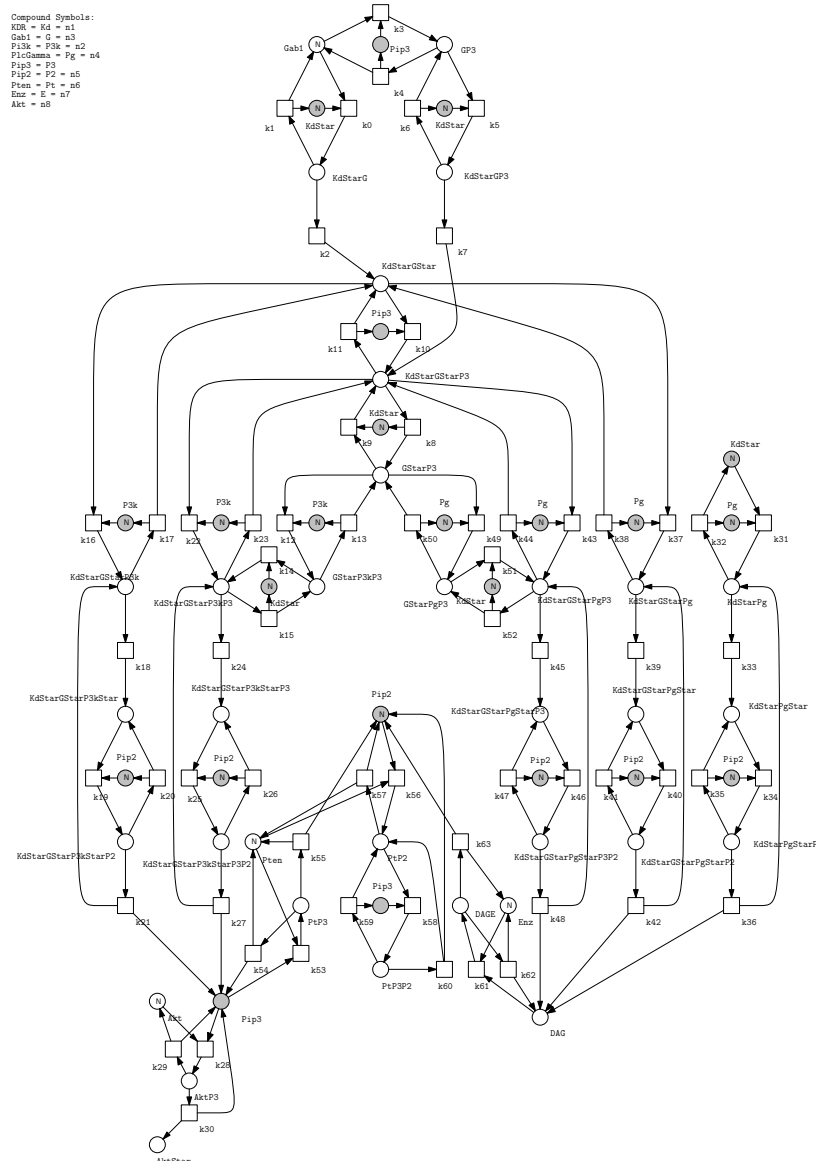


*This form is a summary description of the model entitled “Angiogenesis” proposed for the Model Checking Contest @ Petri Nets. Models can be given in several instances parameterized by scaling parameters. Colored nets can be accompanied by one or many equivalent, unfolded P/T nets. Models are given together with property files (possibly, one per model instance) giving a set of properties to be checked on the model.*

## Description

Angiogenesis, defined as the formation of new vessels from the existing ones, is a topic of great interest in all areas of human biology, particularly to scientists studying vascular development, vascular malformation and cancer biology. Angiogenesis is a complex process involving the activities of many growth factors and relative receptors, which trigger several signaling pathways resulting in different cellular responses. The Petri net was introduced in [1] and refined in [2].

*In March 2020, Pierre Bouvier and Hubert Garavel provided a decomposition of the only one-safe instance of this model into a network of communicating automata. This network is expressed as a Nested-Unit Petri Net (NUPN) that can be found in the “toolspecific” section of the corresponding PNML file.*



*Graphical representation with parameter N. The gray coloured places are logic/fusion places.*

## References

- 1 L. Napione, D. Manini, F. Cordero, A. Horvath, A. Picco, M. D. Pierro, S. Pavan, M. Sereno, A. Veglio, F. Bussolino, and G. Balbo. On the Use of Stochastic Petri Nets in the Analysis of Signal Transduction Pathways for Angiogenesis Process. In Proc. CMSB 2009, pages 281–295. LNCS/LNBI 5688, Springer, 2009.
- 2 F. Cordero, A. Horvath, D. Manini, L. Napione, M. D. Pierro, S. Pavan, A. Picco, A. Veglio, M. Sereno, F. Bussolino, and G. Balbo. Simplification of a complex signal transduction model using invariants and flow equivalent servers. Theor. Comput. Sci., 412(43):6036–6057, 2011.

## Scaling parameter

Parameter name	Parameter description	Chosen parameter values
$N$	initial number of tokens on places Akt, Enz, Gab1, KdStar, P3k, Pg, Pip2 and Pten	1, 5, 10, 15, 20, 25, 50

## Size of the model

Parameter	Number of places	Number of transitions	Number of arcs	Number of units	HWB code
$N = 1$	39	64	185	9	1–8–16
$N = 5$	39	64	185	–	--39
$N = 10$	39	64	185	–	--39
$N = 15$	39	64	185	–	--39
$N = 20$	39	64	185	–	--39
$N = 25$	39	64	185	–	--39
$N = 50$	39	64	185	–	--39

## Structural properties

- ordinary** — all arcs have multiplicity one ..... ✓
- simple free choice** — all transitions sharing a common input place have no other input place ..... ✗<sup>(a)</sup>
- extended free choice** — all transitions sharing a common input place have the same input places ..... ✗<sup>(b)</sup>
- state machine** — every transition has exactly one input place and exactly one output place ..... ✗<sup>(c)</sup>
- marked graph** — every place has exactly one input transition and exactly one output transition ..... ✗<sup>(d)</sup>
- connected** — there is an undirected path between every two nodes (places or transitions) ..... ✓<sup>(e)</sup>
- strongly connected** — there is a directed path between every two nodes (places or transitions) ..... ✗<sup>(f)</sup>
- source place(s)** — one or more places have no input transitions ..... ✗<sup>(g)</sup>
- sink place(s)** — one or more places have no output transitions ..... ✓<sup>(h)</sup>
- source transition(s)** — one or more transitions have no input places ..... ✗<sup>(i)</sup>
- sink transitions(s)** — one or more transitions have no output places ..... ✗<sup>(j)</sup>
- loop-free** — no transition has an input place that is also an output place ..... ✓<sup>(k)</sup>
- conservative** — for each transition, the number of input arcs equals the number of output arcs ..... ✗<sup>(l)</sup>
- subconservative** — for each transition, the number of input arcs equals or exceeds the number of output arcs ..... ✗<sup>(m)</sup>

(a) stated by CÆSAR.BDD version 3.3 on all 7 instances (1, 5, 10, 15, 20, 25, and 50).

(b) transitions “t0” and “k3” share a common input place “Gab1”, but only the former transition has input place “KdStar”.

(c) 57 transitions are not of a state machine, e.g., transition “t0”.

(d) 38 places are not of a marked graph, e.g., place “AktP3”.

(e) stated by CÆSAR.BDD version 2.0 on all 7 instances (1, 5, 10, 15, 20, 25, and 50).

(f) from place “AktStar” one cannot reach place “Akt”.

(g) stated by CÆSAR.BDD version 2.0 on all 7 instances (1, 5, 10, 15, 20, 25, and 50).

(h) place “AktStar” is a sink place.

(i) stated by CÆSAR.BDD version 2.0 on all 7 instances (1, 5, 10, 15, 20, 25, and 50).

(j) stated by CÆSAR.BDD version 2.0 on all 7 instances (1, 5, 10, 15, 20, 25, and 50).

(k) stated by CÆSAR.BDD version 2.0 on all 7 instances (1, 5, 10, 15, 20, 25, and 50).

(l) 57 transitions are not conservative, e.g., transition “t0”.

(m) 33 transitions are not subconservative, e.g., transition “t1”.

**nested units** — *places are structured into hierarchically nested sequential units* <sup>(n)</sup> ..... ? <sup>(o)</sup>

## Behavioural properties

- safe** — *in every reachable marking, there is no more than one token on a place* ..... ? <sup>(p)</sup>  
**dead place(s)** — *one or more places have no token in any reachable marking* ..... ? <sup>(q)</sup>  
**dead transition(s)** — *one or more transitions cannot fire from any reachable marking* ..... ✓  
**deadlock** — *there exists a reachable marking from which no transition can be fired* ..... ✓ <sup>(r)</sup>  
**reversible** — *from every reachable marking, there is a transition path going back to the initial marking* ..... ✗ <sup>(s)</sup>  
**live** — *for every transition  $t$ , from every reachable marking, one can reach a marking in which  $t$  can fire* ..... ✗ <sup>(t)</sup>

## Size of the marking graphs

Parameter	Number of reachable markings	Number of transition firings	Max. number of tokens per place	Max. number of tokens per marking
$N = 1$	110 <sup>(u)</sup>	288 <sup>(v)</sup>	$N$ <sup>(w)</sup>	8 <sup>(x)</sup>
$N = 5$	4.2735E+7 <sup>(y)</sup>	4.8687E+8 <sup>(z)</sup>	$N$ <sup>(aa)</sup>	40 <sup>(ab)</sup>
$N = 10$	8.2265E+11 <sup>(ac)</sup>	1.5636E+13 <sup>(ad)</sup>	$N$ <sup>(ae)</sup>	80 <sup>(af)</sup>
$N = 15$	1 115 538 966 669 107 <sup>(ag)</sup>	?	$N$	$\geq 120$
$N = 20$	351 820 047 967 344 849 <sup>(ah)</sup>	?	$N$	$\geq 160$
$N = 25$	43 090 329 340 850 957 348 <sup>(ai)</sup>	?	$N$	$\geq 200$
$N = 50$	?	?	$N$	$\geq 400$

<sup>(n)</sup> the definition of Nested-Unit Petri Nets (NUPN) is available from <http://mcc.lip6.fr/nupn.php>

<sup>(o)</sup> stated by CÆSAR.BDD version 3.3 to be true on 1 instance(s) out of 7, and false on the remaining 6 instance(s).

<sup>(p)</sup> stated by CÆSAR.BDD version 2.0 to be true on 1 instance(s) out of 7, and false on the remaining 6 instance(s).

<sup>(q)</sup> stated by CÆSAR.BDD version 3.3 to be true on 1 instance(s) out of 7, and unknown on the remaining 6 instance(s).

<sup>(r)</sup> Checked by Marcie on 2013-12-13; confirmed at MCC'2014 by Tapaal on 2 instances and by Lola on 5 instances.

<sup>(s)</sup> has dead states.

<sup>(t)</sup> has dead states.

<sup>(u)</sup> given in [2] and computed by Marcie on 2013-12-13; confirmed by CÆSAR.BDD version 2.0; confirmed at MCC'2014 by Marcie, PNMC, PNXDD, Stratagem, and Tapaal.

<sup>(v)</sup> computed at MCC'2014 by Marcie.

<sup>(w)</sup> confirmed at MCC'20214 by Marcie, PNMC, and Tapaal.

<sup>(x)</sup> computed at MCC'2014 by Marcie, PNMC, and Tapaal.

<sup>(y)</sup> exact value 42 734 935 given in [2] and computed by Marcie on 2013-12-13; confirmed at MCC'2014 by Marcie, PNMC, and PNXDD.

<sup>(z)</sup> computed at MCC'2014 by Marcie.

<sup>(aa)</sup> confirmed at MCC'2014 by Marcie and PNMC.

<sup>(ab)</sup> computed at MCC'2014 by Marcie and PNMC.

<sup>(ac)</sup> exact value 822 645 885 495 computed by Marcie on 2013-12-13; confirmed at MCC'2014 by Marcie, PNMC, and PNXDD.

<sup>(ad)</sup> computed at MCC'2014 by Marcie.

<sup>(ae)</sup> confirmed at MCC'2014 by Marcie and PNMC.

<sup>(af)</sup> computed at MCC'2014 by Marcie and PNMC.

<sup>(ag)</sup> computed by Marcie on 2013-12-13.

<sup>(ah)</sup> computed by Marcie on 2013-12-13.

<sup>(ai)</sup> computed by Marcie on 2013-12-13.