B HFPN Model of the Akt-MAPK Signaling Pathways

The figure below shows the HFPN model of the Akt-MAPK signaling pathways. This pathway model contains 36 molecular species and 42 unknown kinetic rate constants. The equations associated with each transition are shown in Table 1. The nominal values of the rate constants fall within the interval [0.0, 1.0]. The molecular concentrations of the various species fall within the interval [0.0, 5.0]. The nominal values of the rate constants and the initial concentration levels of the molecular species are given in Tables 2 and 3.

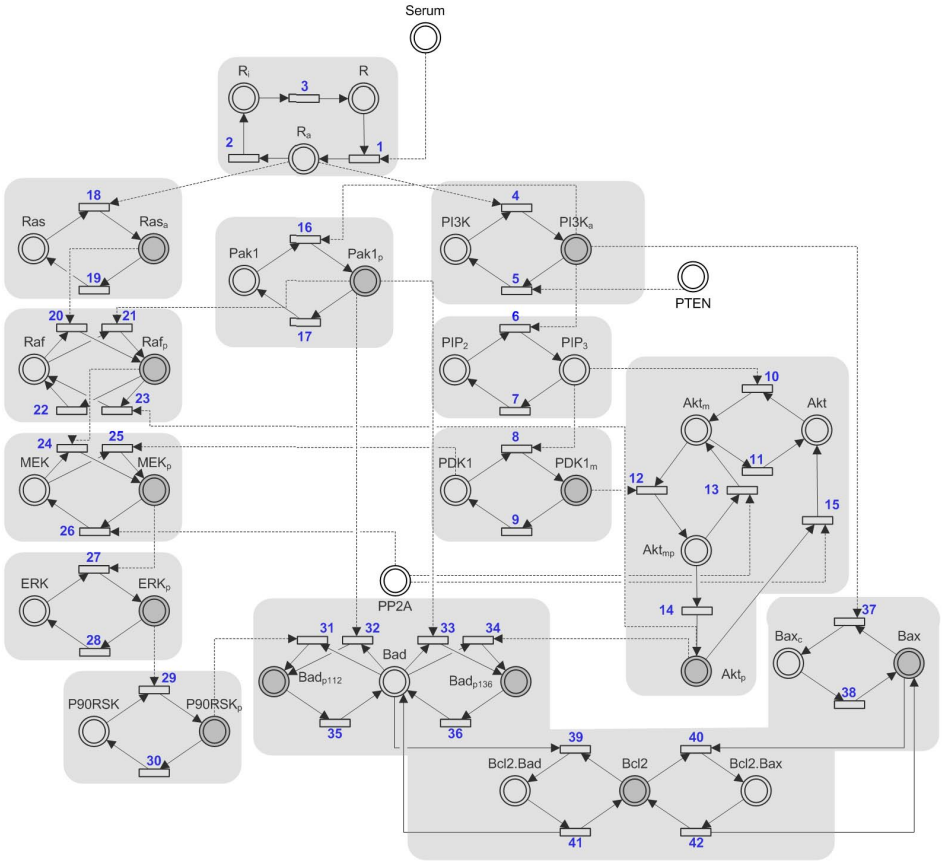

Fig. 1. The HFPN model of the Akt-MAPK pathways. A place node in the model is shaded in gray if data is available for the corresponding molecular species. The light gray boxes indicate the components obtained through pathway decomposition.

Table 1. Equations for the reactions in the pathway. The molecular species are denoted in "[]".

No	Rate Equation	No	Rate Equation	No	Rate Equation	No	Rate Equation
1	$k_1[R]$	12	$k_{12}[PDK1_m][Akt_m]$	23	$k_{23}[Akt_p][Raf_p]$	34	$k_{34}[Akt_p][Bad]$
2	$k_2[R_a]$	13	$k_{13}[PP2A][Akt_{mp}]$	24	$k_{24}[Raf_p][MEK]$	35	$k_{35}[Bad_{p112}]$
3	$k_3[R_i]$	14	$k_{14}[Akt_{mp}]$	25	$k_{25}[PDK1][MEK]$	36	$k_{36}[Bad_{p136}]$
4	$k_4[R_a][PI3K]$	15	$k_{15}[PP2A][Akt_p]$	26	$k_{26}[MEK_p][PP2A]$	37	$k_{37}[PI3K_a][Bax]$
5	$k_5[PTEN][PI3K_a]$	16	$k_{16}[PI3K_a][Pak1]$	27	$k_{27}[MEK_p][ERK]$	38	$k_{38}[Bax_c]$
6	$k_6[PI3K_a][PIP_2]$	17	$k_{17}[Pak1_p]$	28	$k_{28}[ERK_p]$	39	$k_{39}[Bad][Bcl2]$
7	$k_7[PIP_3]$	18	$k_{18}[R_a][Ras]$	29	$k_{29}[ERK_p][P90RSK]$	40	$k_{40}[Bax][Bcl2]$
8	$k_8[PIP_3][PDK1]$	19	$k_{19}[Ras_a]$	30	$k_{30}[P90RSK_p]$	41	$k_{41}[Bcl2.Bad]$
9	$k_9[PDK1_m$	20	$k_{20}[Ras_a][Raf]$	31	$k_{31}[P90RSK_p][Bad]$	42	$k_{42}[Bcl2.Bax]$
10	$k_{10}[PIP_3][Akt]$	21	$k_{21}[Pak1_p][Raf]$	32	$k_{32}[Pak1_p][Bad]$		
11	$k_{11}[Akt_m]$	22	$k_{22}[Raf_p]$	33	$k_{33}[Pak1_p][Bad]$		

Table 2. Nominal values for the unknown kinetic rate constants.

Parameter	Value	Parameter	Value	Parameter	Value	Parameter	Value	Parameter	Value
k_1	0.55	k_{11}	0.65	k_{21}	0.75	k_{31}	0.05	k_{41}	0.95
k_2	0.35	k_{12}	0.65	k_{22}	0.85	k_{32}	0.65	k_{42}	0.45
k_3	0.05	k_{13}	0.65	k_{23}	0.55	k_{33}	0.05		
k_4	0.85	k_{14}	0.75	k_{24}	0.45	k_{34}	0.35		
k_5	0.75	k_{15}	0.55	k_{25}	0.55	k_{35}	0.85		
k_6	0.55	k_{16}	0.05	k_{26}	0.35	k_{36}	0.95		
k_7	0.95	k_{17}	0.95	k_{27}	0.95	k_{37}	0.75		
k_8	0.25	k_{18}	0.25	k_{28}	0.85	k_{38}	0.15		
k_9	0.45	k_{19}	0.35	k_{29}	0.05	k_{39}	0.85		
k_{10}	0.65	k_{20}	0.45	k_{30}	0.35	k_{40}	0.85		

Table 3. Initial concentration levels of the molecular species.

Species	Concentration	Species	Concentration	Species	Concentration	Species	Concentration
Serum	1.0	$PDK1_m$	0.0	Raf_p	0.0	Bax	0.0
PP2A	5.0	Akt	5.0	MEK	5.0	Bax_c	5.0
R	5.0	Akt_m	0.0	MEK_p	0.0	Bcl2	5.0
R_a	0.0	Akt_{mp}	0.0	ERK	5.0	Bcl2.Bad	0.0
R_i	0.0	Akt_p	0.0	ERK_p	0.0	Bcl2.Bax	0.0
PI3K	5.0	Pak1	5.0	P90RSK	5.0	PTEN	1.0
$PI3K_a$	0.0	$Pak1_p$	0.0	$P90RSK_p$	0.0		
PIP_2	5.0	Ras	5.0	Bad	5.0		
PIP_3	0.0	Ras_a	0.0	Bad_{p112}	0.0		
PDK1	5.0	Raf	5.0	Bad_{p136}	0.0		