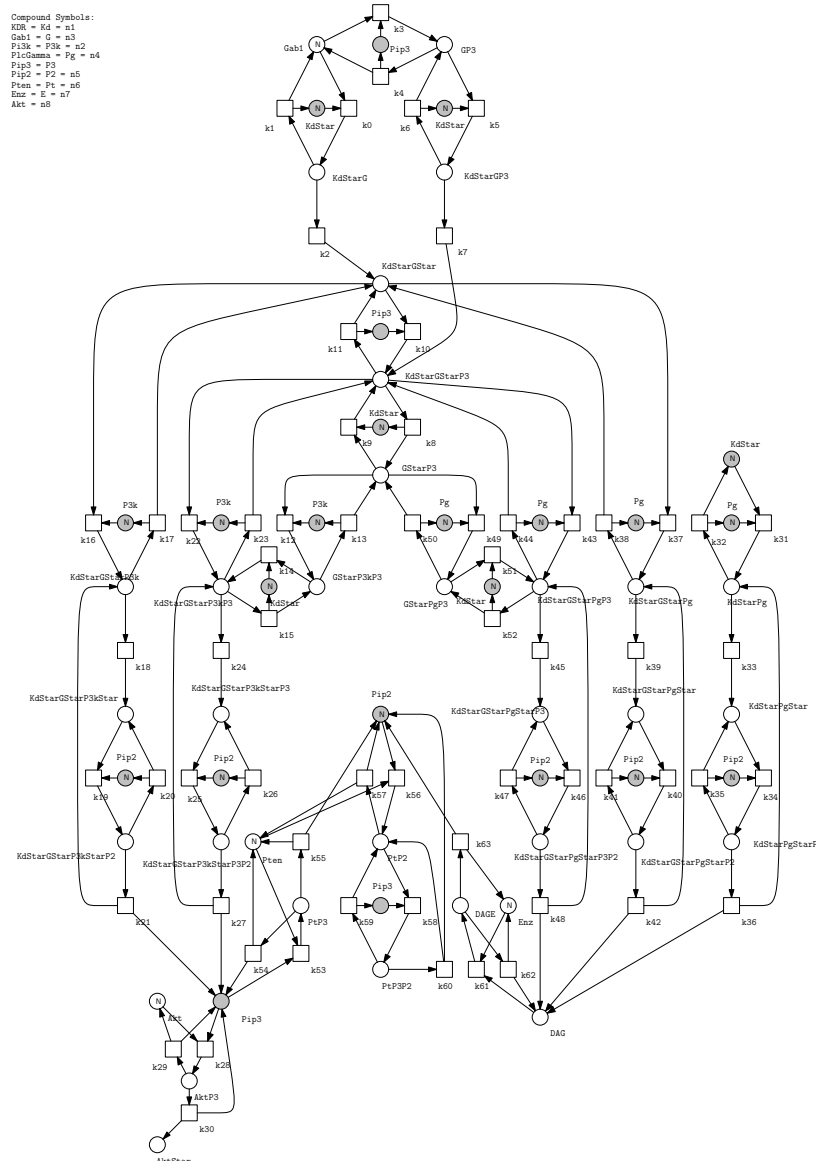


This form is a summary description of the model entitled “Angiogenesis” proposed for the Model Checking Contest @ Petri Nets. Models can be given in several instances parameterized by scaling parameters. Colored nets can be accompanied by one or many equivalent, unfolded P/T nets. Models are given together 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 ✗^(a)
- extended free choice** — all transitions sharing a common input place have the same input places ✗^(b)
- state machine** — every transition has exactly one input place and exactly one output place ✗^(c)
- marked graph** — every place has exactly one input transition and exactly one output transition ✗^(d)
- connected** — there is an undirected path between every two nodes (places or transitions) ✓^(e)
- strongly connected** — there is a directed path between every two nodes (places or transitions) ✗^(f)
- source place(s)** — one or more places have no input transitions ✗^(g)
- sink place(s)** — one or more places have no output transitions ✓^(h)
- source transition(s)** — one or more transitions have no input places ✗⁽ⁱ⁾
- sink transitions(s)** — one or more transitions have no output places ✗^(j)
- loop-free** — no transition has an input place that is also an output place ✓^(k)
- conservative** — for each transition, the number of input arcs equals the number of output arcs ✗^(l)
- subconservative** — for each transition, the number of input arcs equals or exceeds the number of output arcs ✗^(m)

(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* ⁽ⁿ⁾ ? ^(o)

Behavioural properties

- safe** — *in every reachable marking, there is no more than one token on a place* ? ^(p)
dead place(s) — *one or more places have no token in any reachable marking* ? ^(q)
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* ✓ ^(r)
reversible — *from every reachable marking, there is a transition path going back to the initial marking* ✗ ^(s)
live — *for every transition t , from every reachable marking, one can reach a marking in which t can fire* ✗ ^(t)

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 ^(u)	288 ^(v)	N ^(w)	8 ^(x)
$N = 5$	4.2735E+7 ^(y)	4.8687E+8 ^(z)	N ^(aa)	40 ^(ab)
$N = 10$	8.2265E+11 ^(ac)	1.5636E+13 ^(ad)	N ^(ae)	80 ^(af)
$N = 15$	1 115 538 966 669 107 ^(ag)	?	N	≥ 120
$N = 20$	351 820 047 967 344 849 ^(ah)	?	N	≥ 160
$N = 25$	43 090 329 340 850 957 348 ^(ai)	?	N	≥ 200
$N = 50$?	?	N	≥ 400

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

^(o) 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).

^(p) 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).

^(q) 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).

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

^(s) has dead states.

^(t) has dead states.

^(u) 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.

^(v) computed at MCC'2014 by Marcie.

^(w) confirmed at MCC'20214 by Marcie, PNMC, and Tapaal.

^(x) computed at MCC'2014 by Marcie, PNMC, and Tapaal.

^(y) 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.

^(z) computed at MCC'2014 by Marcie.

^(aa) confirmed at MCC'2014 by Marcie and PNMC.

^(ab) computed at MCC'2014 by Marcie and PNMC.

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

^(ad) computed at MCC'2014 by Marcie.

^(ae) confirmed at MCC'2014 by Marcie and PNMC.

^(af) computed at MCC'2014 by Marcie and PNMC.

^(ag) computed by Marcie on 2013-12-13.

^(ah) computed by Marcie on 2013-12-13.

^(ai) computed by Marcie on 2013-12-13.