Model Checking Cancer Automata

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Outline

- What is **cancer**?
- How to model it?
- How to **extend/improve** the model?
- What are the **verification results**?
- **Conclusion** and **possible future works**


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BOTSWANA
MADAGASCAR
Java

PLANNING

ANALYZE

DESIGN

SOFTWARE ENGINEERING

VALIDATION

AND VERIFICATION

. . . . .

Cancer as a system?

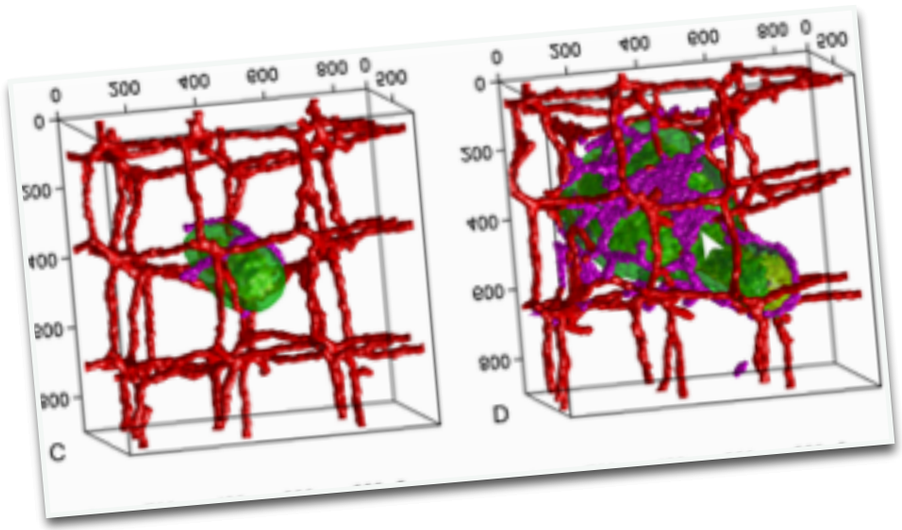
Cancer

is a progressive disease

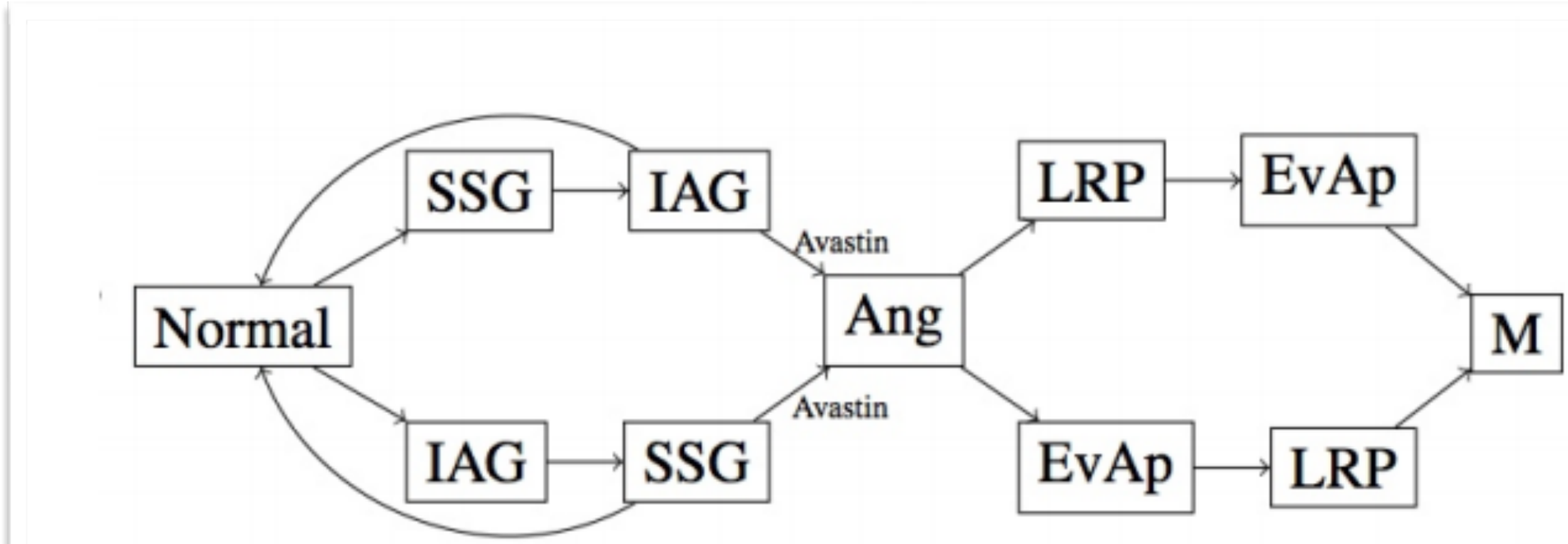
is a disease of all ages

one of the most common cause of death in the US and Europe

Cancer Models



- ***Mathematical model***
- ***3D Simulation***

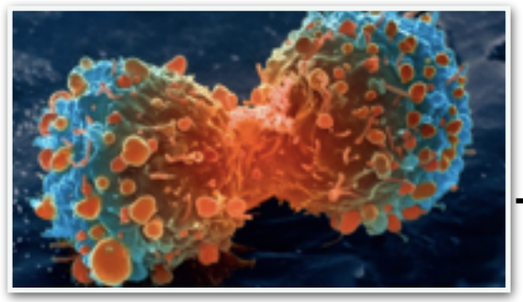


Cancer Hybrid automata


Evading apoptosis
Limitless replicative potential
Sustained angiogenesis
Tissue invasion & metastasis
Hallmarks of Cancer
Evading immune surveillance
DNA damage stress
Oxidative stress
Mitotic stress
O2
ATP

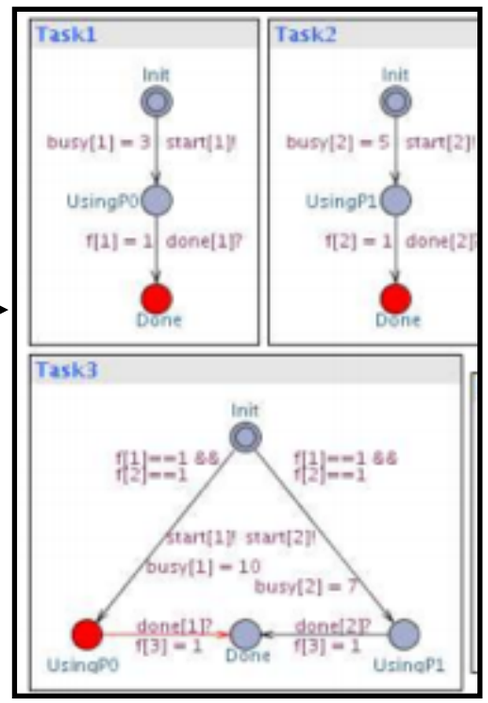
Cancer Models

System



Cancer

Automata



Specification

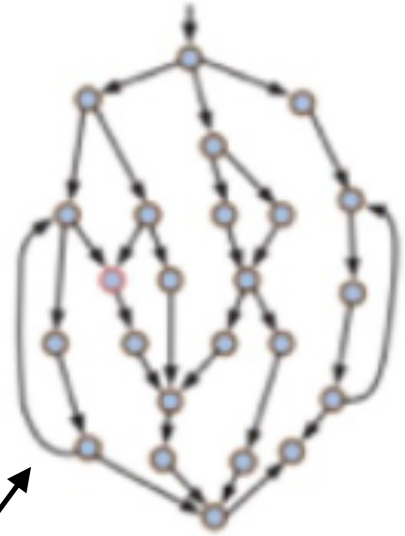
E[] !c.Stage4

TCTL & PTCL (UPPAAL Query Language

System requirements

progression of cancer

Model checker



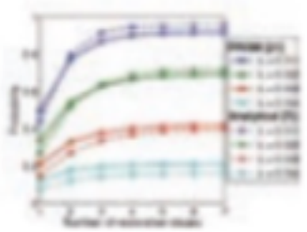
UPPAAL

Promela Spin

Qualitative/ Quantitive properties

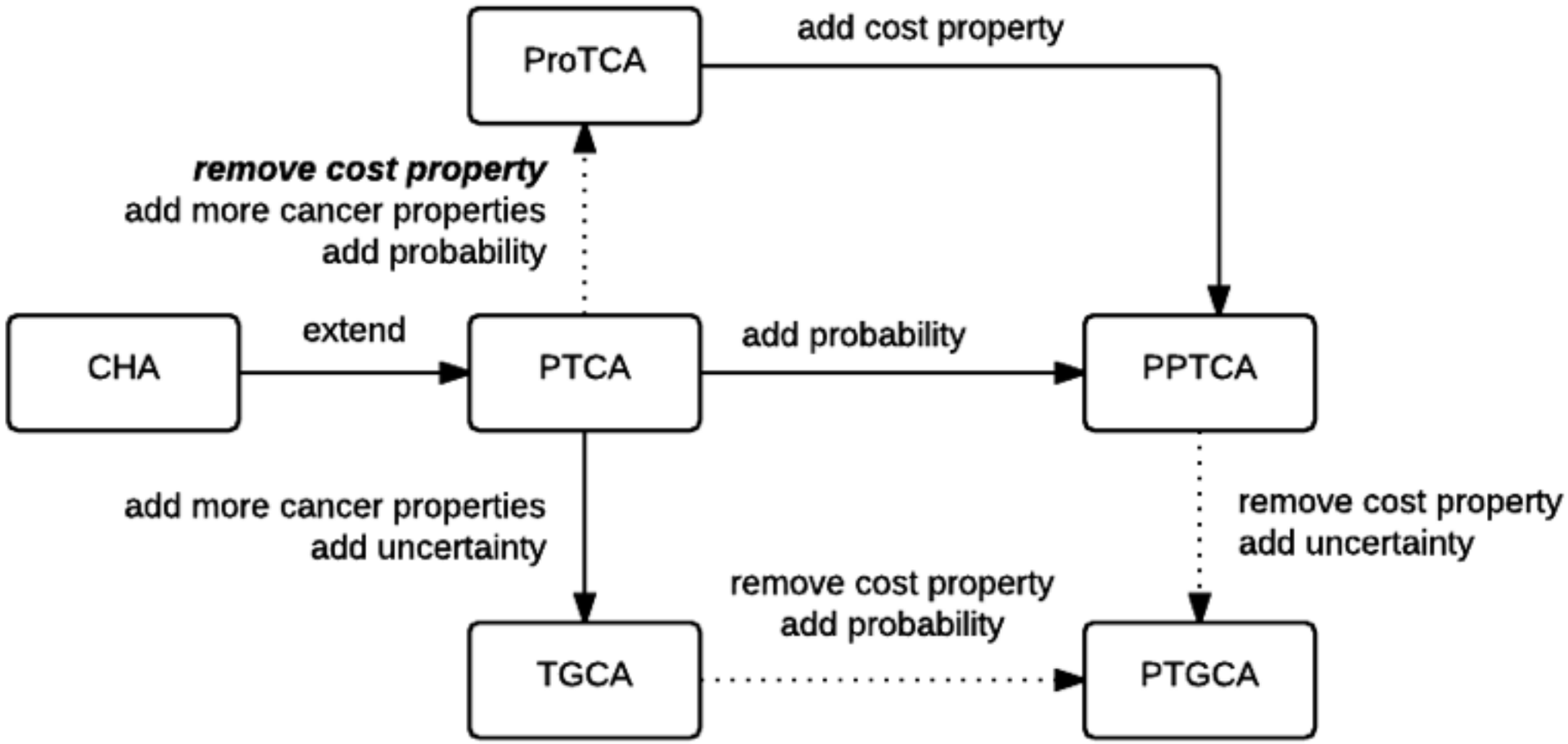
Verification results

Numerical results



Diagnostics

Extending the model



Priced Timed Cancer Automata (PTCA)

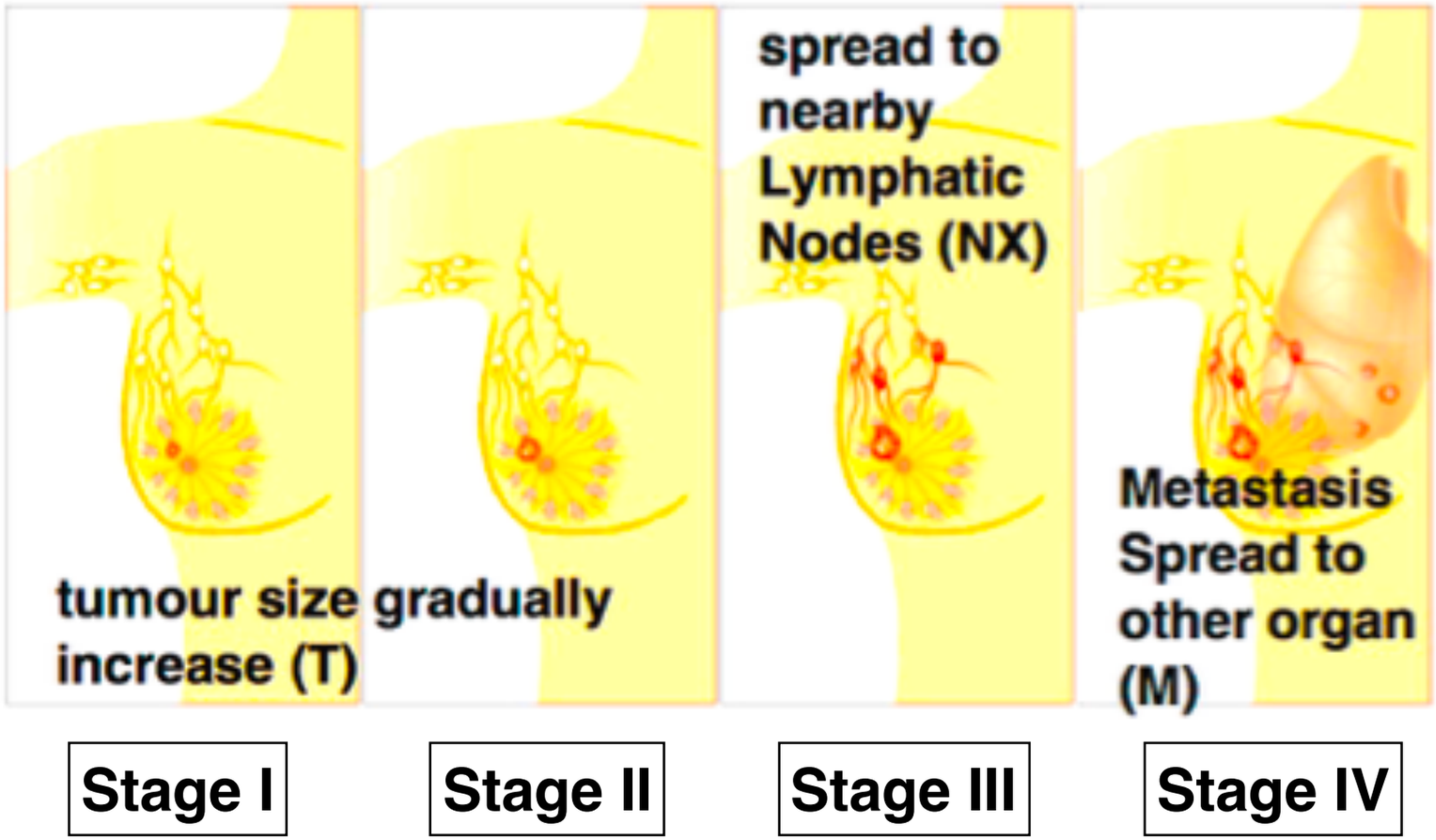
Probabilistic Timed Cancer Automata (ProTCA)

Timed Game Cancer Automata (TGCA)

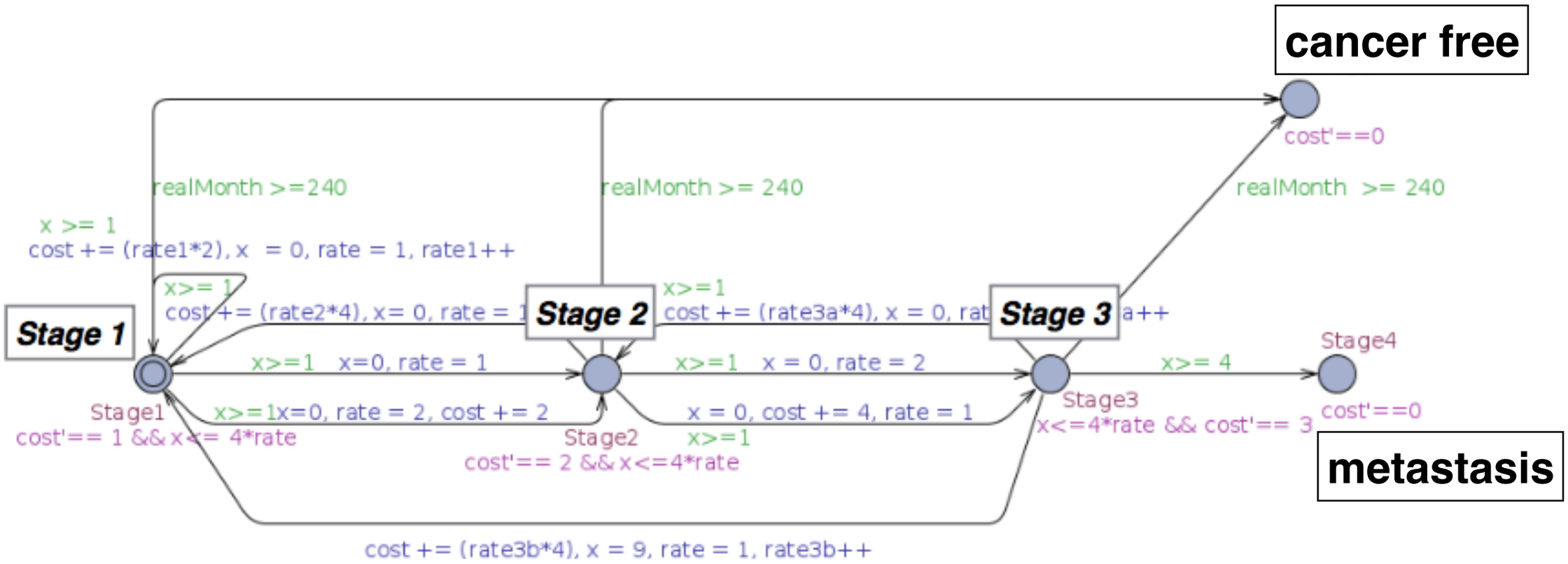
Probabilistic Timed Game Cancer Automata (PTGCA)

TMN Staging

- Tumour size
- Affected Lymphatic Nodes
- Metastasis



Priced Timed Cancer Automata (PTCA)

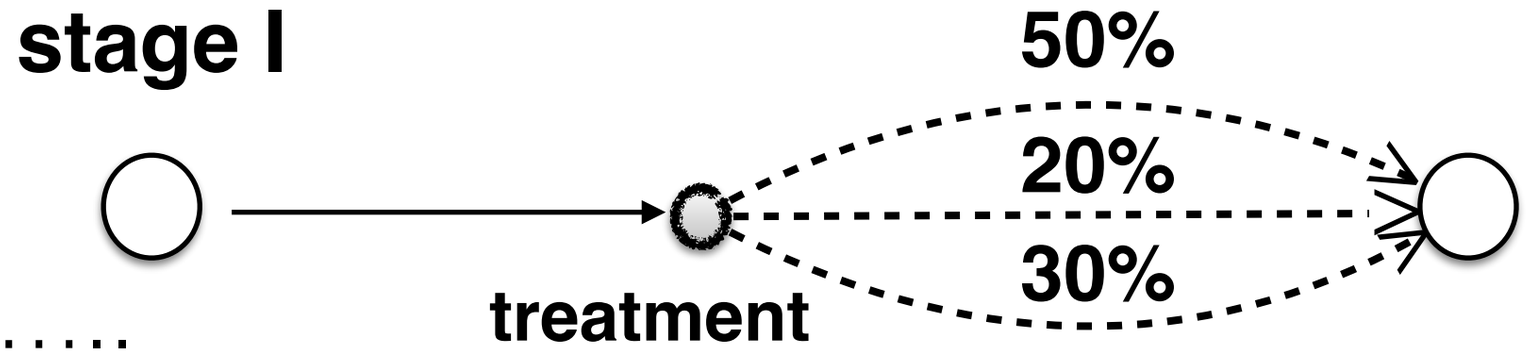


Property specifications

E<> canFree :

there is exists a path where eventually cancer free condition is reached

Probabilistic Timed Cancer Automata (ProTCA)



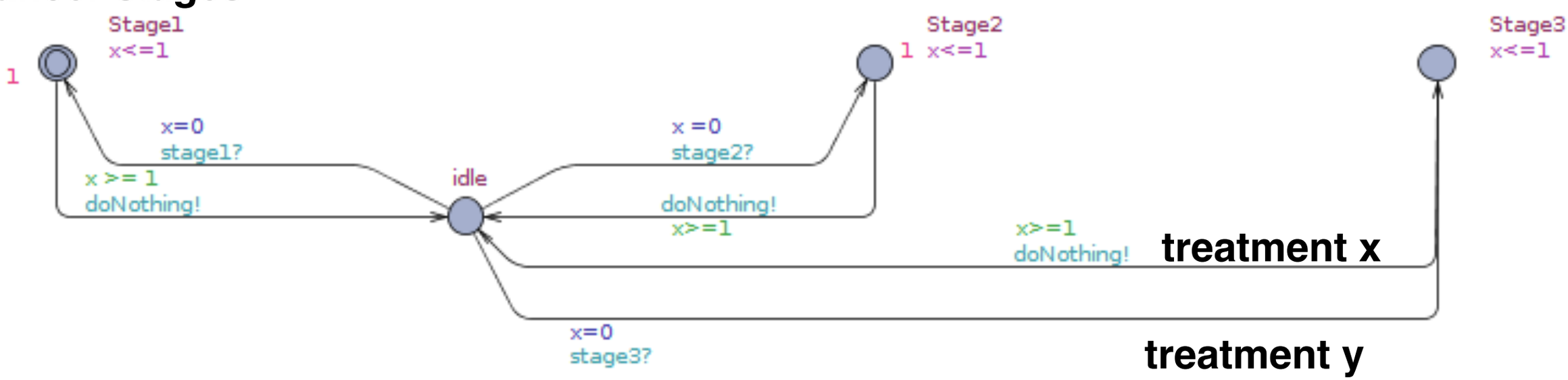
Measuring **Prognosis rate/ Therapy** success rate by using **strategy automata**

Cormobidities

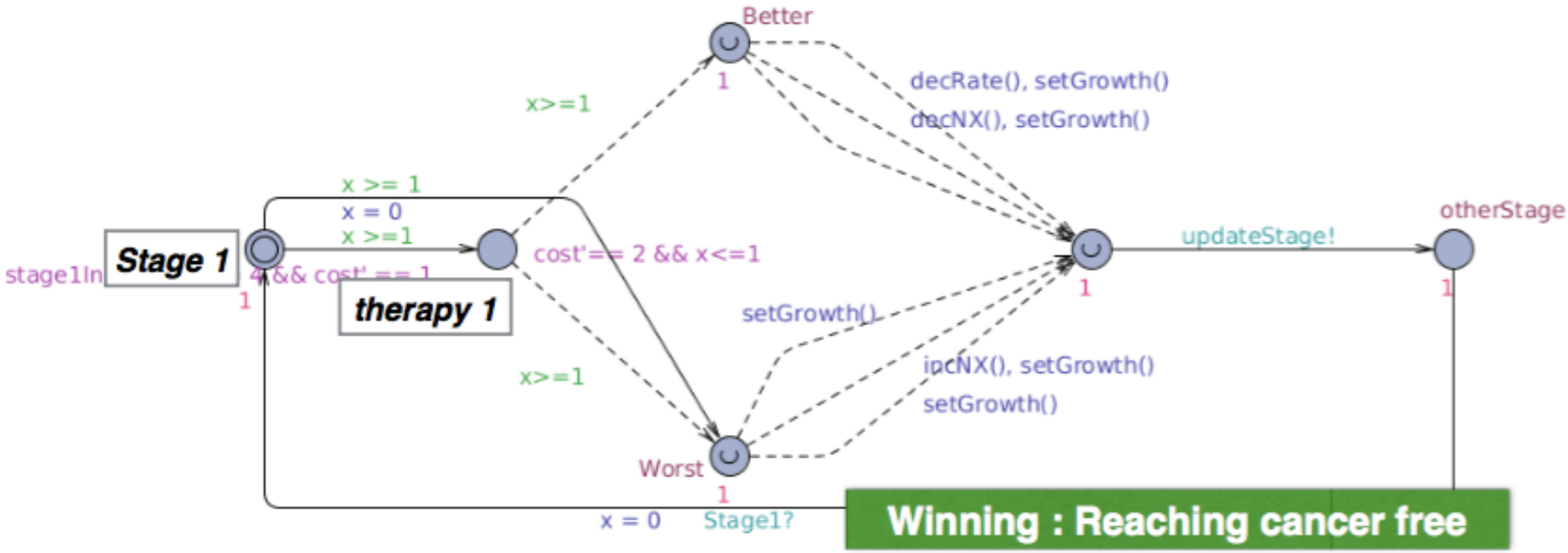
liver automata

Strategy Automata

cancer stages



Timed Game Cancer Automata (TGCA)



Winning : Reaching cancer free

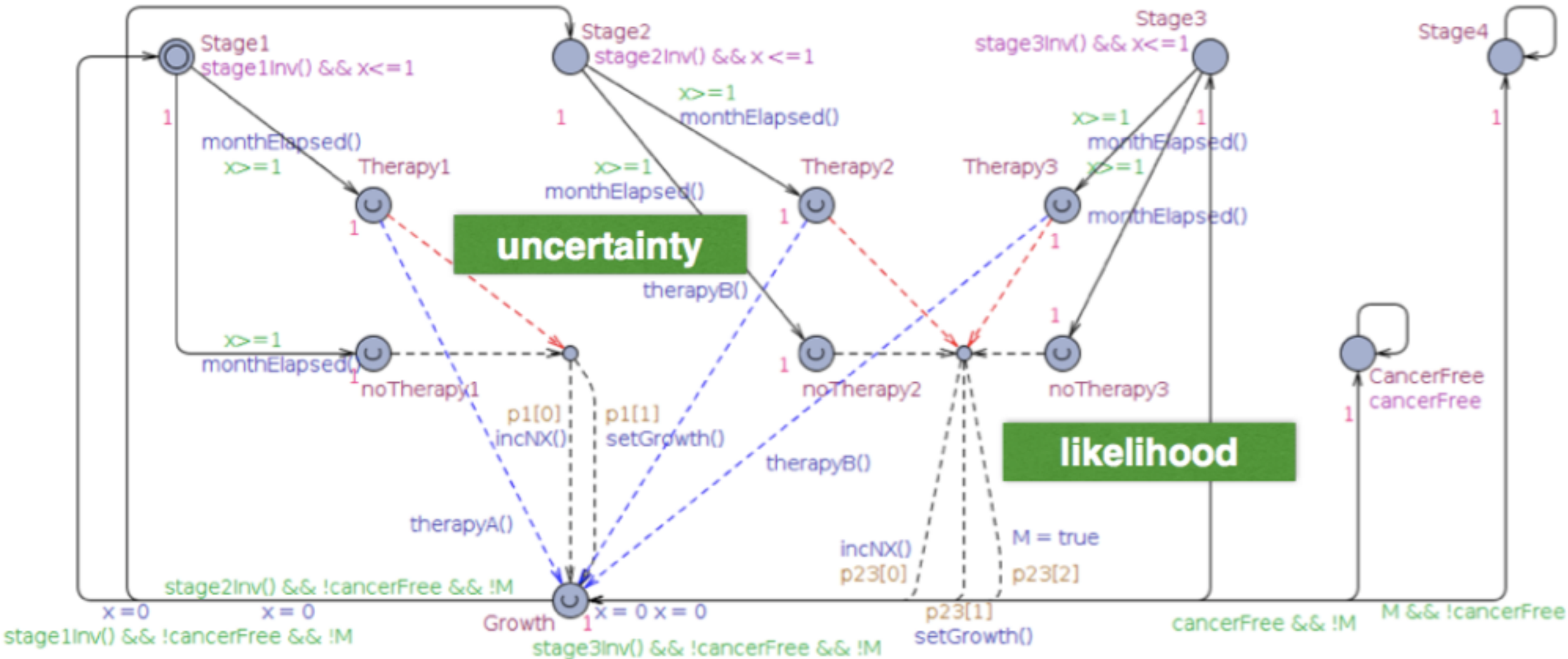
Losing : reaching Metastasis

Finding a winning strategy…

control: A[] !s4.Stage4

control: A[!s4.stage4 U free.CF]

Probabilistic Timed Game Cancer Automata



Property Specifications

TCTL:

E[] (!cha.Stage4) finding a pathway to avoid metastasis

PTCL:

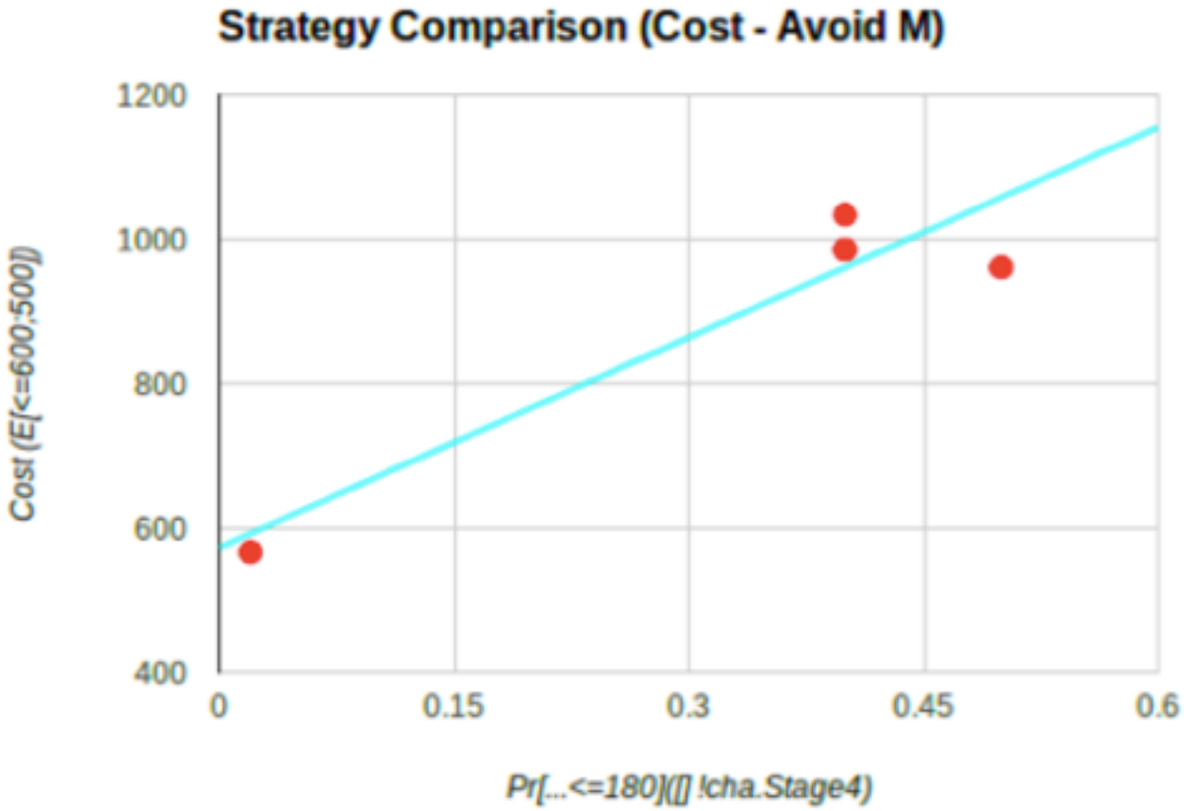
Pr[xRealMonth <= 300] ([] !cha.Stage4) the probability to avoid metastasis

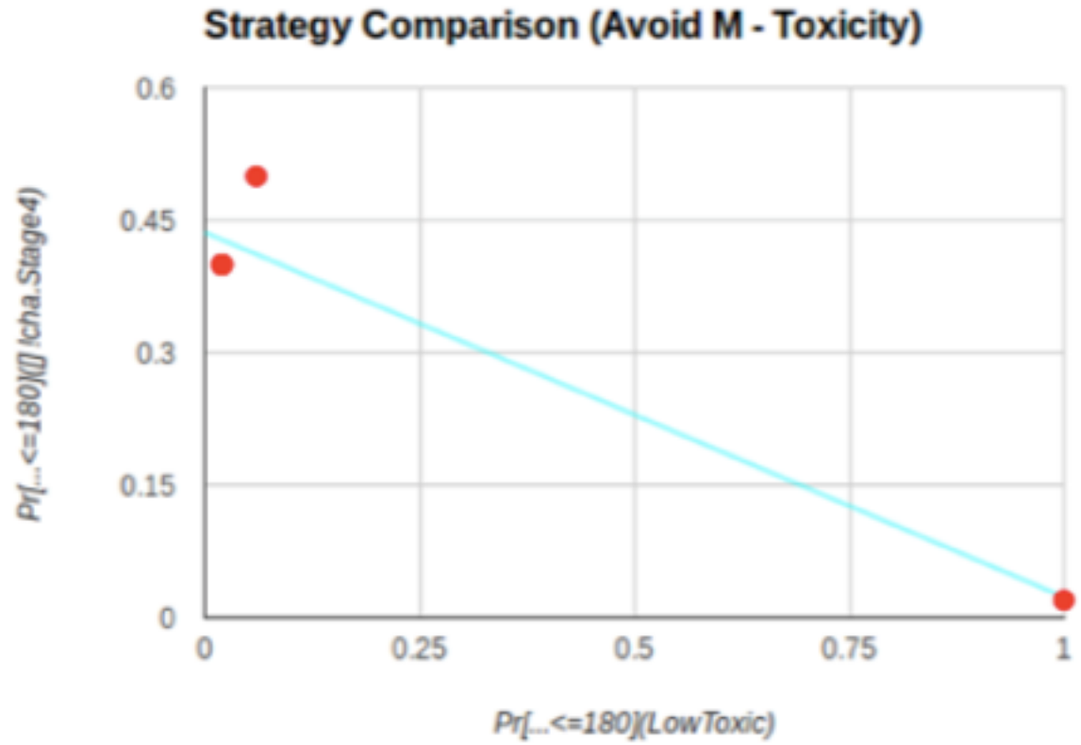
E[<=600; 500] (max: cha.cost) the cost estimation

Pr[xRealMonth in <= 180] ([] liver.LowToxicLevel) the probability of having low liver toxicity

simulate 1 [xrm<=300] logD, M*1000, NX*500 simulate the growth of cancer

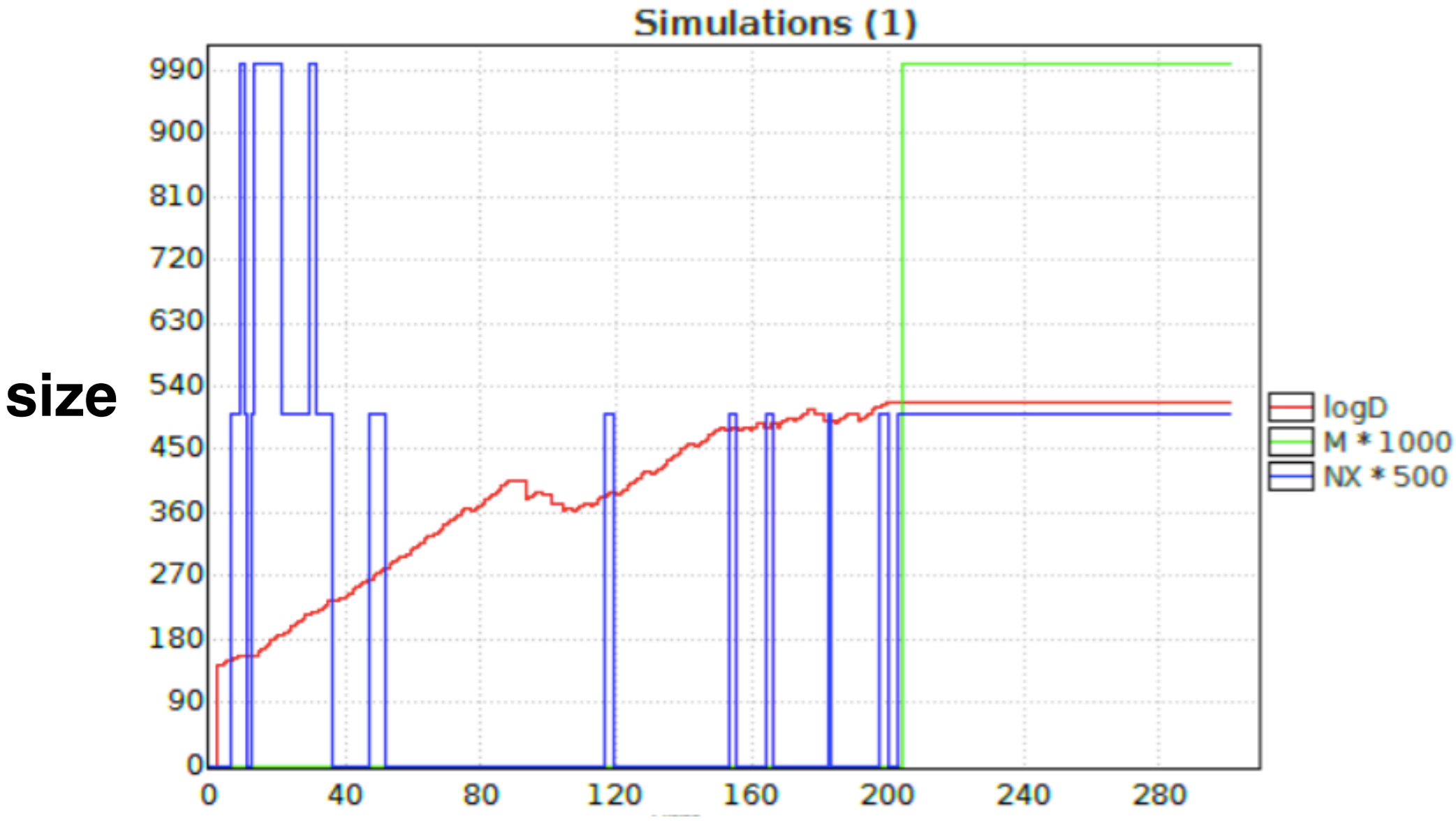
Result





The PPTCA strategy comparison

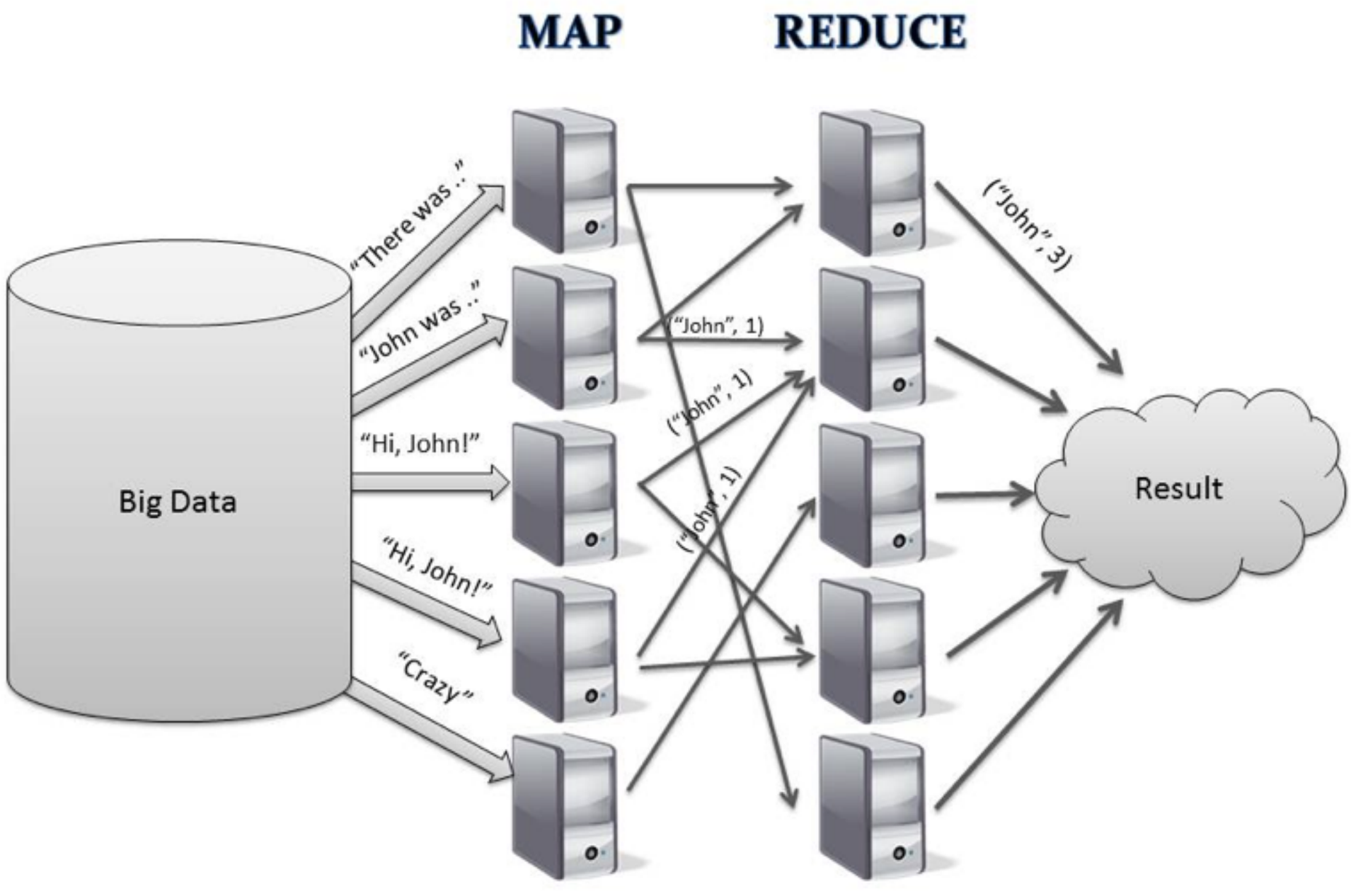
Result


Simulations (1)
size
990
900
810
720
630
540
450
360
270
180
90
0
0
40
80
120
160
200
240
280
time (months)
logD
M * 1000
NX * 500

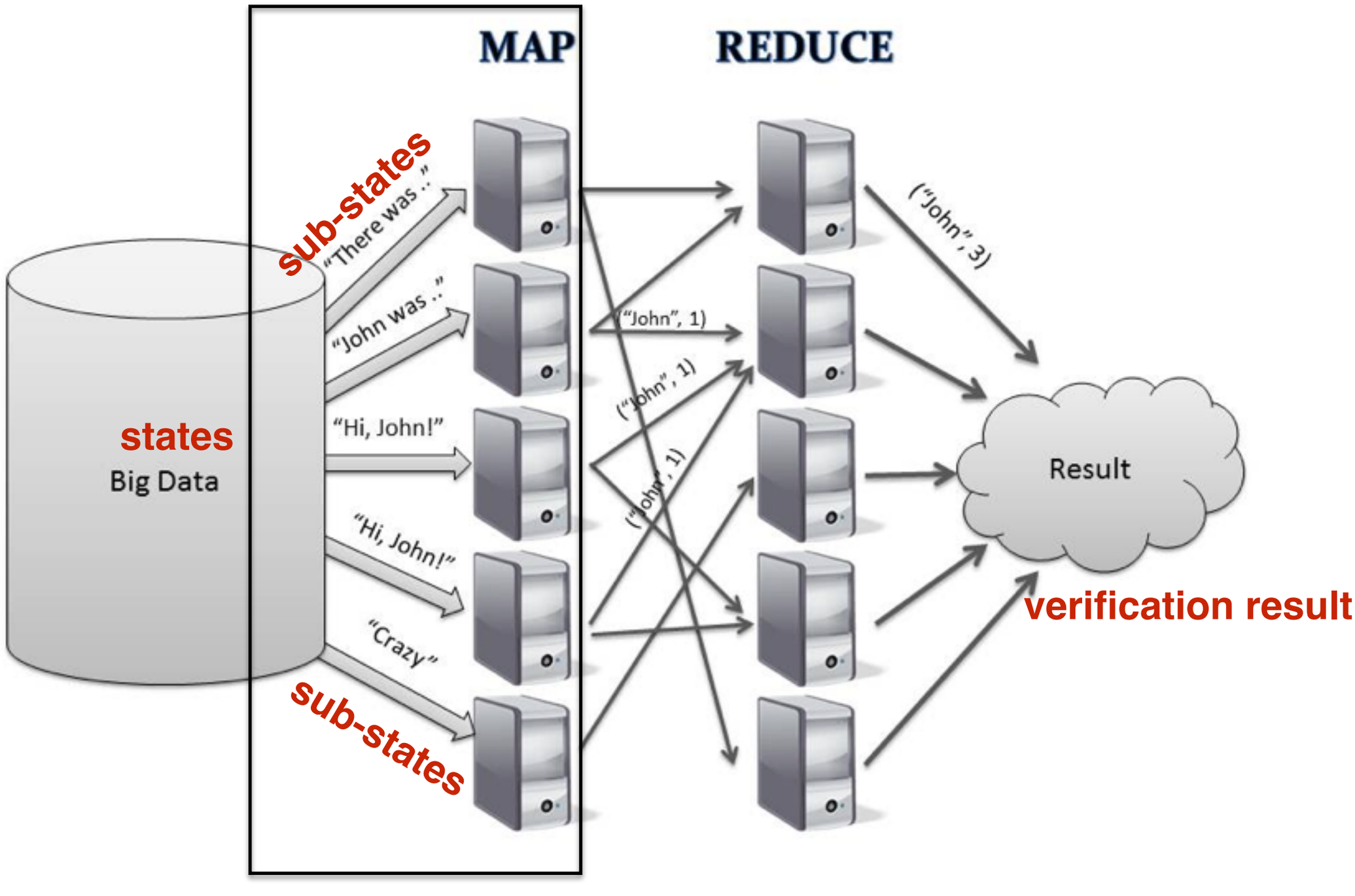
Conclusion & Future works

- (improve) Data Collections
- (include) experts participation

- **(avoid) State Space Explosion**



- **(avoid) State Space Explosion**



Conclusion & Future works

- **Cancer Automata as the generic model**

THANK YOU