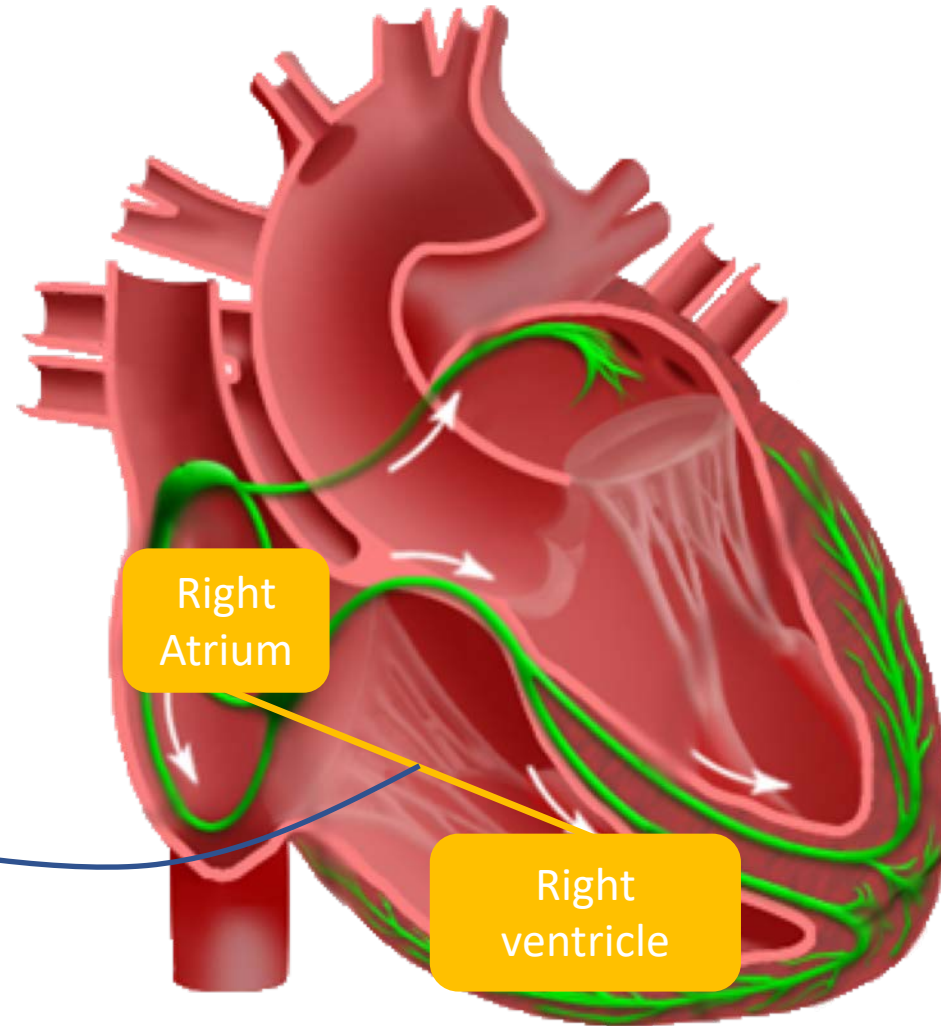


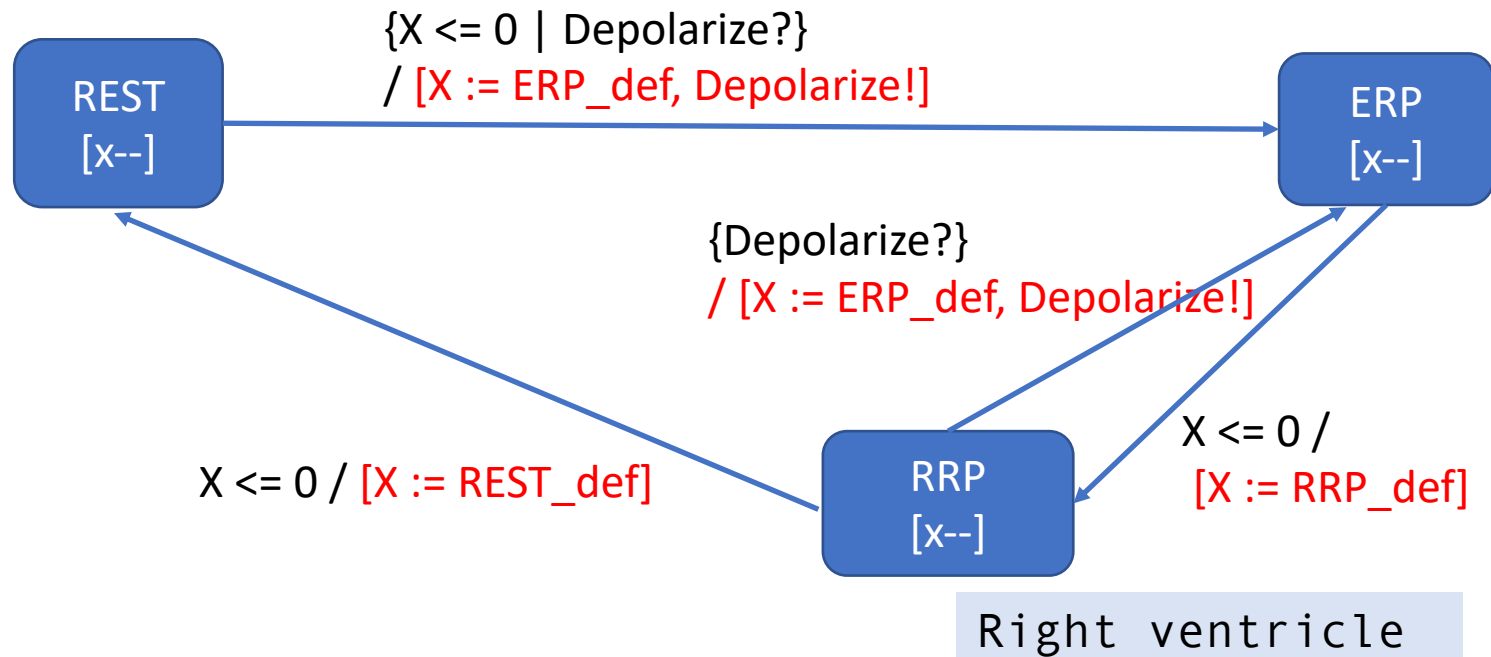
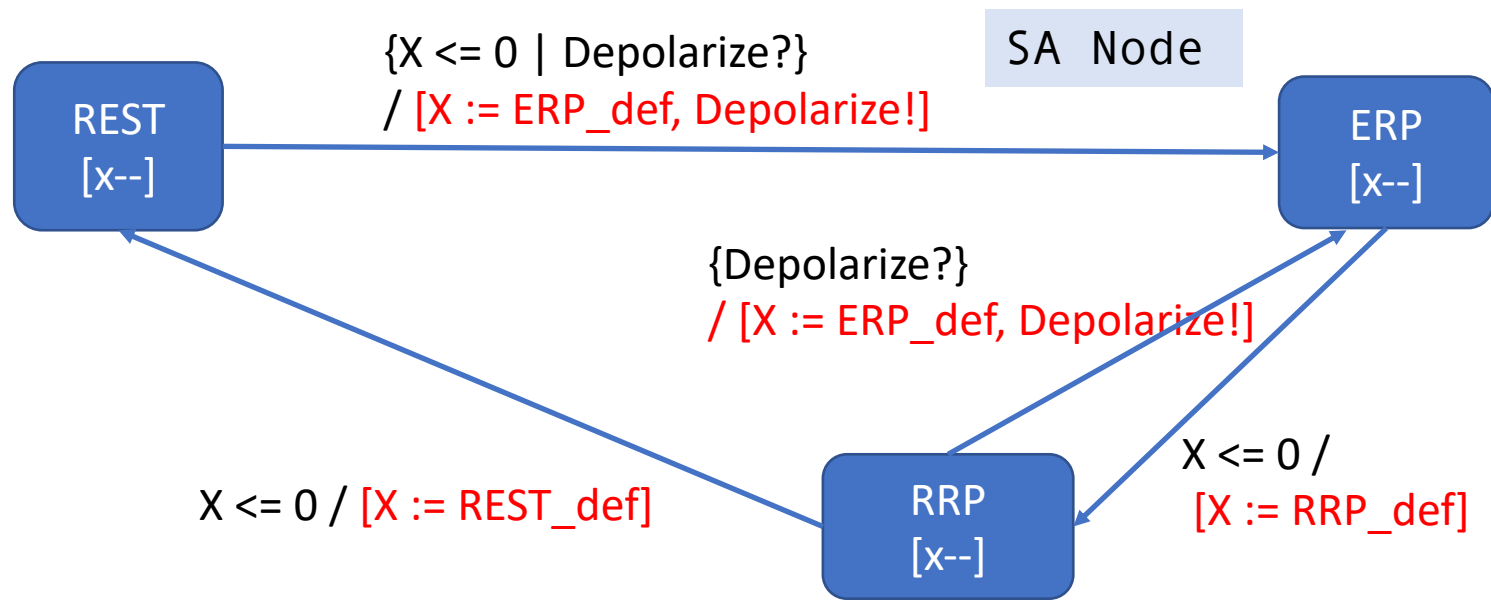
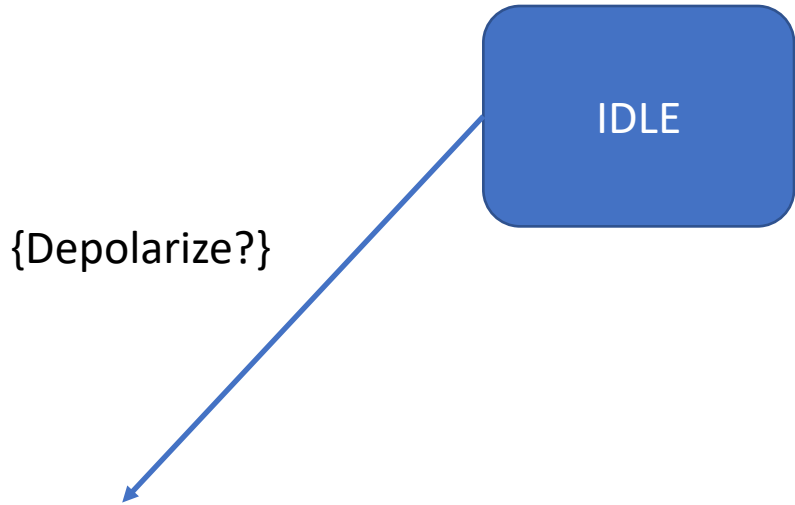
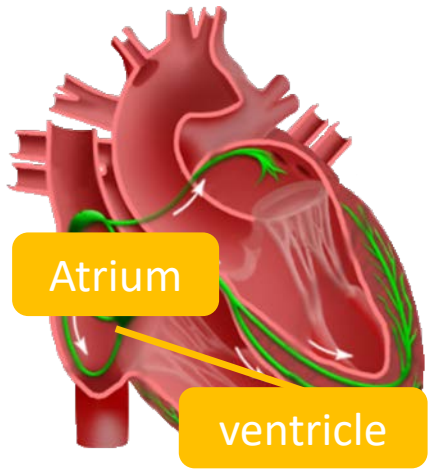


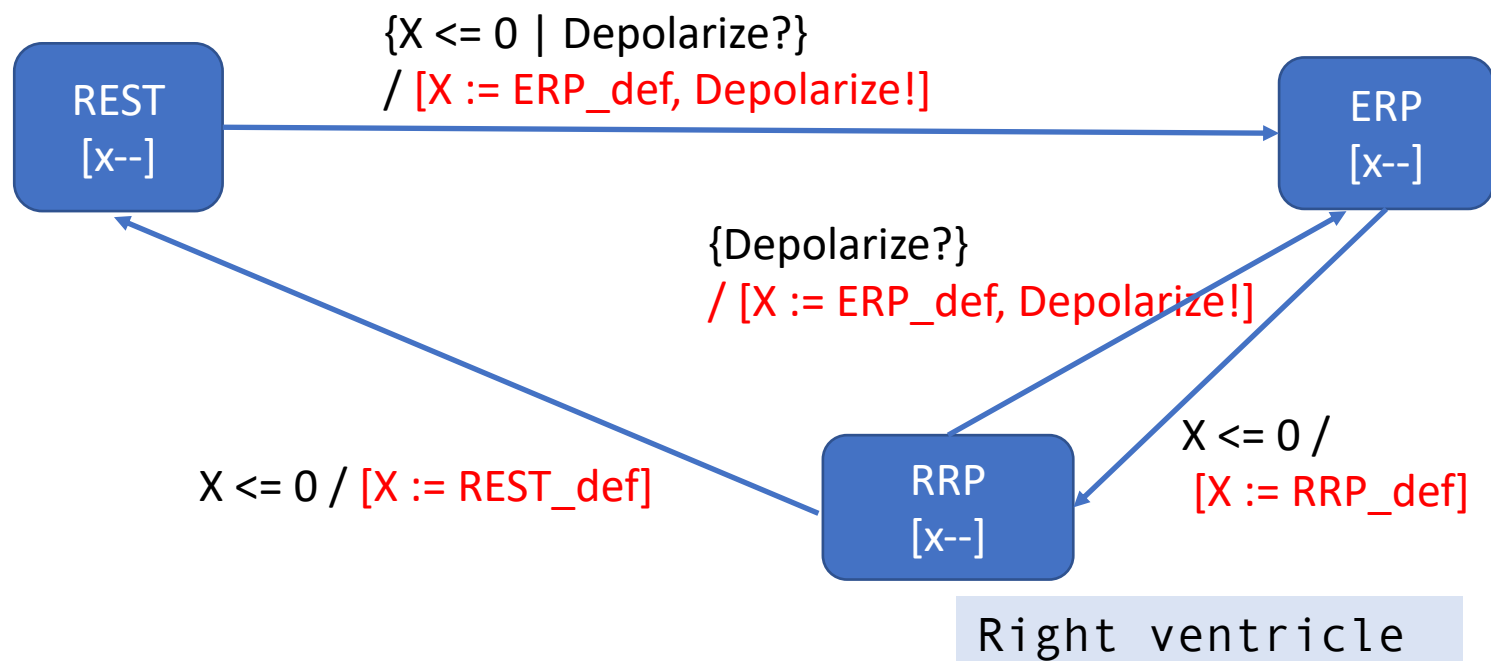
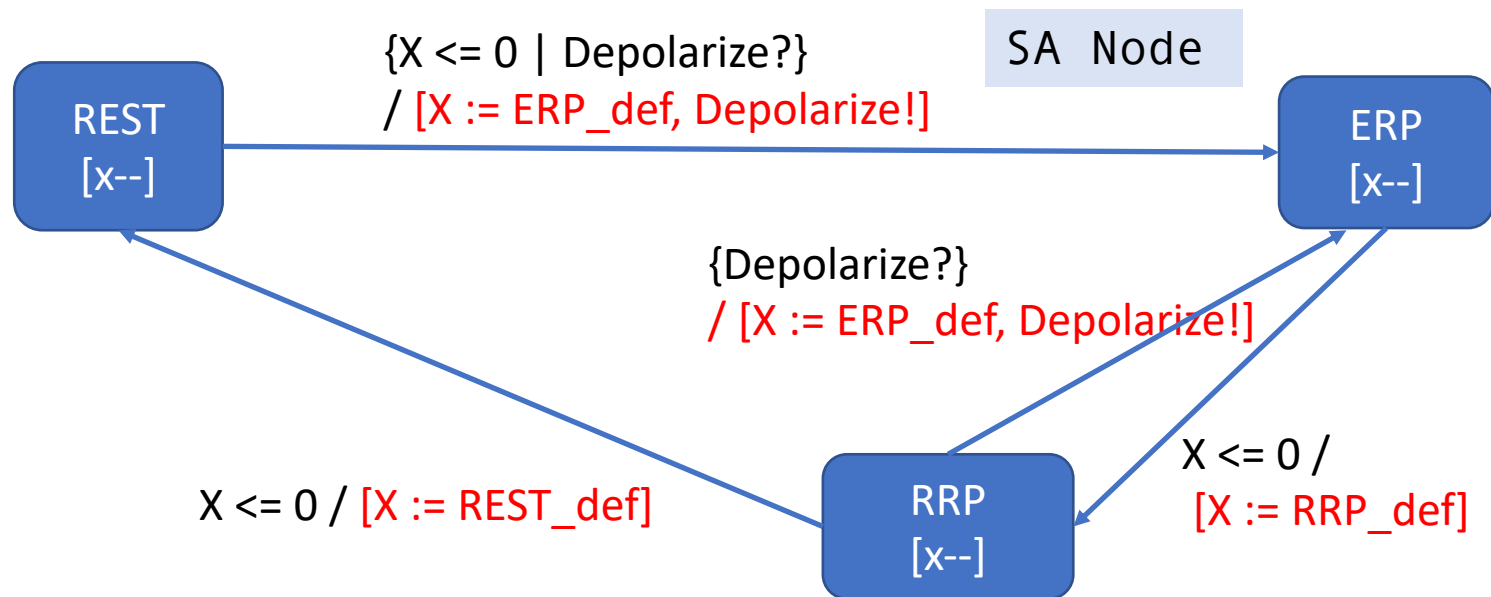
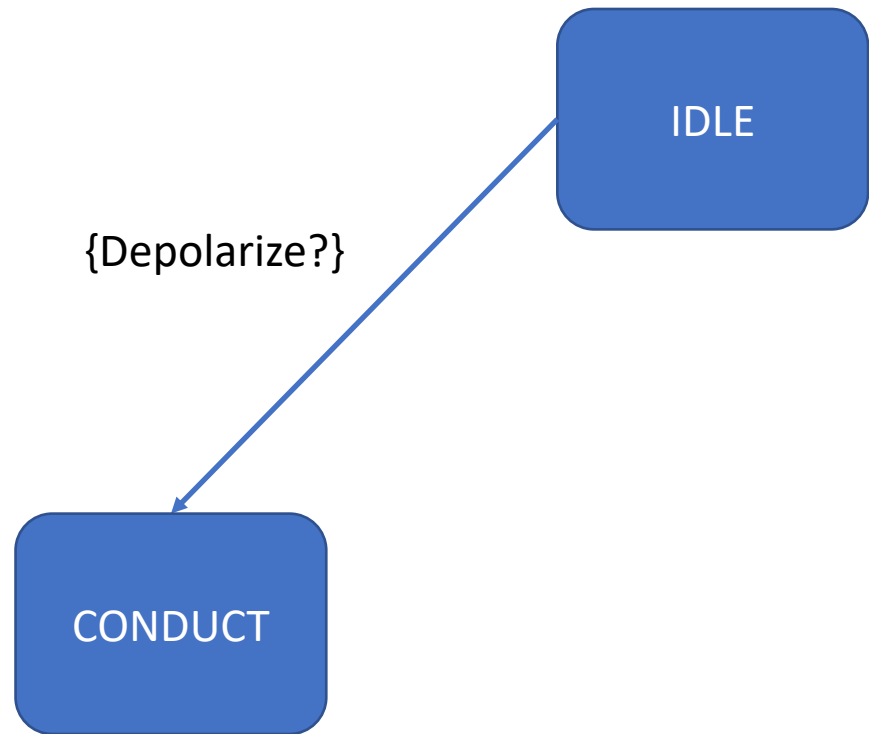
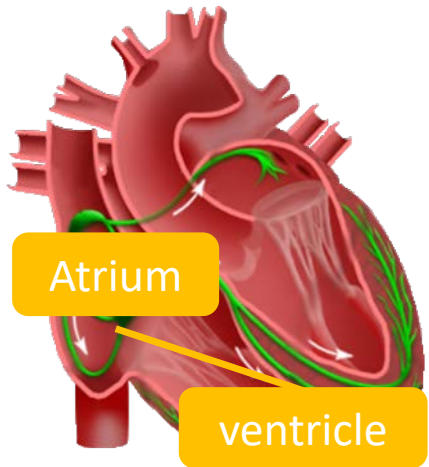


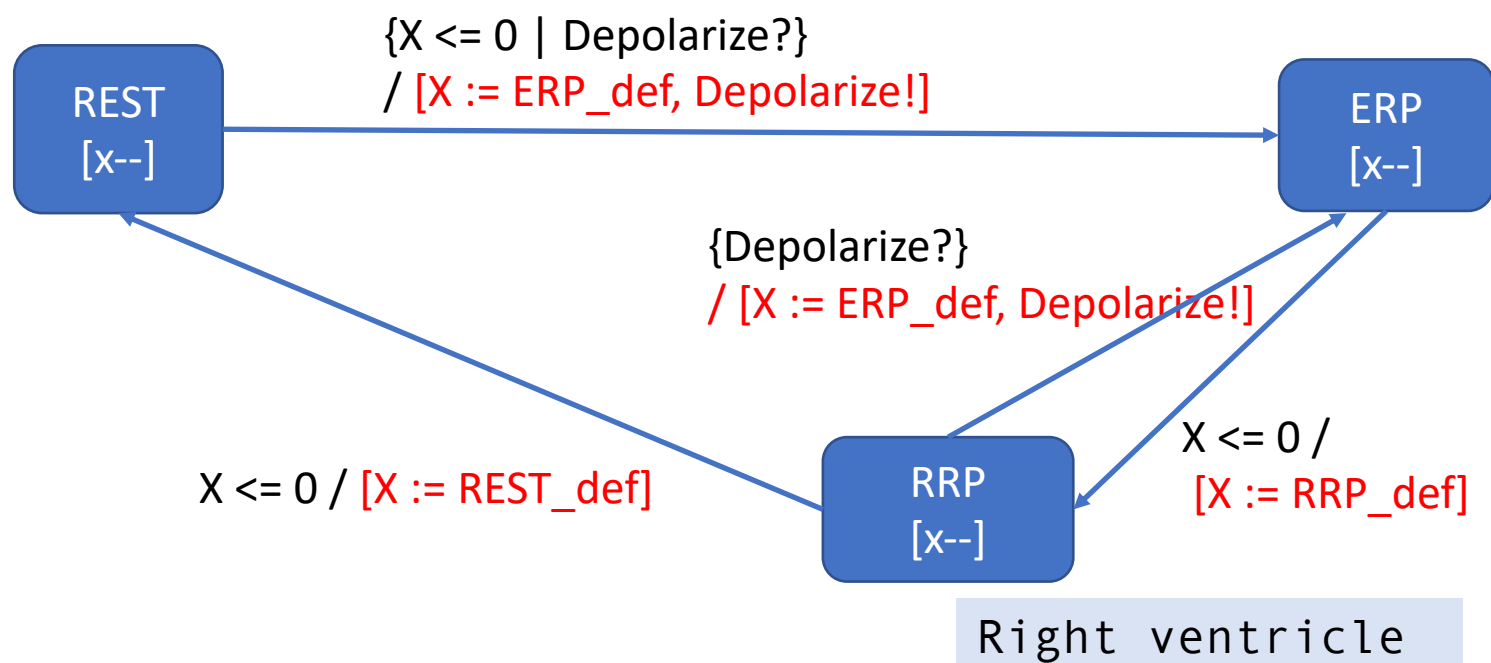
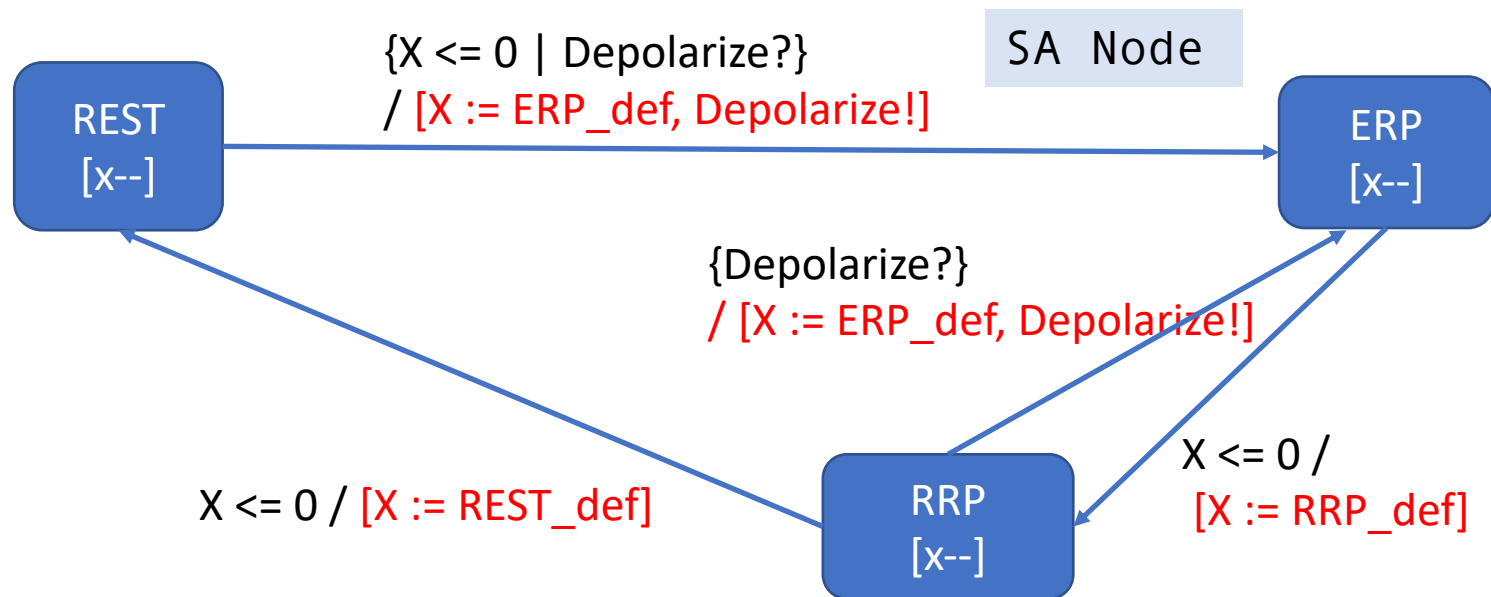
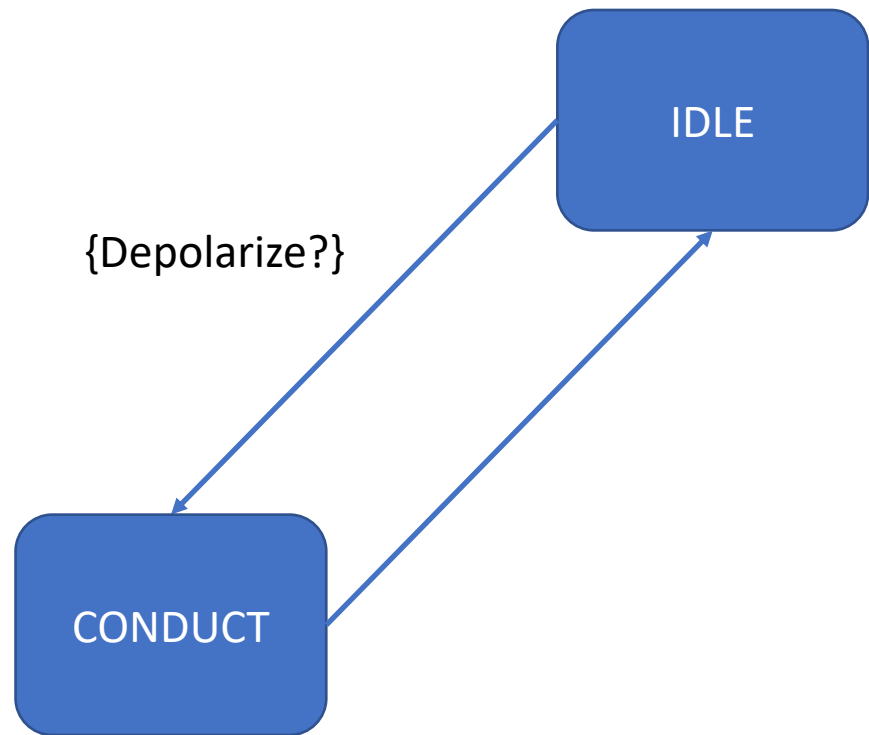
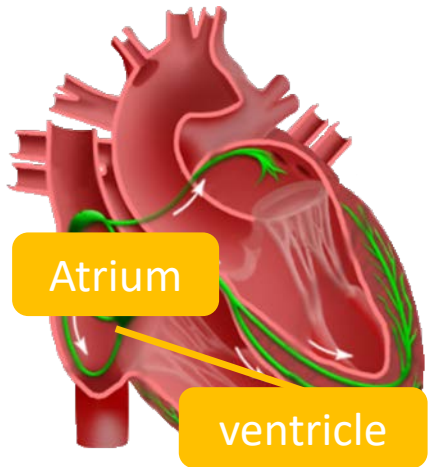
A timed automaton model of conduction paths

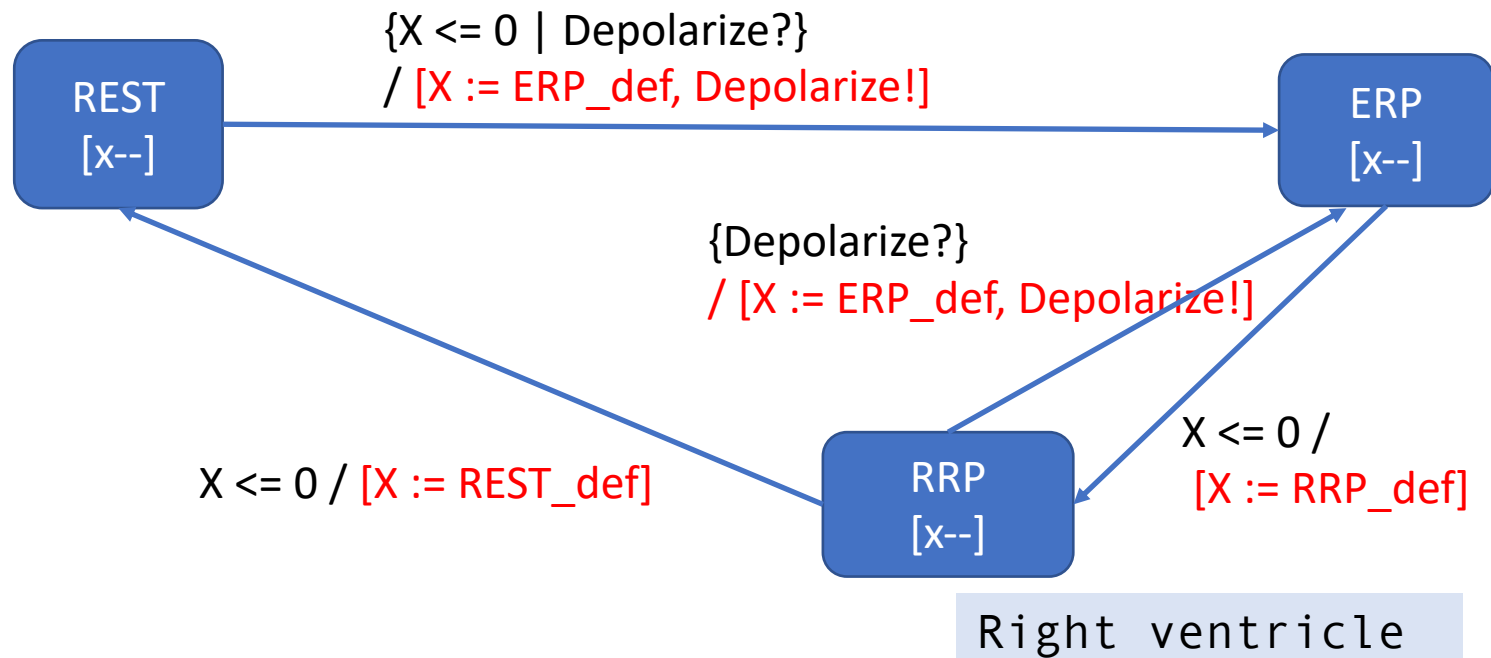
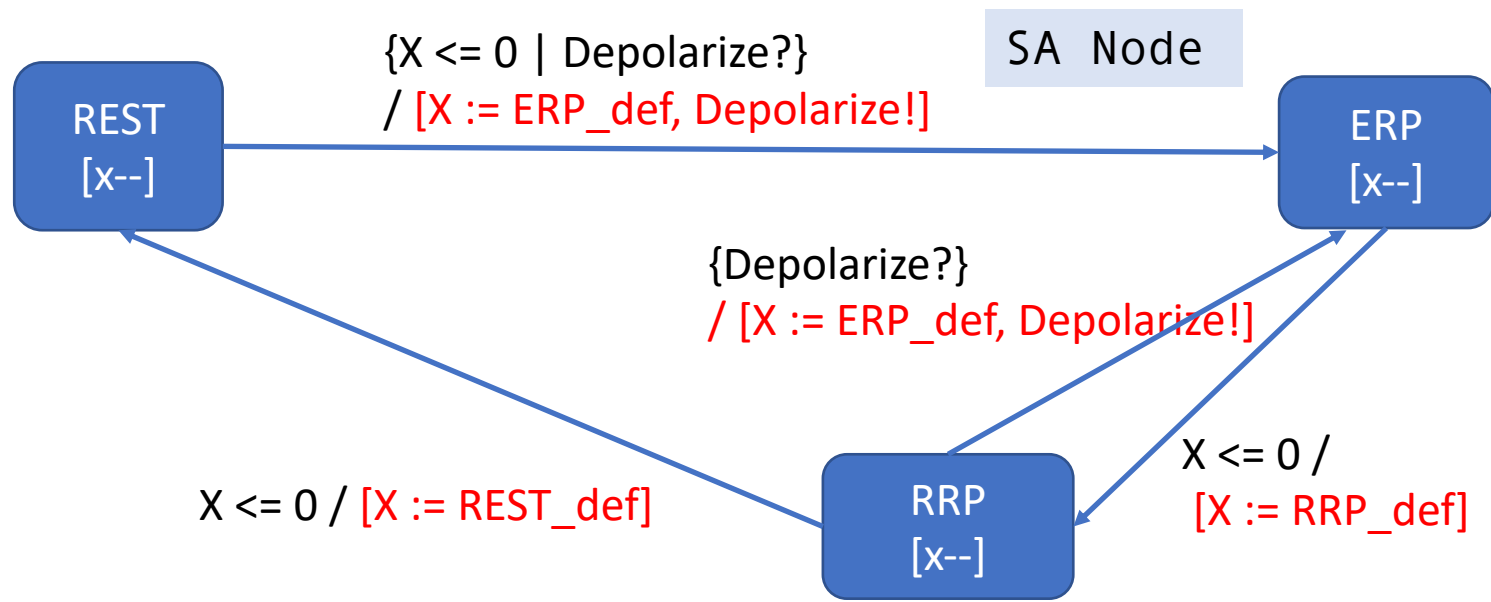
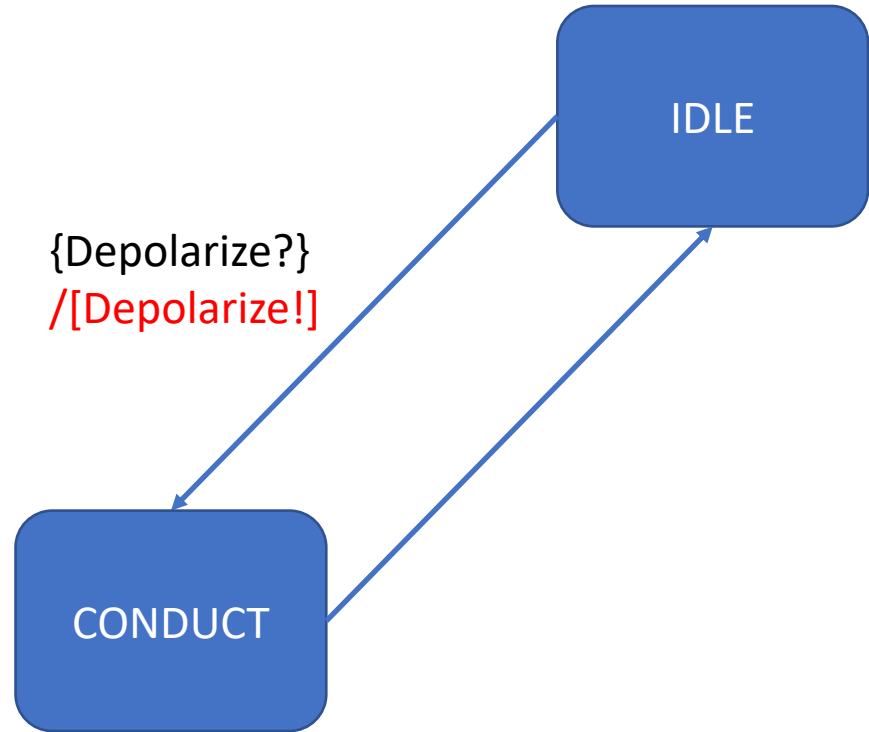
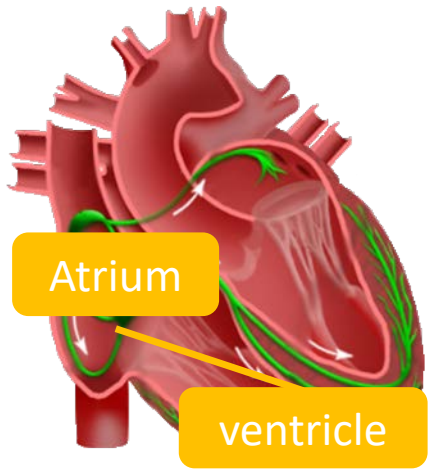
Model this conduction path (which is a piece of tissue) as a different kind of timed automaton.

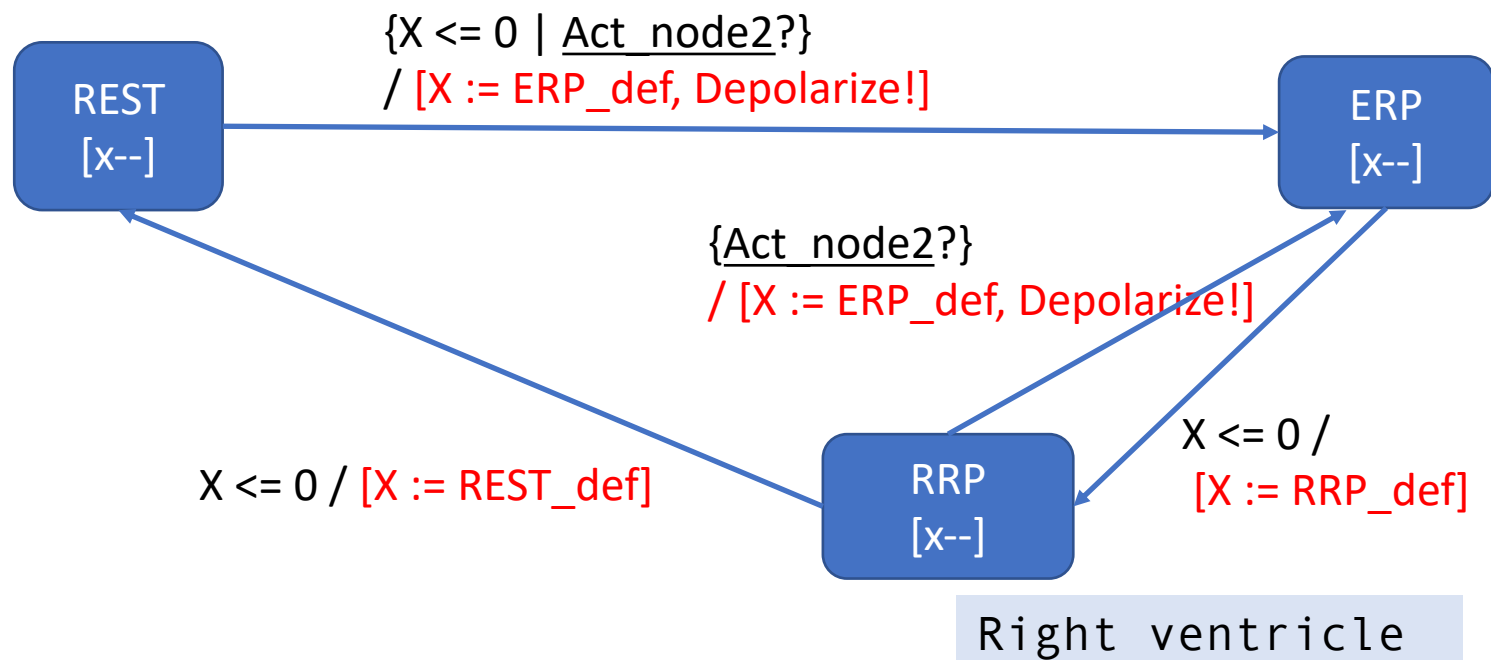
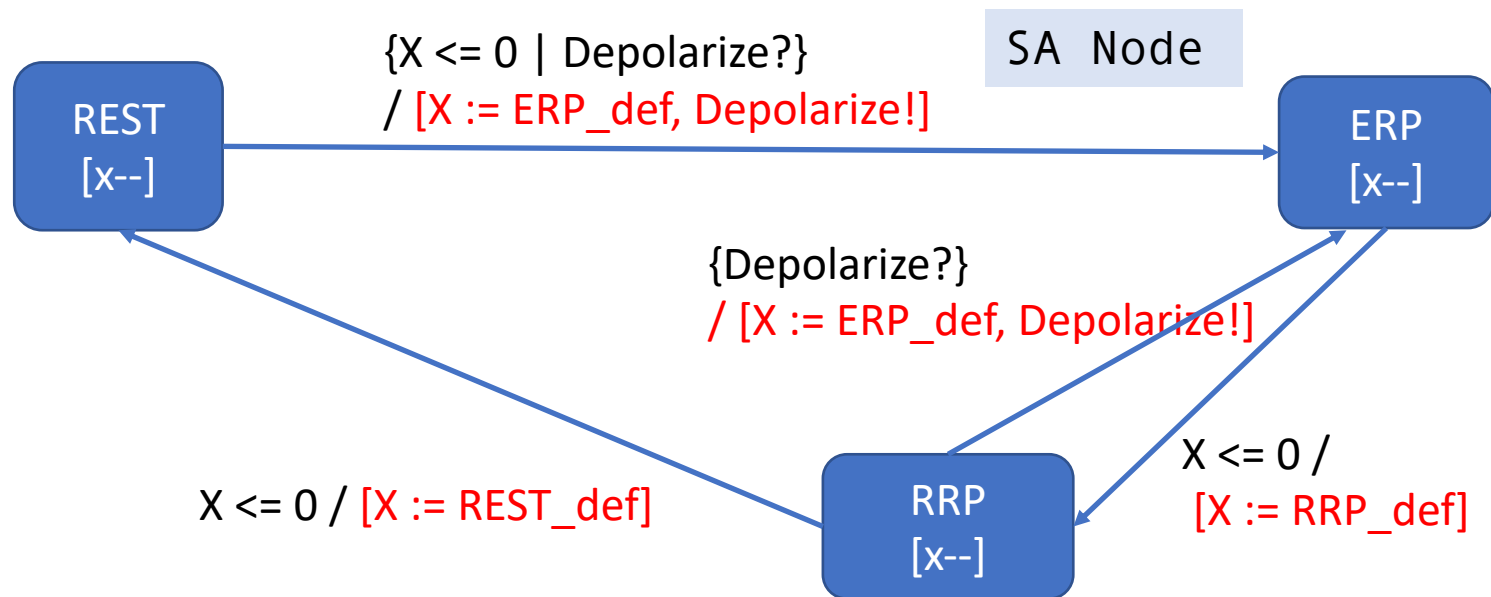
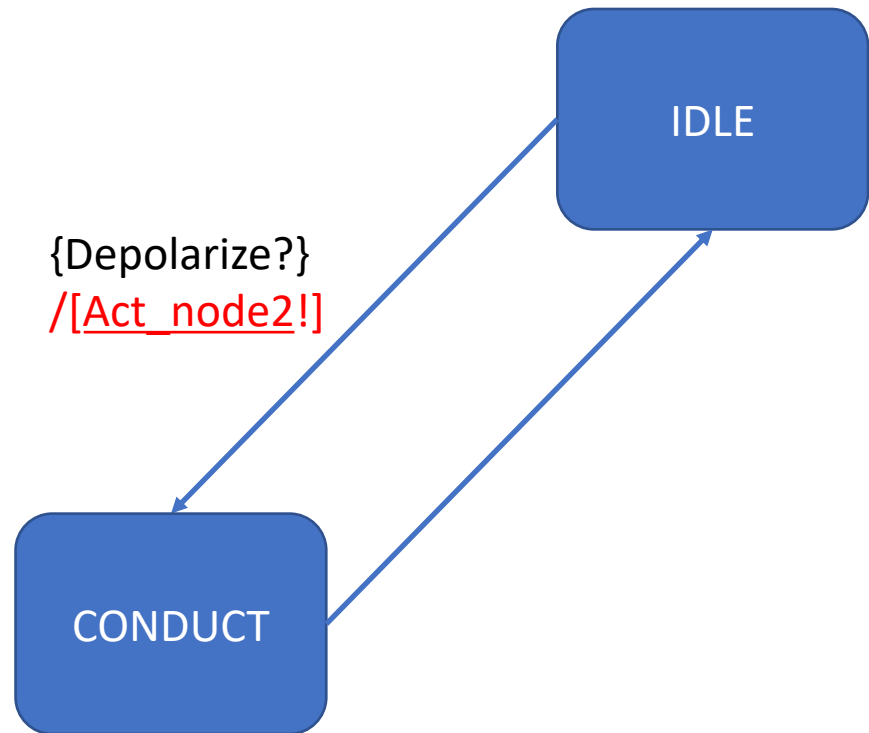
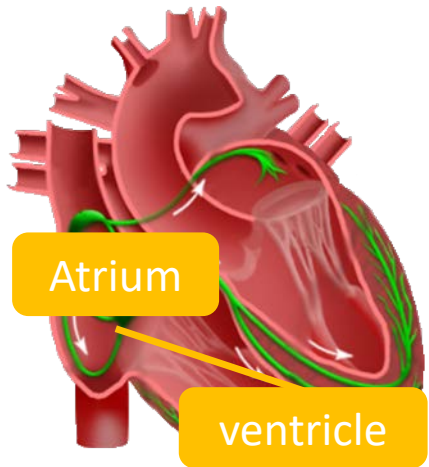


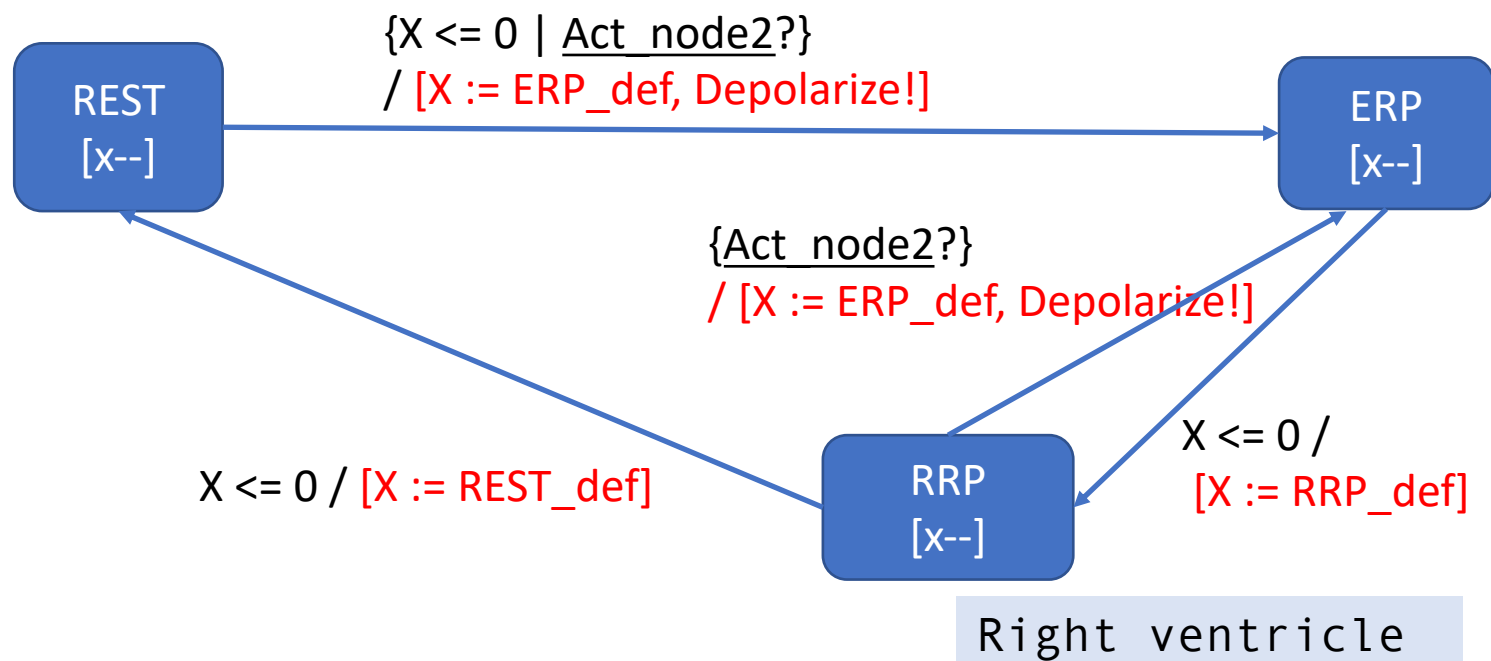
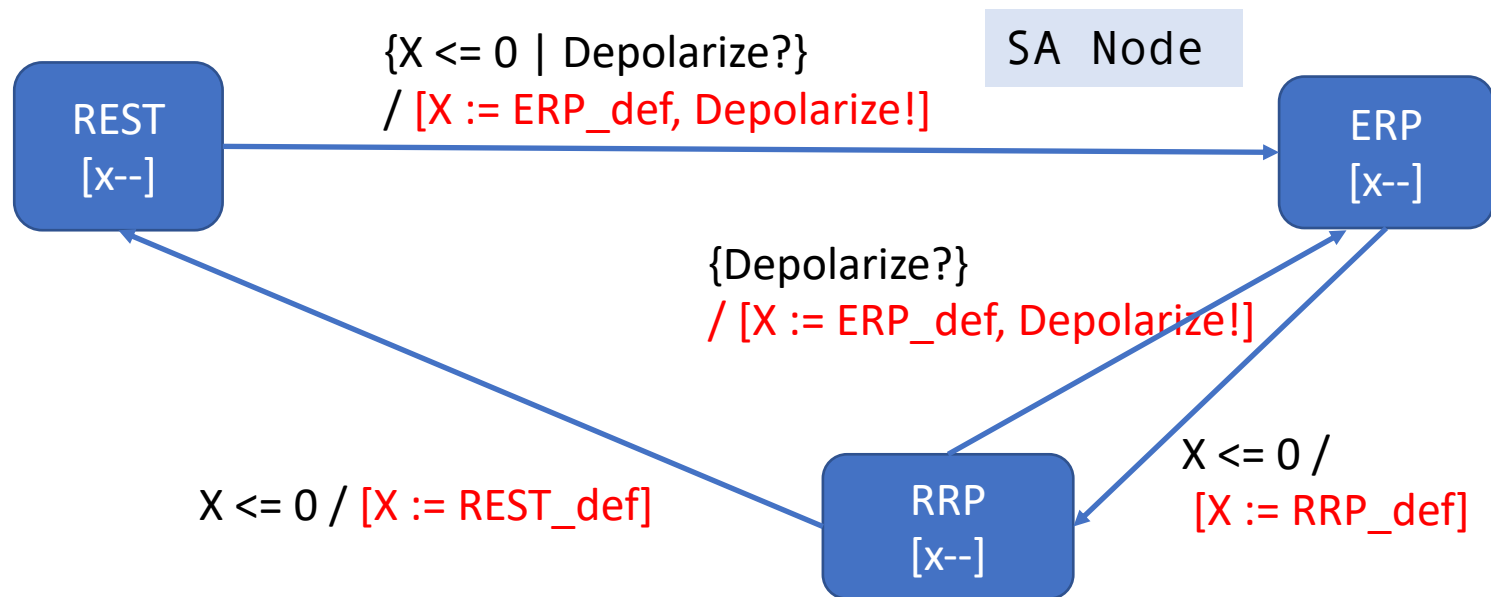
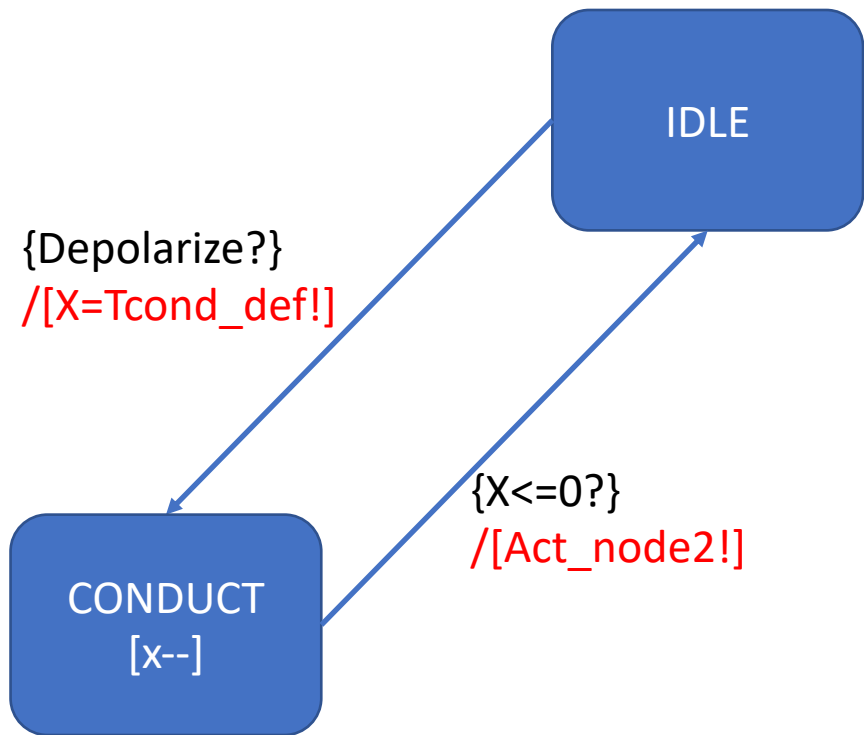
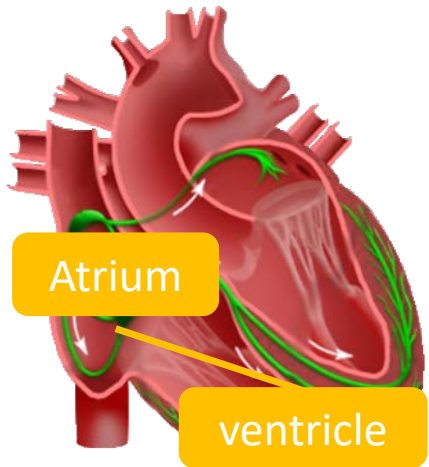


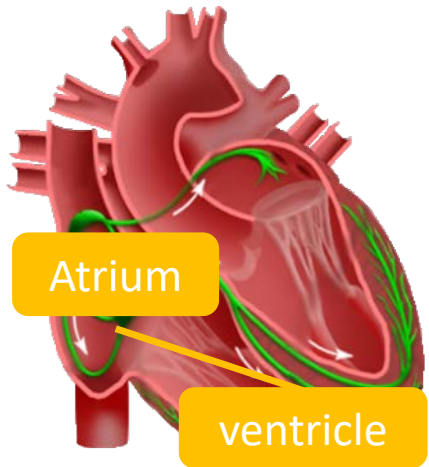




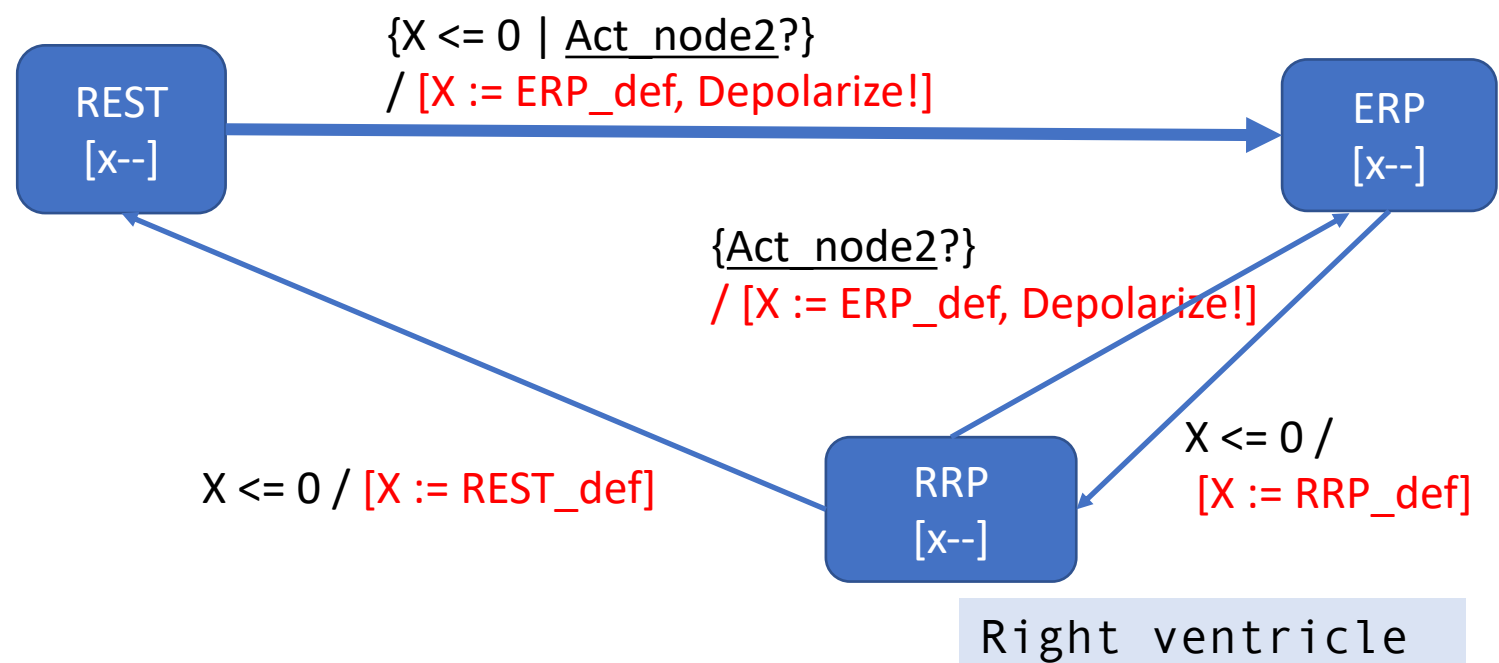
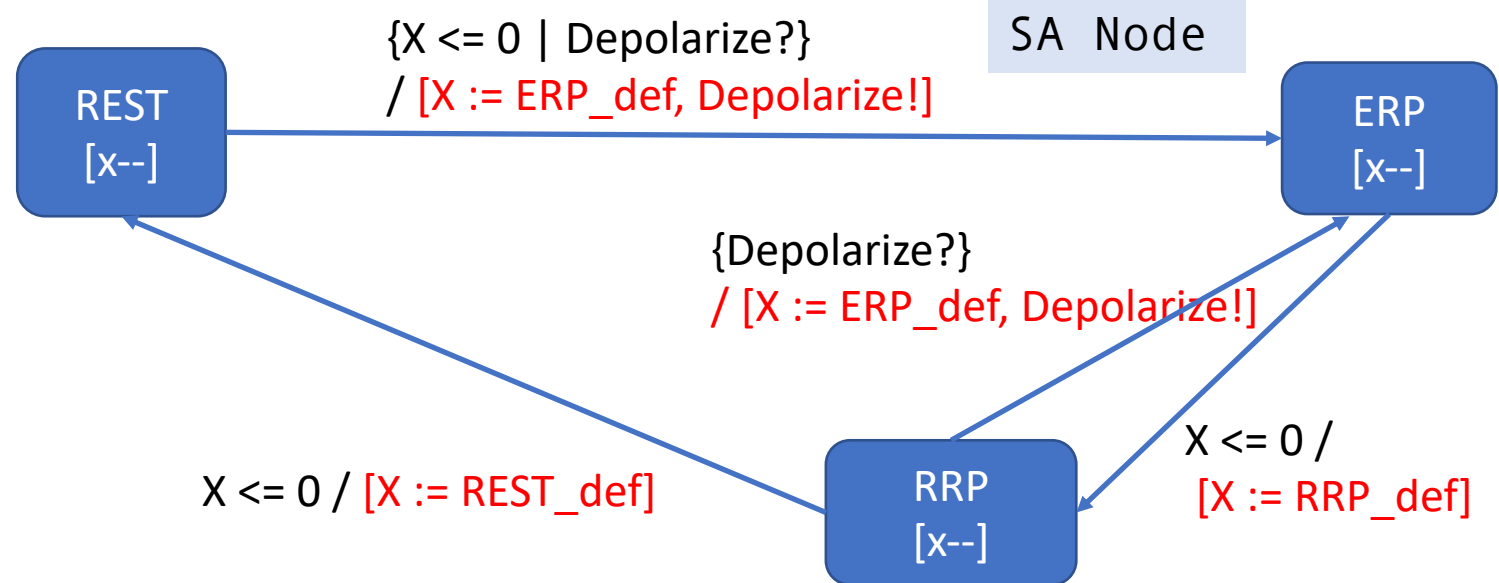
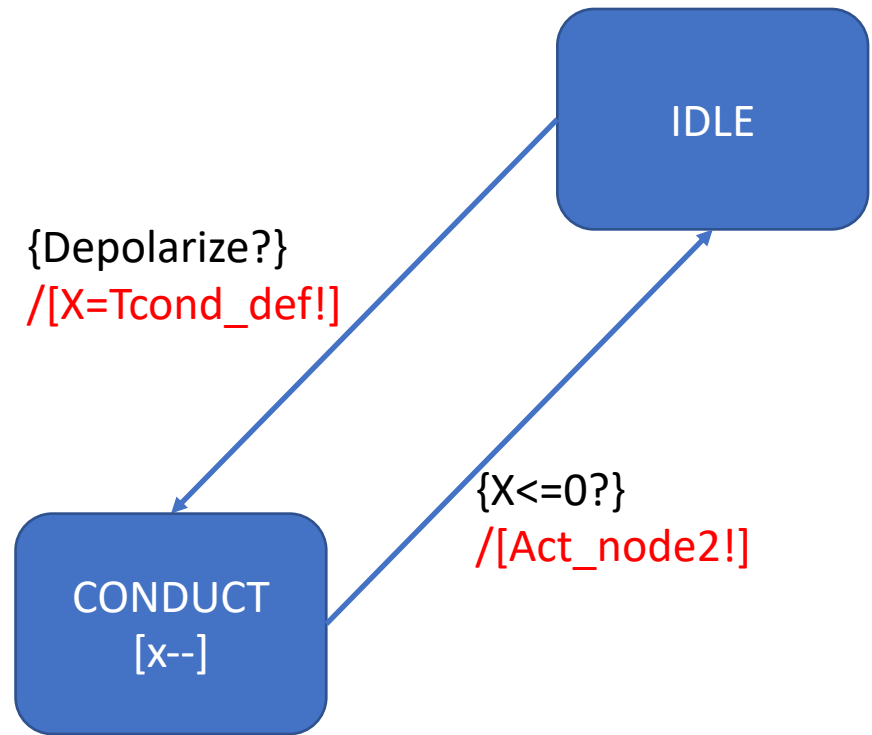


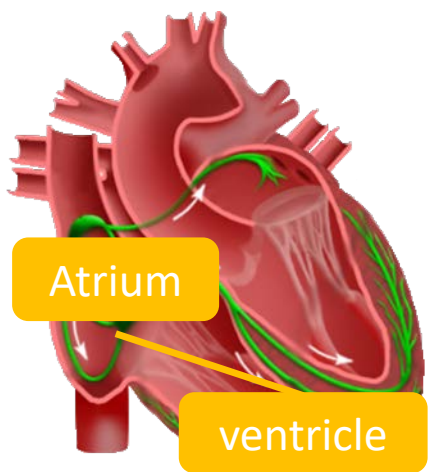




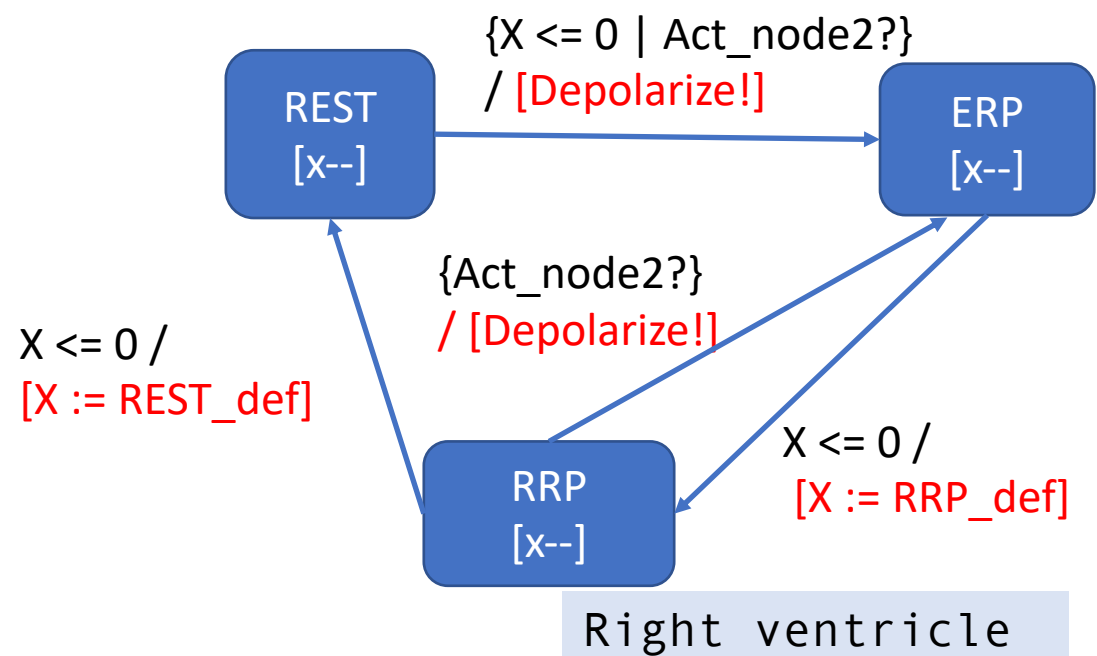
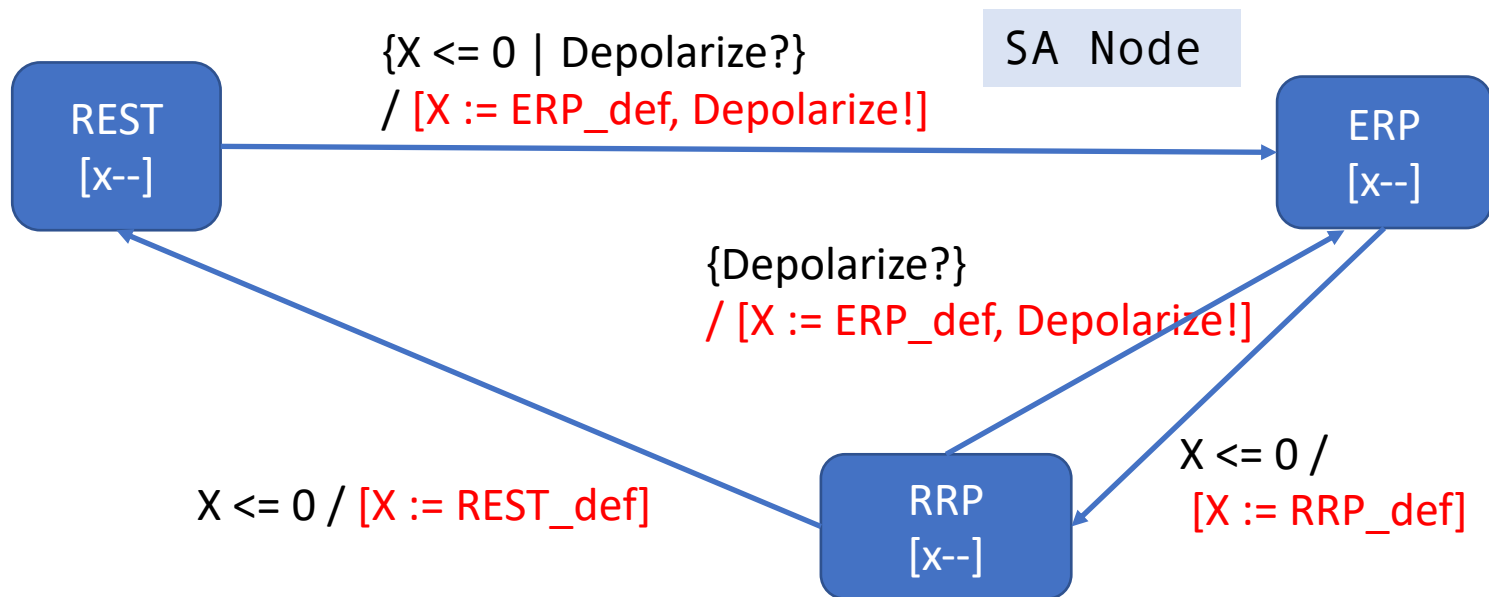
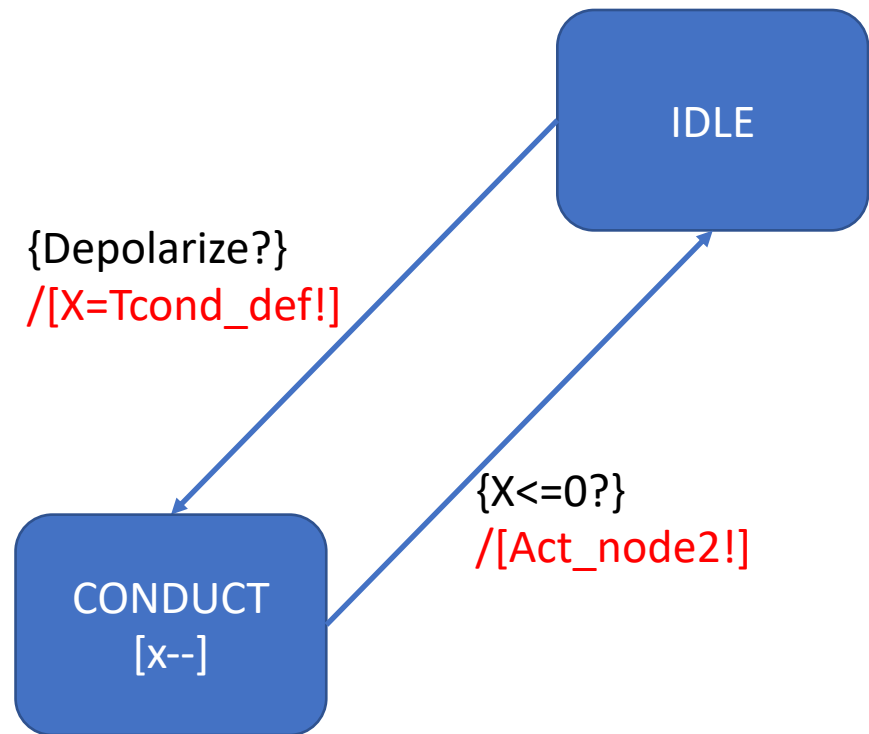


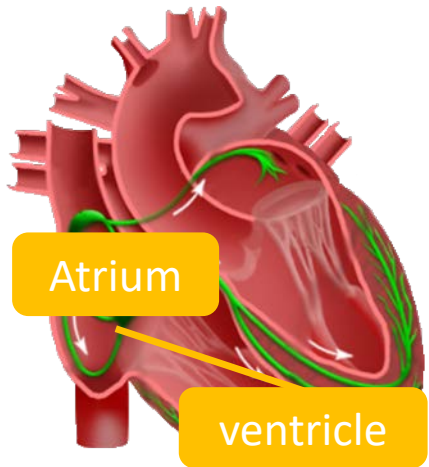
Retrograde Conduction



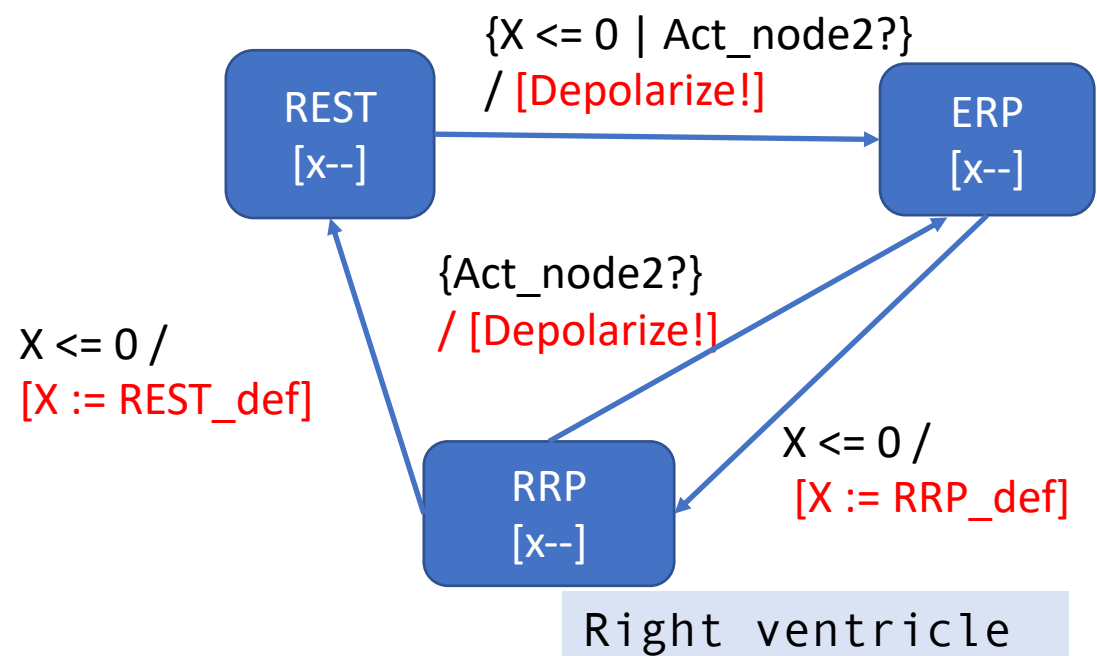
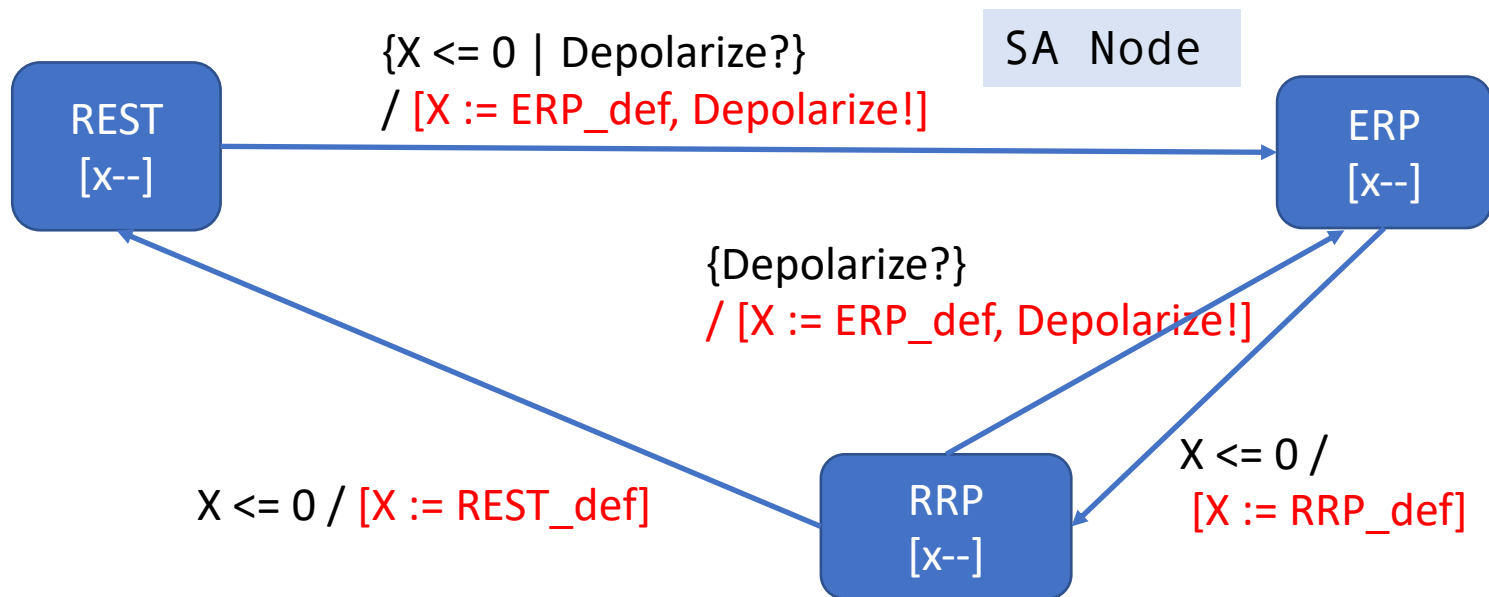
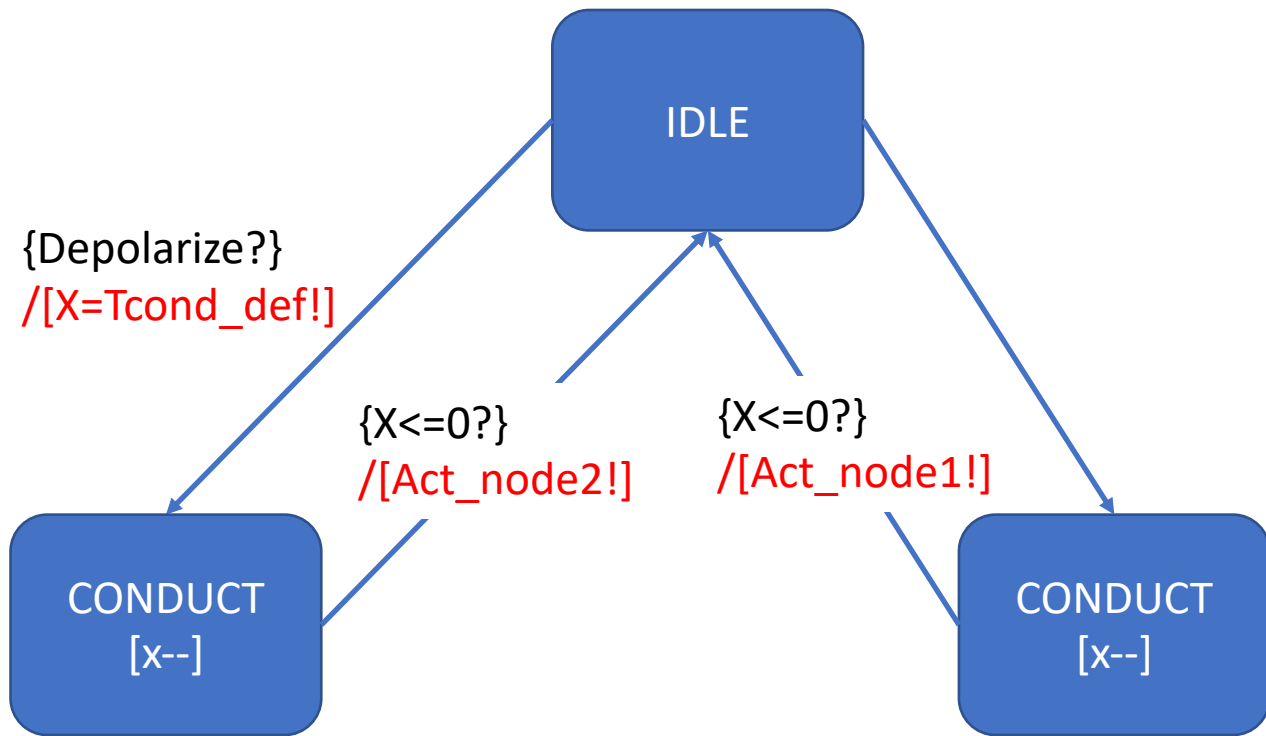


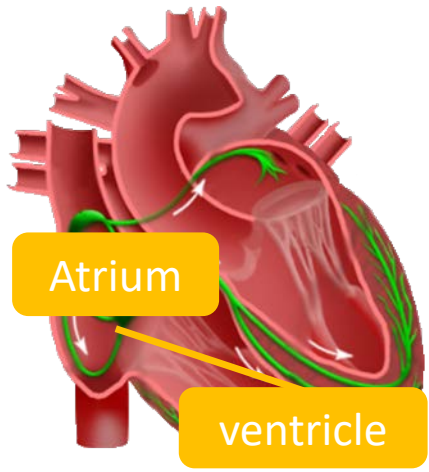
Retrograde Conduction



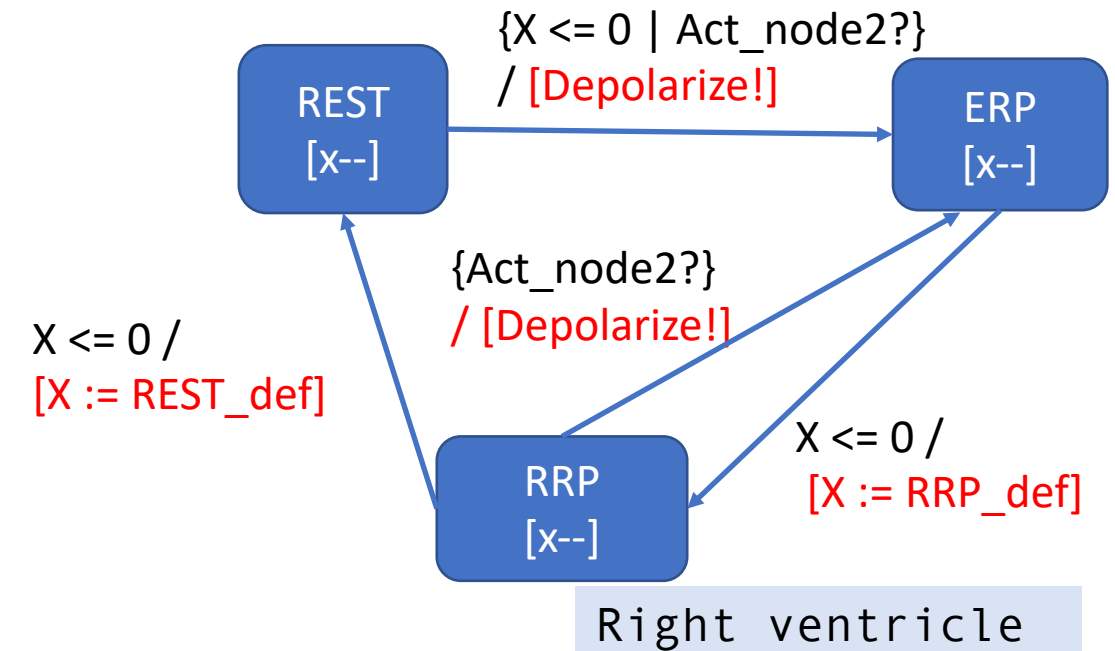
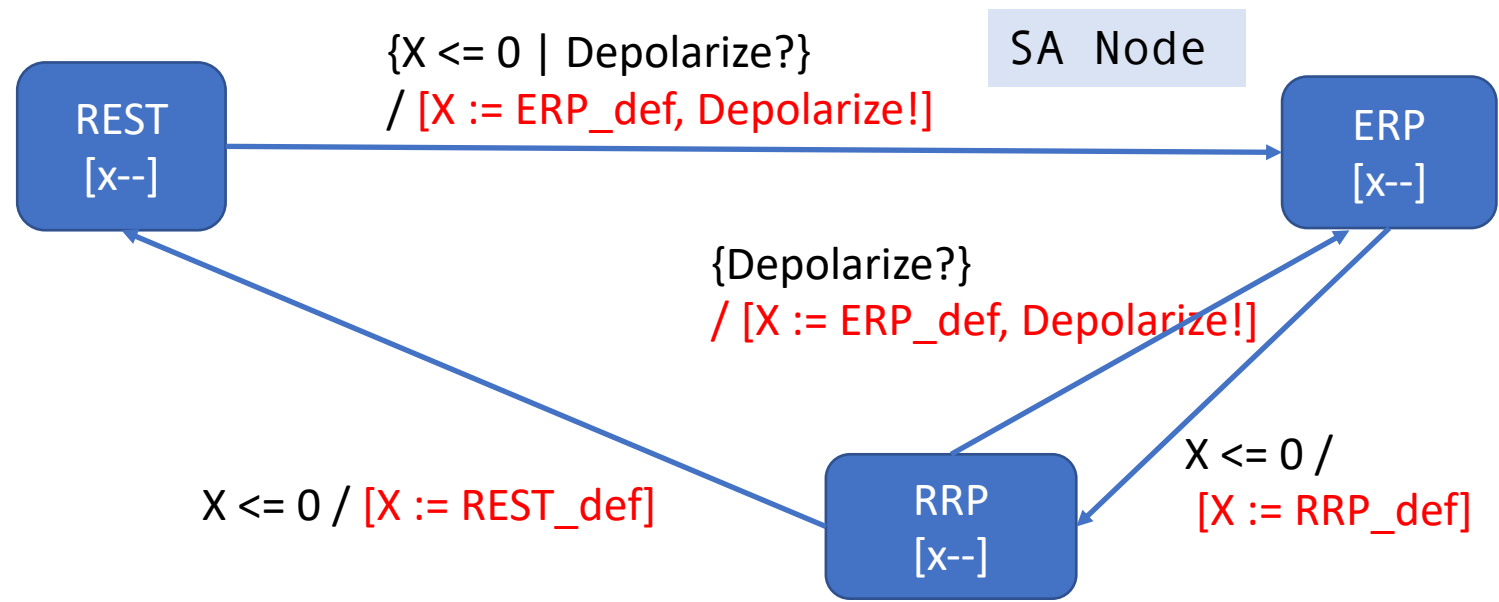
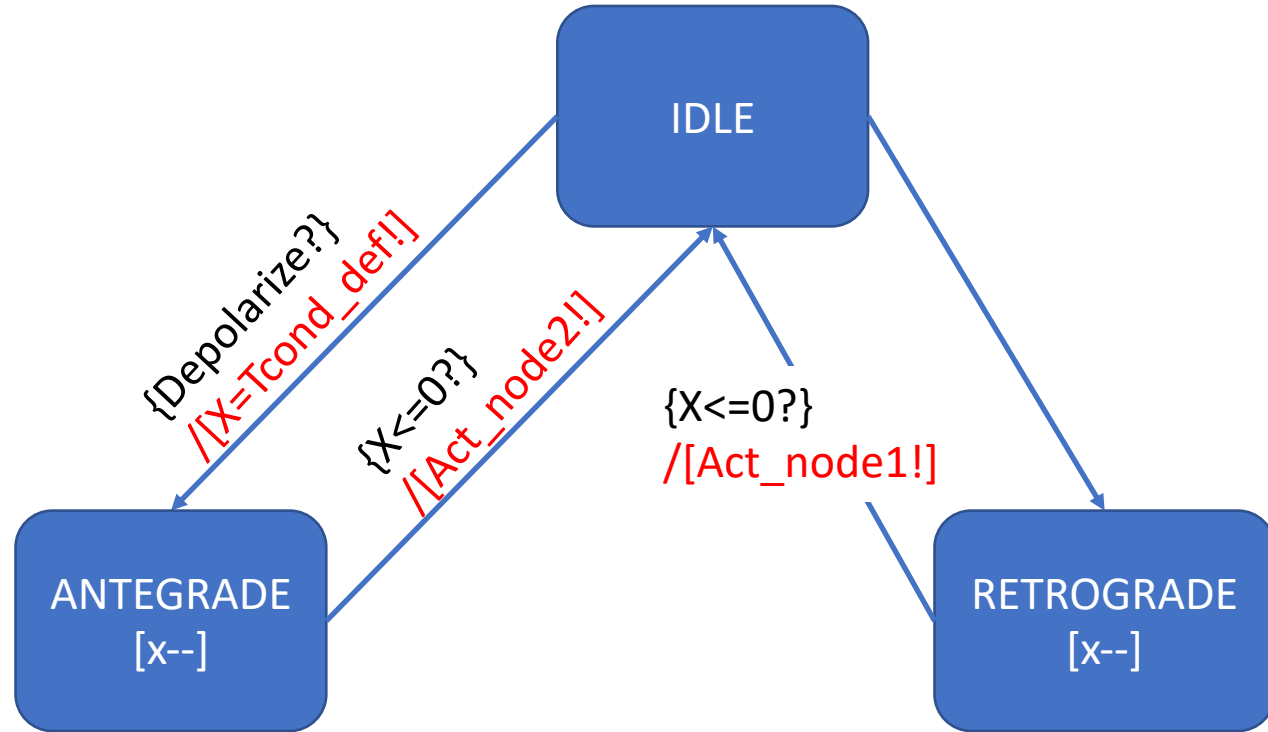


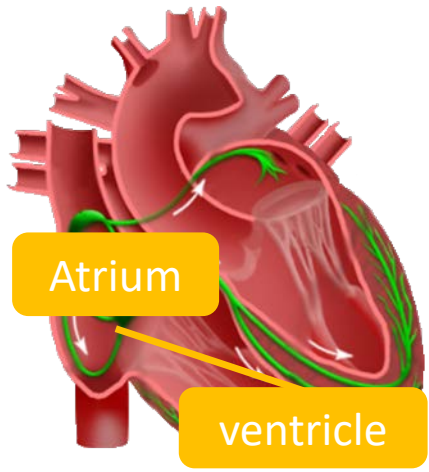
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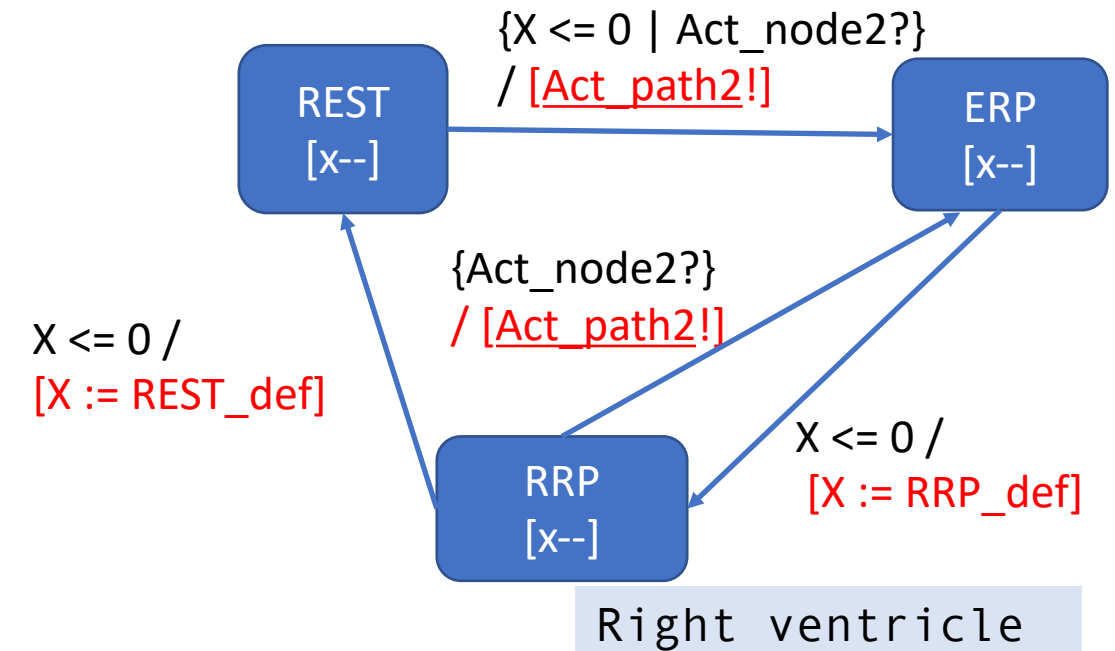
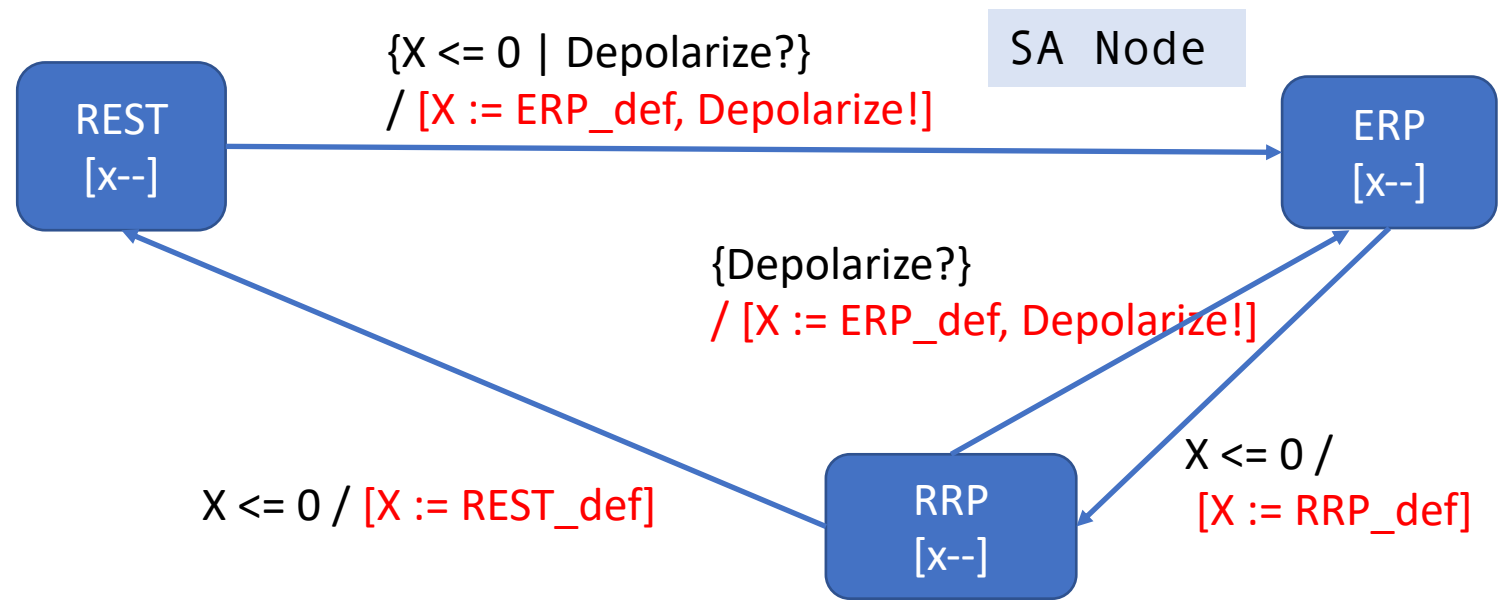
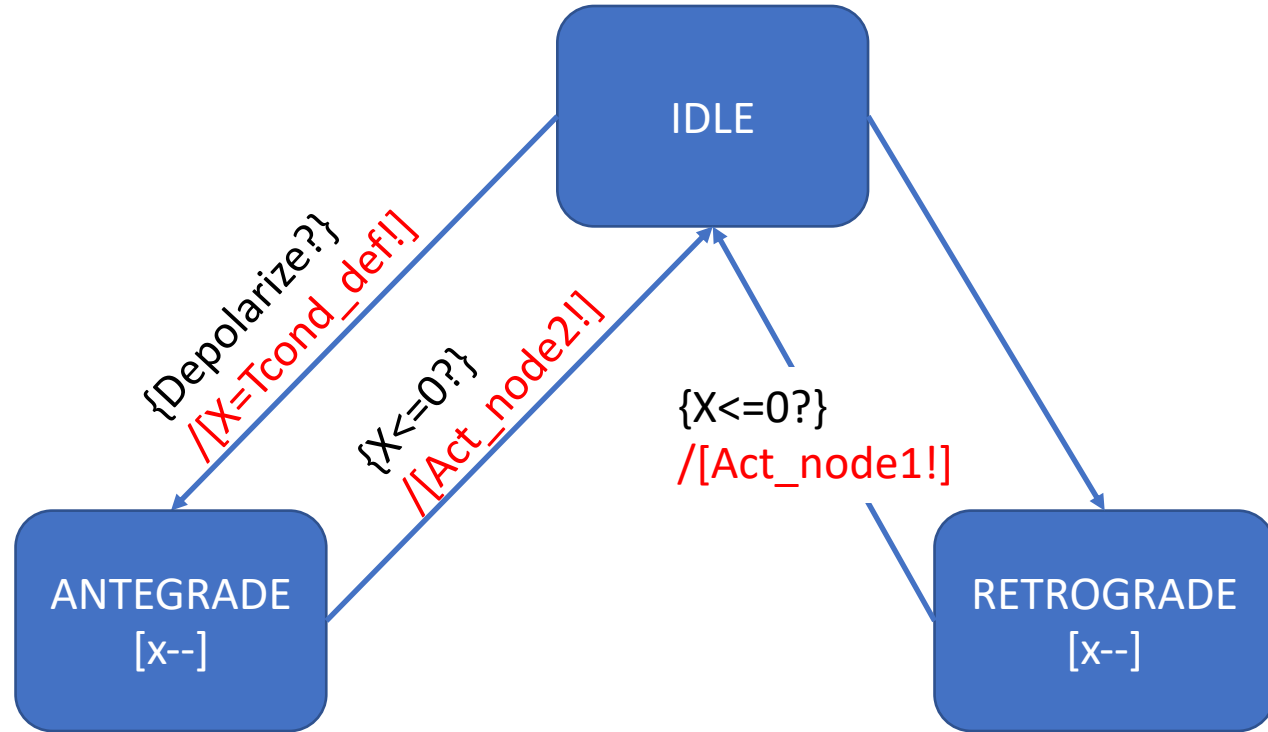


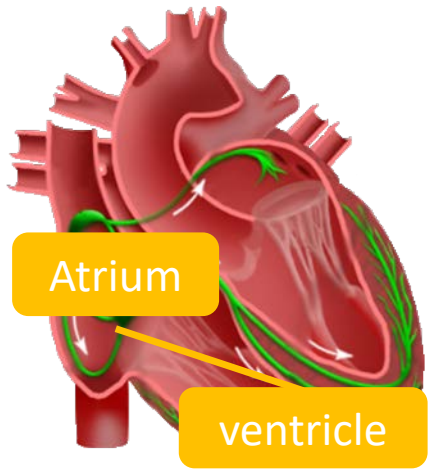
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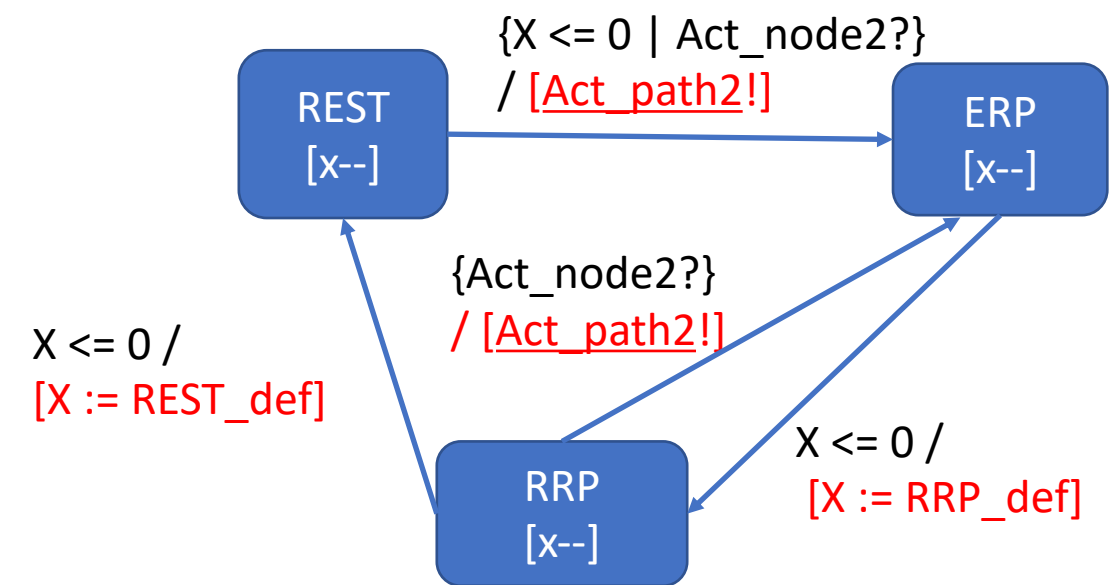
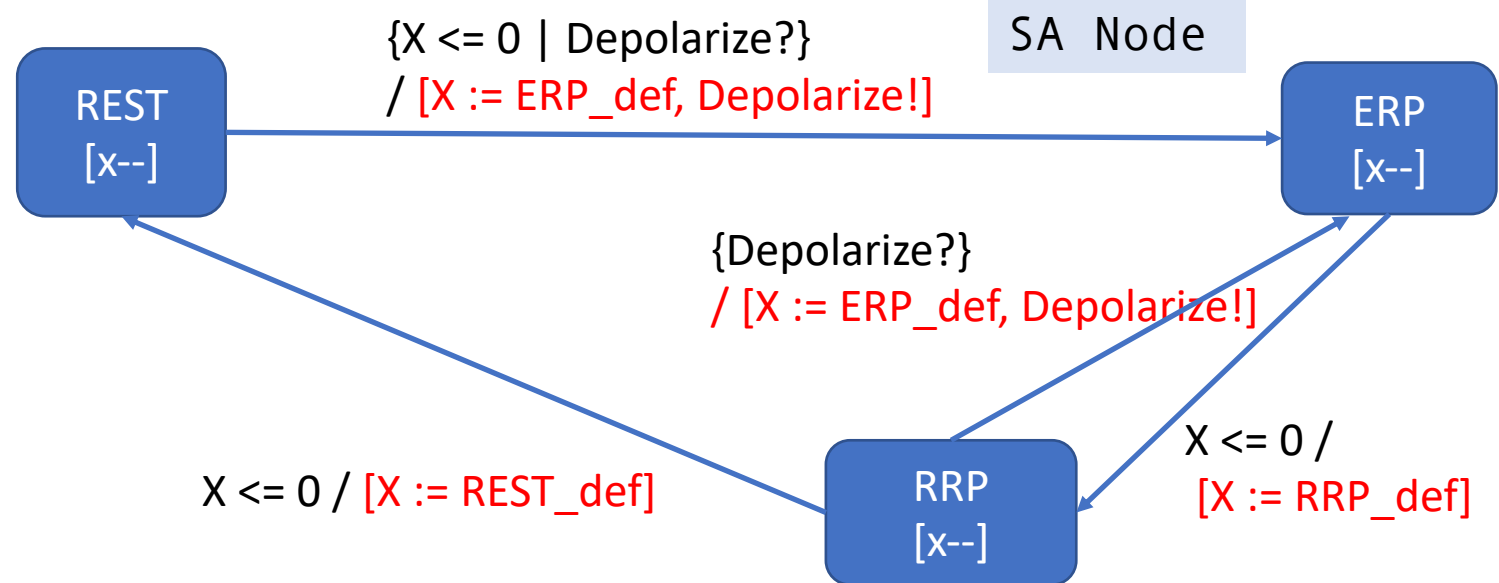
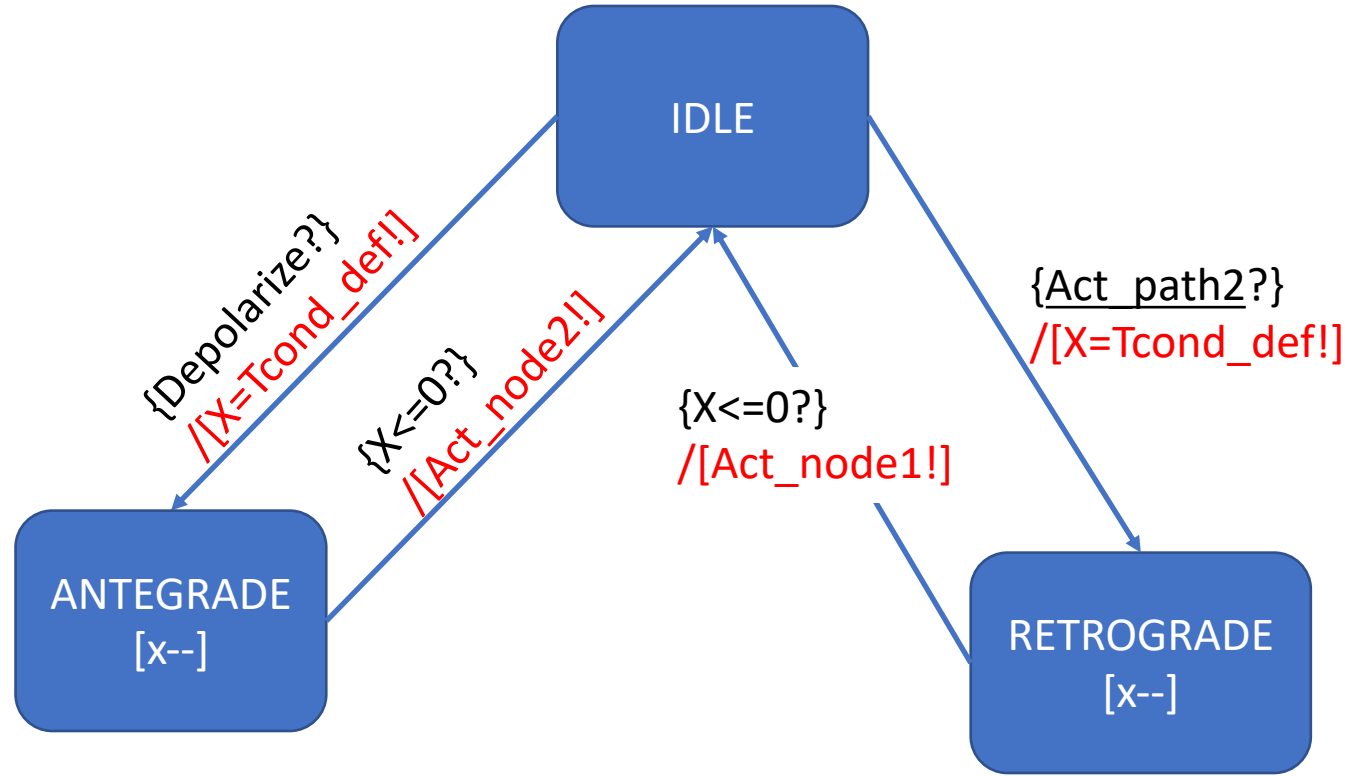


Retrograde Conduction

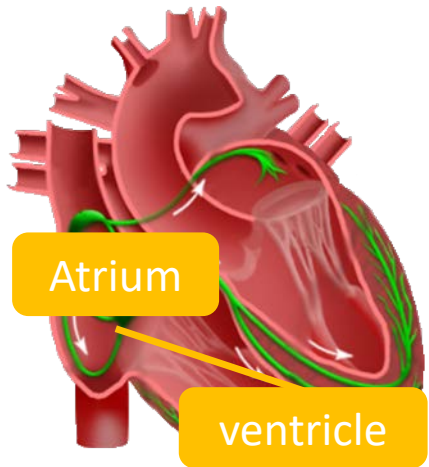




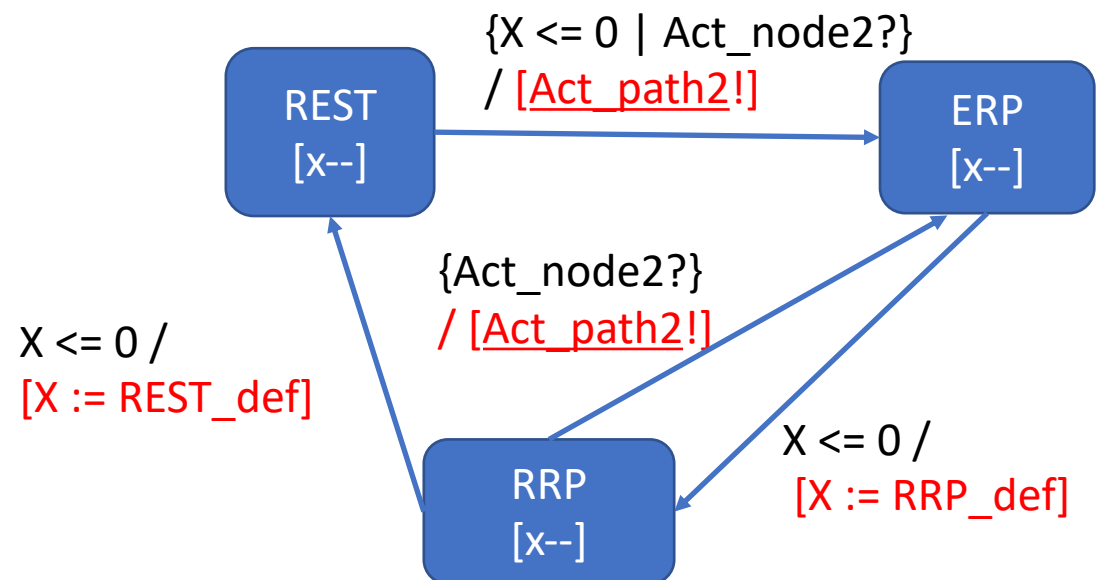
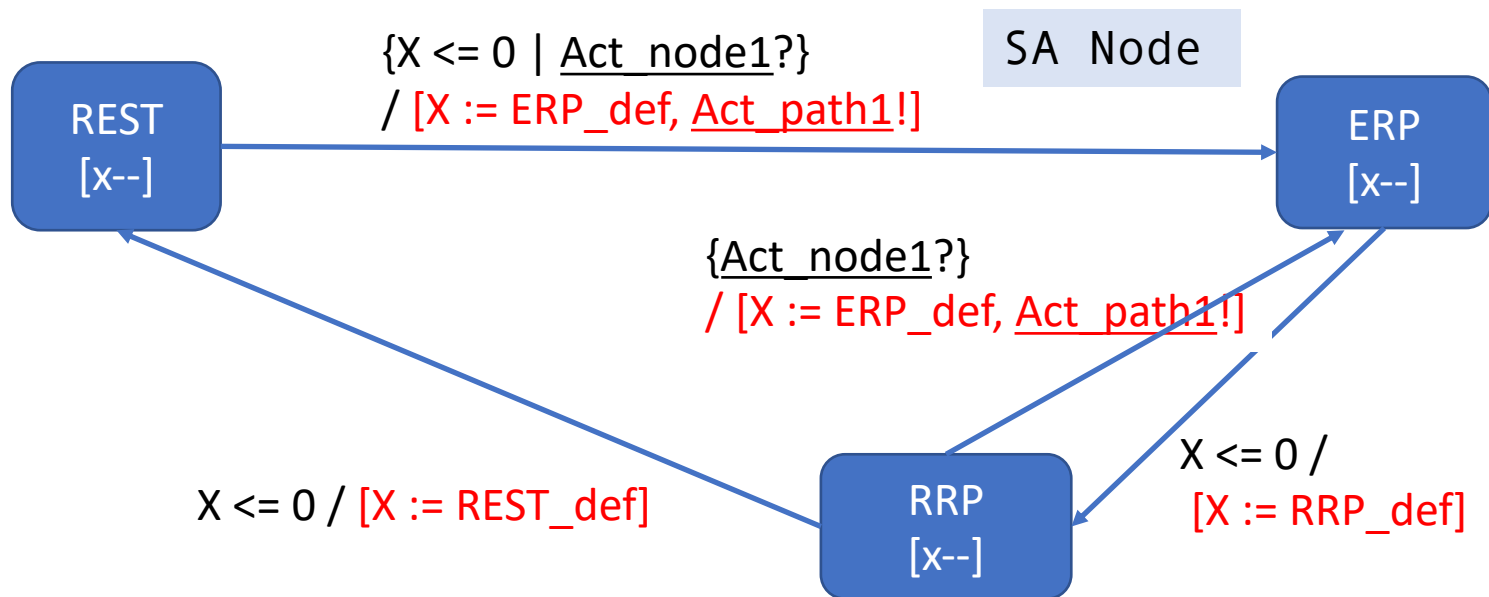
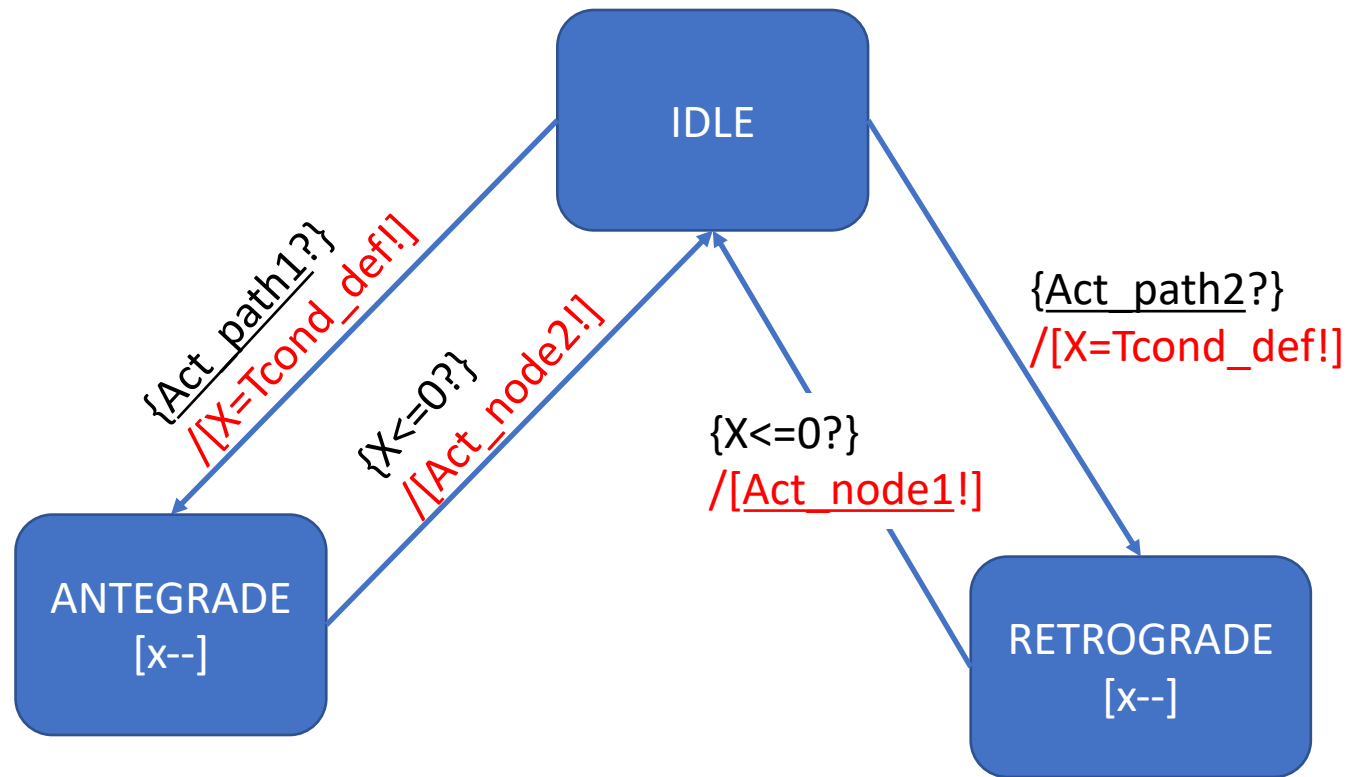
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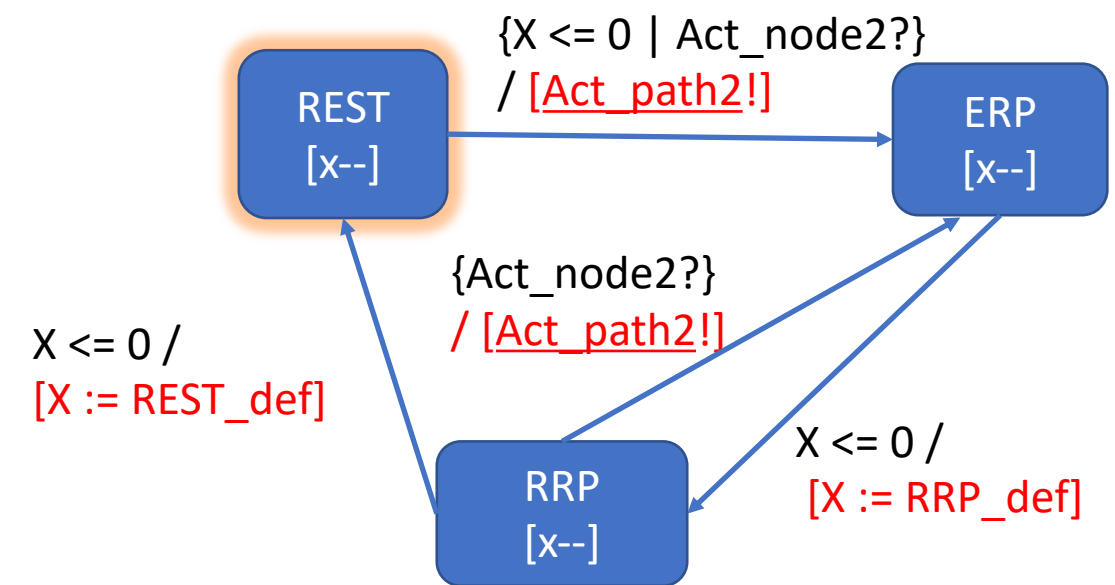
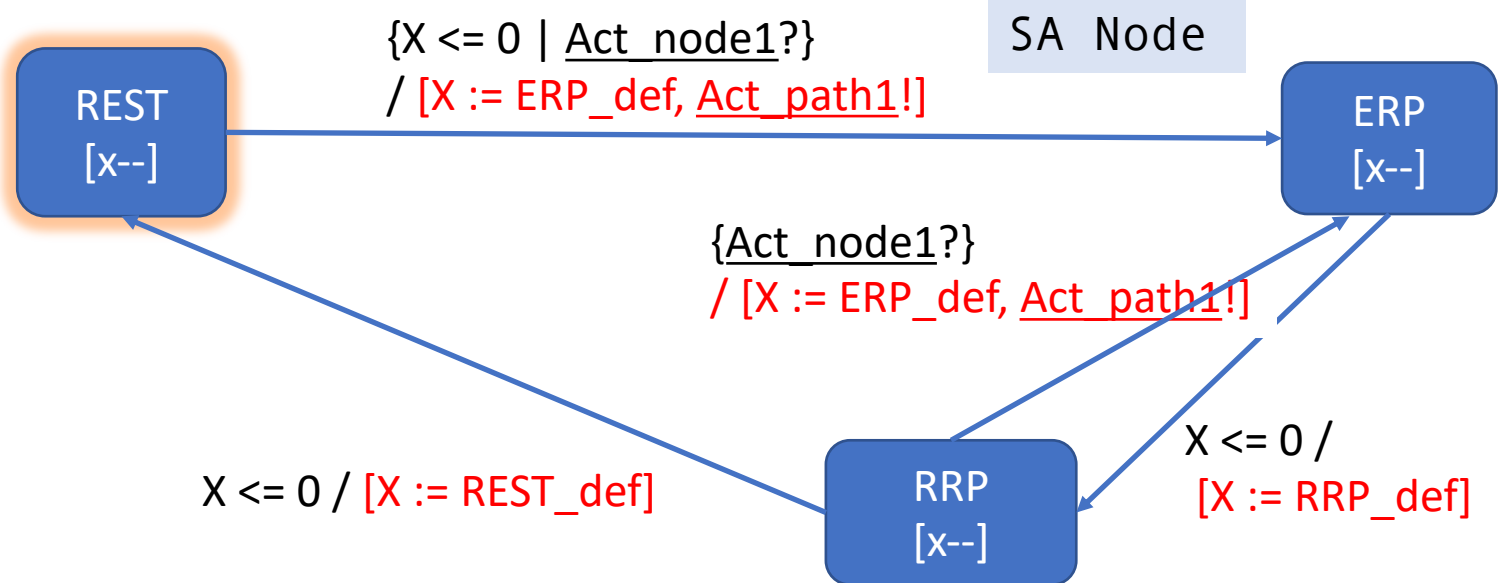
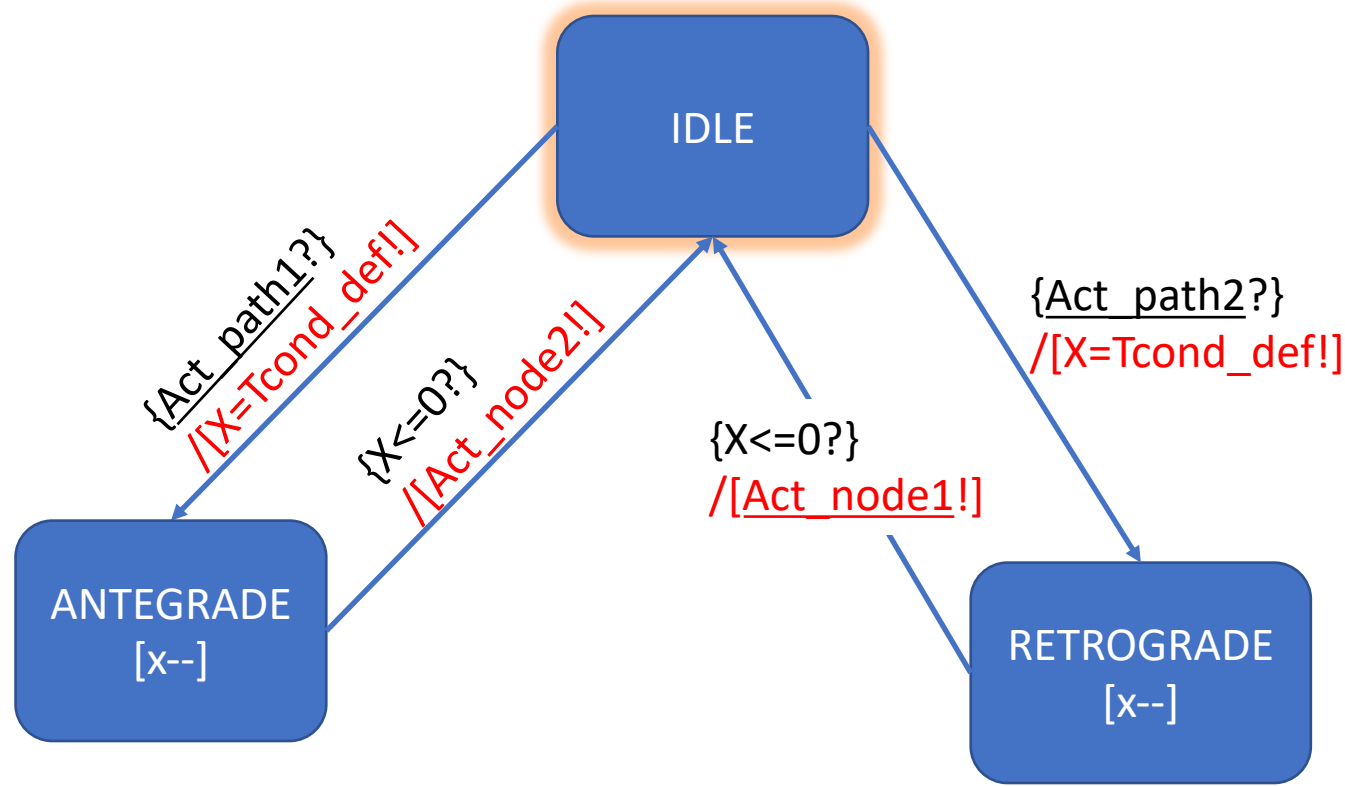
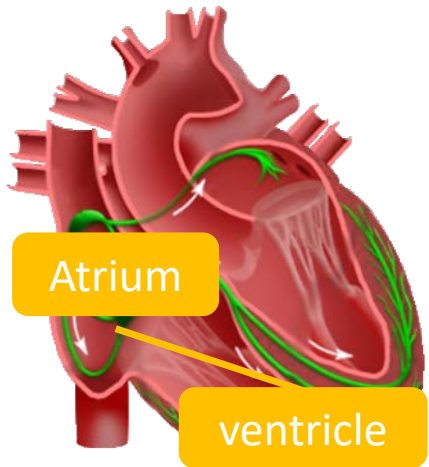
Right ventricle



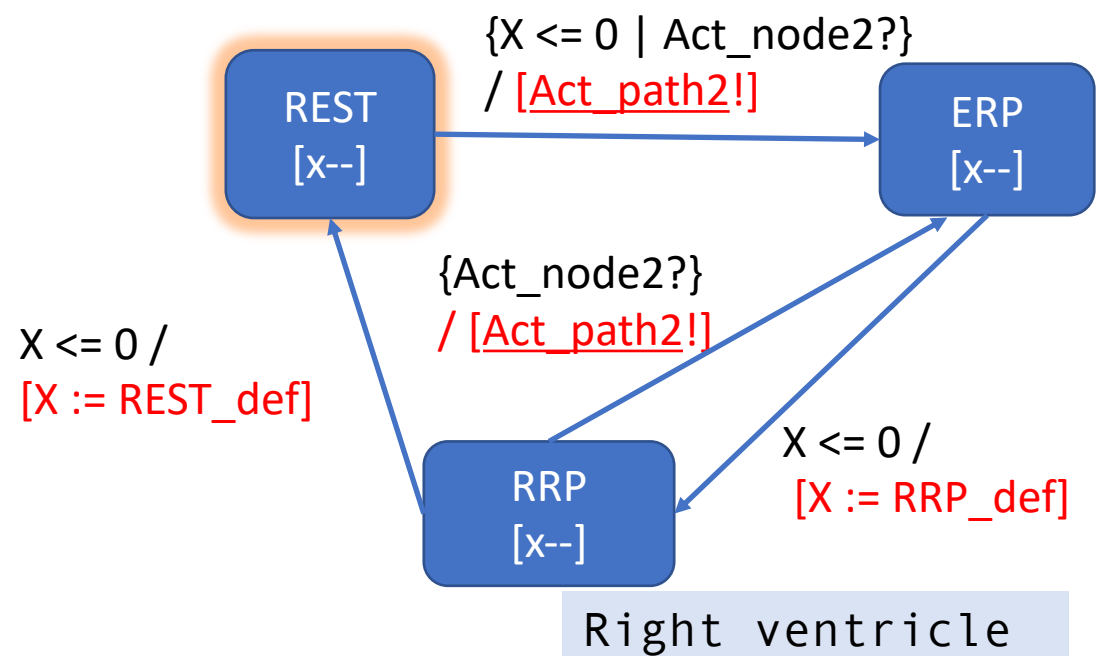
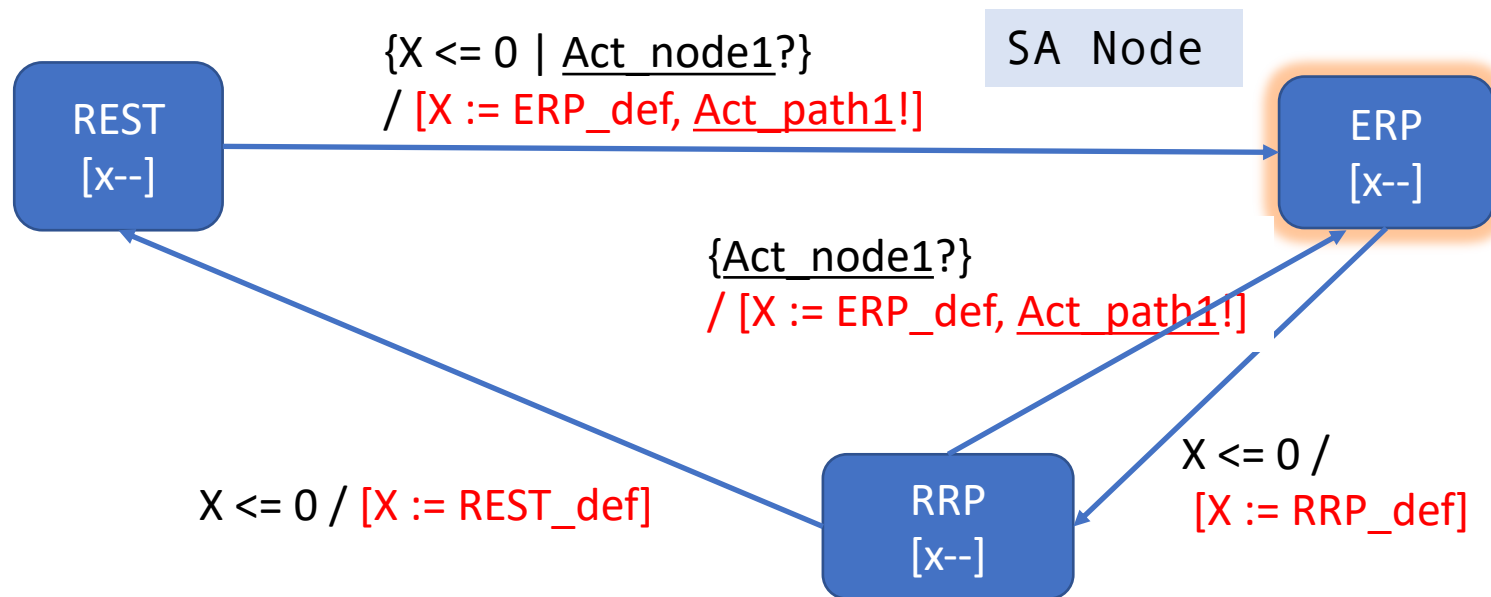
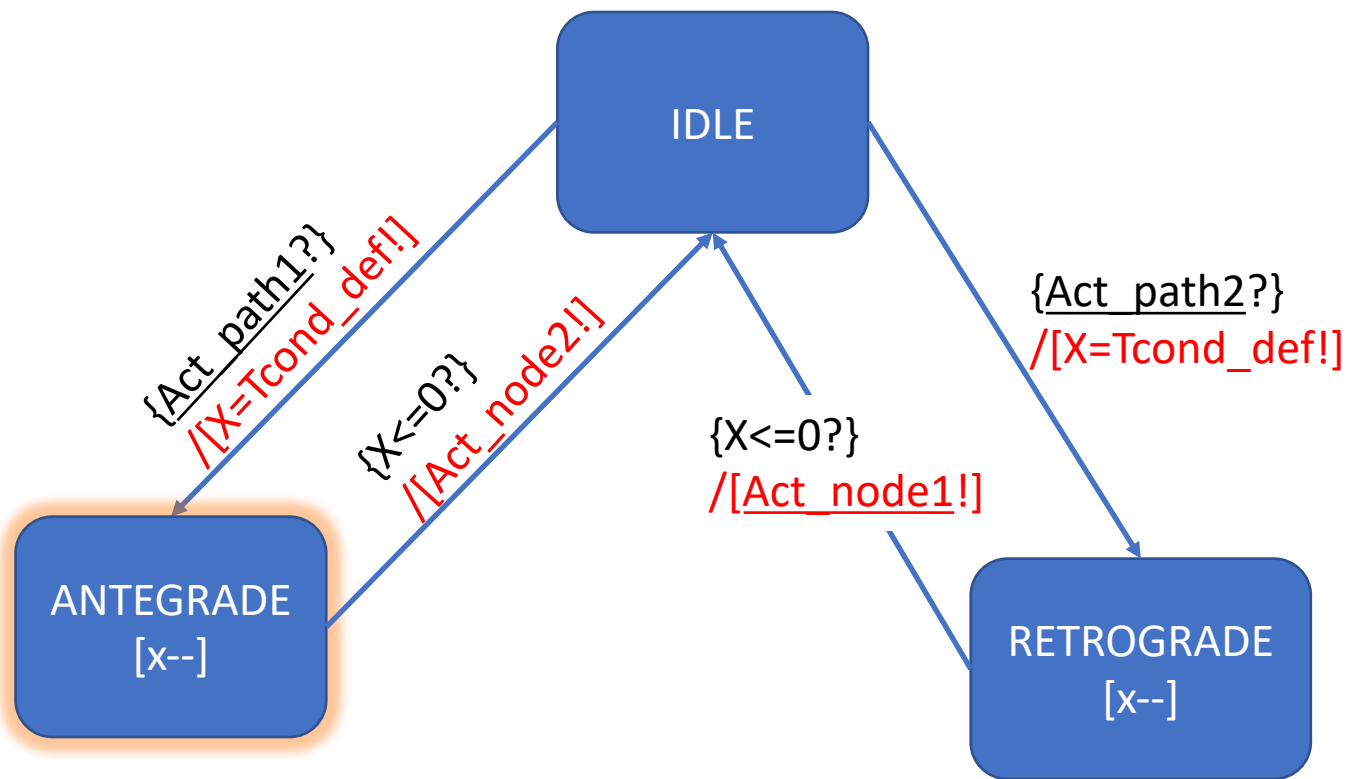
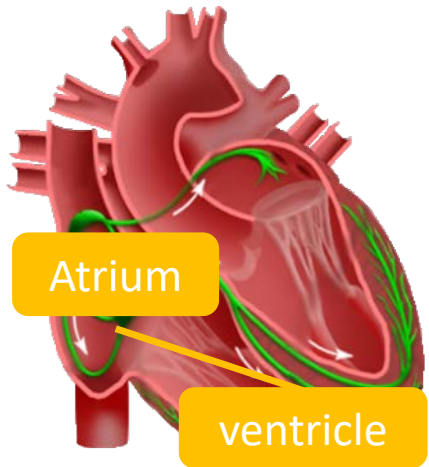
Uniform naming

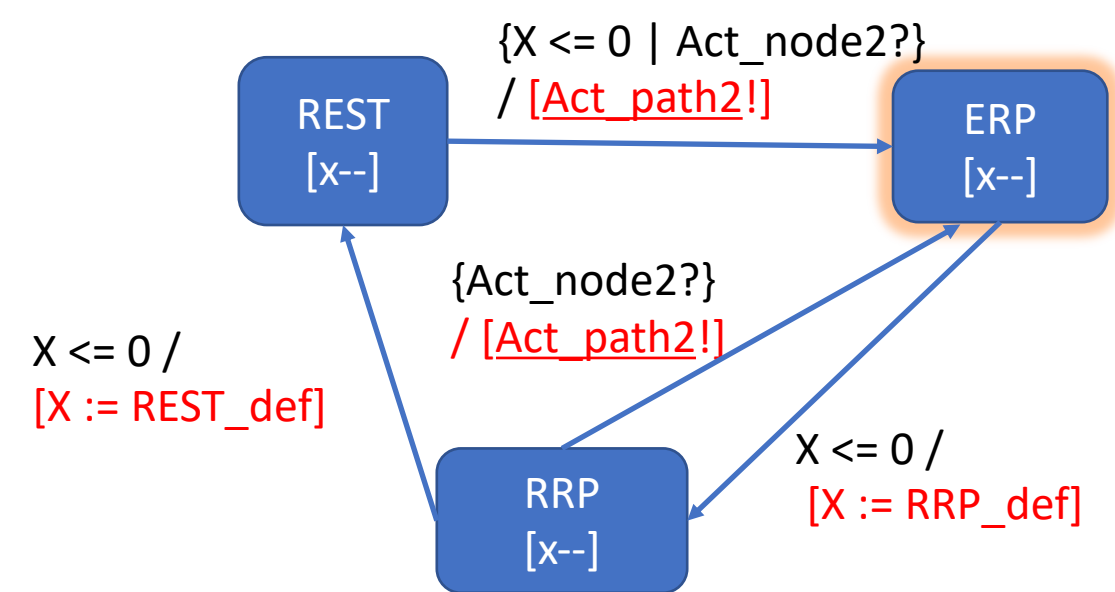
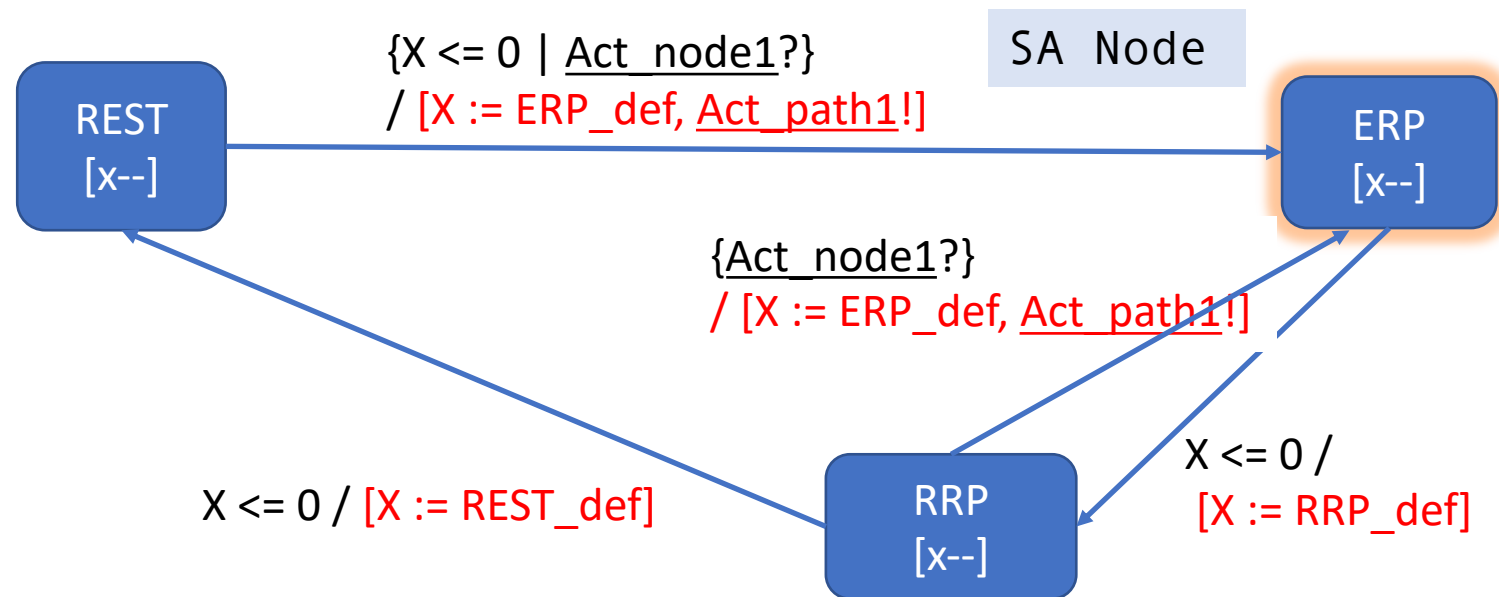
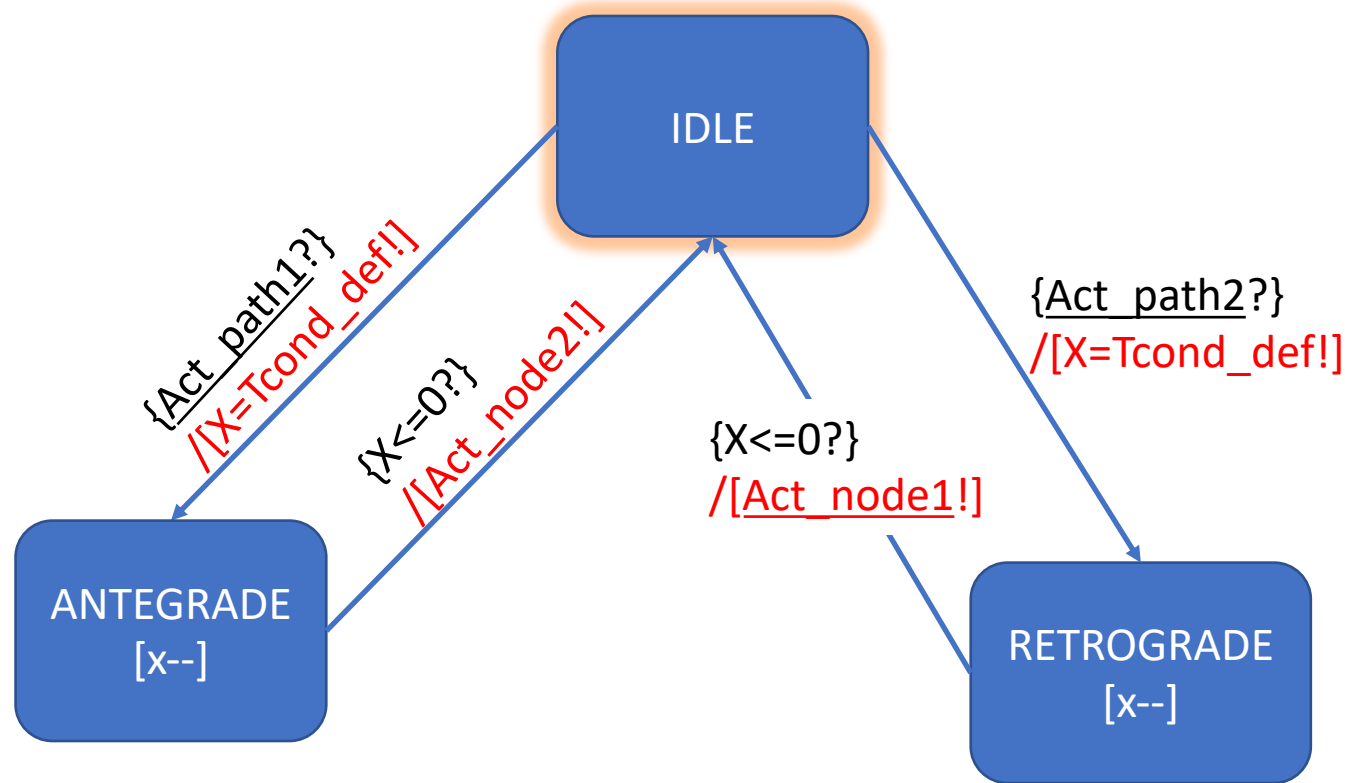
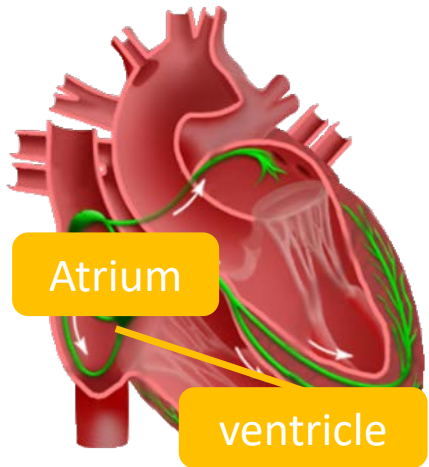


Right ventricle

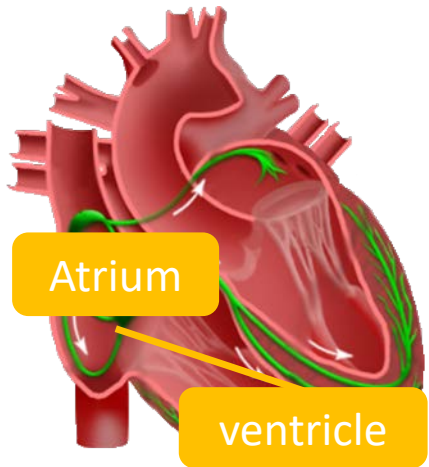


Right ventricle

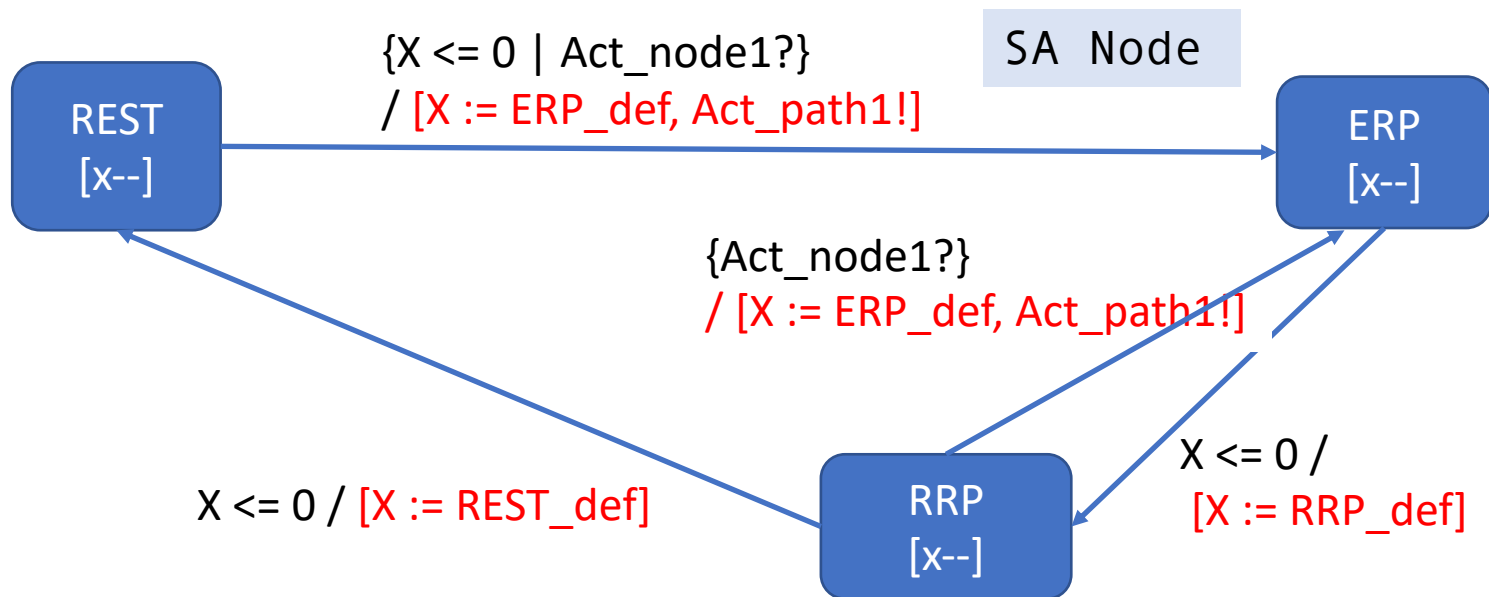
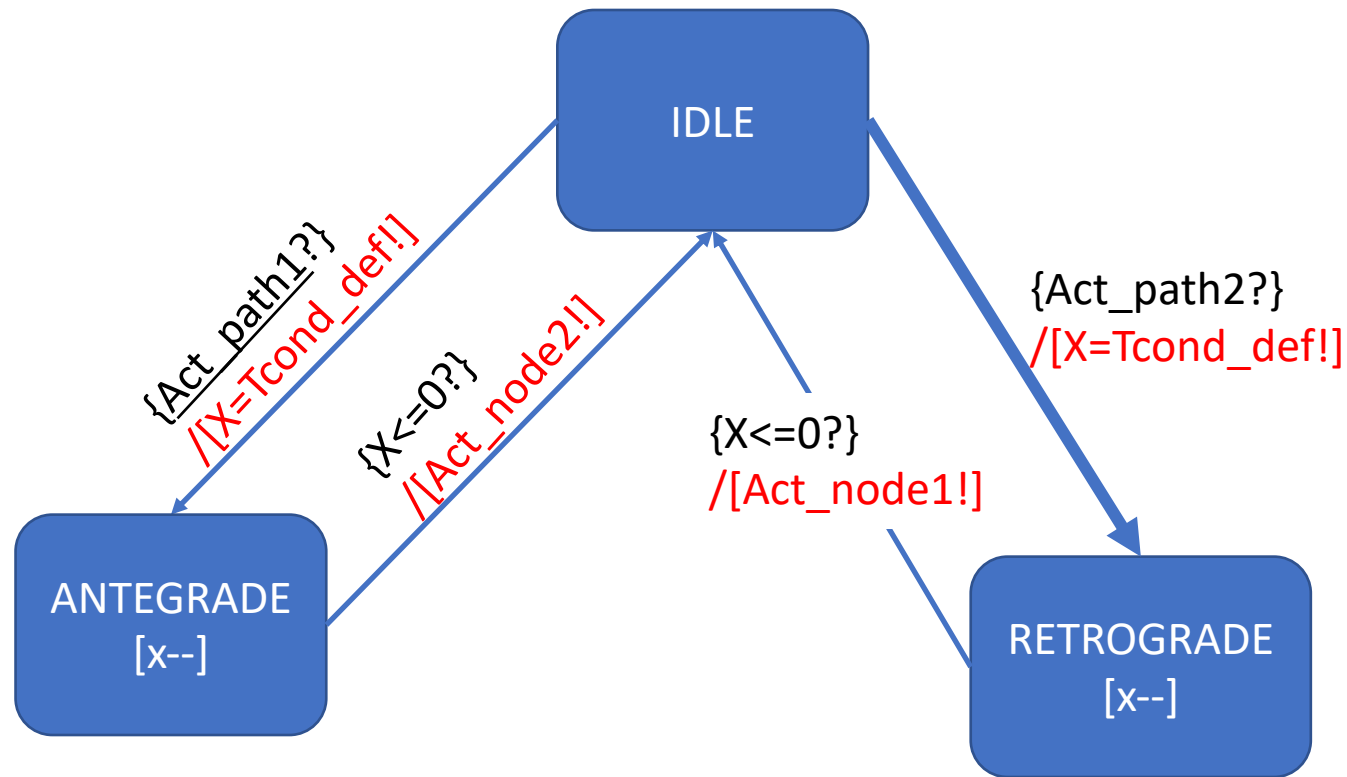




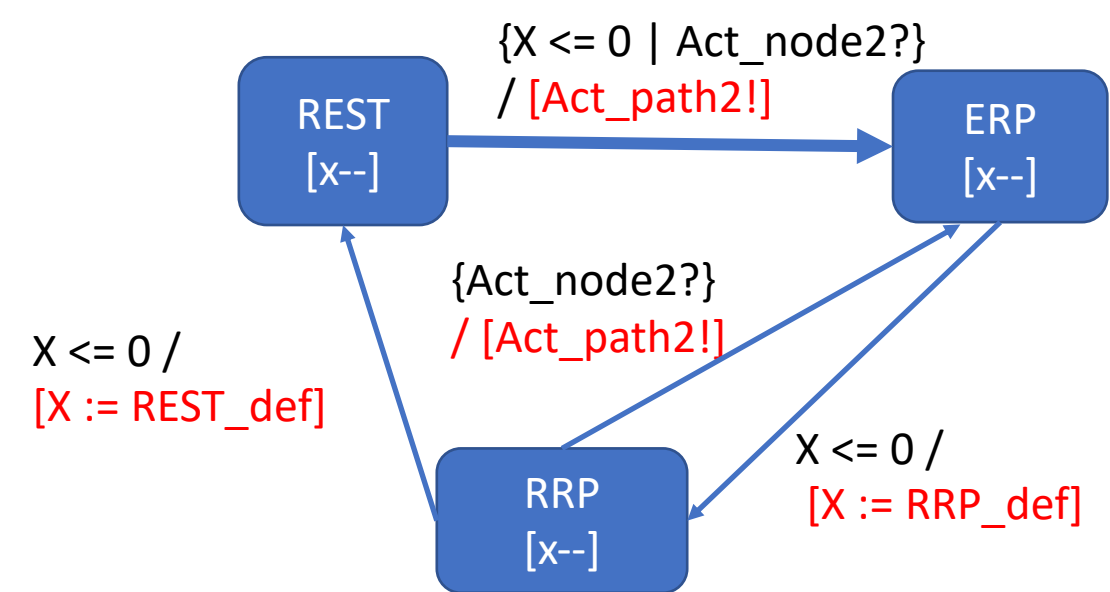
Right ventricle



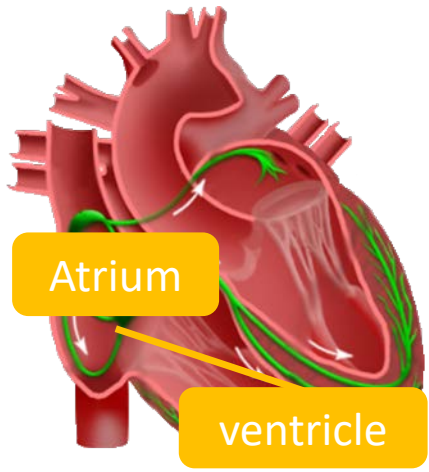
Infinite loop?



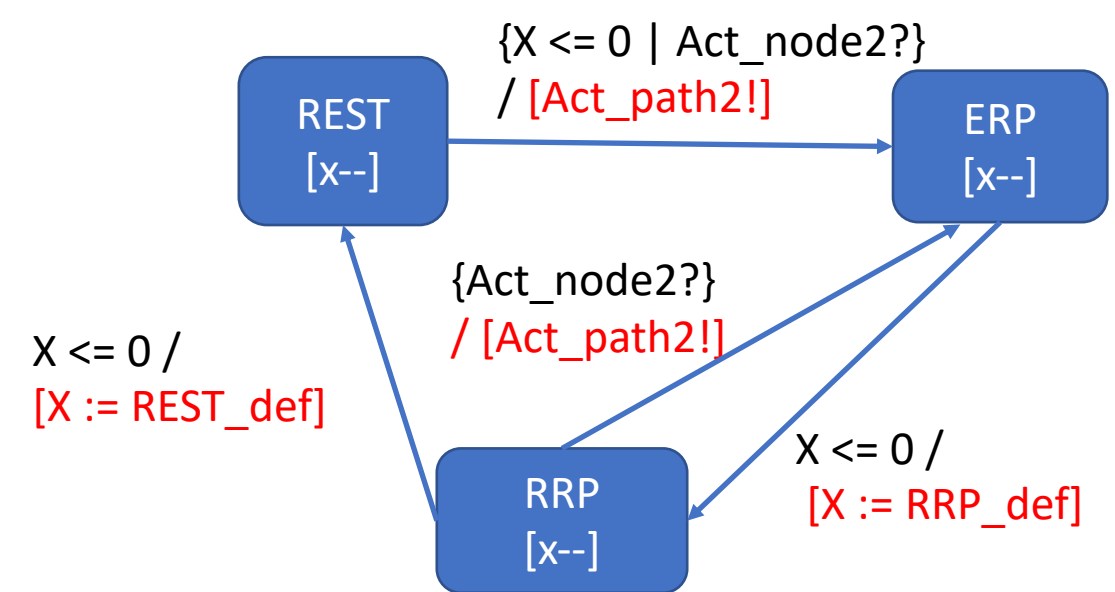
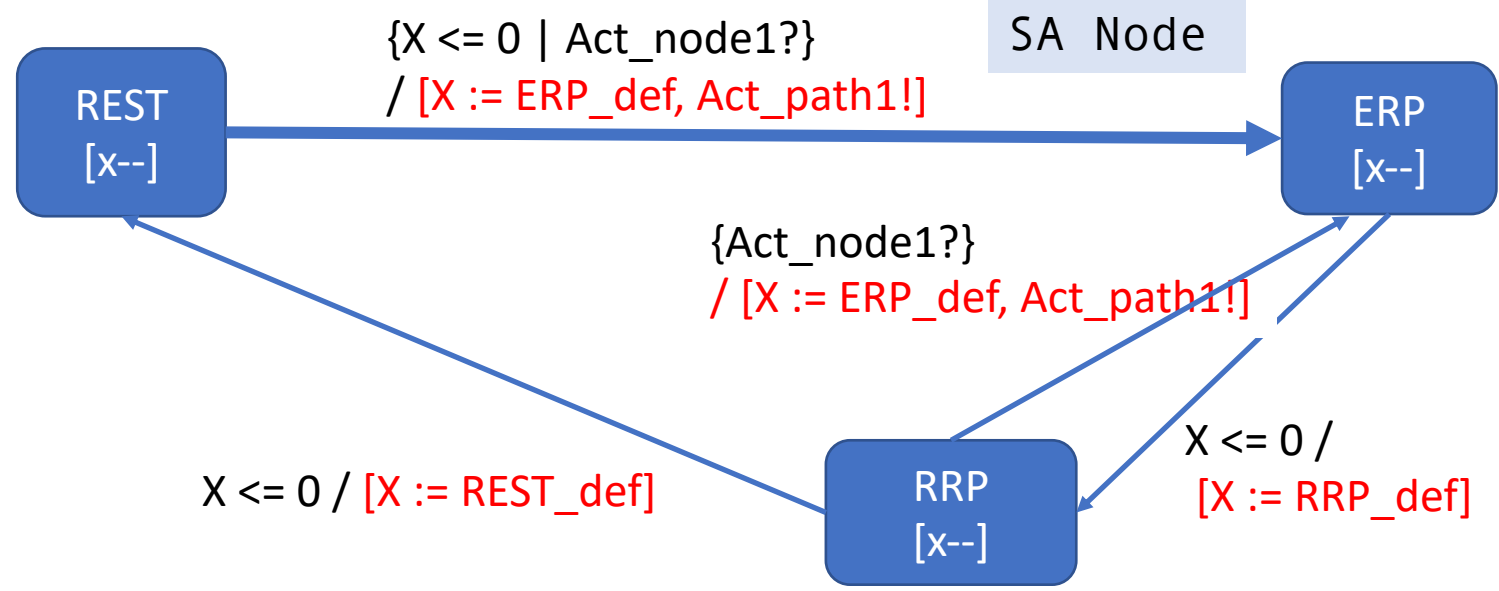
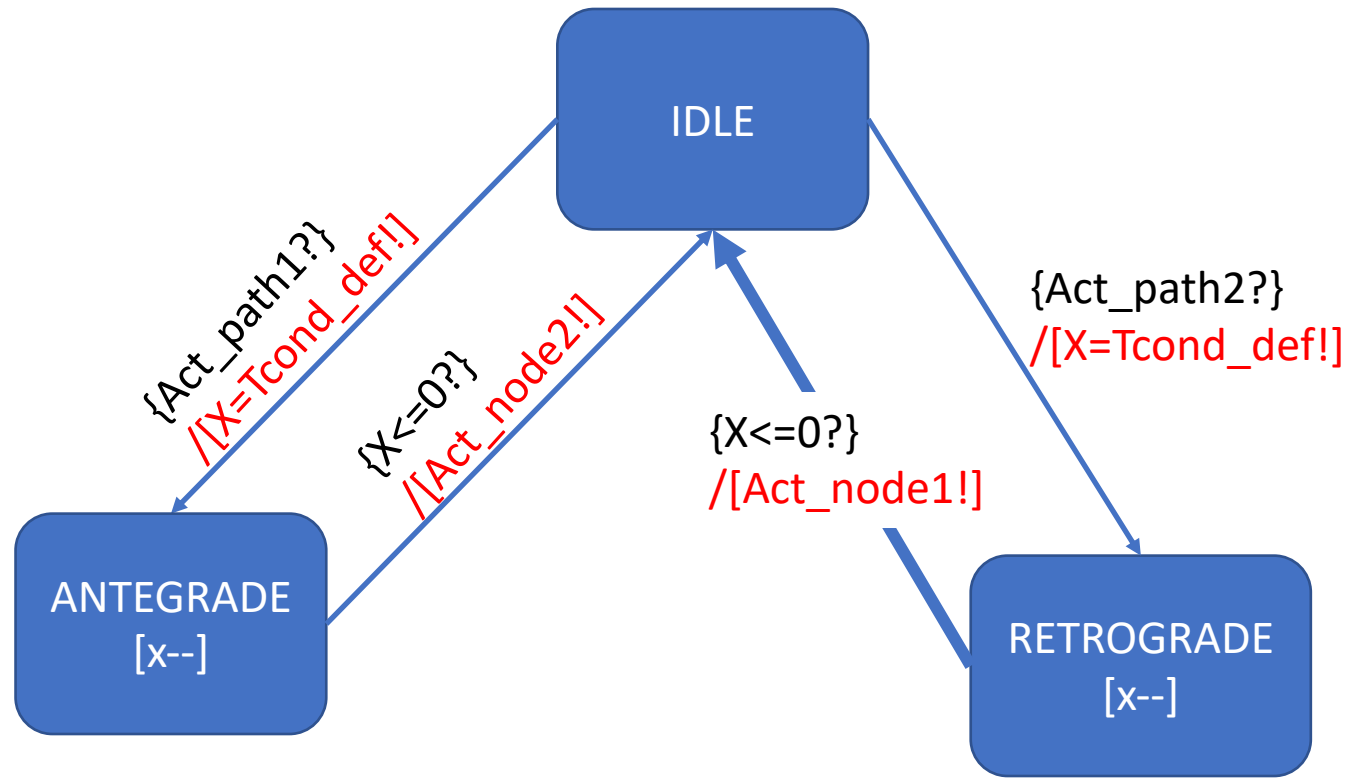
SA Node



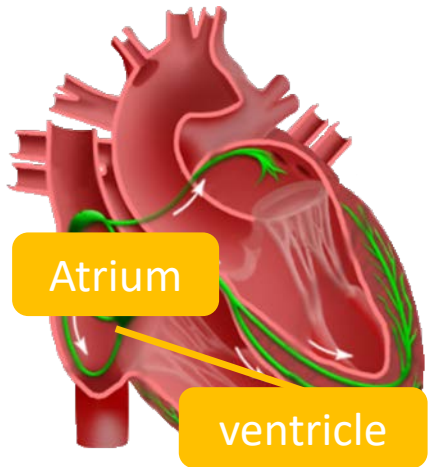
Right ventricle



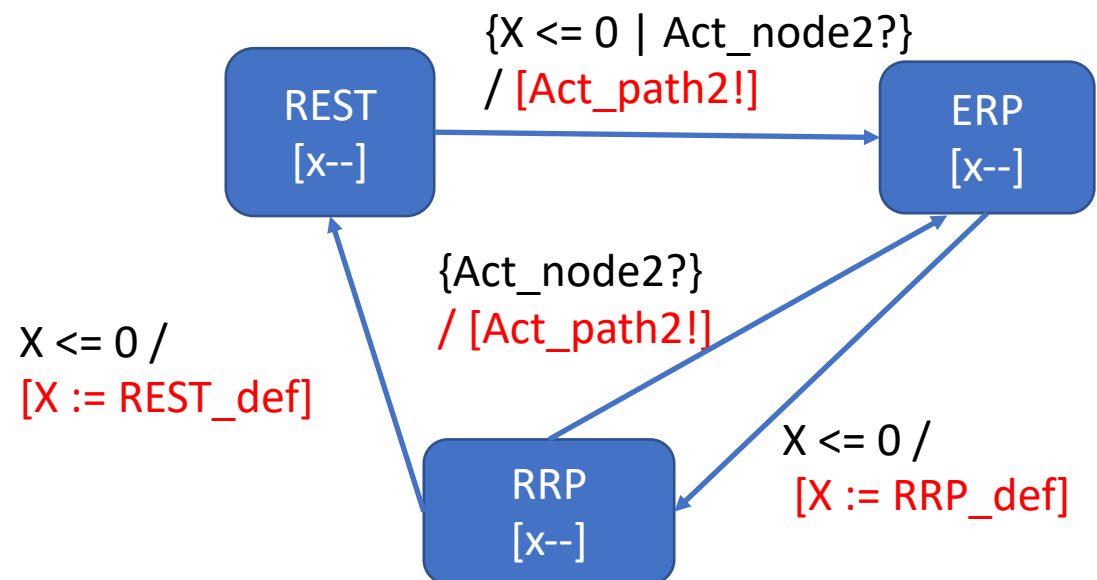
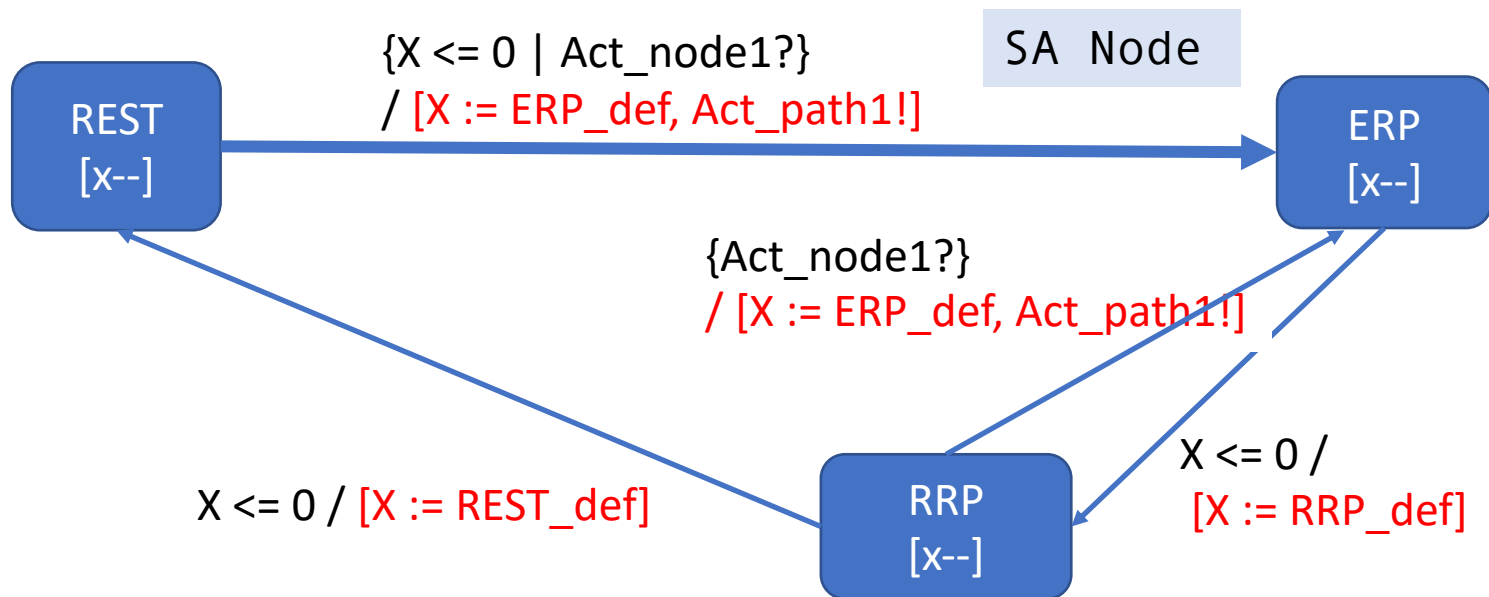
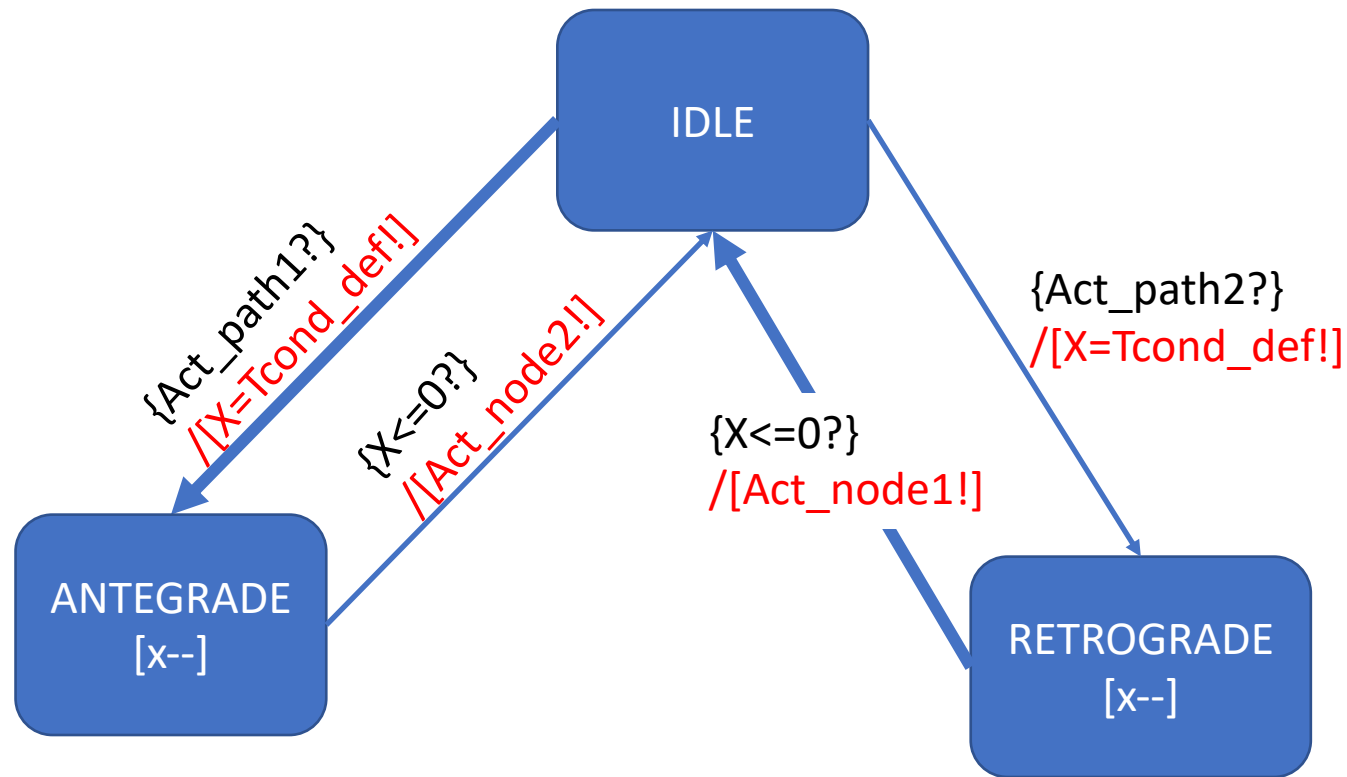
Infinite loop?



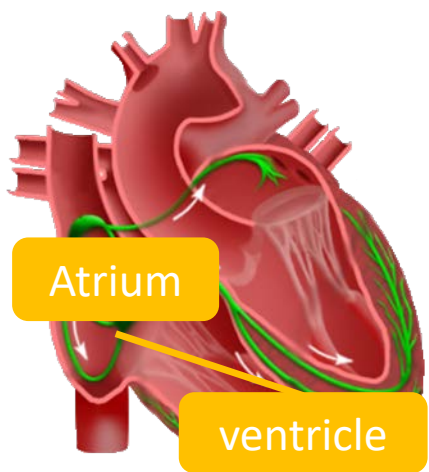
Right ventricle



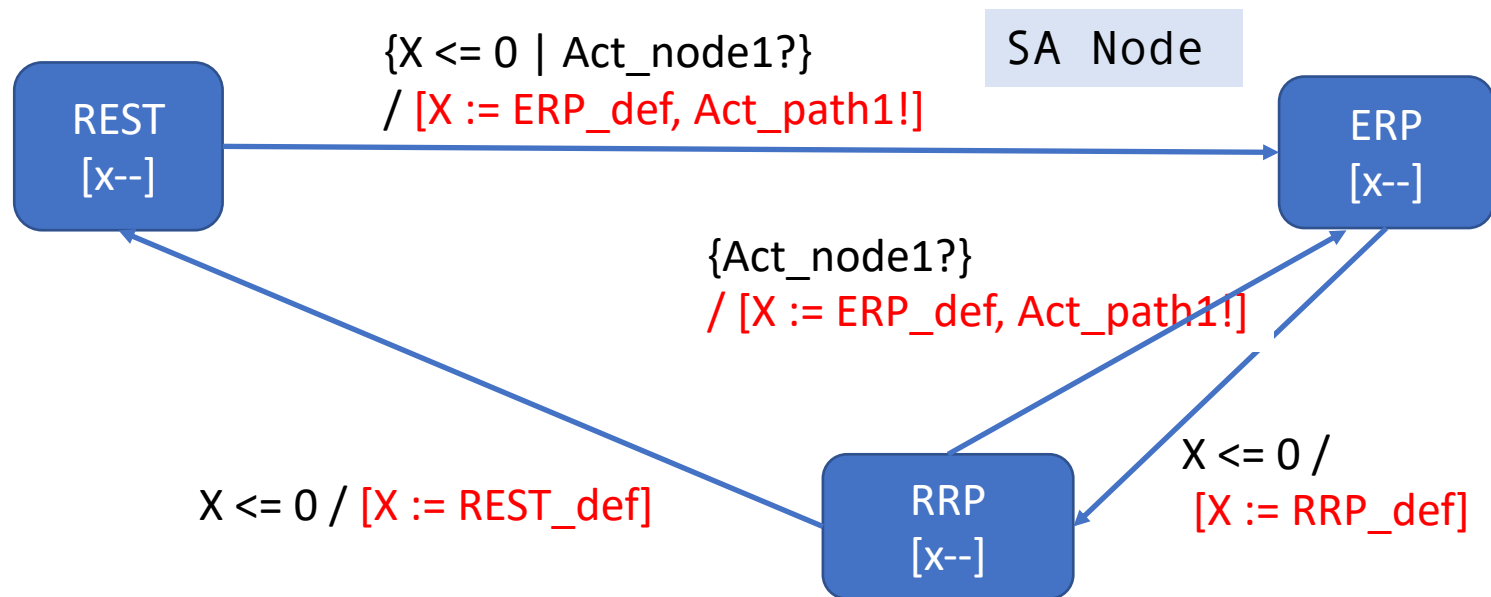
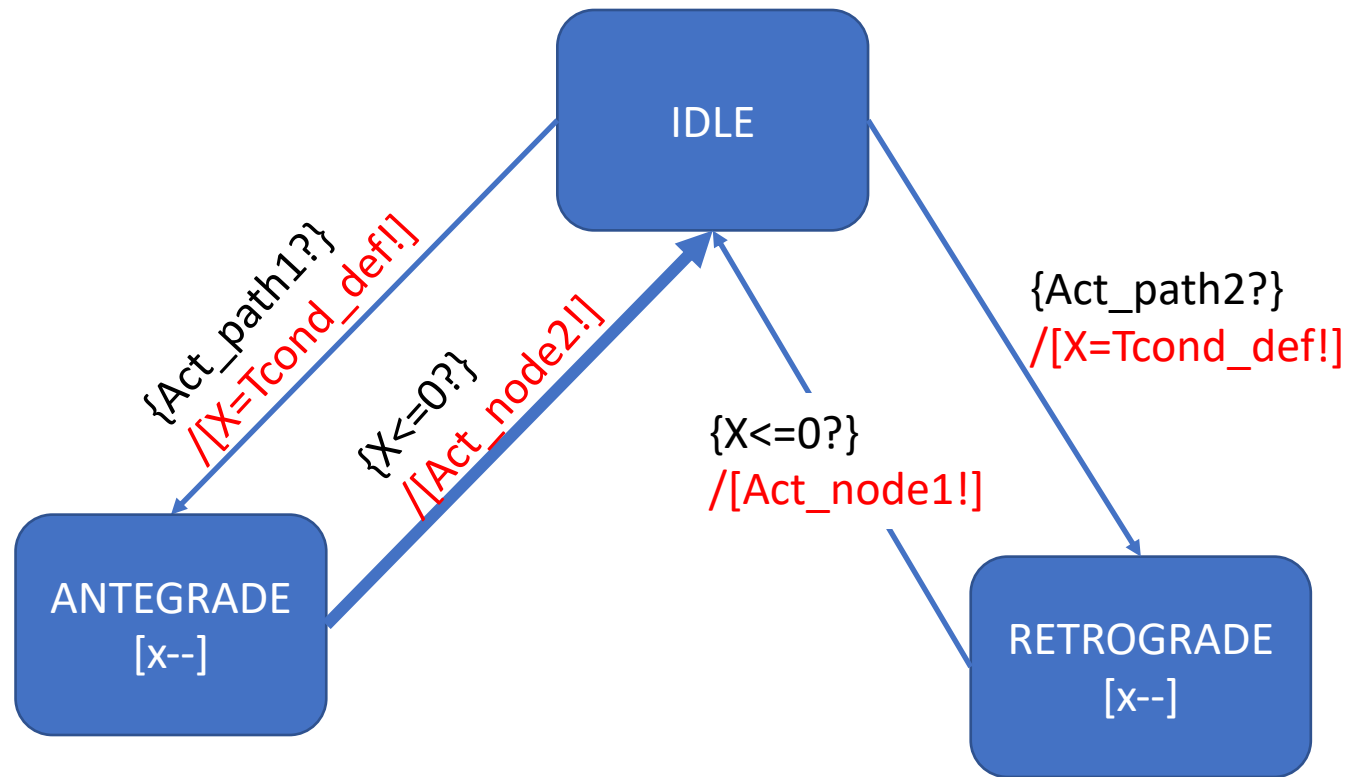
Infinite loop?



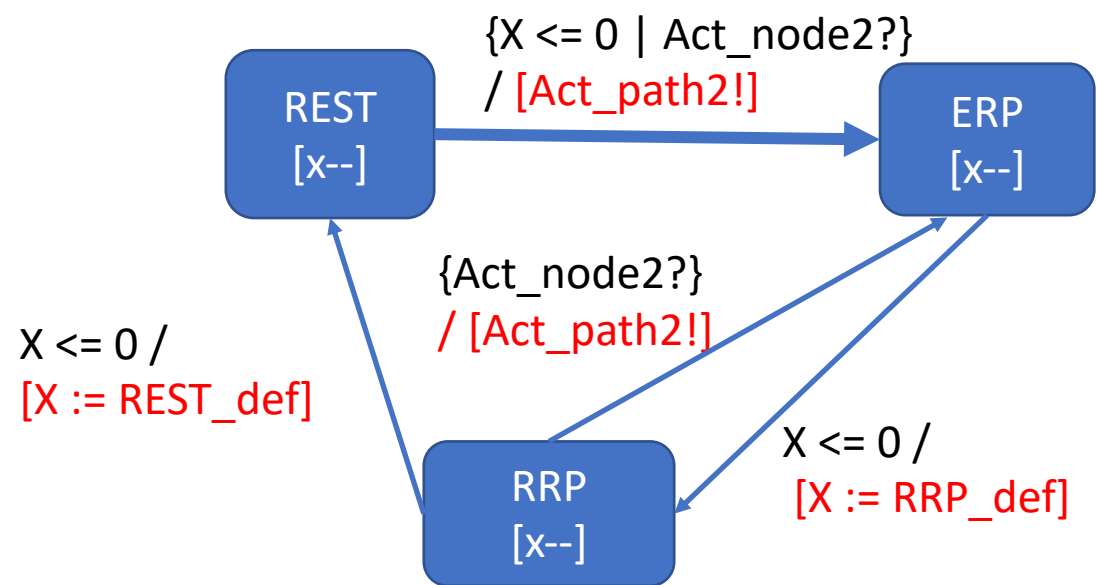
Right ventricle



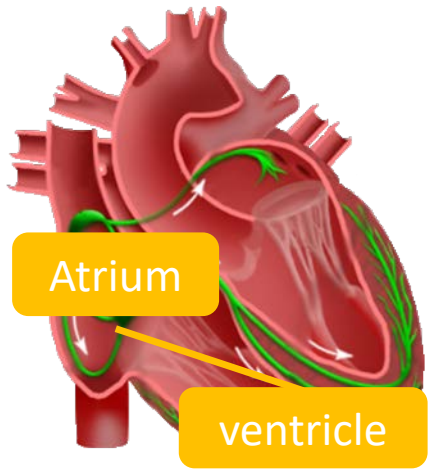
Infinite loop!



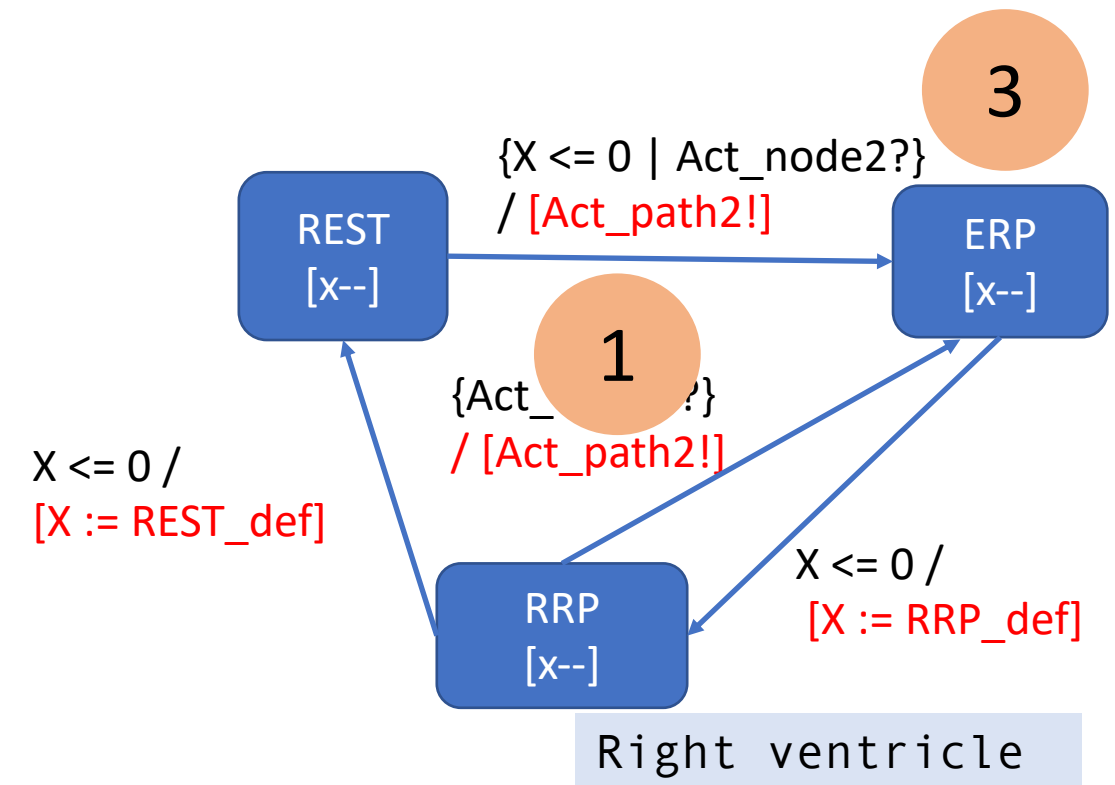
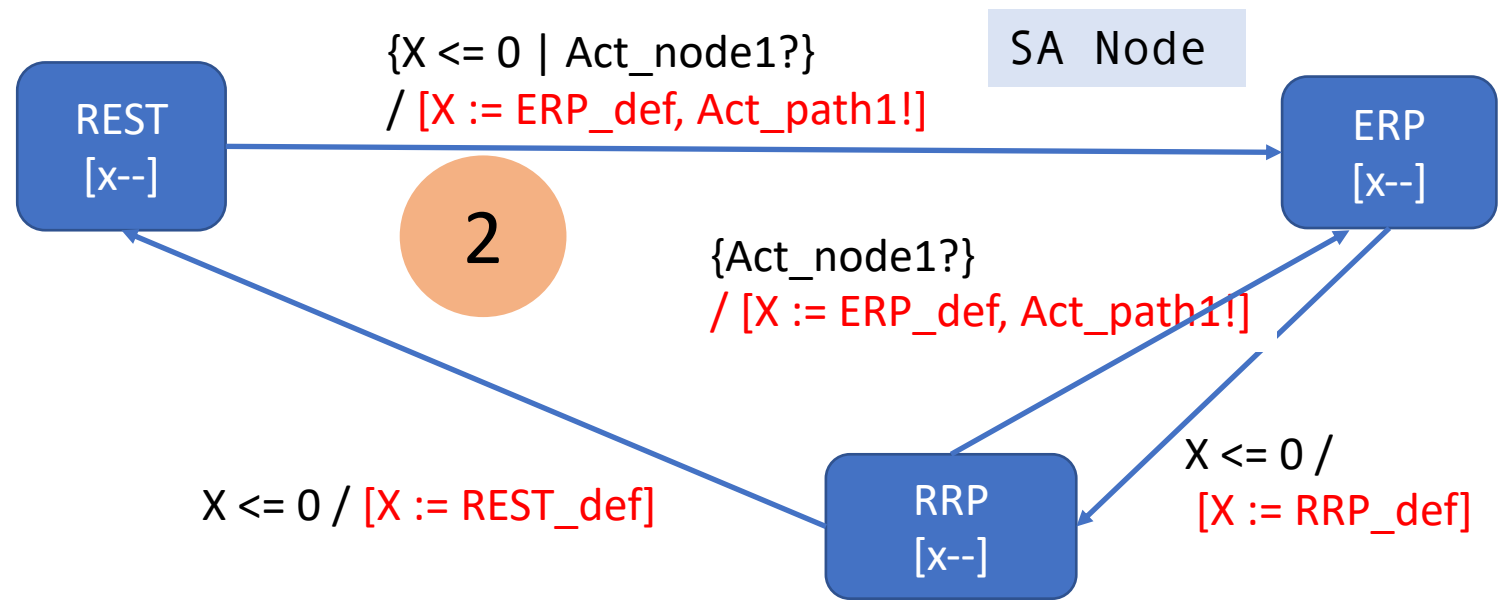
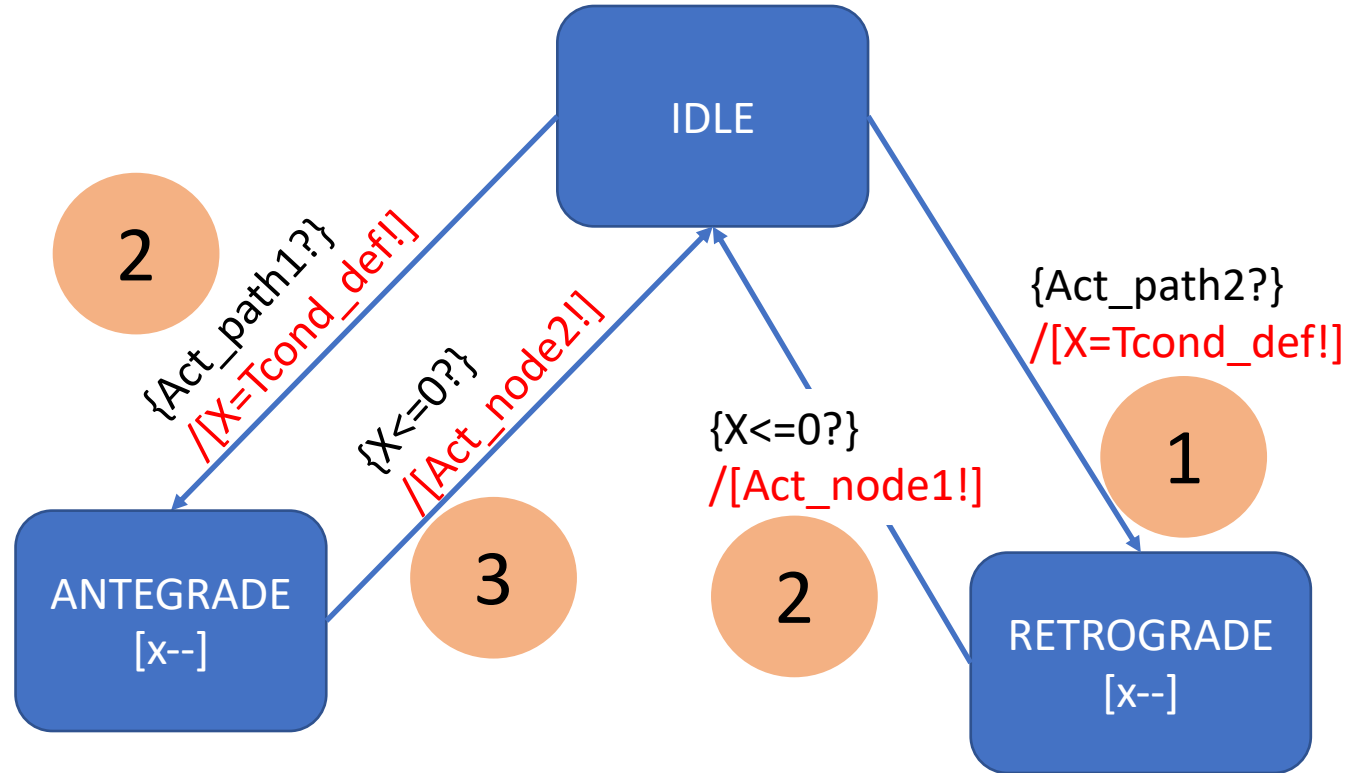
SA Node

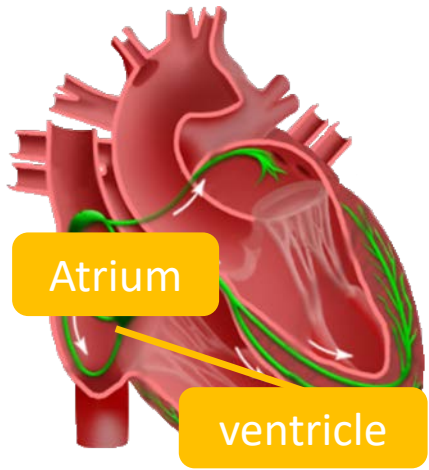


Right ventricle

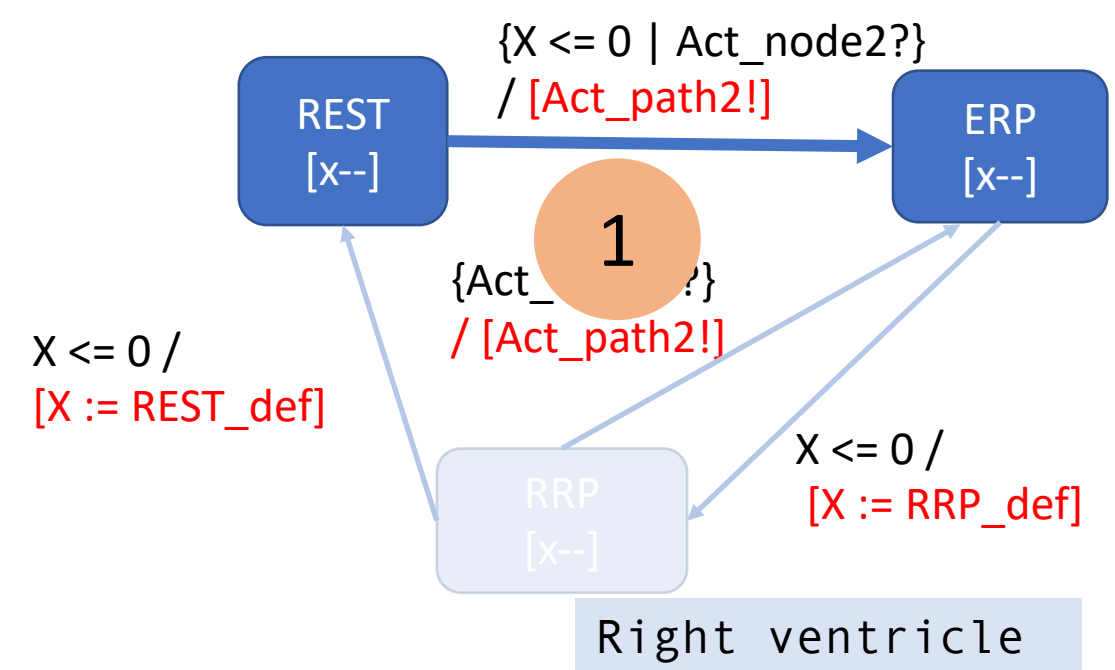
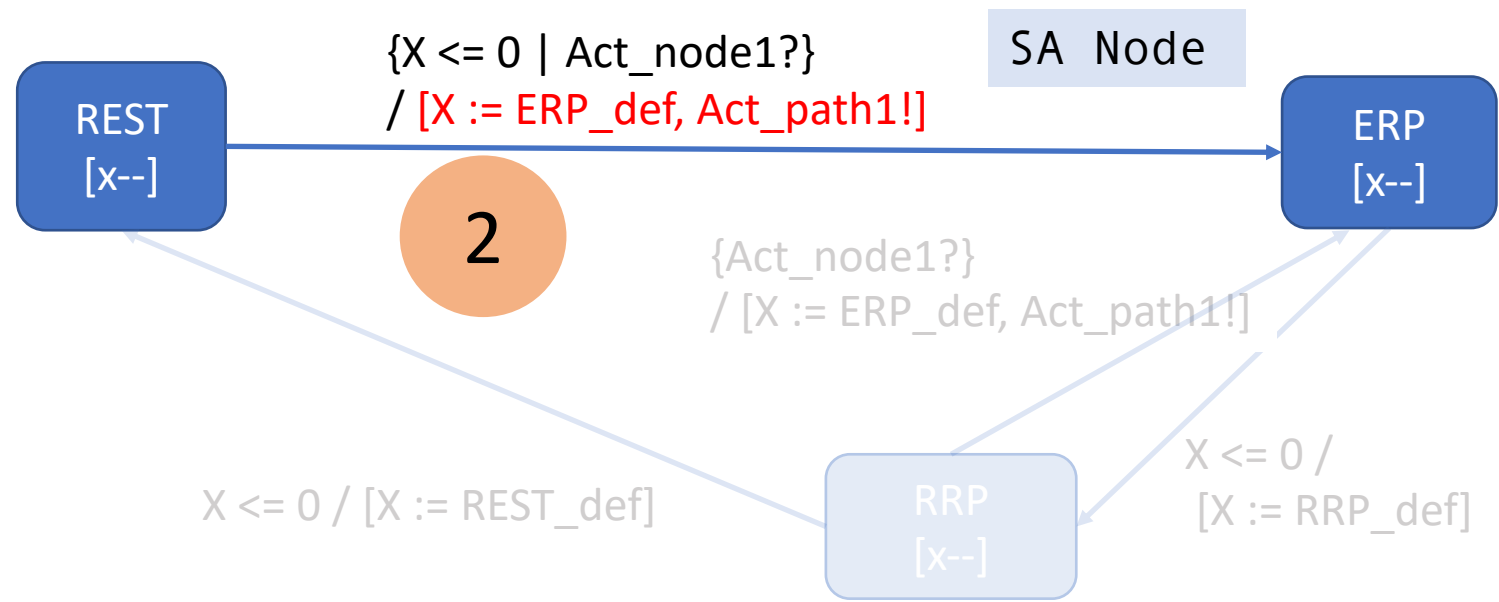
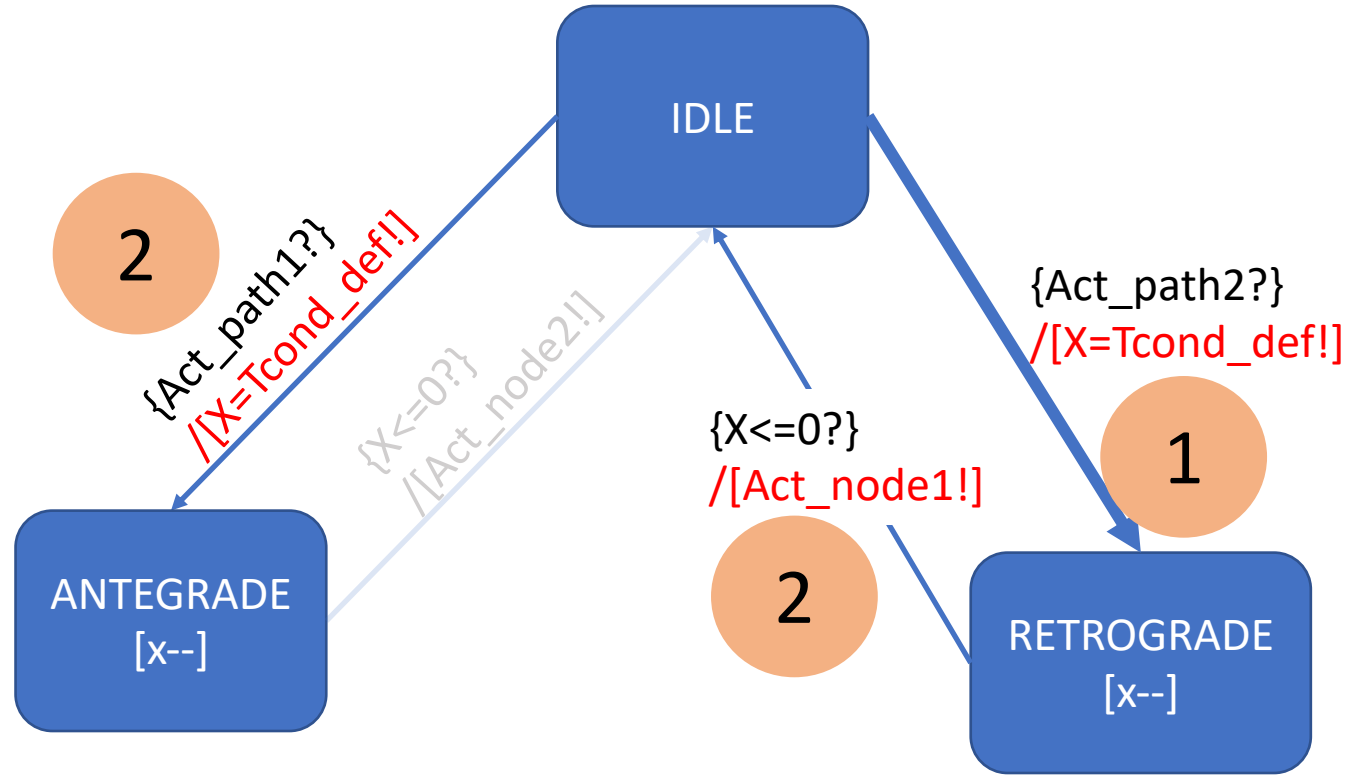


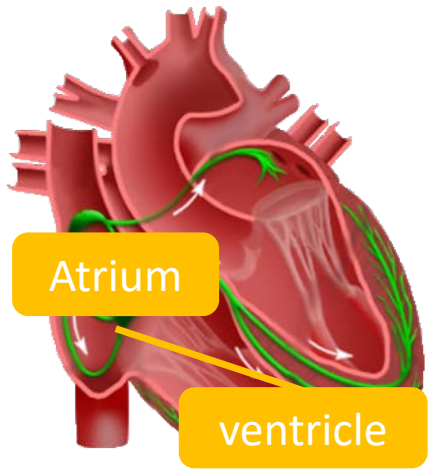
Infinite loop!



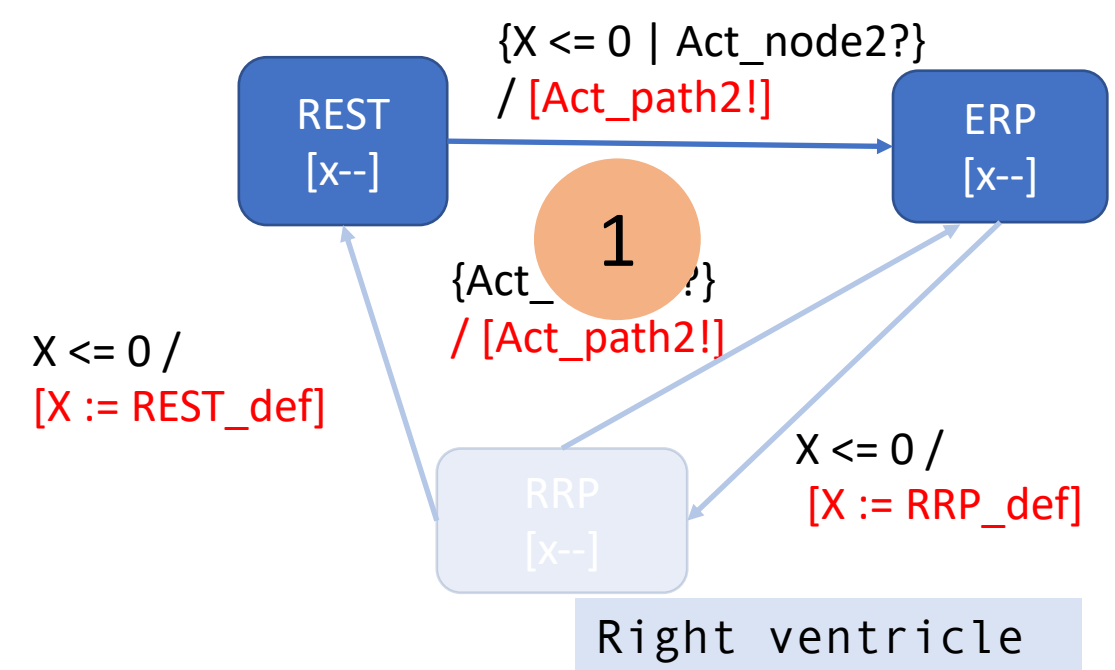
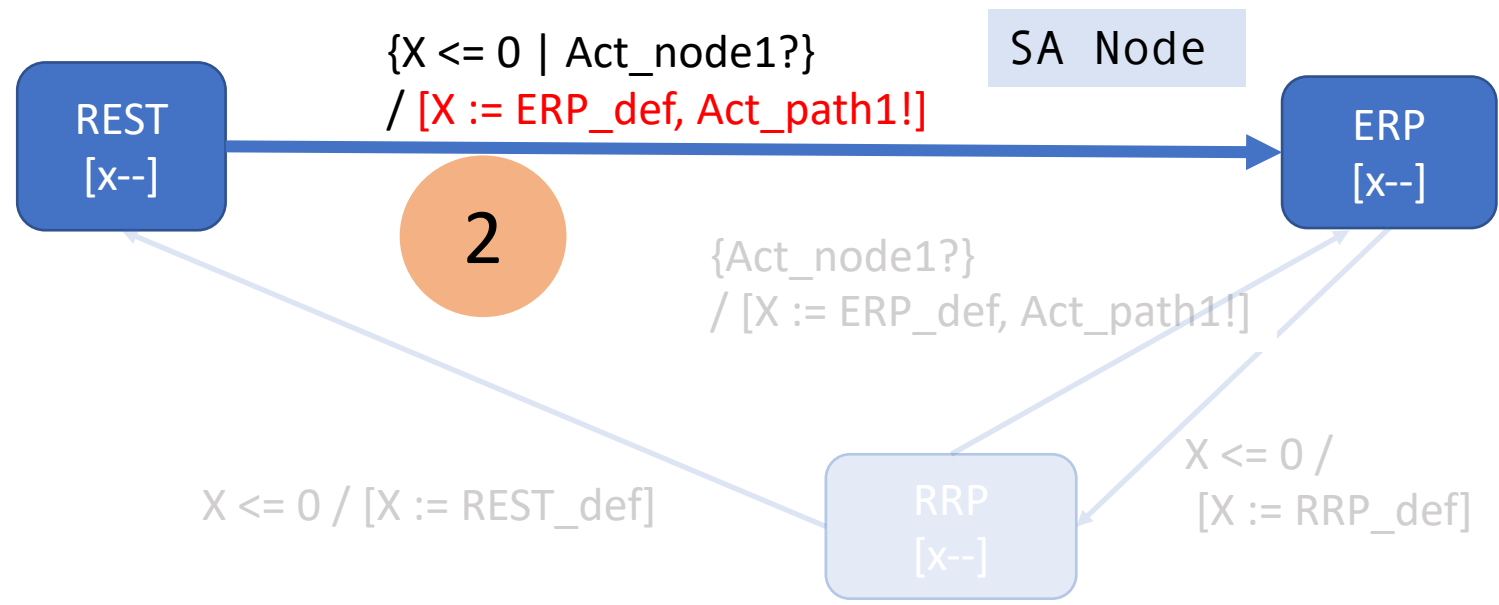
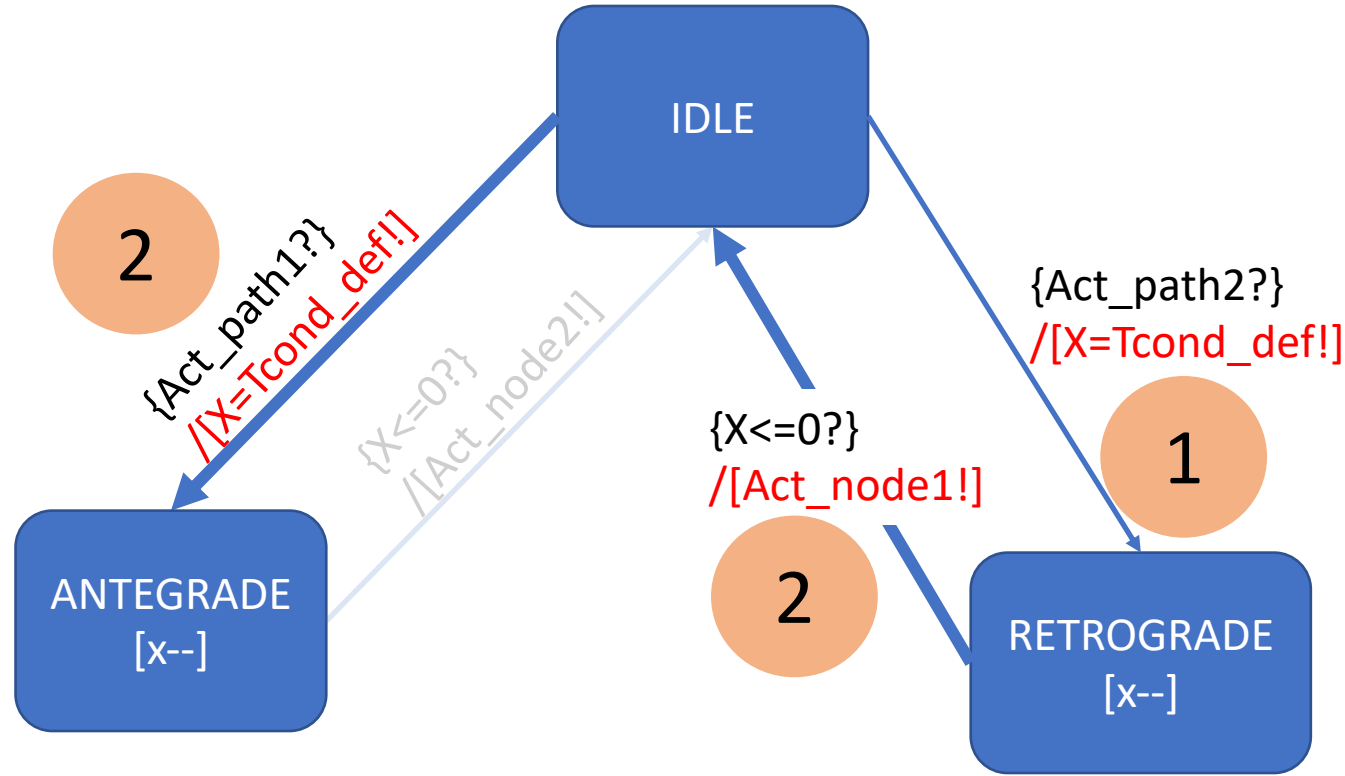


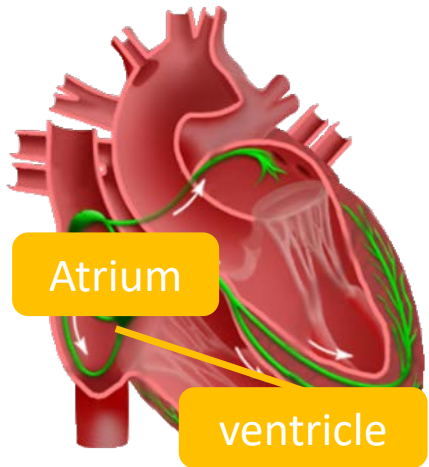
Breaking the Infinite loop



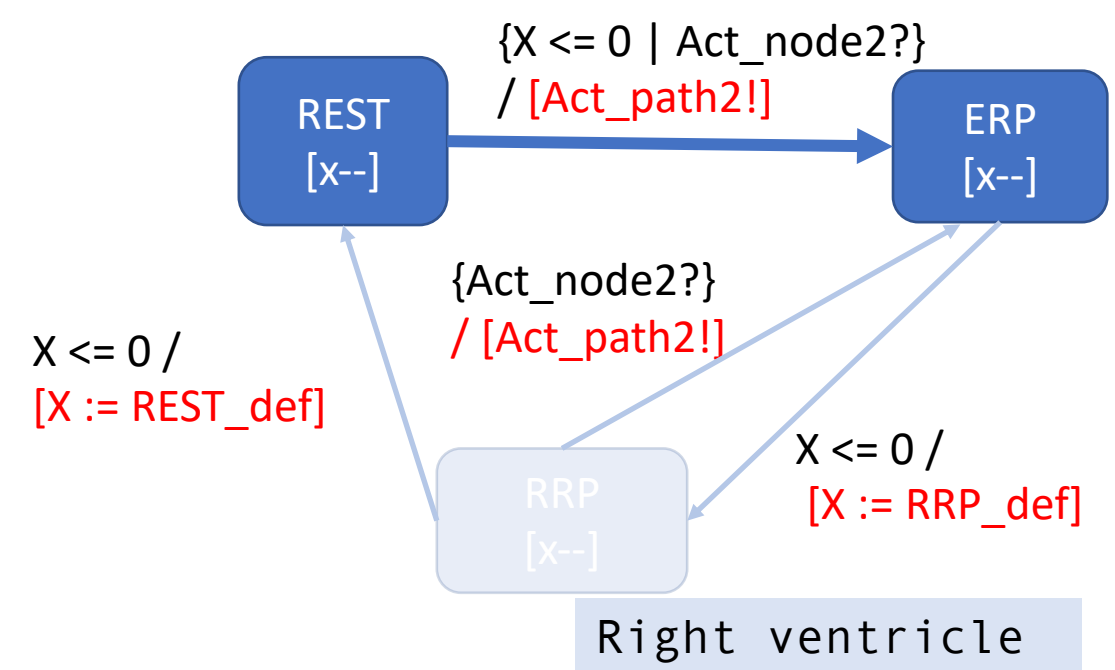
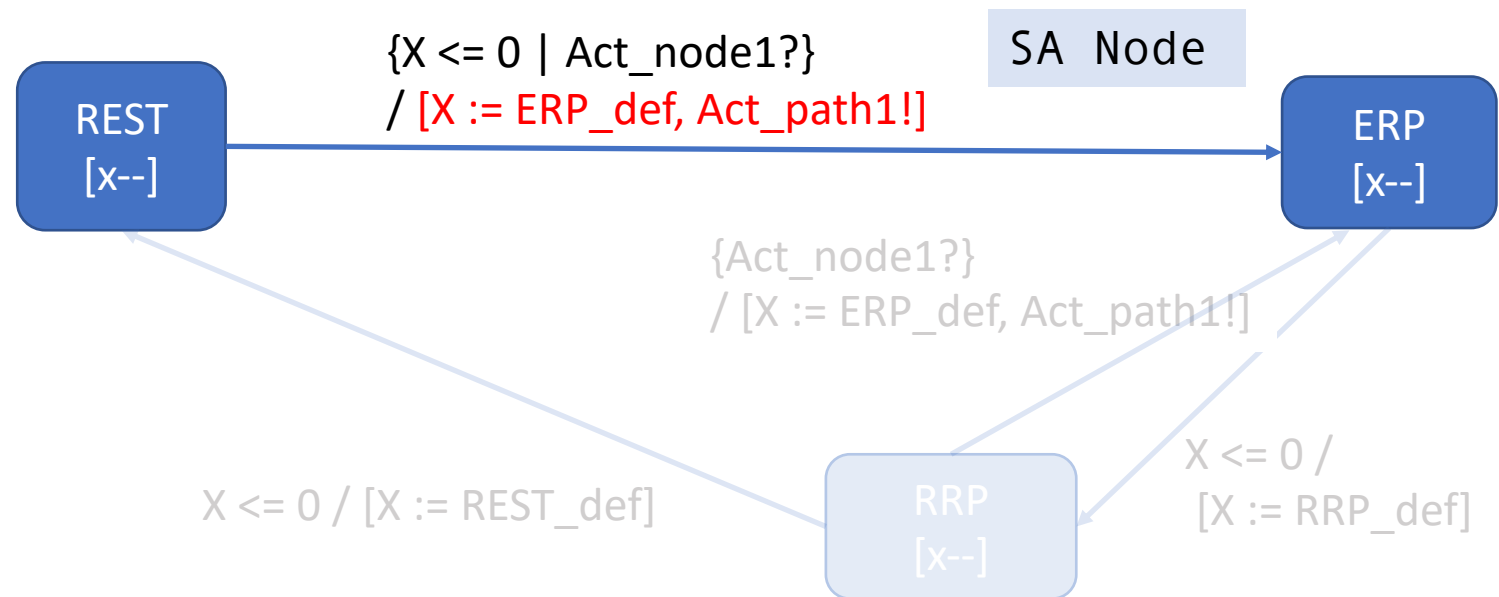
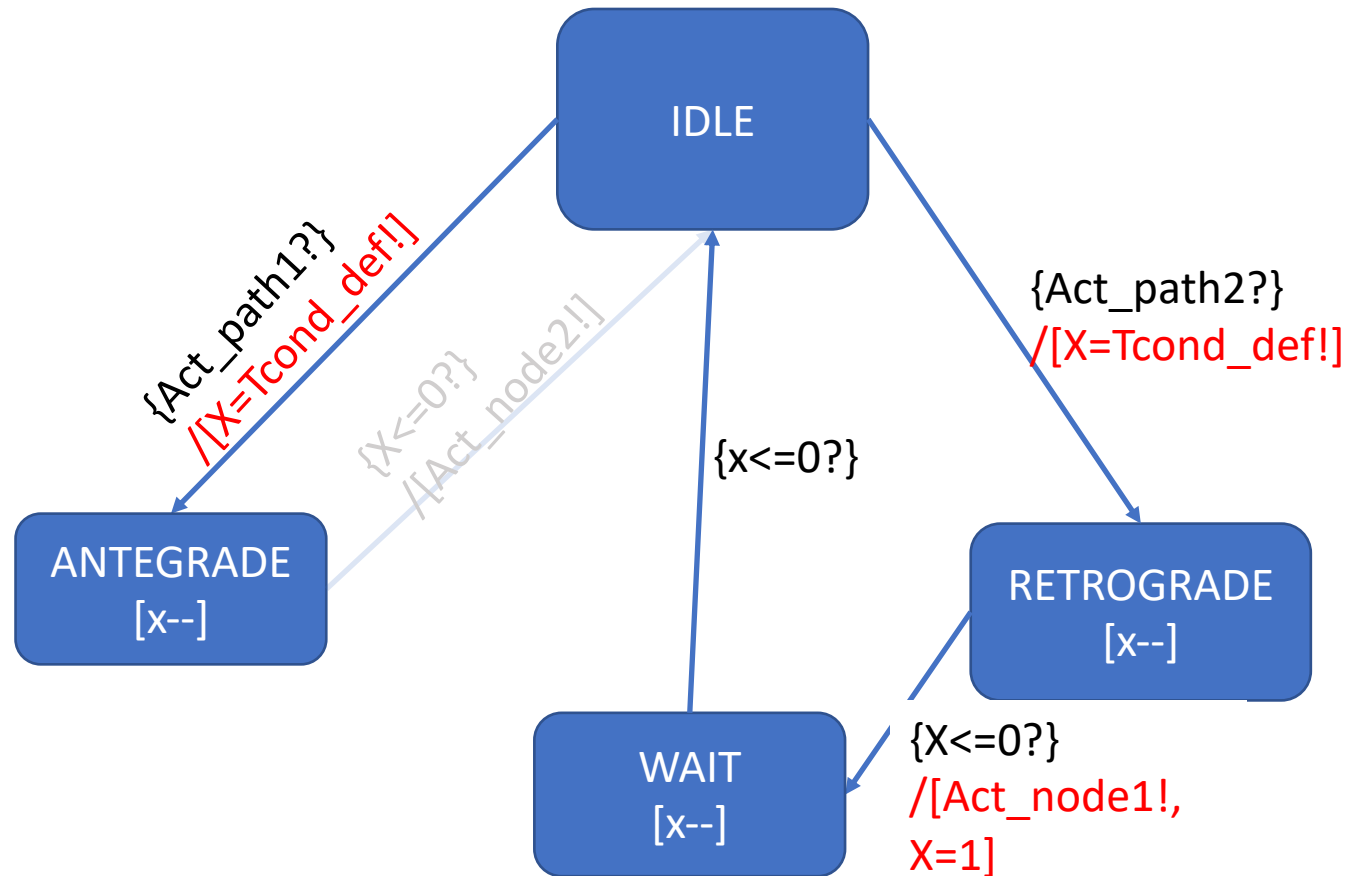


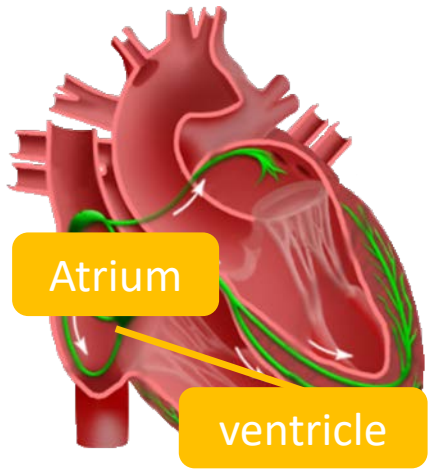
Breaking the Infinite loop



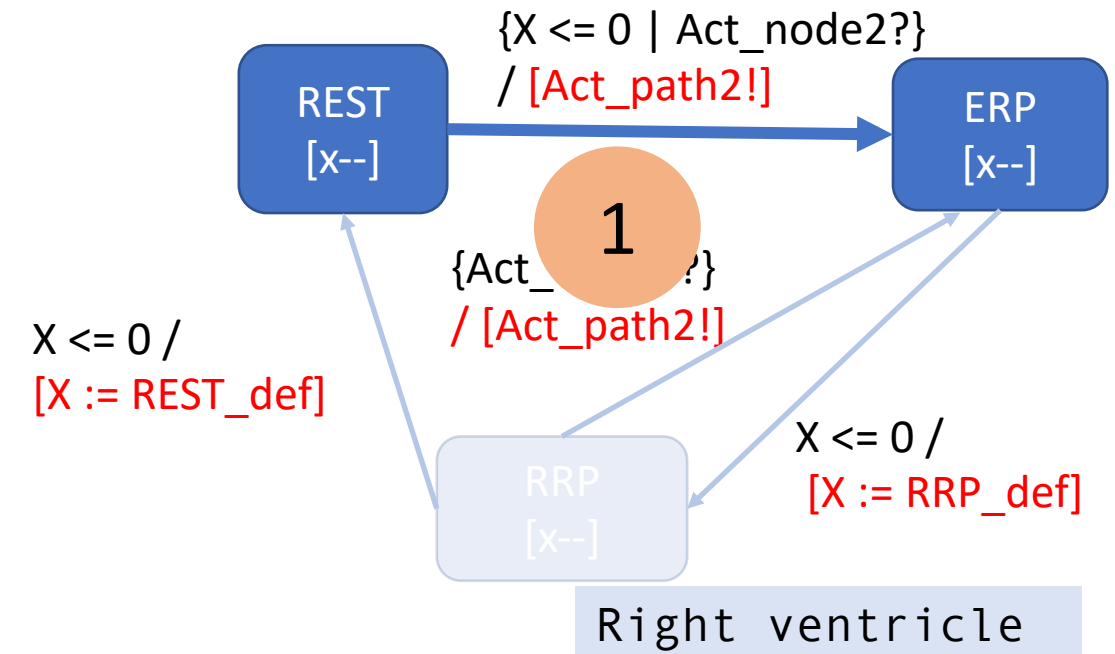
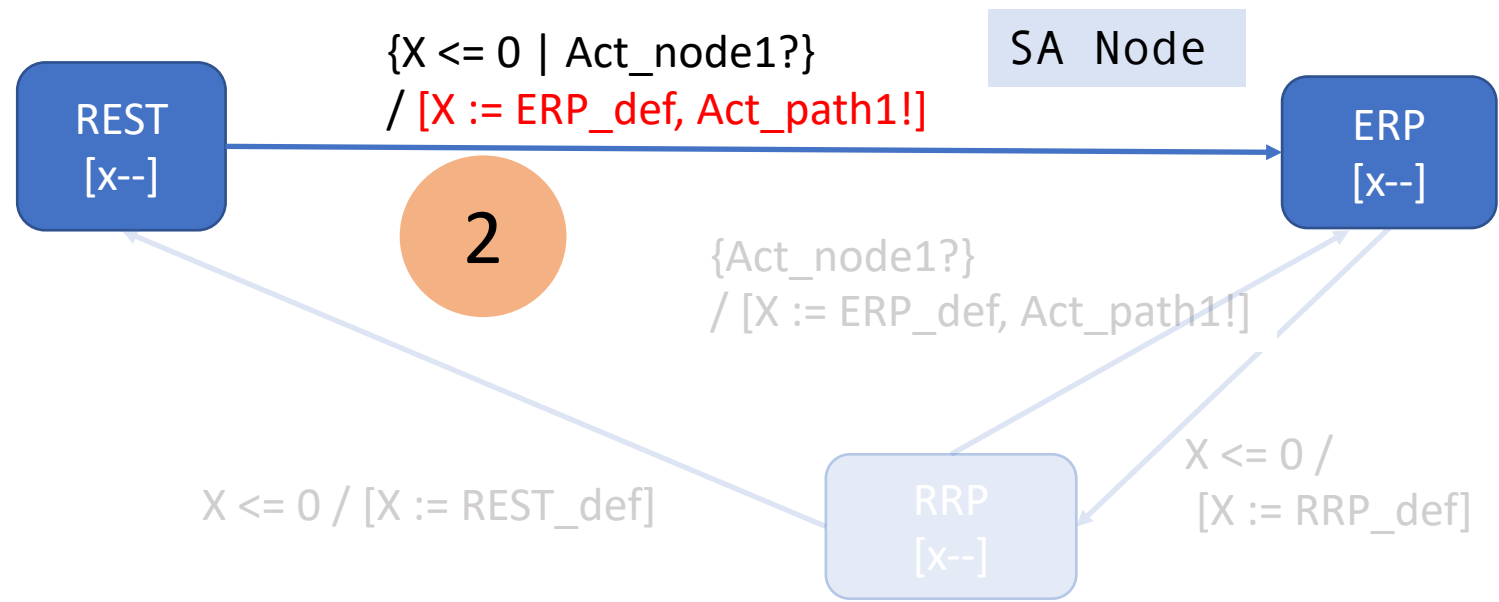
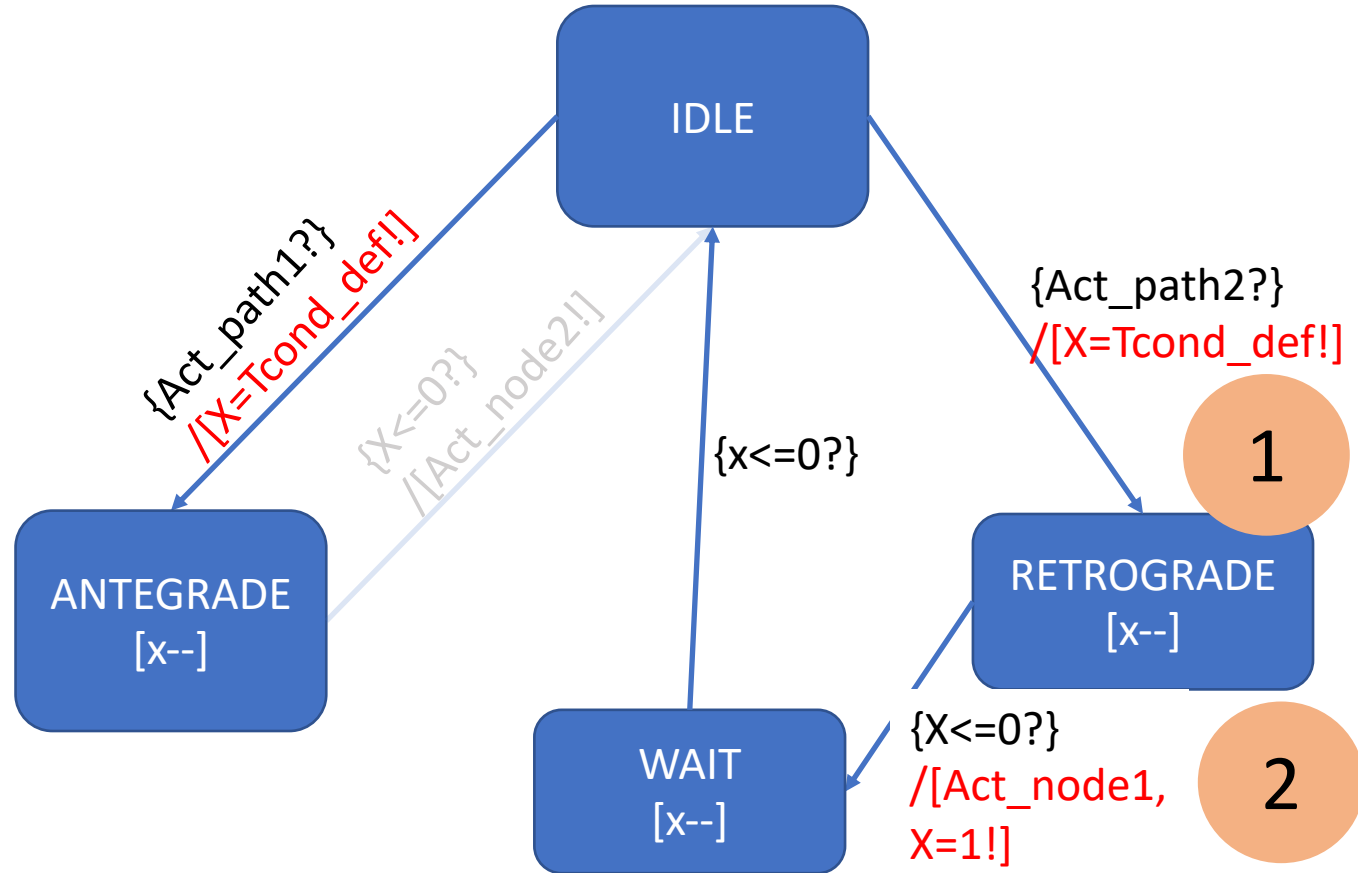


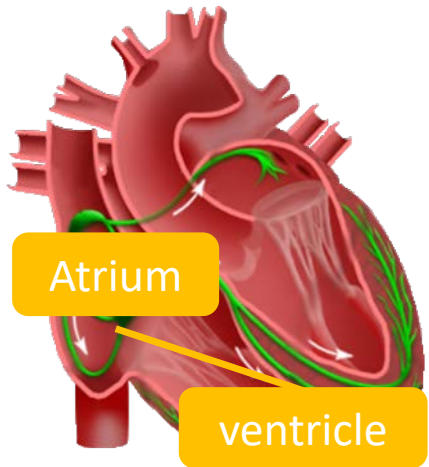
Breaking the Infinite loop



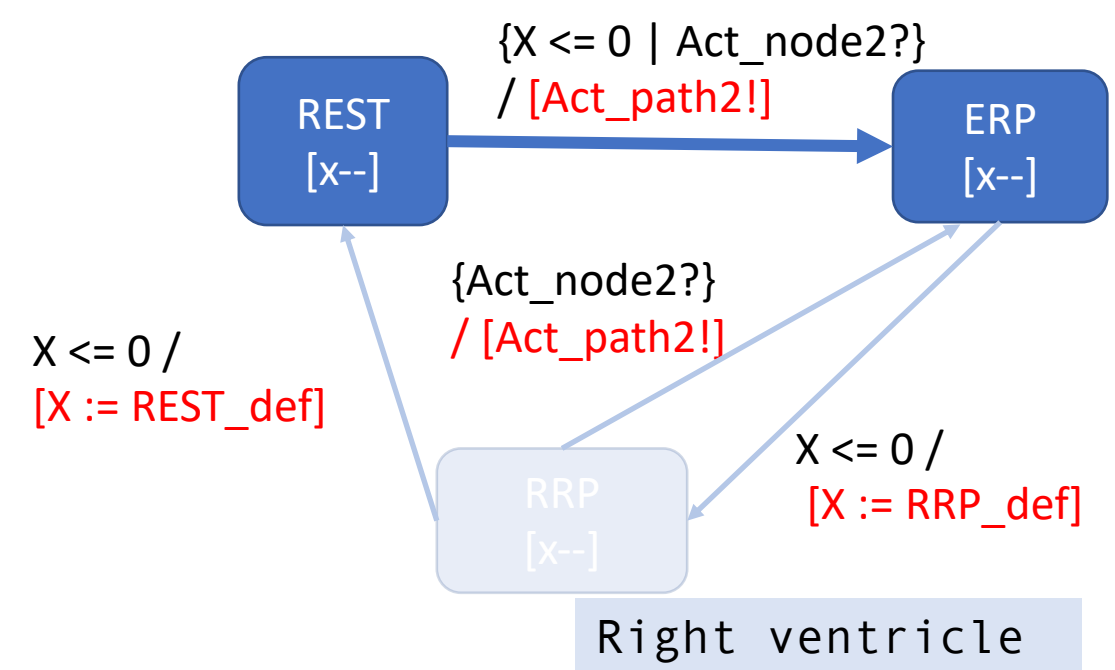
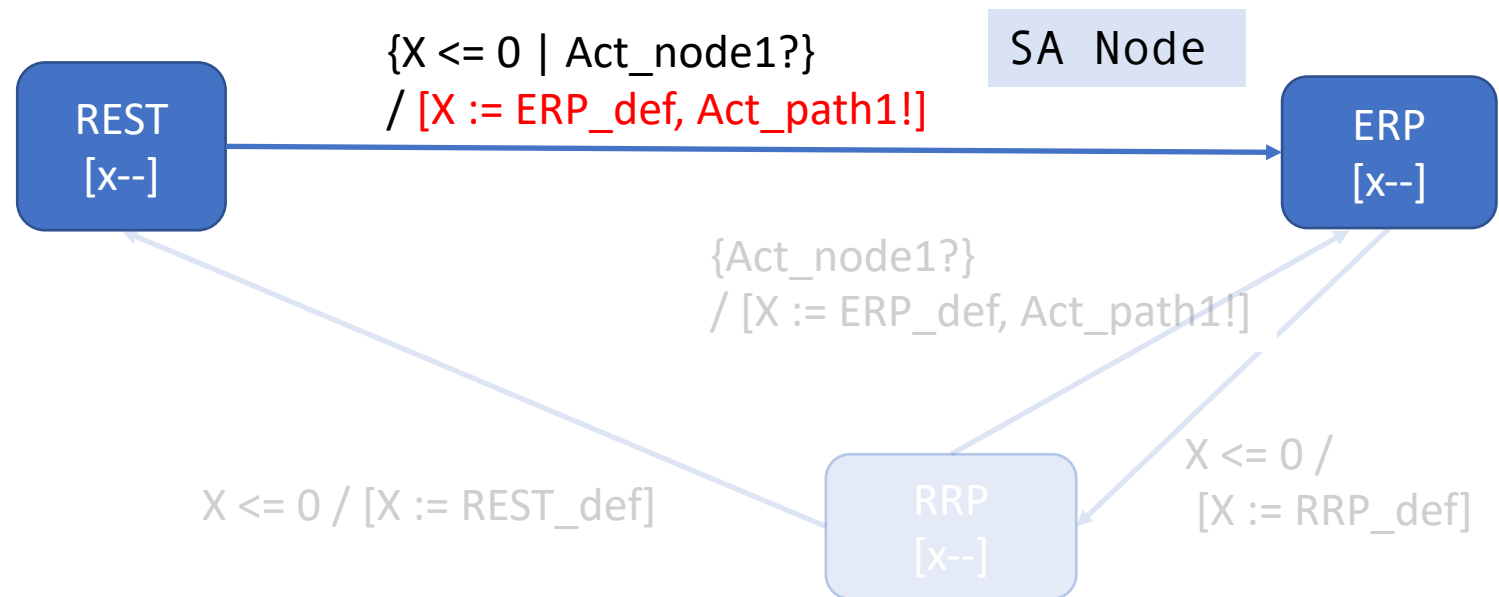
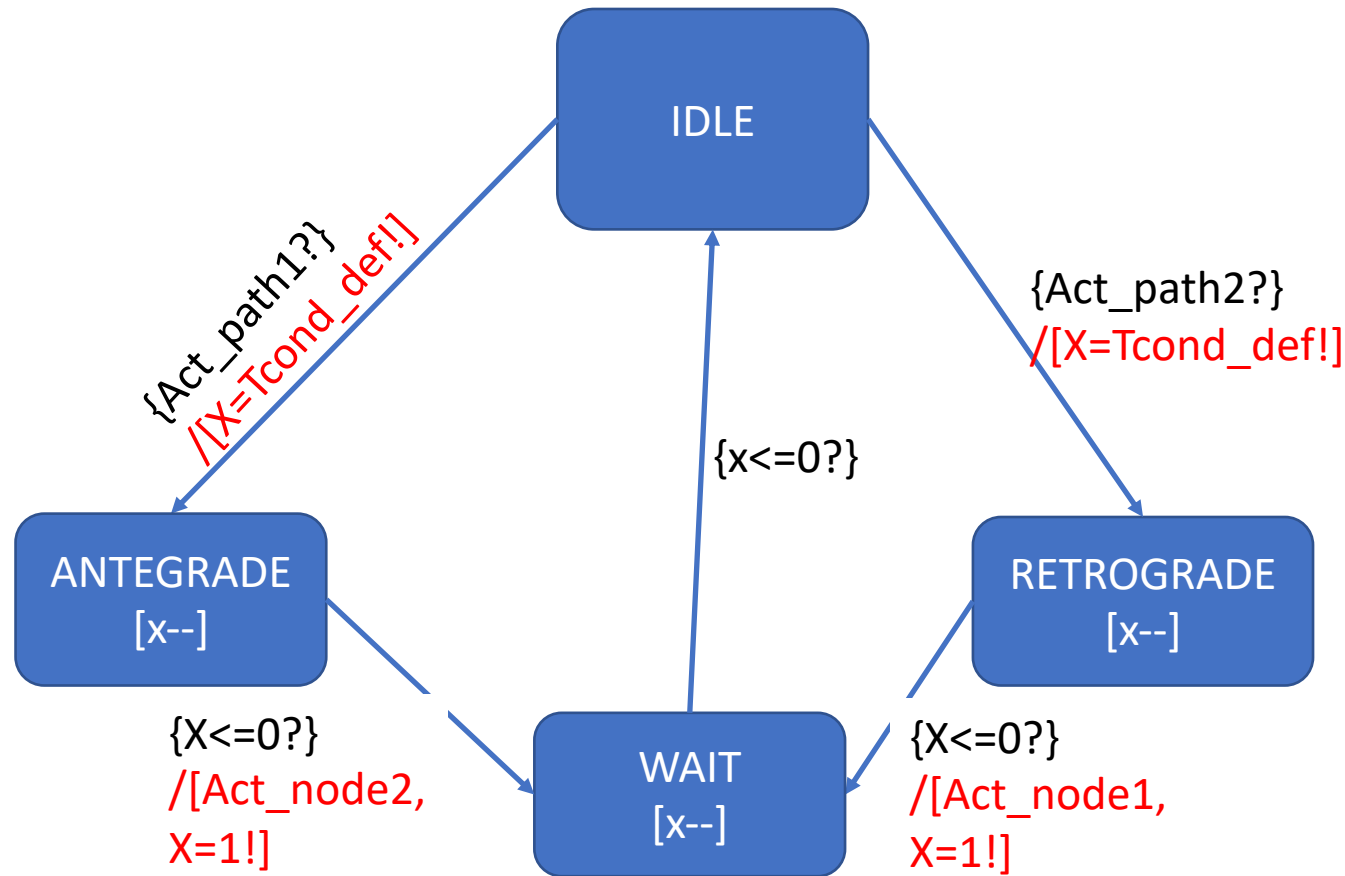


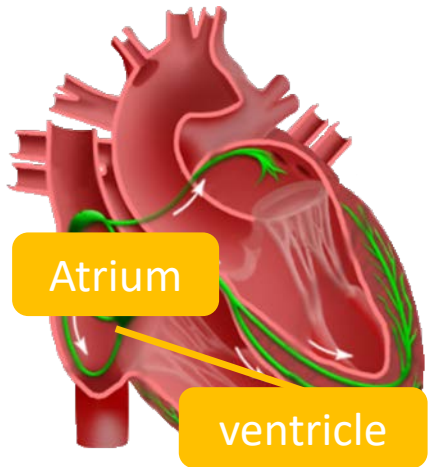
Breaking the Infinite loop



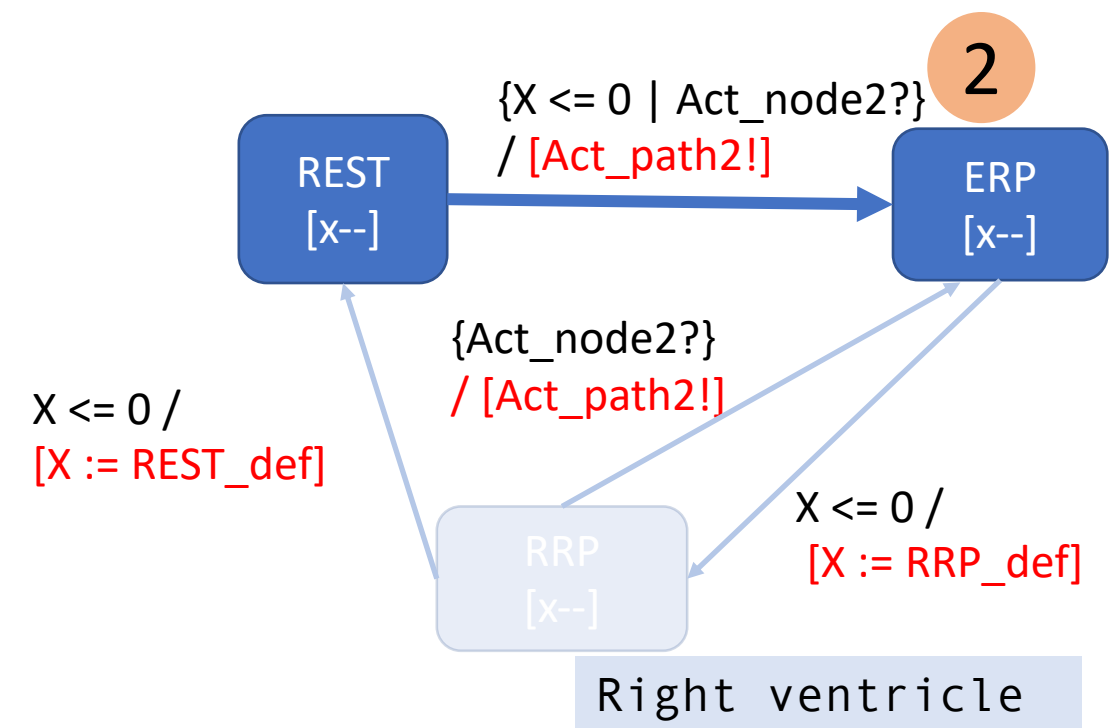
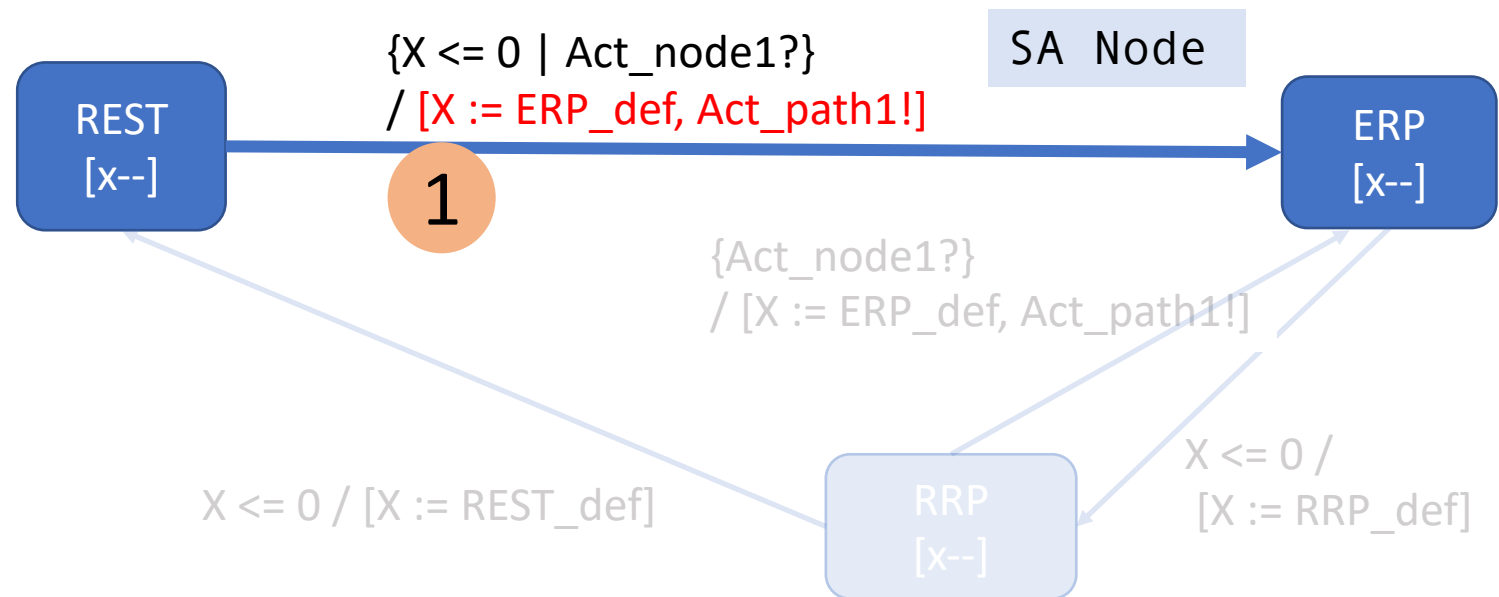
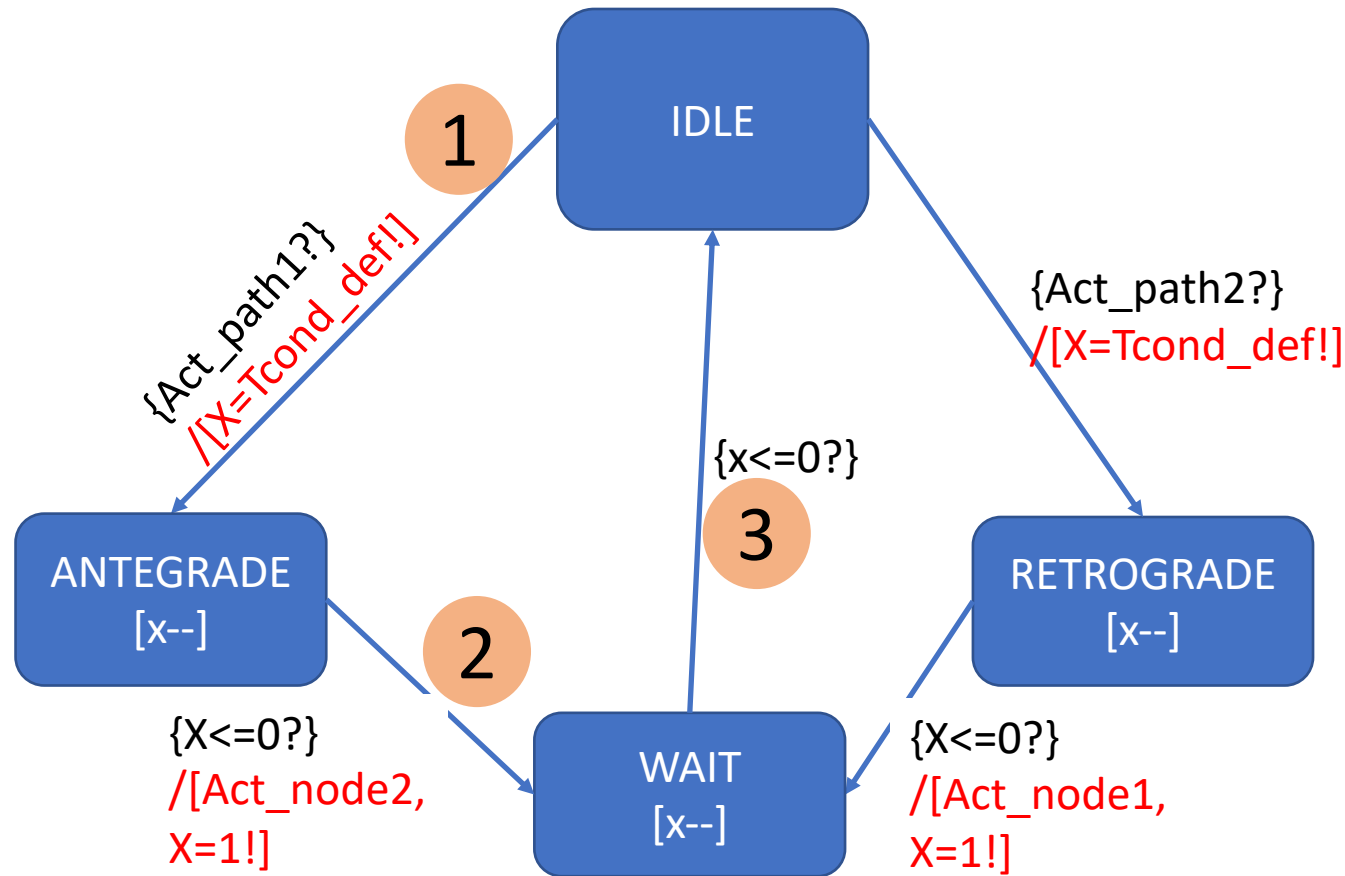


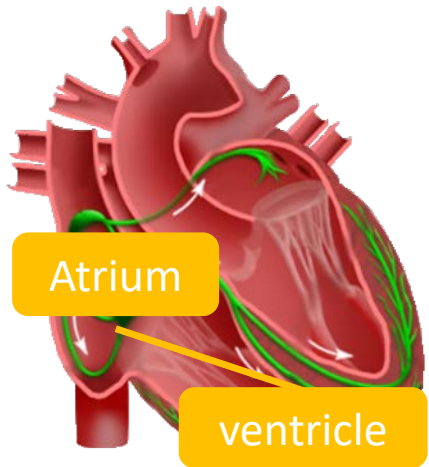
Breaking the Infinite loop



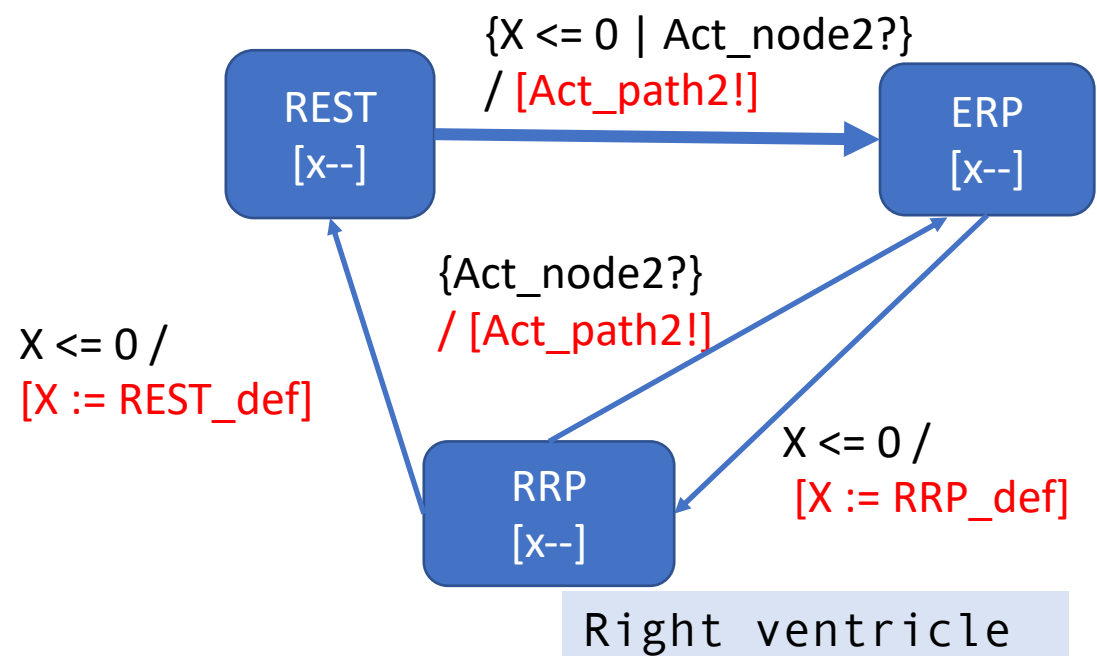
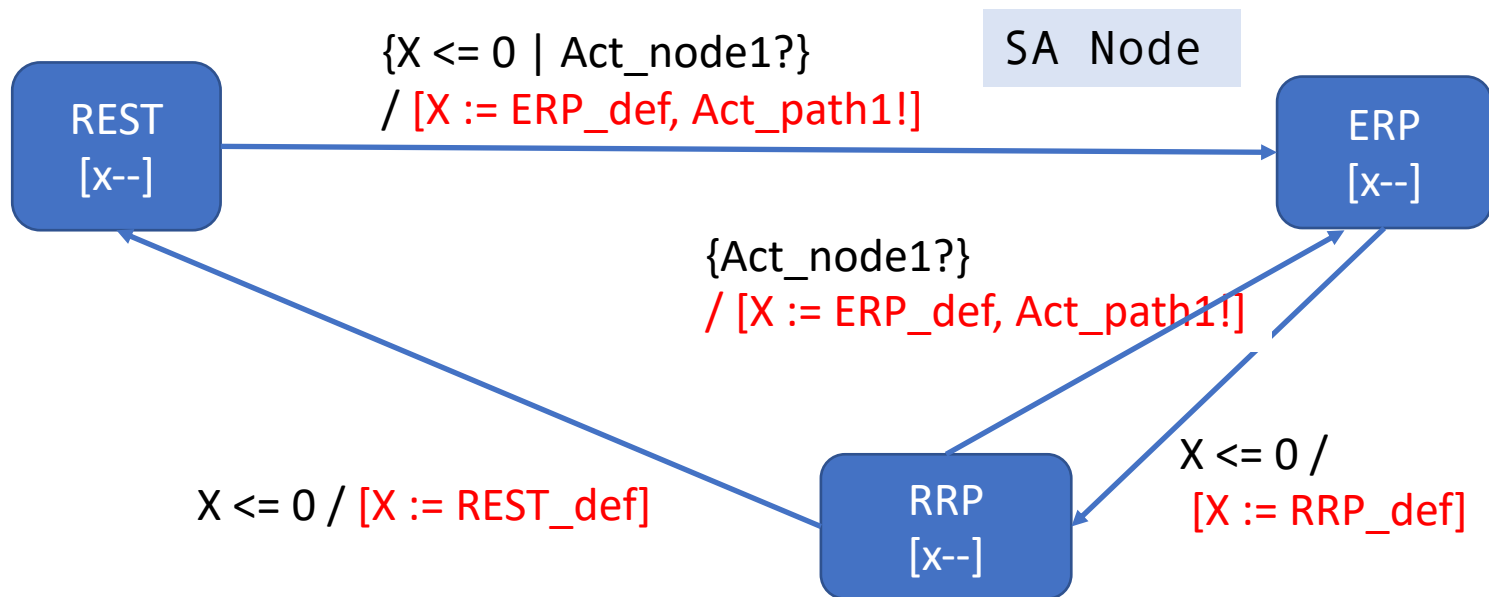
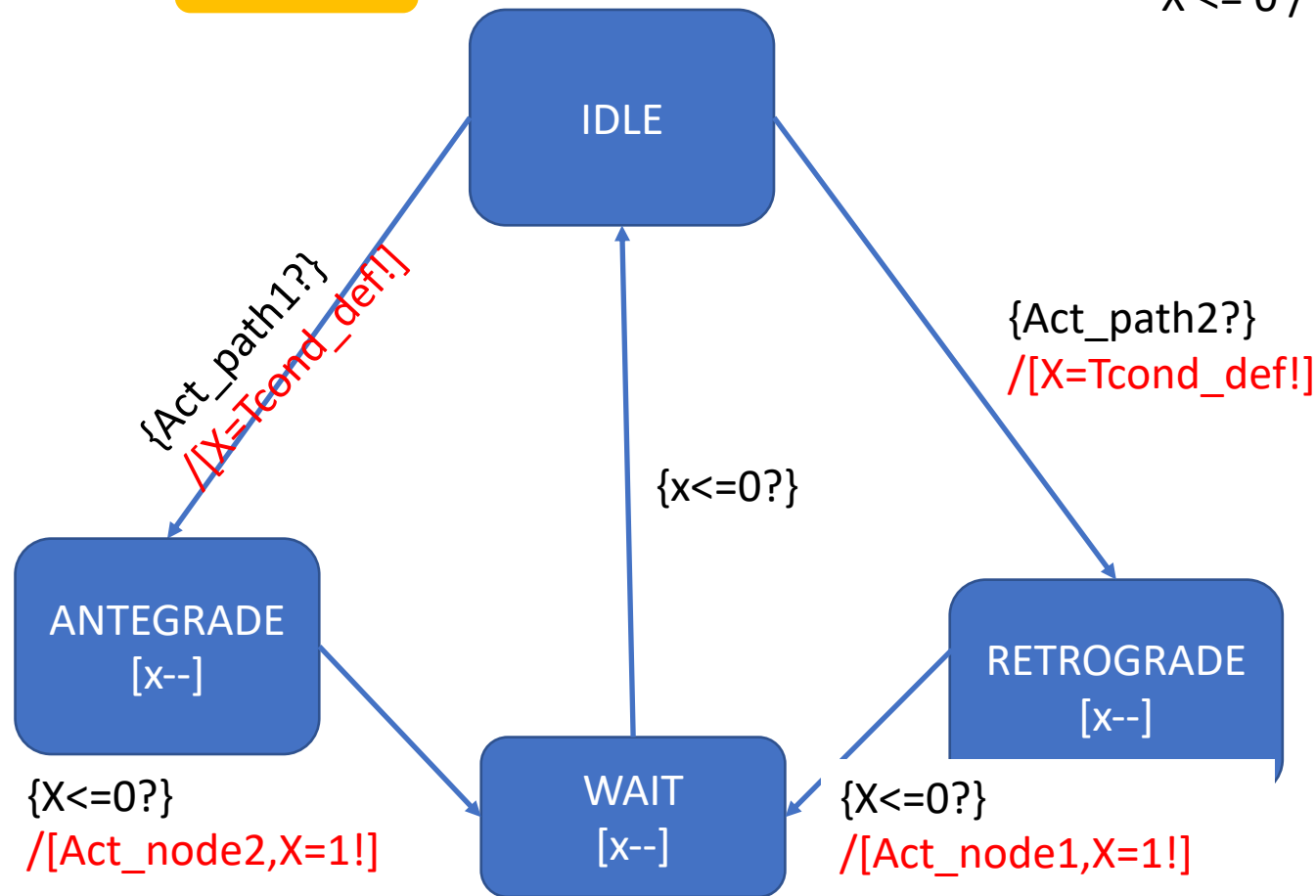


Breaking the Infinite loop

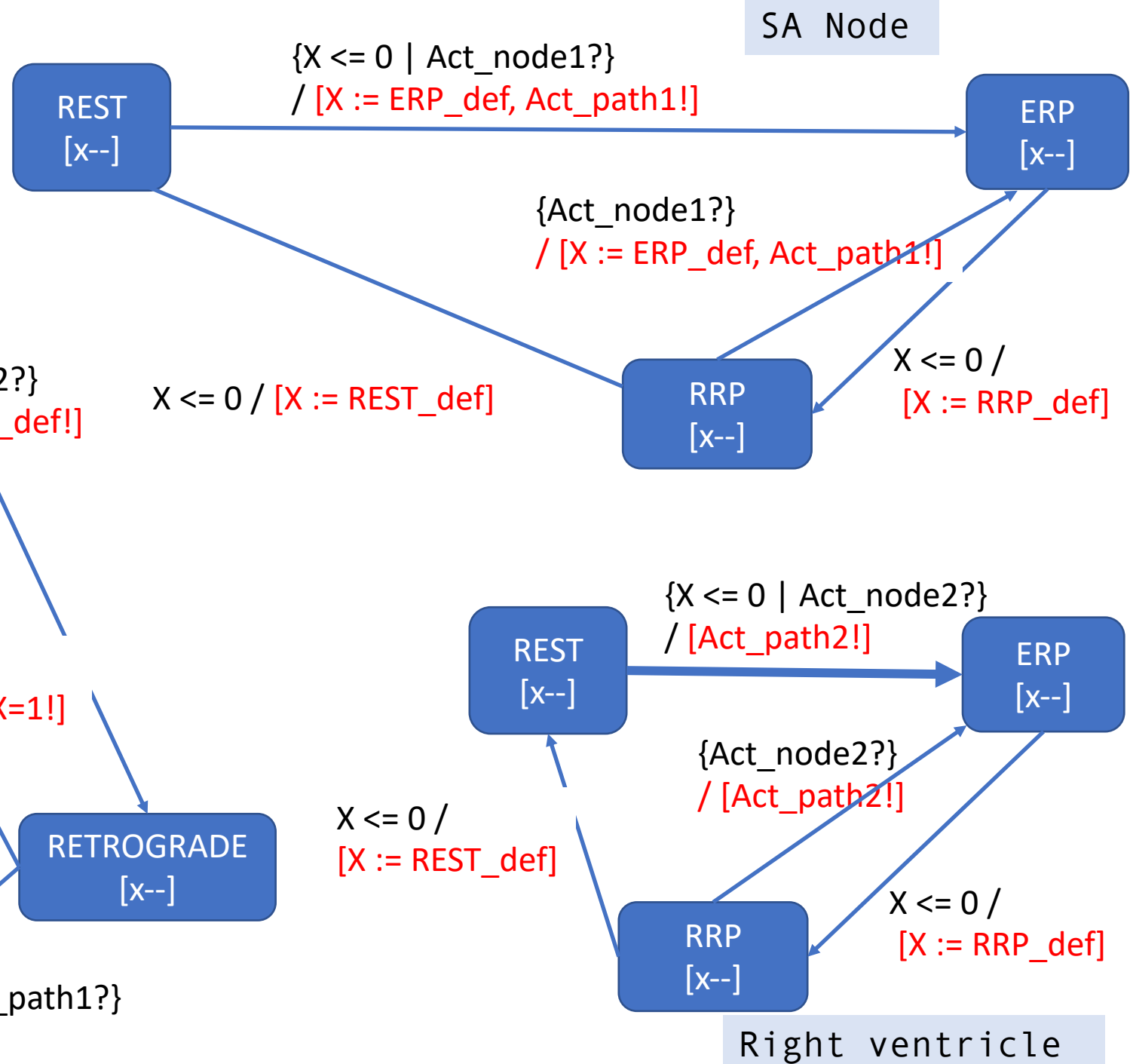
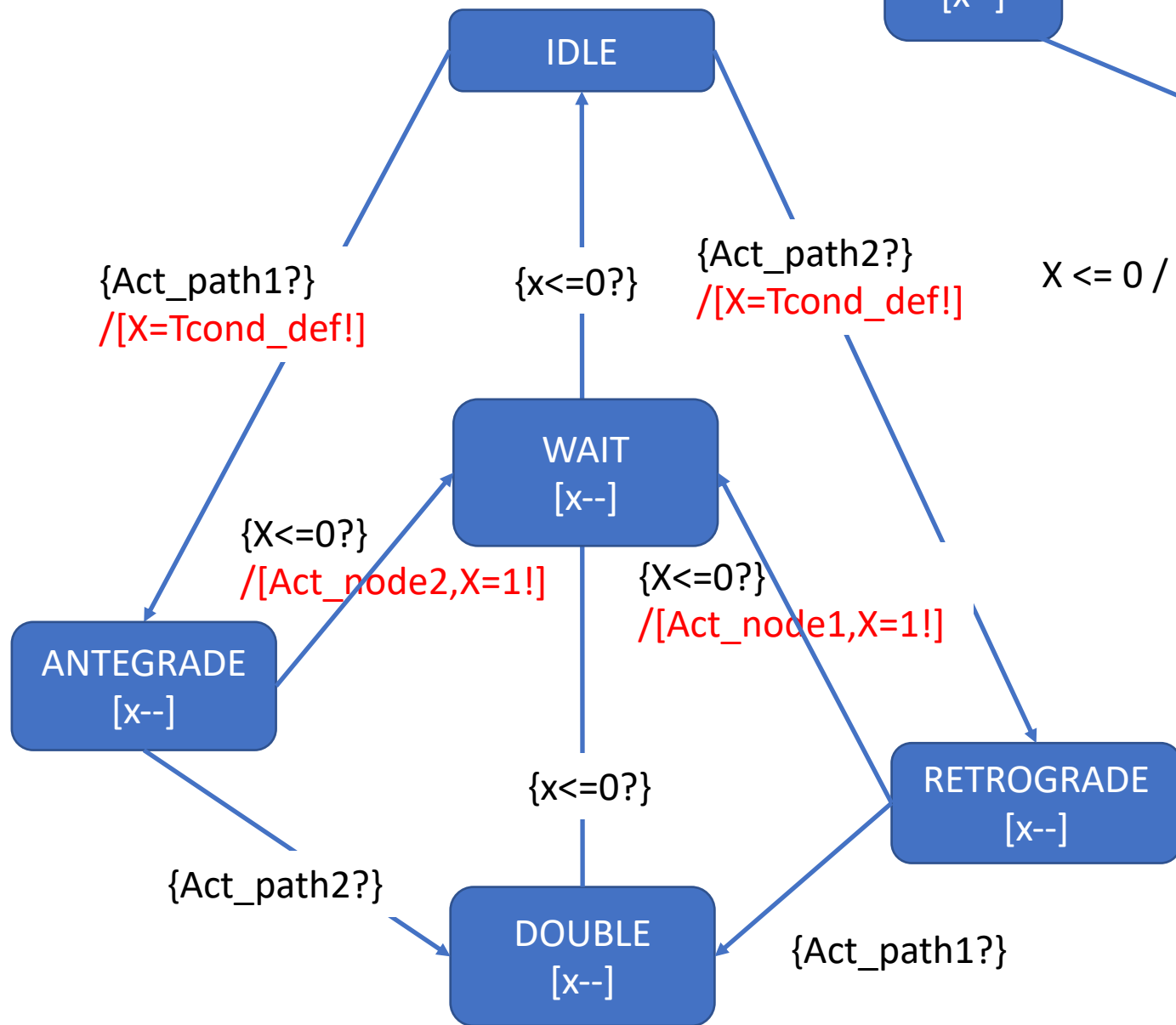




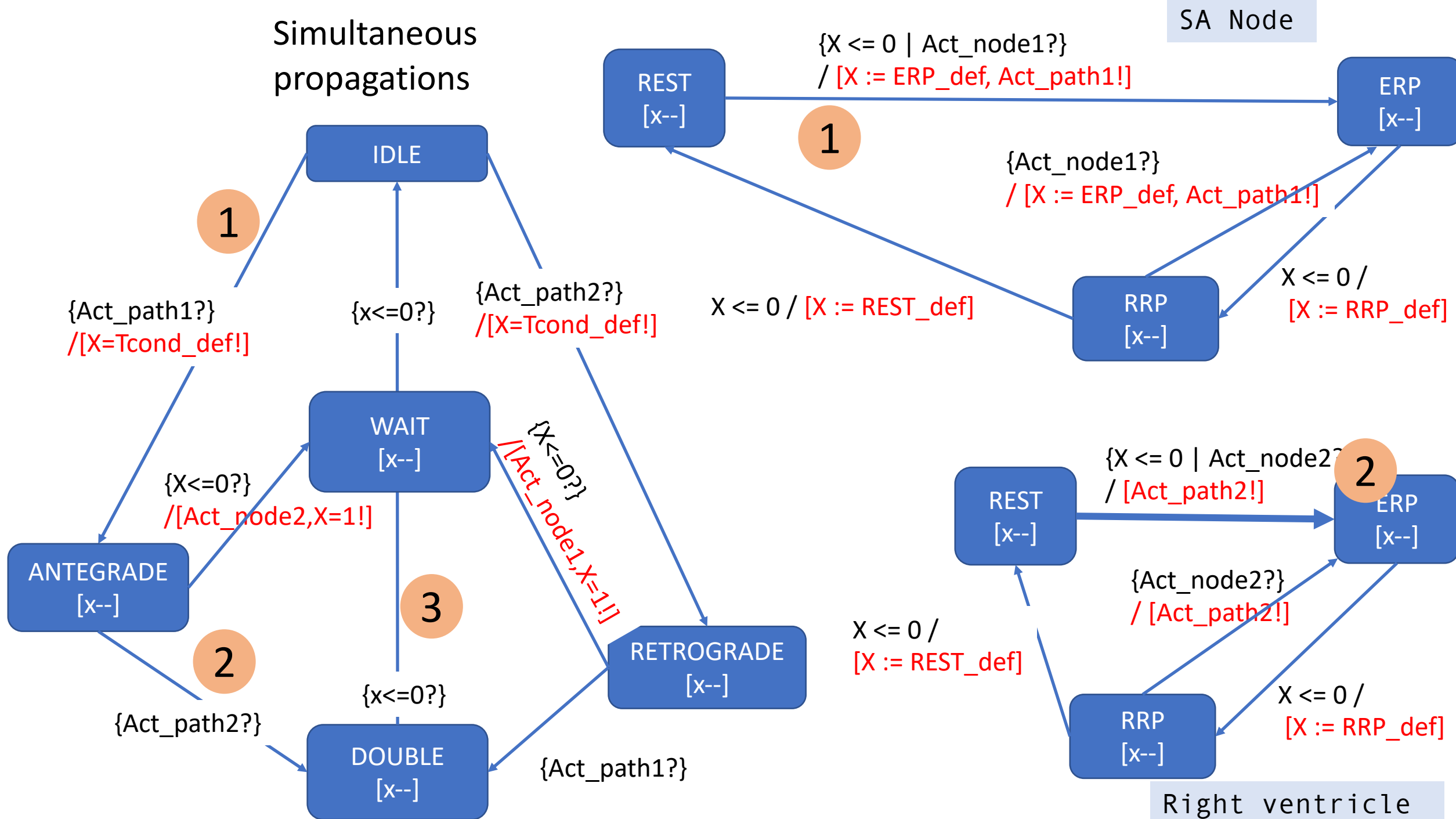
Simultaneous propagations



Simultaneous propagations

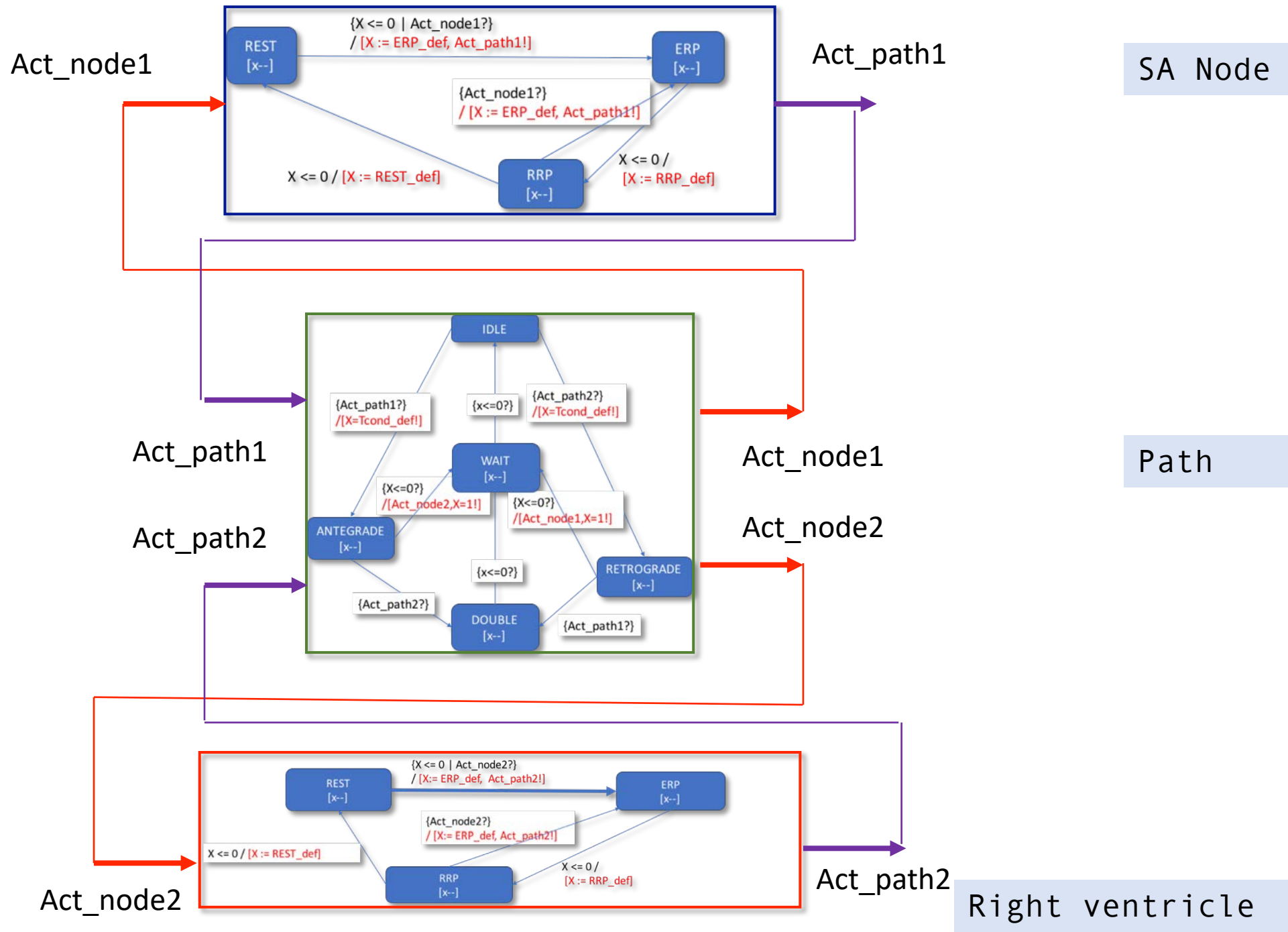


Simultaneous propagations



Messages

N
P
N



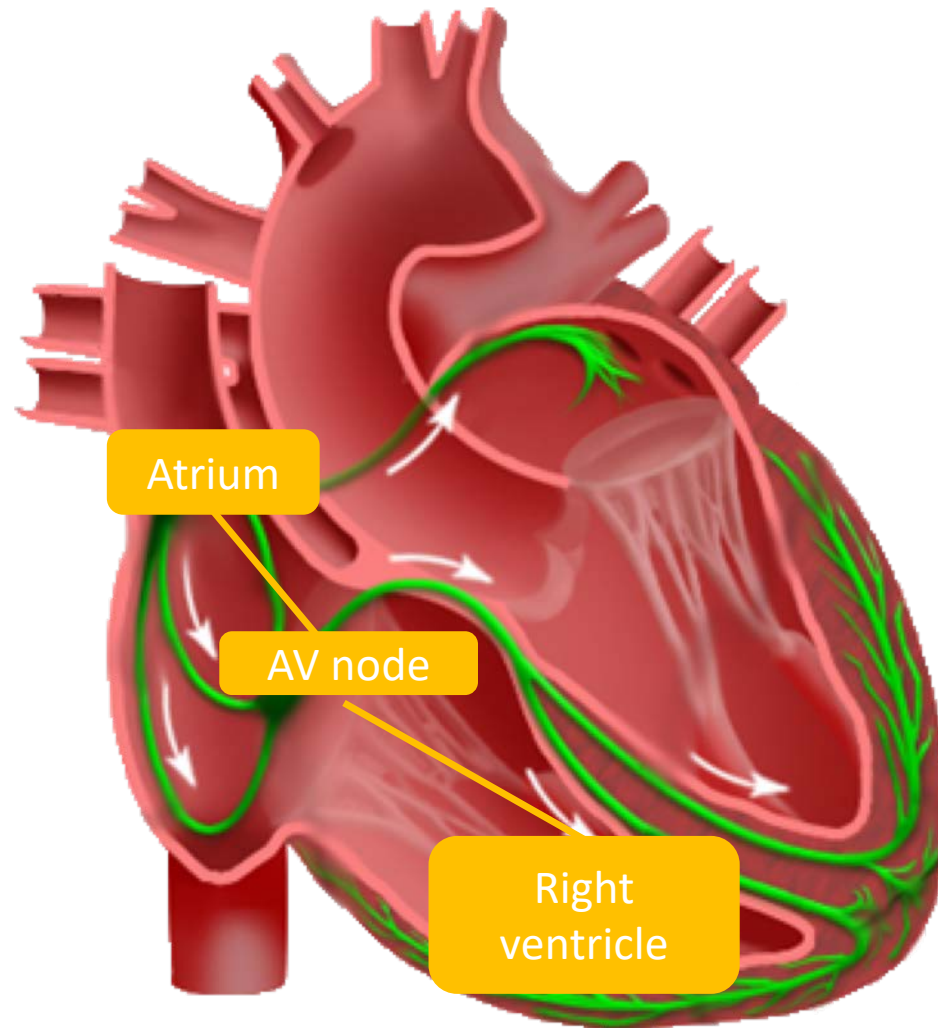
SA Node

Path

Right ventricle

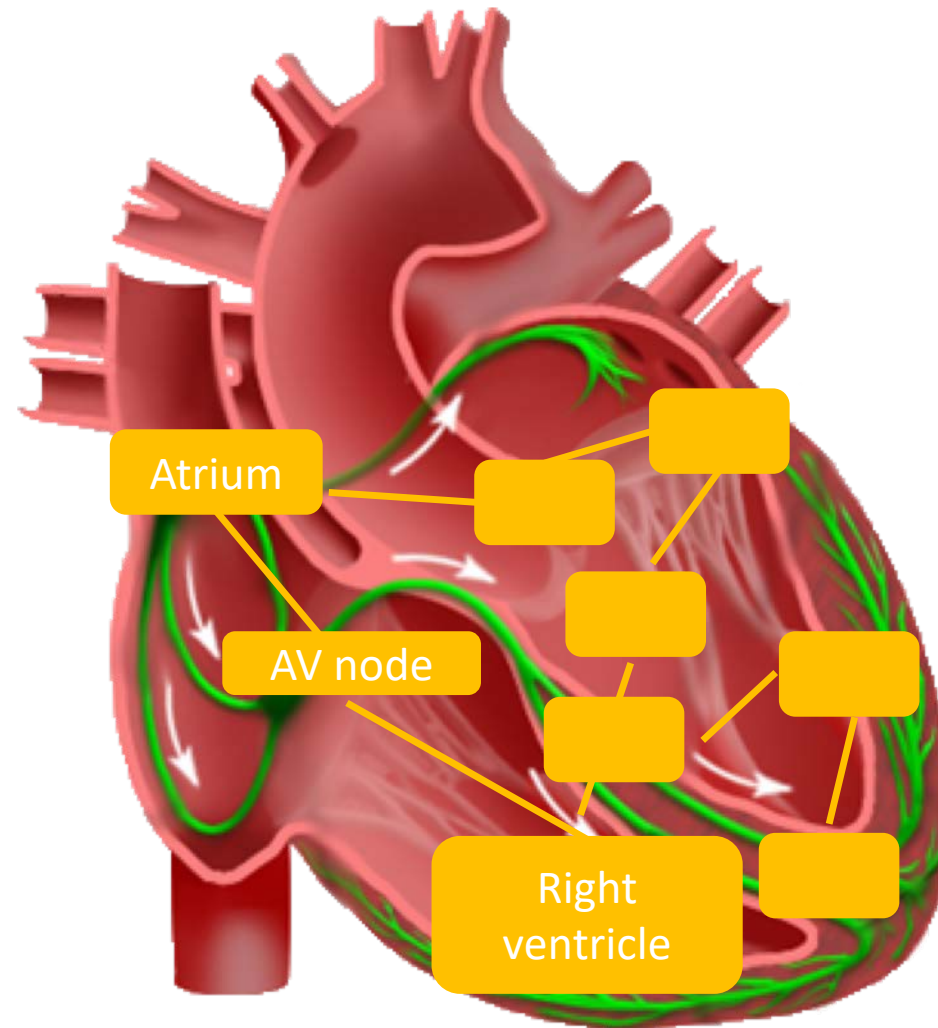
NPNPN

Of course, can add more tissue (more nodes) for a finer granularity model.



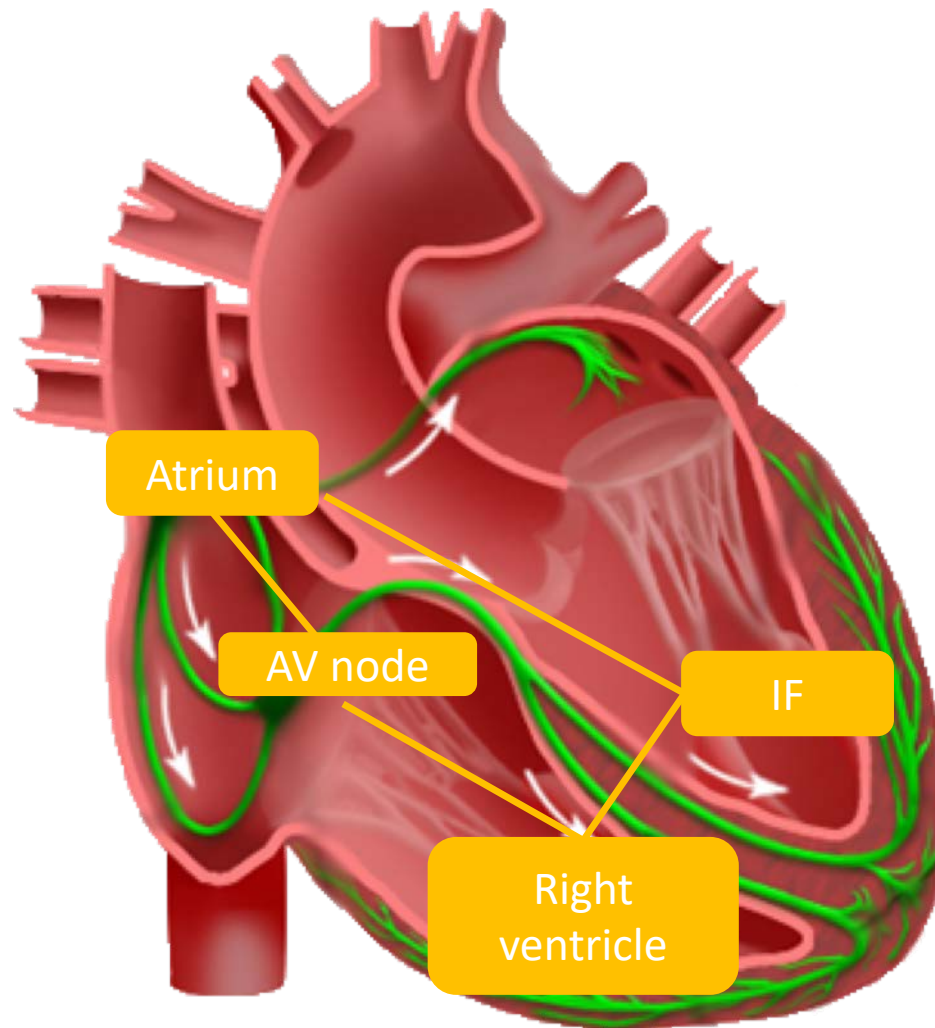
NPNPN

Scalability and refinement:
Model refinement means to make the model more accurate, more faithful to reality...It is important to create a model that is refinable so when the computational resources are available, it is easy to create a more refined model and get more accurate results.



Irritable focus

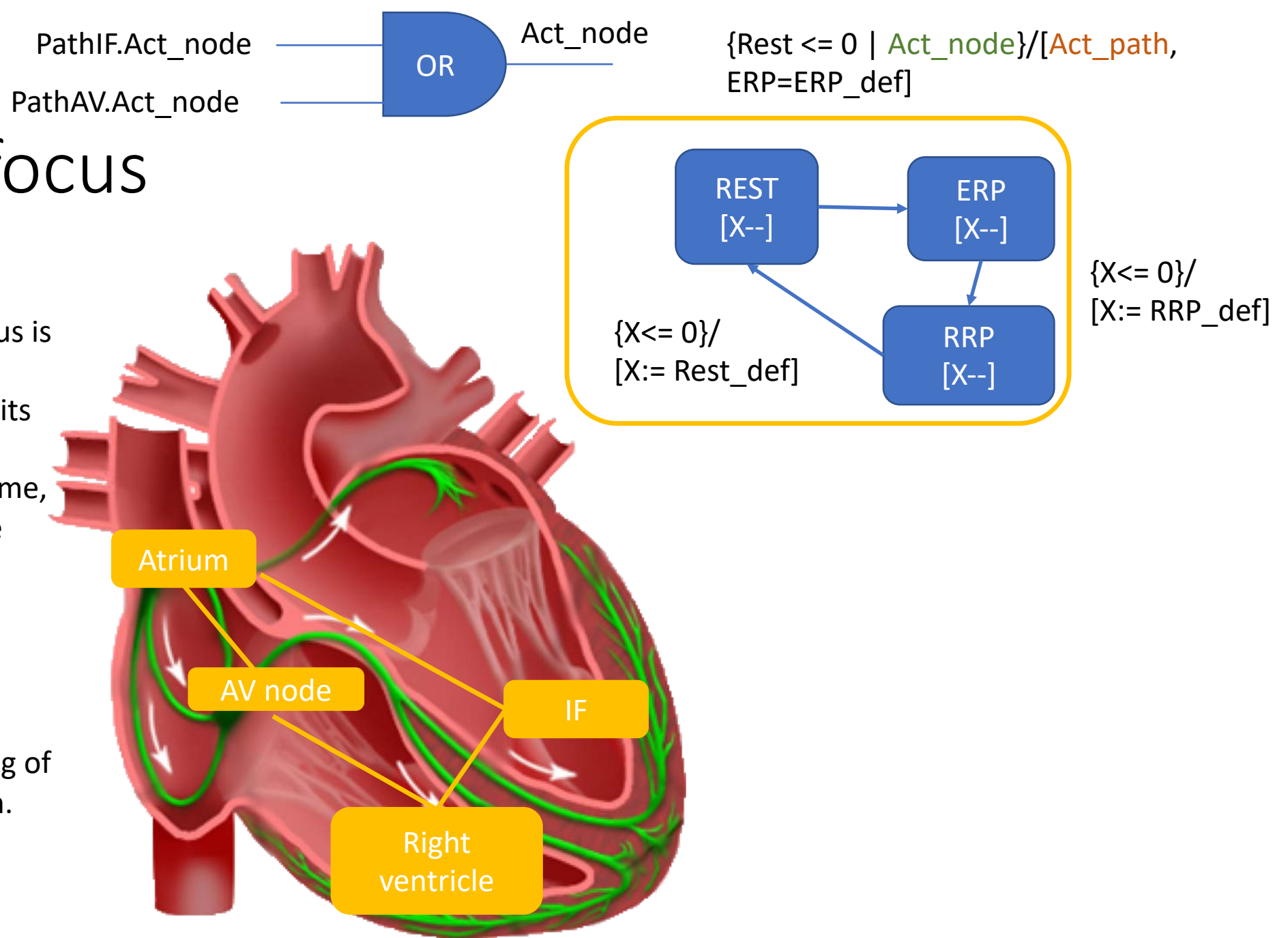
An irritable focus is a piece of tissue that starts depolarizing on its own for a brief (or extended) period of time, sometimes driving the rhythm or otherwise disturbing it.



Irritable focus

Recall: an irritable focus is a piece of tissue that starts depolarizing on its own for a brief (or extended) period of time, sometimes driving the rhythm or otherwise disturbing it.

Note also the modeling of retrograde conduction.

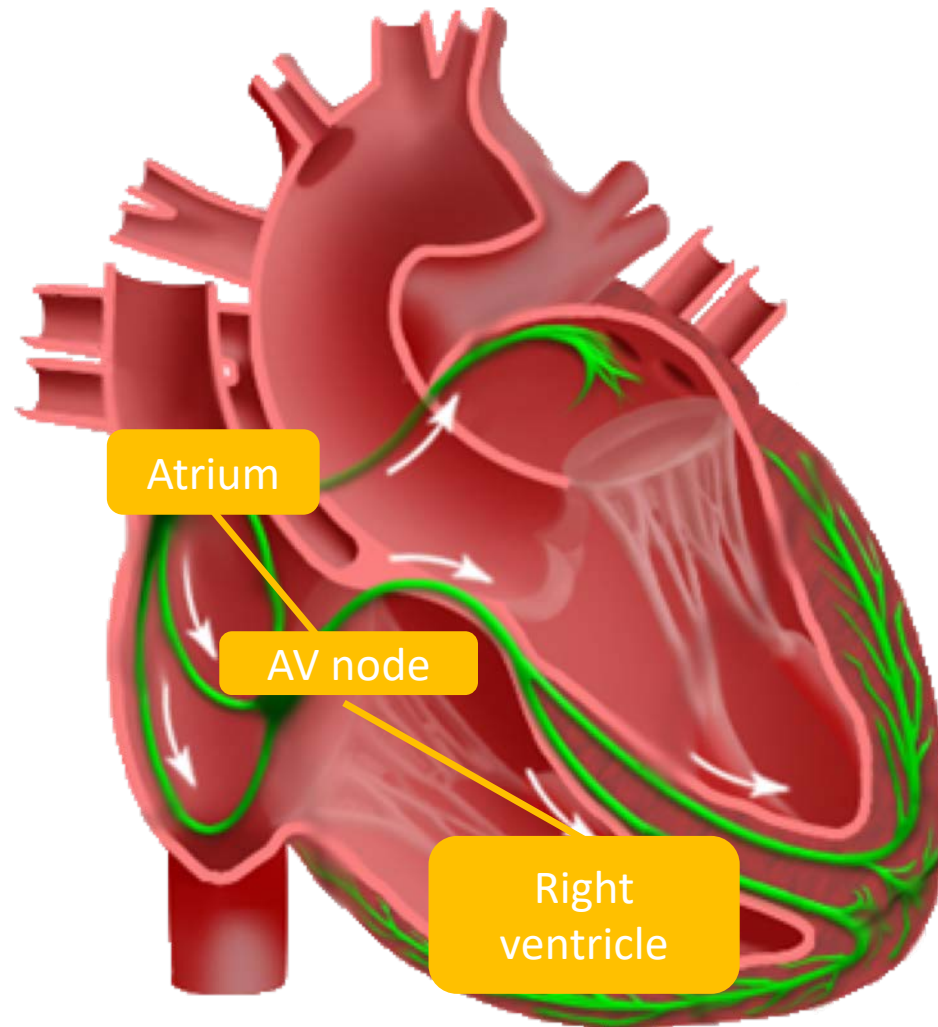


Atrio-Ventricular (AV) Node

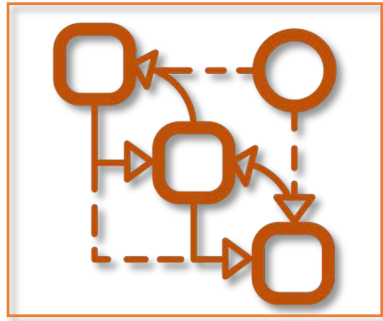
The AV node adds a delay between atria and ventricles. This delay allows the ventricles to fill with blood before they contract to pump that blood out to the body.

It also acts as a rate controller: if atria beat too fast, every few beats will be dropped by the AV node and won't make it to the ventricles. That's because those events fall in the AV's ERP.

The ERP of the AV node *increases* as the excitations come closer together.



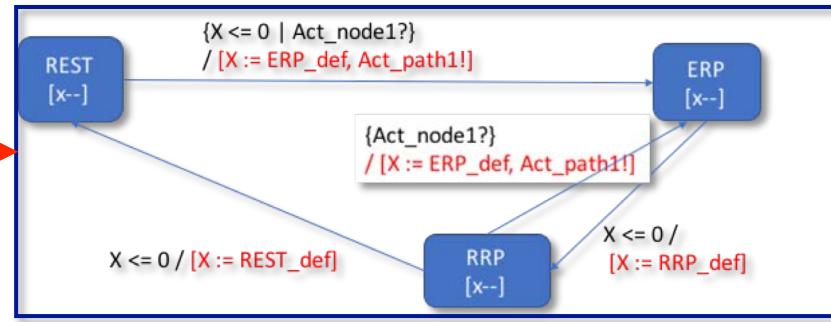
ASense
VSense



Pacemaker

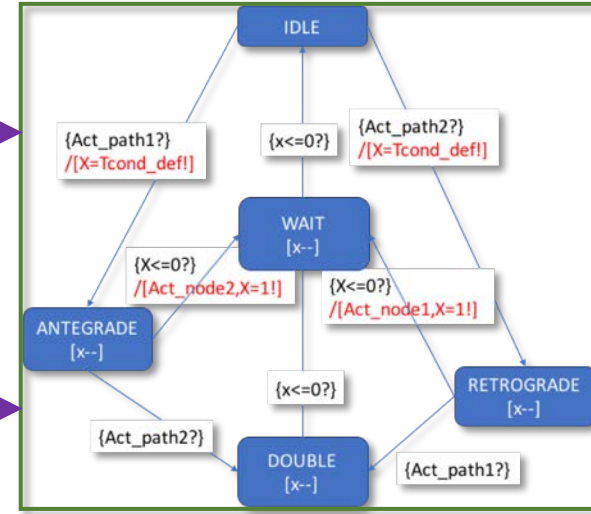
APace
VPace

Act_node1



Act_path1

Act_path1

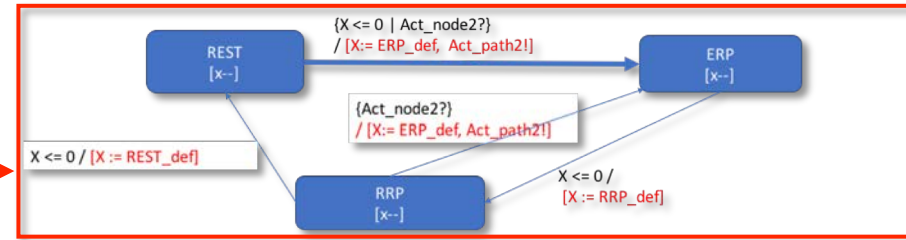


Act_path2

Act_node1

Act_node2

Act_node2



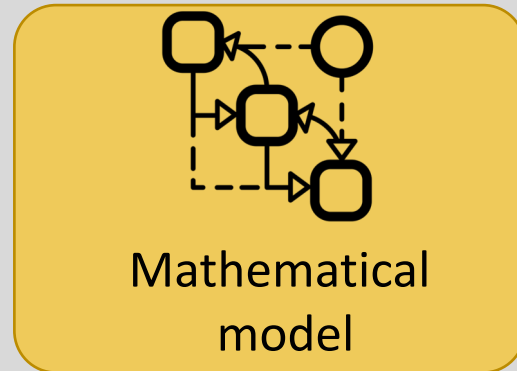
Act_path2

Heart as a network of timed automata: So What?

- A timed automaton is a mathematical object with clear *semantics*: we understand how it behaves and can analyze that behavior.
- A mathematical model allows us to do a more rigorous checking of correctness than we could without one. *We can prove things about its behavior.*

Model Checking

Does



satisfy

$F p \wedge q$

?

Formal notation

Linear Temporal Logic

Transition Systems – Mathematical understanding.
Linear Temporal Logic – Expressing requirements formally.
Model checking
UPPAAL