Supplemental Material

Competitive Tuning Among Ca^{2+}/Calmodulin-Dependent Proteins: Analysis of *in silico* Model Robustness and Parameter Variability

Matthew C. Pharris, Neal Patel, and Tamara L. Kinzer-Ursem

Table S1. Calmodulin binding proteins and their chemical reaction

Protein	Description and Chemical Reactions
Adenylyl Cyclase 1 (AC1)	A prominent, membrane-associated Adenylyl Cyclase isoform in hippocampal neurons. Binds CaM at its C_{1b} domain and, when activated, converts ATP to cAMP. $AC1 + CaM_{iN,jC} \leftrightarrow AC1\_CaM_{iN,jC}$ $2\ Ca^{2+} + AC1\_CaM_{iN,jC} \leftrightarrow AC1\_CaM_{(i+1)N,jC}$ $2\ Ca^{2+} + AC1\_CaM_{iN,jC} \leftrightarrow AC1\_CaM_{iN,(j+1)C}$ $AC1\_CaM_{iN,jC} \rightarrow AC1\_CaM_{iN,jC} + cAMP$
Adenylyl Cyclase 8 (AC8)	A prominent, Adenylyl Cyclase isoform in hippocampal neurons. Binds Ca^{2+}/CaM at both its N- and C-termini, which are explicitly accounted for in this work. Ca^{2+}/CaM-AC8ct (C-terminus-bound AC8) may bind ATP for conversion to cAMP. $AC8nt + CaM_{iN,jC} \leftrightarrow AC8nt\_CaM_{iN,jC}$ $2\ Ca^{2+} + AC8nt\_CaM_{iN,jC} \leftrightarrow AC8nt\_CaM_{(i+1)N,jC}$ $2\ Ca^{2+} + AC8nt\_CaM_{iN,jC} \leftrightarrow AC8nt\_CaM_{iN,(j+1)C}$ $AC8ct + CaM_{iN,jC} \leftrightarrow AC8ct\_CaM_{iN,jC}$ $2\ Ca^{2+} + AC8ct\_CaM_{iN,jC} \leftrightarrow AC8ct\_CaM_{(i+1)N,jC}$ $2\ Ca^{2+} + AC8ct\_CaM_{iN,jC} \leftrightarrow AC8ct\_CaM_{iN,(j+1)C}$ $AC8ct\_CaM_{iN,jC} \rightarrow AC8ct\_CaM_{iN,jC} + cAMP$
Ca^{2+}/CaM-dependent kinase II (CaMKII)	Ca^{2+}/CaM-dependent kinase. Highly expressed in brain, and especially hippocampal tissue. In this work, CaMKII is modeled as monomers which, when active, may dimerize and subsequently become Ca^{2+}/CaM-independent via autophosphorylation. Active CaMKII phosphorylates many downstream proteins such as the GluA1 subunit of AMPA receptors. $CaMKII + CaM_{iN,jC} \leftrightarrow CaMKII\_CaM_{iN,jC}$ $Ca^{2+} + CaMKII\_CaM_{iN,jC} \leftrightarrow CaMKII\_CaM_{(i+1)N,jC}$ $Ca^{2+} + AC8nt\_CaM_{iN,jC} \leftrightarrow AC8nt\_CaM_{iN,(j+1)C}$ $CaMKII\_CaM_{iN,jC} + CaMKII\_CaM_{iN,jC} \leftrightarrow Dimer_{(iN,jC),(iN,jC)} \rightarrow pCaMKII\_CaM_{iN,jC} + CaMKII\_CaM_{iN,jC}$ $CaMKII\_CaM_{iN,jC} + pCaMKII\_CaM_{iN,jC} \leftrightarrow pDimer_{(iN,jC),(iN,jC)} \rightarrow pCaMKII\_CaM_{iN,jC} + pCaMKII\_CaM_{iN,jC}$ $CaMKII\_CaM_{iN,jC} + GluA1 \leftrightarrow CaMKII_{iN,jC}\_GluA1 \rightarrow CaMKII\_CaM_{iN,jC} + GluA1_{p831}$ $CaMKII\_CaM_{iN,jC} + GluA1_{p845} \leftrightarrow CaMKII_{iN,jC}\_GluA1_{p845} \rightarrow CaMKII\_CaM_{iN,jC} + GluA1_{p831p845}$ $pCaMKII\_CaM_{iN,jC} + GluA1 \leftrightarrow pCaMKII_{iN,jC}\_GluA1 \rightarrow pCaMKII\_CaM_{iN,jC} + GluA1_{p831}$ $pCaMKII\_CaM_{iN,jC} + GluA1_{p845} \leftrightarrow pCaMKII_{iN,jC}\_GluA1_{p845} \rightarrow pCaMKII\_CaM_{iN,jC} + GluA1_{p831p845}$
Calcineurin (CaN)	A Ca^{2+}/CaM-dependent serine/threonine phosphatase. For simplicity, our models are restricted only to binding of Ca^{2+}/CaM to the catalytic CaNA subunit.

	CaN + $CaM_{iN,jC}$ ↔ $CaN\_CaM_{iN,jC}$ Ca^{2+} + $CaN\_CaM_{iN,jC}$ ↔ $CaN\_CaM_{(i+1)N,jC}$ Ca^{2+} + $CaN\_CaM_{iN,jC}$ ↔ $CaN\_CaM_{iN,(j+1)C}$
Myosin Light Chain Kinase (MLCK)	A putatively abundant CBP in dendritic spines, which we model using kinetic parameters derived from studies on smooth muscle. MLCK+ $CaM_{iN,jC}$ ↔ $MLCK\_CaM_{iN,jC}$ Ca^{2+} + $MLCK\_CaM_{iN,jC}$ ↔ $MLCK\_CaM_{(i+1)N,jC}$ Ca^{2+} + $MLCK\_CaM_{iN,jC}$ ↔ $MLCK\_CaM_{iN,(j+1)C}$
Neurogranin (Ng)	A membrane-associated protein, and one of the few proteins that strongly binds CaM in absence of Ca^{2+}. Ng+ $CaM_{iN,jC}$ ↔ $Ng\_CaM_{iN,jC}$ Ca^{2+} + $Ng\_CaM_{iN,jC}$ ↔ $Ng\_CaM_{(i+1)N,jC}$ Ca^{2+} + $Ng\_CaM_{iN,jC}$ ↔ $Ng\_CaM_{iN,(j+1)C}$
Nitric Oxide Synthetase (NOS)	Typically a membrane-associated protein that binds tightly to CaM and generates Nitric Oxide from citrulline and arginine. NOS+ $CaM_{iN,jC}$ ↔ $NOS\_CaM_{iN,jC}$ Ca^{2+} + $NOS\_CaM_{iN,jC}$ ↔ $NOS\_CaM_{(i+1)N,jC}$ Ca^{2+} + $NOS\_CaM_{iN,jC}$ ↔ $NOS\_CaM_{iN,(j+1)C}$
Phosphodiesterase 1 (PDE1)	A Ca^{2+}/CaM dependent phosphodiesterase that cleaves cAMP into AMP. PDE1+ $CaM_{iN,jC}$ ↔ $PDE1\_CaM_{iN,jC}$ Ca^{2+} + $PDE1\_CaM_{iN,jC}$ ↔ $PDE1\_CaM_{(i+1)N,jC}$ Ca^{2+} + $PDE1\_CaM_{iN,jC}$ ↔ $PDE1\_CaM_{iN,(j+1)C}$ $PDE1\_CaM_{iN,jC}$ + cAMP → $PDE1\_CaM_{iN,jC}$ + AMP

Reaction parameters are provided in Table S3. Bidirectional arrows denote reversibility; Unidirectional arrows indicate irreversible reactions. Under-scores denote protein complexes. Subscripts i and j pertain to the 4-state model and denote total Ca^{2+} at the CaM N- and C-terminus, respectively. Therefore, in the 4-state model, i and j may be either 0 or 2 independently of each other. In the 2-state model, i and j must both either be 0 or 2. Prefix p denotes phosphorylated players. The corresponding system of differential equations are found in Supplemental Material section entitled "Model Equations".

Table S2. Non-calmodulin binding proteins included in model and their respective chemical reactions

Phosphodiesterase 4 (PDE4)	PDE4 is not Ca^{2+}/CaM dependent but plays a significant role in regulating the levels of cAMP in cells by cleaving cAMP into AMP. Phosphorylation by active PKAc increases the enzymatic activity of PDE4 [4]. PDE4 + PKAc ↔ PDE4_PKAc → PKAc + pPDE4 PDE4 + cAMP → PDE4 + AMP pPDE4 + cAMP → pPDE4 + AMP
Protein kinase A (PKA, also known as cAMP-dependent kinase)	Binds up to four cAMP, liberating catalytic subunits that bind and phosphorylate a number of downstream targets such as PDE4 and GluA1 [4,5]. Reaction subscripts: numbers denote bound cAMP, R denotes auto-inhibition, C denotes a catalytic subunit. PKA + cAMP ↔ R2C2_cAMP R2C2_cAMP + cAMP ↔ R2C2_$cAMP_2$ R2C2_$cAMP_2$ + cAMP ↔ R2C2_$cAMP_3$ R2C2_$cAMP_3$ + cAMP ↔ R2C2_$cAMP_4$ R2C2_$cAMP_4$ ↔ R2C_$cAMP_4$ + PKAc R2C_$cAMP_4$ ↔ R2_$cAMP_4$ + PKAc R2_$cAMP_4$ ↔ R2 + 4 AMP PKAc + PKAinhibitor ↔ PKAi R2 + PKAi ↔ R2C + PKAinhibitor R2C + PKAi ↔ PKA + PKAinhibitor
Inhibitor 1 (Inh-1 or I1)	Inhibitor 1 may become phosphorylated at Ser-35 by PKAc, and phosphorylated Ip35 is able to bind and inhibit the activity of protein phosphatase 1 (PP1). Activated CaN-CaM is able to de-phosphorylate Ip35 back to the original I1 state. I1 + PKAc ↔ I1_PKAc → Ip35 + PKAc Ip35 + PP1 ↔ Ip35_PP1 Ip35 + CaN_$CaM_{iN,jC}$ ↔ Ip35_CaN_$CaM_{iN,jC}$ → I1 + CaN_$CaM_{iN,jC}$
Protein Phosphatase 1 (PP1)	PP1 + pCaMKII_$CaM_{iN,jC}$ ↔ PP1_ pCaMKII_$CaM_{iN,jC}$ → PP1 + CaMKII_$CaM_{iN,jC}$ PP1 + $GluA1_{p831}$ ↔ PP1_$GluA1_{p831}$→ PP1 + GluA1 PP1 + $GluA1_{p845}$ ↔ PP1_$GluA1_{p845}$→ PP1 + GluA1 PP1 + $GluA1_{p831p845}$ ↔ PP1_$GluA1_{p831p845}$→ PP1 + $GluA1_{p845}$
GluA1	One of four subunits of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA receptor). Is phosphorylated at amino acid residue Ser-831 by CaMKII and residue Ser-845 by PKA [4,6]. Increase AMPA phosphorylation is implicated in synaptic plasticity, and GluA1-p845 may be necessary for exocytosis of AMPARs to the synaptic membrane [6]. GluA1 + PKA4 ↔ GluA1_PKA4 GluA1 + PKAc ↔ GluA1_PKAc → $GluA1_{p845}$ + PKAc GluA1 + CaMKII_$CaM_{iN,jC}$ ↔ GluA1_CaMKII_$CaM_{iN,jC}$ → $GluA1_{p831}$ + CaMKII_$CaM_{iN,jC}$ GluA1 + pCaMKII_$CaM_{iN,jC}$ ↔ GluA1_pCaMKII_$CaM_{iN,jC}$ → $GluA1_{p831}$ + pCaMKII_$CaM_{iN,jC}$ $GluA1_{p845}$ + CaMKII_$CaM_{iN,jC}$ ↔ $GluA1_{p845}$_CaMKII_$CaM_{iN,jC}$ → $GluA1_{p831p845}$ + CaMKII_$CaM_{iN,jC}$ $GluA1_{p845}$ + pCaMKII_$CaM_{iN,jC}$ ↔ $GluA1_{p845}$_pCaMKII_$CaM_{iN,jC}$ → $GluA1_{p831p845}$ + pCaMKII_$CaM_{iN,jC}$ $GluA1_{p831}$ + PKAc ↔ $GluA1_{p831}$_PKAc → $GluA1_{p831p845}$ + PKAc

Reaction parameters are provided in Table S3. Bidirectional arrows denote reversibility; Unidirectional arrows indicate irreversible reactions. Under-scores denote protein complexes. Subscripts i and j pertain to the 4-state model and denote total Ca^{2+} at the CaM N- and C-terminus, respectively. Therefore, in the 4-state model, i and j may be either 0 or 2 independently of each other. In the 2-state model, i and j must both either be 0 or 2. Prefix p denotes phosphorylated players. The corresponding system of differential equations are found in Supplemental Material section entitled "Model Equations".

Equation S1. Calculation of C_b for Figure 3.

In Figure 3, we deploy a metric first utilized in a previous publication (Romano et al. 2017 PLoS Comp Biol). In that publication, the metric C_b is defined as the time-averaged concentration of CaM-bound CBP at a given Ca^{2+} frequency. C_b is mathematically represented in Equation 1 below.

$$(1)\ C_b = \frac{1}{t_f - t_0} \int_{t=t_0}^{t_f} \sum_{i=0}^{2} \sum_{j=0}^{2} [T_b CaM4]\, dt$$

$$(2)\ C_b = \frac{1}{t_f - t_0} \int_{t=t_0}^{t_f} \sum_{i=0}^{2} \sum_{j=0}^{2} \left[T_b CaMN_i C_j\right] dt$$

$$T_b = \{AC1, AC8nt, AC8ct, CaMKII, CaN, MLCK, Ng, NOS, PDE1\}$$

Where the subscript b indexes the binding partners, so the average bound concentration for a given binding partner (C_b) is found by integrating the total concentration of that binding partner (T_b) bound to each CaM state ($CaMN_iC_j$, i and j = 0, 1, or 2) over the stimulation period (t_o until t_f) and dividing by the stimulus duration (t_f - t_o). Note that dividing by stimulus duration is necessary because we reduce $t_f - t_o$ in order to limit computational expense at high frequencies. To compare relative levels of CaM-binding across various proteins and experimental conditions, for each binding partner we normalize C_b by its peak value from among all the Ca^{2+} frequencies simulated.

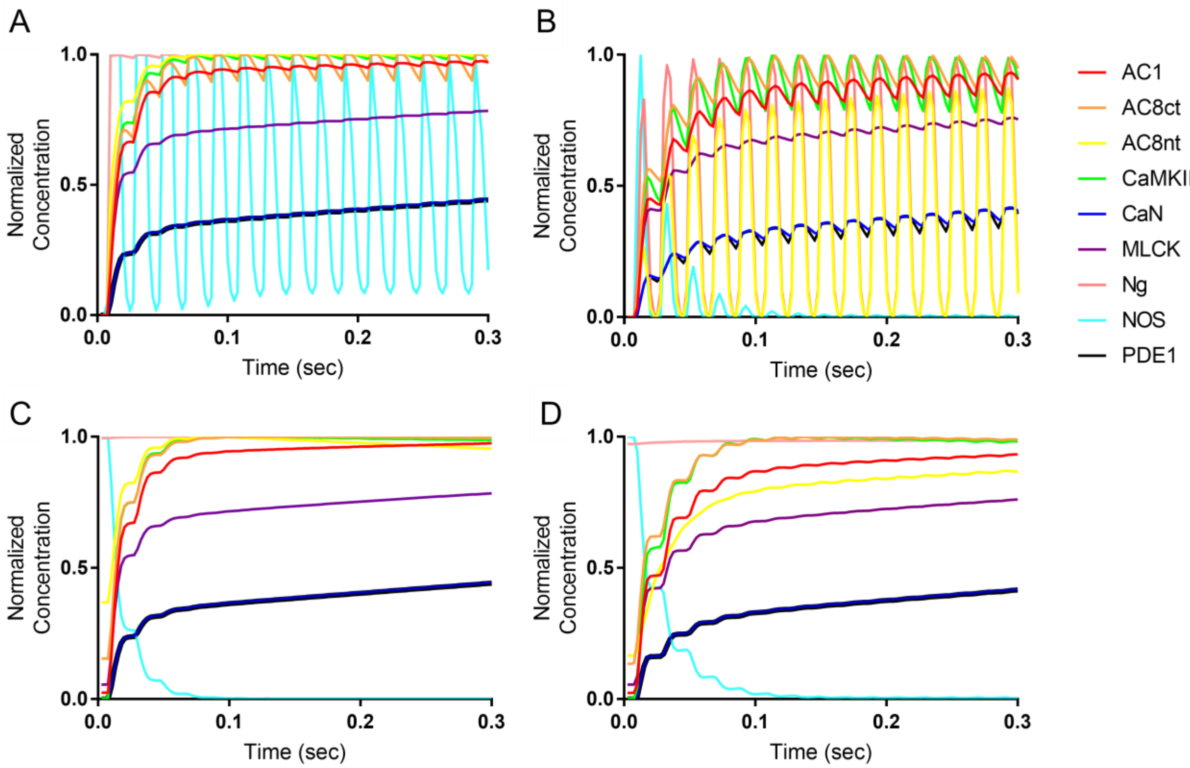

Figure S1. 2-state vs 4-state time-course comparison at 50Hz. (A, B) Response of binding models to 50 Hz Ca^{2+} frequency stimulation, monitoring each CBP bound to Ca^{2+}-saturated CaM_4 for the **(A)** 2-state and **(B)** 4-state models. **(C, D)** Response of binding models to 50 Hz Ca^{2+} frequency stimulation, monitoring the cumulative concentration of each CBP bound to any Ca^{2+}/CaM state for the **(C)** 2-state and **(D)** 4-state models.

Table S3. Sensitivity Analysis of Kinetic Parameters at 10 Hz Ca^{2+} and WT Ng.

Parameter	PRCC
$k_p^{AC1CaM4}$	0.736
$k_{on}^{AC1CaM4}$	0.568
$k_p^{KCaM4GluA1}$	0.550
$k_{on}^{CaMKIIGluA1}$	0.540
k_{on}^{KCaM4}	-0.560
$k_p^{PDE4cAMP}$	-0.771

*****Note that both CaMKII- and AC-associated parameters are both implicated as significant in this analysis.

Table S4. Sensitivity Analysis of Initial Concentrations at 10 vs 100 Hz Ca^{2+} with WT Ng.

Parameter	PRCC 10 Hz	Parameter	PRCC 100 Hz
$concCaM$	0.898	$concCaM$	0.893
$concGluA1$	0.708	$concGluA1$	0.775
$concAC1$	0.578	$concAC1$	0.632
$concCaMKII$	-0.540	$concPKA$	0.556
$concPDE4$	-0.747	$concCaMKII$	-0.597
		$concPDE4$	-0.758

*At both 10 Hz and 100 Hz, that [CaM] and [GluA1] are highly significant lends confidence to our sensitivity analysis results.

Table S5. Model parameter values

Parameter	Description	Value Used	Reference(s)
Ca^{2+} binding to CaM			
k_{on}^{2N}	2 Ca^{2+} binding to CaM N-terminus	100.0 $\mu M^{-1}s^{-1}$	[1] [26]
k_{off}^{2N}	2 Ca^{2+} dissociation from CaM N-terminus	750.0 s^{-1}	[1] [26]
K_{D}^{2N}	Equilibrium binding of 2 Ca^{2+} to CaM N-terminus	7.5 μM	[1] [26]
k_{on}^{2C}	2 Ca^{2+} binding to CaM C-terminus	4.0 $\mu M^{-1}s^{-1}$	[1] [26]
k_{off}^{2C}	2 Ca^{2+} dissociation from CaM C-terminus	9.25 s^{-1}	[1] [26]
K_{D}^{2C}	Equilibrium binding of 2 Ca^{2+} to CaM C-terminus	2.32 μM	[1] [26]
CaM binding to AC1			
$k_{on}^{AC1CaM0}$	CaM0 binding to AC1	0.00166 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{AC1CaM0}$	CaM0 dissociation from AC1	0.9 s^{-1}	[3] [26]
$K_{D}^{AC1CaM0}$	Equilibrium binding of CaM0 to AC1	542.0 μM	[4] [26]
$k_{on}^{AC1CaM2N}$	CaM2N binding to AC1	0.156 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{AC1CaM2N}$	CaM2N dissociation from AC1	0.9 s^{-1}	[3] [26]
$K_{D}^{AC1CaM2N}$	Equilibrium binding of CaM2N to AC1	5.78 μM	[4] [26]
$k_{on}^{AC1CaM2C}$	CaM2C binding to AC1	0.064 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{AC1CaM2C}$	CaM2C dissociation from AC1	0.9 s^{-1}	[3] [26]
$K_{D}^{AC1CaM2C}$	Equilibrium binding of CaM2C to AC1	14.1 μM	[4] [26]
$k_{on}^{AC1CaM4}$	CaM4 binding to AC1	6.0 $\mu M^{-1}s^{-1}$	[5] [26]
$k_{off}^{AC1CaM4}$	CaM4 dissociation from AC1	0.9 s^{-1}	[5] [26]
$K_{D}^{AC1CaM4}$	Equilibrium binding of CaM4 to AC1	0.15 μM	[2] [26]
Ca^{2+} binding to AC1-CaM			
k_{on}^{AC12N}	2 Ca^{2+} binding to AC1-CaM N-terminus	100.0 $\mu M^{-1}s^{-1}$	[6] [26]
k_{off}^{AC12N}	2 Ca^{2+} dissociation from AC1-CaM N-terminus	8.0 s^{-1}	[8] [26]
K_{D}^{AC12N}	Equilibrium binding of 2 Ca^{2+} to AC1-CaM N-terminus	0.08 μM	[2] [26]
k_{on}^{AC12C}	2 Ca^{2+} binding to AC1-CaM C-terminus	4.0 $\mu M^{-1}s^{-1}$	[6] [26]
k_{off}^{AC12C}	2 Ca^{2+} dissociation from AC1-CaM C-terminus	1.2 s^{-1}	[8] [26]
K_{D}^{AC12C}	Equilibrium binding of 2 Ca^{2+} to AC1-CaM C-terminus	0.3 μM	[2] [26]
CaM binding to AC8 N-terminus			
$k_{on}^{AC8ntCaM0}$	CaM0 binding to AC8 N-terminus	0.00828 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{AC8ntCaM0}$	CaM0 dissociation from AC8 N-terminus	1.0 s^{-1}	[3] [26]
$K_{D}^{AC8ntCaM0}$	Equilibrium binding of CaM0 to AC8 N-terminus	121.0 μM	[4] [26]
$k_{on}^{AC8ntCaM2N}$	CaM2N binding to AC8 N-terminus	0.00828 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{AC8ntCaM2N}$	CaM2N dissociation from AC8 N-terminus	1.0 s^{-1}	[3] [26]
$K_{D}^{AC8ntCaM2N}$	Equilibrium binding of CaM2N to AC8 N-terminus	121.0 μM	[4] [26]
$k_{on}^{AC8ntCaM2C}$	CaM2C binding to AC8 N-terminus	1.25 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{AC8ntCaM2C}$	CaM2C dissociation from AC8 N-terminus	1.0 s^{-1}	[3] [26]
$K_{D}^{AC8ntCaM2C}$	Equilibrium binding of CaM2C to AC8 N-terminus	0.8 μM	[4] [26]
$k_{on}^{AC8ntCaM4}$	CaM4 binding to AC8 N-terminus	1.25 $\mu M^{-1}s^{-1}$	[5] [26]
$k_{off}^{AC8ntCaM4}$	CaM4 dissociation from AC8 N-terminus	1.0 s^{-1}	[5] [26]
$K_{D}^{AC8ntCaM4}$	Equilibrium binding of CaM4 to AC8 N-terminus	0.8 μM	[2] [26]

Ca^{2+} binding to AC8(N-terminus)-CaM			
$k_{on}^{AC8nt2N}$	2 Ca^{2+} binding to AC8(N-terminus)-CaM N-terminus	100.0 $\mu M^{-1}s^{-1}$	[6] [26]
$k_{off}^{AC8nt2N}$	2 Ca^{2+} dissociation from AC8(N-terminus)-CaM N-terminus	750.0 s^{-1}	[8] [26]
$K_{D}^{AC8nt2N}$	Equilibrium binding of 2 Ca^{2+} to AC8(N-terminus)-CaM N-terminus	7.5 μM	[2] [26]
$k_{on}^{AC8nt2C}$	2 Ca^{2+} binding to AC8(N-terminus)-CaM C-terminus	4.0 $\mu M^{-1}s^{-1}$	[6] [26]
$k_{off}^{AC8nt2C}$	2 Ca^{2+} dissociation from AC8(N-terminus)-CaM C-terminus	0.5 s^{-1}	[8] [26]
$K_{D}^{AC8nt2C}$	Equilibrium binding of 2 Ca^{2+} to AC8(N-terminus)-CaM C-terminus	0.125 μM	[2] [26]
CaM binding to AC8 C-terminus			
$k_{on}^{AC8ctCaM0}$	CaM0 binding to AC8 C-terminus	0.00267 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{AC8ctCaM0}$	CaM0 dissociation from AC8 C-terminus	1.0 s^{-1}	[3] [26]
$K_{D}^{AC8ctCaM0}$	Equilibrium binding of CaM0 to AC8 C-terminus	375.0 μM	[4] [26]
$k_{on}^{AC8ctCaM2N}$	CaM2N binding to AC8 C-terminus	1.25 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{AC8ctCaM2N}$	CaM2N dissociation from AC8 C-terminus	1.0 s^{-1}	[3] [26]
$K_{D}^{AC8ctCaM2N}$	Equilibrium binding of CaM2N to AC8 C-terminus	0.8 μM	[4] [26]
$k_{on}^{AC8ctCaM2C}$	CaM2C binding to AC8 C-terminus	0.00267 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{AC8ctCaM2C}$	CaM2C dissociation from AC8 C-terminus	1.0 s^{-1}	[3] [26]
$K_{D}^{AC8ctCaM2C}$	Equilibrium binding of CaM2C to AC8 C-terminus	375.0 μM	[4] [26]
$k_{on}^{AC8ctCaM4}$	CaM4 binding to AC8 C-terminus	1.25 $\mu M^{-1}s^{-1}$	[5] [26]
$k_{off}^{AC8ctCaM4}$	CaM4 dissociation from AC8 C-terminus	1.0 s^{-1}	[5] [26]
$K_{D}^{AC8ctCaM4}$	Equilibrium binding of CaM4 to AC8 C-terminus	0.8 μM	[2] [26]
Ca^{2+} binding to AC8(C-terminus)-CaM			
$k_{on}^{AC8ct2N}$	2 Ca^{2+} binding to AC8(C-terminus)-CaM N-terminus	100.0 $\mu M^{-1}s^{-1}$	[6] [26]
$k_{off}^{AC8ct2N}$	2 Ca^{2+} dissociation from AC8(C-terminus)-CaM N-terminus	1.6 s^{-1}	[8] [26]
$K_{D}^{AC8ct2N}$	Equilibrium binding of 2 Ca^{2+} to AC8(C-terminus)-CaM N-terminus	0.016 μM	[2] [26]
$k_{on}^{AC8ct2C}$	2 Ca^{2+} binding to AC8(C-terminus)-CaM C-terminus	4.0 $\mu M^{-1}s^{-1}$	[6] [26]
$k_{off}^{AC8ct2C}$	2 Ca^{2+} dissociation from AC8(C-terminus)-CaM C-terminus	9.25 s^{-1}	[8] [26]
$K_{D}^{AC8ct2C}$	Equilibrium binding of 2 Ca^{2+} to AC8(C-terminus)-CaM C-terminus	2.31 μM	[2] [26]
CaM binding to CaN			
k_{on}^{PPCaM0}	CaM0 binding to CaN	0.0000000798 $\mu M^{-1}s^{-1}$	[2] [26]
k_{off}^{PPCaM0}	CaM0 dissociation from CaN	0.000319 s^{-1}	[3] [26]
K_{D}^{PPCaM0}	Equilibrium binding of CaM0 to CaN	3999.0 μM	[4] [26]
$k_{on}^{PPCaM2N}$	CaM2N binding to CaN	0.000416 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{PPCaM2N}$	CaM2N dissociation from CaN	0.000319 s^{-1}	[3] [26]
$K_{D}^{PPCaM2N}$	Equilibrium binding of CaM2N to CaN	0.768 μM	[4] [26]

$k_{on}^{PPCaM2C}$	CaM2C binding to CaN	0.000123 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{PPCaM2C}$	CaM2C dissociation from CaN	0.000319 s^{-1}	[3] [26]
$K_{D}^{PPCaM2C}$	Equilibrium binding of CaM2C to CaN	2.59 μM	[4] [26]
k_{on}^{PPCaM4}	CaM4 binding to CaN	0.64 $\mu M^{-1}s^{-1}$	[9-11] [26]
k_{off}^{PPCaM4}	CaM4 dissociation from CaN	0.000319 s^{-1}	[9-11] [26]
K_{D}^{PPCaM4}	Equilibrium binding of CaM4 to CaN	0.000498 μM	[9-11] [26]
Ca^{2+} binding to CaN-CaM			
k_{on}^{PP2N}	2 Ca^{2+} binding to CaN-CaM N-terminus	100.0 $\mu M^{-1}s^{-1}$	[6] [26]
k_{off}^{PP2N}	2 Ca^{2+} dissociation from CaN-CaM N-terminus	12.0 s^{-1}	[2] [26]
K_{D}^{PP2N}	Equilibrium binding of 2 Ca^{2+} to CaN-CaM N-terminus	0.12 μM	[12] [26]
k_{on}^{PP2C}	2 Ca^{2+} binding to CaN-CaM C-terminus	4.0 $\mu M^{-1}s^{-1}$	[6] [26]
k_{off}^{PP2C}	2 Ca^{2+} dissociation from CaN-CaM C-terminus	0.6 s^{-1}	[2] [26]
K_{D}^{PP2C}	Equilibrium binding of 2 Ca^{2+} to CaN-CaM C-terminus	0.15 μM	[12] [26]
CaM binding to CaMKII			
k_{on}^{KCaM0}	CaM0 binding to CaMKII	0.0038 $\mu M^{-1}s^{-1}$	[1] [26]
k_{off}^{KCaM0}	CaM0 dissociation from CaMKII	5.5 s^{-1}	[1] [26]
K_{D}^{KCaM0}	Equilibrium binding of CaM0 to CaMKII	1.45 mM	[2] [26]
k_{on}^{KCaM2N}	CaM2N binding to CaMKII	0.12 $\mu M^{-1}s^{-1}$	[1] [26]
k_{off}^{KCaM2N}	CaM2N dissociation from CaMKII	1.7 s^{-1}	[1] [26]
K_{D}^{KCaM2N}	Equilibrium binding of CaM2N to CaMKII	14.2 μM	[1] [26]
k_{on}^{KCaM2C}	CaM2C binding to CaMKII	0.92 $\mu M^{-1}s^{-1}$	[1] [26]
k_{off}^{KCaM2C}	CaM2C dissociation from CaMKII	6.8 s^{-1}	[1] [26]
K_{D}^{KCaM2C}	Equilibrium binding of CaM2C to CaMKII	7.39 μM	[1] [26]
k_{on}^{KCaM4}	CaM4 binding to CaMKII	30.0 $\mu M^{-1}s^{-1}$	[1] [26]
k_{off}^{KCaM4}	CaM4 dissociation from CaMKII	1.7 s^{-1}	[1] [26]
K_{D}^{KCaM4}	Equilibrium binding of CaM4 to CaMKII	0.0567 μM	[1] [26]
Ca^{2+} binding to CaMKII-CaM			
k_{on}^{K2N}	2 Ca^{2+} binding to CaMKII-CaM N-terminus	76.0 $\mu M^{-1}s^{-1}$	[1] [26]
k_{off}^{K2N}	2 Ca^{2+} dissociation from CaMKII-CaM N-terminus	33.0 s^{-1}	[1] [26]
K_{D}^{K2N}	Equilibrium binding of 2 Ca^{2+} to CaMKII-CaM N-terminus	0.43 μM	[2] [26]
k_{on}^{K2C}	2 Ca^{2+} binding to CaMKII-CaM C-terminus	44.0 $\mu M^{-1}s^{-1}$	[1] [26]
k_{off}^{K2C}	2 Ca^{2+} dissociation from CaMKII-CaM C-terminus	2.7 s^{-1}	[1] [26]
K_{D}^{K2C}	Equilibrium binding of 2 Ca^{2+} to CaMKII-CaM C-terminus	0.0614 μM	[2] [26]
CaM binding to MLCK			
k_{on}^{MKCaM0}	CaM0 binding to MLCK	0.00717 $\mu M^{-1}s^{-1}$	[2] [26]
k_{off}^{MKCaM0}	CaM0 dissociation from MLCK	0.132 s^{-1}	[3] [26]
K_{D}^{MKCaM0}	Equilibrium binding of CaM0 to MLCK	18.4 μM	[4] [26]
$k_{on}^{MKCaM2N}$	CaM2N binding to MLCK	2.34 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{MKCaM2N}$	CaM2N dissociation from MLCK	0.132 s^{-1}	[3] [26]
$K_{D}^{MKCaM2N}$	Equilibrium binding of CaM2N to MLCK	0.0564 μM	[4] [26]
$k_{on}^{MKCaM2C}$	CaM2C binding to MLCK	0.170 $\mu M^{-1}s^{-1}$	[2] [26]

$k_{off}^{MKCaM2C}$	CaM2C dissociation from MLCK	0.132 s^{-1}	[3] [26]
$K_D^{MKCaM2C}$	Equilibrium binding of CaM2C to MLCK	0.776 μM	[4] [26]
k_{on}^{MKCaM4}	CaM4 binding to MLCK	55.5 $\mu M^{-1}s^{-1}$	[13-15] [26]
k_{off}^{MKCaM4}	CaM4 dissociation from MLCK	0.132 s^{-1}	[13-15] [26]
K_D^{MKCaM4}	Equilibrium binding of CaM4 to MLCK	0.00238 μM	[13-15] [26]
Ca^{2+} binding to MLCK-CaM			
k_{on}^{MK2N}	2 Ca^{2+} binding to MLCK-CaM N-terminus	100.0 $\mu M^{-1}s^{-1}$	[6] [26]
k_{off}^{MK2N}	2 Ca^{2+} dissociation from MLCK-CaM N-terminus	2.3 s^{-1}	[15-18] [26]
K_D^{MK2N}	Equilibrium binding of 2 Ca^{2+} to MLCK-CaM N-terminus	0.023 μM	[2] [26]
k_{on}^{MK2C}	2 Ca^{2+} binding to MLCK-CaM C-terminus	4.0 $\mu M^{-1}s^{-1}$	[6] [26]
k_{off}^{MK2C}	2 Ca^{2+} dissociation from MLCK-CaM C-terminus	0.39 s^{-1}	[15-18] [26]
K_D^{MK2C}	Equilibrium binding of 2 Ca^{2+} to MLCK-CaM C-terminus	0.098 μM	[2] [26]
Ca^{2+} binding to Ng-CaM			
k_{on}^{NgCaM0}	CaM0 binding to Ng	28.0 $\mu M^{-1}s^{-1}$	[19] [26]
k_{off}^{NgCaM0}	CaM0 dissociation from Ng	36.0 s^{-1}	[19] [26]
K_D^{NgCaM0}	Equilibrium binding of CaM0 to Ng	1.29 μM	[19] [26]
$k_{on}^{NgCaM2N}$	CaM2N binding to Ng	28.0 $\mu M^{-1}s^{-1}$	[19] [26]
$k_{off}^{NgCaM2N}$	CaM2N dissociation from Ng	36.0 s^{-1}	[19] [26]
$K_D^{NgCaM2N}$	Equilibrium binding of CaM2N to Ng	1.29 μM	[19] [26]
$k_{on}^{NgCaM2C}$	CaM2C binding to Ng	2.0 $\mu M^{-1}s^{-1}$	[19] [26]
$k_{off}^{NgCaM2C}$	CaM2C dissociation from Ng	136.0 s^{-1}	[19] [26]
$K_D^{NgCaM2C}$	Equilibrium binding of CaM2C to Ng	68.0 μM	[19] [26]
k_{on}^{NgCaM4}	CaM4 binding to Ng	2.0 $\mu M^{-1}s^{-1}$	[19] [26]
k_{off}^{NgCaM4}	CaM4 dissociation from Ng	136.0 s^{-1}	[19] [26]
K_D^{NgCaM4}	Equilibrium binding of CaM4 to Ng	68.0 μM	[19] [26]
Ca^{2+} binding to Ng-CaM			
k_{on}^{Ng2N}	2 Ca^{2+} binding to Ng-CaM N-terminus	100.0 $\mu M^{-1}s^{-1}$	[19] [26]
k_{off}^{Ng2N}	2 Ca^{2+} dissociation from Ng-CaM N-terminus	750.0 s^{-1}	[19] [26]
K_D^{Ng2N}	Equilibrium binding of 2 Ca^{2+} to Ng-CaM N-terminus	7.5 μM	[19] [26]
k_{on}^{Ng2C}	2 Ca^{2+} binding to Ng-CaM C-terminus	426.0 $\mu M^{-1}s^{-1}$	[19] [26]
k_{off}^{Ng2C}	2 Ca^{2+} dissociation from Ng-CaM C-terminus	418.0 s^{-1}	[19] [26]
K_D^{Ng2C}	Equilibrium binding of 2 Ca^{2+} to Ng-CaM C-terminus	0.98 μM	[19] [26]
CaM binding to NOS			
$k_{on}^{NOSCaM0}$	CaM0 binding to NOS	0.135 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{NOSCaM0}$	CaM0 dissociation from NOS	0.01 s^{-1}	[3] [26]
$K_D^{NOSCaM0}$	Equilibrium binding of CaM0 to NOS	0.074 μM	[4] [26]
$k_{on}^{NOSCaM2N}$	CaM2N binding to NOS	0.135 $\mu M^{-1}s^{-1}$	[2] [26]
$k_{off}^{NOSCaM2N}$	CaM2N dissociation from NOS	0.01 s^{-1}	[3] [26]
$K_D^{NOSCaM2N}$	Equilibrium binding of CaM2N to NOS	0.074 μM	[4] [26]
$k_{on}^{NOSCaM2C}$	CaM2C binding to NOS	1.25 $\mu M^{-1}s^{-1}$	[2] [26]

$k_{off}^{NOSCaM2C}$	CaM2C dissociation from NOS	0.01 s^{-1}	[3] [26]
$K_{D}^{NOSCaM2C}$	Equilibrium binding of CaM2C to NOS	0.008 μM	[4] [26]
$k_{on}^{NOSCaM4}$	CaM4 binding to NOS	1.25 $\mu M^{-1}s^{-1}$	[20-22] [26]
$k_{off}^{NOSCaM4}$	CaM4 dissociation from NOS	0.01 s^{-1}	[20-22] [26]
$K_{D}^{NOSCaM4}$	Equilibrium binding of CaM4 to NOS	0.008 μM	[20-24] [26]
Ca^{2+} binding to NOS-CaM			
k_{on}^{NOS2N}	2 Ca^{2+} binding to NOS-CaM N-terminus	100.0 $\mu M^{-1}s^{-1}$	[6] [26]
k_{off}^{NOS2N}	2 Ca^{2+} dissociation from NOS-CaM N-terminus	750.0 s^{-1}	[25] [26]
K_{D}^{NOS2N}	Equilibrium binding of 2nd Ca^{2+} to NOS-CaM N-terminus	7.5 μM	[2] [26]
k_{on}^{NOS2C}	2 Ca^{2+} binding to NOS-CaM C-terminus	4.0 $\mu M^{-1}s^{-1}$	[6] [26]
k_{off}^{NOS2C}	2 Ca^{2+} dissociation from NOS-CaM C-terminus	1.0 s^{-1}	[25] [26]
K_{D}^{NOS2C}	Equilibrium binding of 2 Ca^{2+} to NOS-CaM C-terminus	0.25 μM	[2] [26]
CaM binding to PDE1			
$k_{on}^{PDE1CaM0}$	CaM0 binding to PDE1	0.0000000138 $\mu M^{-1}s^{-1}$	[2]
$k_{off}^{PDE1CaM0}$	CaM0 dissociation from PDE1	0.001 s^{-1}	[3]
$K_{D}^{PDE1CaM0}$	Equilibrium binding of CaM0 to PDE1	72463.8 μM	[4]
$k_{on}^{PDE1CaM2N}$	CaM2N binding to PDE1	0.00002 $\mu M^{-1}s^{-1}$	[2]
$k_{off}^{PDE1CaM2N}$	CaM2N dissociation from PDE1	0.001 s^{-1}	[3]
$K_{D}^{PDE1CaM2N}$	Equilibrium binding of CaM2N to PDE1	50 μM	[4]
$k_{on}^{PDE1CaM2C}$	CaM2C binding to PDE1	0.00013 $\mu M^{-1}s^{-1}$	[2]
$k_{off}^{PDE1CaM2C}$	CaM2C dissociation from PDE1	0.001 s^{-1}	[3]
$K_{D}^{PDE1CaM2C}$	Equilibrium binding of CaM2C to PDE1	7.69 μM	[4]
$k_{on}^{PDE1CaM4}$	CaM4 binding to PDE1	0.18182 $\mu M^{-1}s^{-1}$	[28]
$k_{off}^{PDE1CaM4}$	CaM4 dissociation from PDE1	0.001 s^{-1}	[28]
$K_{D}^{PDE1CaM4}$	Equilibrium binding of CaM4 to PDE1	0.0055 μM	[28]
Ca^{2+} binding to PDE1-CaM			
k_{on}^{PDE12N}	2 Ca^{2+} binding to PDE1-CaM N-terminus	750.0 $\mu M^{-1}s^{-1}$	[6]
k_{off}^{PDE12N}	2 Ca^{2+} dissociation from PDE1-CaM N-terminus	25 s^{-1}	[2]
K_{D}^{PDE12N}	Equilibrium binding of 2 Ca^{2+} to PDE1-CaM N-terminus	0.033 μM	[4]
k_{on}^{PDE12C}	2 Ca^{2+} binding to PDE1-CaM C-terminus	204 $\mu M^{-1}s^{-1}$	[6]
k_{off}^{PDE12C}	2 Ca^{2+} dissociation from PDE1-CaM C-terminus	1.02 s^{-1}	[2]
K_{D}^{PDE12C}	Equilibrium binding of 2 Ca^{2+} to PDE1-CaM C-terminus	0.005 μM	[4]
CaMKII binding to CaMKII			
k_{on}^{CaMKII}	CaMKII binding to CaMKII	45 $\mu M^{-1}s^{-1}$	[1]
k_{off}^{CaMKII}	CaMKII dissociation from CaMKII	2250 s^{-1}	[1]
K_{D}^{CaMKII}	Equilibrium binding of CaMKII to CaMKII	50 μM	[1]
$k_{on}^{CaMKIIp}$	CaMKII binding pCaMKII	45 $\mu M^{-1}s^{-1}$	[1]
$k_{off}^{CaMKIIp}$	CaMKII dissociation from pCaMKII	2250 s^{-1}	[1]
$K_{D}^{CaMKIIp}$	Equilibrium binding of CaMKII to pCaMKII	50 μM	[1]
CaMKII phosphorylation			
$k_{p}^{CaMKIICaM0}$	Autophosphorylation of CaMKII-CaM0	0 s^{-1}	[1]

$k_p^{CaMKIICaM2N}$	Autophosphorylation of CaMKII-CaM2N	0.120 s^{-1}	[1]
$k_p^{CaMKIICaM2C}$	Autophosphorylation of CaMKII-CaM2C	0.064 s^{-1}	[1]
$k_p^{CaMKIICaM4}$	Autophosphorylation of CaMKII-CaM4	0.875 s^{-1}	[1]
AC1 mediated catalysis of ATP			
k_{cat}^{AC1CaM}	Catalysis of ATP by AC1-CaM0	0 s^{-1}	[27][28]
$k_{cat}^{AC1CaM2N}$	Catalysis of ATP by AC1-CaM2N	0.77897 s^{-1}	[27][28]
$k_{cat}^{AC1CaM2C}$	Catalysis of ATP by AC1-CaM2C	0.41545 s^{-1}	[27][28]
$k_{cat}^{AC1CaM4}$	Catalysis of ATP by AC1-CaM4	5.68 s^{-1}	[27][28]
AC8ct mediated catalysis of ATP			
$k_{cat}^{AC8ctCaM}$	Catalysis of ATP by AC8ct-CaM0	0 s^{-1}	[27][28]
$k_{cat}^{AC8ctCaM2N}$	Catalysis of ATP by AC8ct-CaM2N	0.3895 s^{-1}	[27][28]
$k_{cat}^{AC8ctCaM2C}$	Catalysis of ATP by AC8ct-CaM2C	0.2077 s^{-1}	[27][28]
$k_{cat}^{AC8ctCaM4}$	Catalysis of ATP by AC8ct-CaM4	2.84 s^{-1}	[27][28]
PDE1 mediated catalysis of cAMP			
$k_{cat}^{PDE1cAMP}$	Catalysis of cAMP by PDE1	11.0 s^{-1}	[28]
cAMP binding to PKA			
k_{on}^{cAMP1}	Association of first cAMP to PKA	54 $\mu M^{-1}s^{-1}$	[29]
k_{off}^{cAMP1}	Dissociation of first cAMP to PKA	33 s^{-1}	[29]
k_{on}^{cAMP2}	Association of second cAMP to PKA	54 $\mu M^{-1}s^{-1}$	[29]
k_{off}^{cAMP2}	Dissociation of second cAMP to PKA	33 s^{-1}	[29]
k_{on}^{cAMP3}	Association of third cAMP to PKA	75 $\mu M^{-1}s^{-1}$	[29]
k_{off}^{cAMP3}	Dissociation of third cAMP to PKA	110 s^{-1}	[29]
k_{on}^{cAMP4}	Association of fourth cAMP to PKA	75 $\mu M^{-1}s^{-1}$	[29]
k_{off}^{cAMP4}	Dissociation of fourth cAMP to PKA	32.05 s^{-1}	[29]
PKAc reaction pathway			
k_{split}^{PKAc}	Dissociation of PKAc from R2C2	60 s^{-1}	[29]
k_{join}^{PKAc}	Association of PKAc to R2C	18 $\mu M^{-1}s^{-1}$	[29]
$k_{on}^{PKAinhib}$	Association of PKA to PKA Inhibitor	59 $\mu M^{-1}s^{-1}$	[29]
$k_{off}^{PKAinhib}$	Dissociation of PKAc from PKA Inhibitor	1 s^{-1}	[29]
k_p^{PDE4}	PDE4 phosphorylation by PKAc	0.125 s^{-1}	[28]
PDE4 mediated catalysis of cAMP			
$k_{cat}^{cAMPPDE4}$	PDE4 mediated catalysis of cAMP	17.23 s^{-1}	[28]
$k_{cat}^{cAMPpPDE4}$	pPDE4 mediated catalysis of cAMP	34.5 s^{-1}	[28]
PKA4 binding to GluA1			
$k_{on}^{PKA4GluA1}$	PKA4 binding to GluA1	0.402 $\mu M^{-1}s^{-1}$	[27]
$k_{off}^{PKA4GluA1}$	PKA4 dissociation from GluA1	24.0 s^{-1}	[27]
$K_D^{PKA4GluA1}$	Equilibrium binding of PKA4 to GluA1	59.7 μM	[27]
GluA1 phosphorylation at s845 site by PKAc			
$k_{on}^{PKAc845}$	PKAc binding to GluA1	4.02 $\mu M^{-1}s^{-1}$	[27]
$k_{off}^{PKAc845}$	PKAc dissociation to GluA1	24.0 s^{-1}	[27]
$K_D^{PKAc845}$	Equilibrium binding of PKAc to GluA1	5.97 μM	[27]
$k_p^{PKAc845}$	Phosphorylation of s845 site by PKAc	6.0 s^{-1}	[27]
GluA1 phosphorylation at s831 by CaMKII			
$k_{on}^{CaMKII831}$	CaMKII binding to GluA1	0.02224 $\mu M^{-1}s^{-1}$	[27]
$k_{off}^{CaMKII831}$	CaMKII dissociation to GluA1	1.6 s^{-1}	[27]
$K_D^{CaMKII831}$	Equilibrium binding of CaMKII to GluA1	71.94 μM	[27]

$k_p^{CaMKII831}$	Phosphorylation of s831 site by CaMKII	0.4 s^{-1}	[27]
GluA1 phosphorylation at s831 by pCaMKII			
$k_{on}^{pCaMKII831}$	pCaMKII binding to GluA1	0.0278 $\mu M^{-1}s^{-1}$	[27]
$k_{off}^{pCaMKII831}$	pCaMKII dissociation to GluA1	2 s^{-1}	[27]
$K_D^{pCaMKII831}$	Equilibrium binding of pCaMKII to GluA1	71.94 μM	[27]
$k_p^{pCaMKII831}$	Phosphorylation of s831 site by pCaMKII	0.5 s^{-1}	[27]
PP1-CaMKII Reactions			
$k_{on}^{PP1CaMKII}$	Association of PP1 to pCaMKII	0.0006 $\mu M^{-1}s^{-1}$	[30]
$k_{off}^{PP1CaMKII}$	Dissociation of PP1 to pCaMKII	0.34 s^{-1}	[30]
$k_p^{PP1CaMKII}$	De-phosphorylation by PP1 of pCaMKII	0.086 s^{-1}	[30]
Inh-1 Reactions with PKAc and CaN			
k_{on}^{I1PKAc}	Association of Inh-1 to PKAc	1.4 $\mu M^{-1}s^{-1}$	[28]
k_{off}^{I1PKAc}	Dissociation of Inh-1 from PKAc	5.6 s^{-1}	[28]
k_p^{I1PKAc}	Phosphorylation of Inh-1 by PKAc	1.4 s^{-1}	[28]
k_{on}^{pI1PP1}	Association of PP1 to pInh-1	1 $\mu M^{-1}s^{-1}$	[28]
k_{off}^{pI1PP1}	Dissociation of PP1 from pInh-1	0.0011 s^{-1}	[28]
k_{on}^{pI1CaN}	Association of pInh-1 with CaN	2.33 $\mu M^{-1}s^{-1}$	[28]
k_{off}^{pI1CaN}	Dissociation of pInh-1 from CaN	11.2 s^{-1}	[28]
$k_p^{pI1CaNCaM2C}$	De-phosphorylation of pInh-1 by CaN-CaM2C	0.2048 s^{-1}	[28][31]
$k_p^{pI1CaNCaM2N}$	De-phosphorylation of pInh-1 by CaN-CaM2N	0.384 s^{-1}	[28][31]
$k_p^{pI1CaNCaM4}$	De-phosphorylation of pInh-1 by CaN-CaM4	2.8 s^{-1}	[28][31]
De-phosphorylation of GluA1 by PP1			
$k_{on}^{p845PP1}$	Association of PP1 with phosphor-S845	0.218 $\mu M^{-1}s^{-1}$	[28]
$k_{off}^{p845PP1}$	Dissociation of PP1 from phosphor-S845	0.17 s^{-1}	[28]
$k_p^{p845PP1}$	De-phosphorylation by PP1 at phosphor-S845	0.0425 s^{-1}	[28]
$k_{on}^{p831PP1}$	Association of PP1 with phosphor-S831	0.219 $\mu M^{-1}s^{-1}$	[28]
$k_{off}^{p831PP1}$	Dissociation of PP1 from phosphor-S831	0.35 s^{-1}	[28]
$k_p^{p831PP1}$	De-phosphorylation by PP1 at phosphor-S831	0.0875	[28]
De-phosphorylation of GluA1 by CaN			
$k_{on}^{p845CaN}$	Association of CaN with phospho-S845	2.01 $\mu M^{-1}s^{-1}$	[28]
$k_{off}^{p845CaN}$	Dissociation of CaN from phospho-S845	8 s^{-1}	[28]
$k_p^{p831CaNCaM2C}$	De-phosphorylation of pS845 by CaN-CaM2C	0.274 s^{-1}	[28][31]
$k_p^{p831CaNCaM2N}$	De-phosphorylation of pS845 by CaN-CaM2N	0.146 s^{-1}	[28][31]
$k_p^{p831CaNCaM4}$	De-phosphorylation of pS845 by CaN-CaM4	2 s^{-1}	[28][31]
Initial Concentrations			
$[Ca^{2+}]_{t=0}$	Initial concentration of Ca^{2+}	0.005 μM	[26]
$[CaM]_{t=0}$	Initial concentration of CaM	33 μM	[26]
$[AC1]_{t=0}$	Initial concentration of AC1	42 μM	[26]
$[AC8nt]_{t=0}$	Initial concentration of AC8nt	42 μM	[26]
$[AC8ct]_{t=0}$	Initial concentration of AC8ct	42 μM	[26]
$[CaN]_{t=0}$	Initial concentration of CaN	0.5 μM	[26]
$[CaMKII]_{t=0}$	Initial concentration of CaMKII	74 μM	[26]

$[MLCK]_{t=0}$	Initial concentration of MLCK	5 μM	[26]
$[Ng]_{t=0}$	Initial concentration of Ng	52 μM	[26]
$[NOS]_{t=0}$	Initial concentration of NOS	1 μM	[26]
$[PDE1]_{t=0}$	Initial concentration of PDE1	2.25 μM	[28][32]
$[PDE4]_{t=0}$	Initial concentration of PDE4	3 μM	[28]
$[PP1]_{t=0}$	Initial concentration of ATP	1.47 μM	[28][30]
$[Inh\text{-}1]_{t=0}$	Initial concentration of AMP	1.422 μM	[28][29]
$[PKA]_{t=0}$	Initial concentration of PKA	2.2 μM	[28][29]
$[PKA\ Inhib]_{t=0}$	Initial concentration of PKA Inhibitor	0.259 μM	[29]
$[GluA1]_{t=0}$	Initial concentration of GluA1	11.6 μM	[27]

References:

[1] S. Pepke et al., "A Dynamic Model of Interactions of Ca^{2+}, Calmodulin, and Catalytic Subunits of Ca^{2+}/Calmodulin-Dependent Protein Kinase II," *PLoS Comput. Biol.*, vol. 6, no. 2, p. e1000675, 2010.

[2] Calculated from the relationship $K_D = \frac{k_{off}}{k_{on}}$

[3] Assume that Ca^{2+} binding does not affect the rate of protein dissociation from CaM

[4] Calculated from the thermodynamic principle of microscopic reversibility

[5] M. Kim et al., "Colocalization of Protein Kinase A with Adenylyl Cyclase Enhances Protein Kinase A Activity during Long-Lasting Long-Term-Potentiation," *PLoS Comput. Biol.*, vol. 7, no. 6, p. e1002084, 2011.

[6] Assume that protein binding does not affect the rate of Ca^{2+} association to CaM

[7] Assume that protein binding does not affect the fast dissociation rate(s) of Ca^{2+} from CaM

[8] N. Masada et al., "Distinct Mechanisms of Calmodulin Binding and Regulation of Adenylyl Cyclases 1 and 8," *Biochem.*, vol. 51, no. 40, pp. 7917-7929, 2012.

[9] A.R. Quintana et al., "Kinetics of calmodulin binding to calcineurin," *BBRC*, vol. 334, pp. 674-680, 2005.

[10] M.J. Hubbard and C.B. Klee, "Calmodulin Binding by Calcineurin," *J. Biol. Chem.*, vol. 262, no. 31, pp. 15062-15070, 1987.

[11] E. Takano, M. Hatanaka, and M. Maki, "Real-time analysis of the calcium-dependent interaction between calmodulin and a synthetic oligopeptide of calcineurin by a surface plasmon resonance biosensor," *FEBS Letters*, vol. 352, pp. 247-250, 1994.*

[12] P.M. Stemmer and C.B. Klee, "Dual Calcium Ion Regulation of Calcineurin by Calmodulin and Calcineurin B," *Biochem.*, vol. 33, pp. 6859-6866, 1994.

[13] K. Torok and D.R. Trentham, "Mechanism of 2-Chloro-(ε-amino-Lys_{75})-[6-[4-(N,N-diethylamino)phenyl]-1,3,5-triazin-4-yl]calmodulin Interactions with Smooth Muscle Myosin Light Chain Kinase and Derived Peptides," *Biochem.*, vol. 33, pp. 12807-12820, 1994.

[14] R. Kasturi, C. Vasulka, and J.D. Johnson, "Ca^{2+}, Caldesmon, and Myosin Light Chain Kinase Exchange with Calmodulin," *J. Biol. Chem.*, vol. 268, pp. 7958-7964, 1993.

[15] M.C. Potier et al., "The Human Myosin Light Chain Kinase (MLCK) from Hippocampus: Cloning, Sequencing, Expression, and Localization to 3qcen-q21," *Genomics*, vol. 29, no. 3, pp. 562-570, 1995.†

[17] J.D. Johnson et al., "Effects of Myosin Light Chain Kinase and Peptides on Ca^{2+} Exchange with the N- and C-terminal Ca^{2+} Binding Sites of Calmodulin," *J. Biol. Chem.*, pp. 761-767, 1996.

[18] O.B. Peersen, T.S. Madsen, and J.J. Falke, "Intermolecular tuning of calmodulin by target peptides and proteins: Differential effects of Ca^{2+} binding and implications for kinase activation," *Protein Sci.*, vol. 6, pp. 794-807, 1997.*

[19] Y. Kubota, J. Putkey, and M. Waxham, "Neurogranin Controls the Spatiotemporal Pattern of Postsynaptic Ca^{2+}/CaM signaling," *Biophys. J.*, vol. 93, pp. 3848-3859, 2007.

[20] J.L. McMurry et al., "Rate, Affinity and Calcium Dependence of Nitric Oxide Synthase Isoform Binding to the Primary Physiological Regulator Calmodulin," *FEBS J.*, vol. 278, pp. 4943-4954, 2011.

[21] G. Wu, V. Berka, and A. Tsai, "Binding Kinetics of Calmodulin with Target Peptides of Three Nitric Oxide Synthase Isozymes," *J. Inorg. Biochem.*, vol. 105, pp. 1226-1237, 2011.*

[22] M. Zoche et al., "Distinct Molecular Recognition of Calmodulin-Binding Sites in the Neuronal and Macrophage Nitric Oxide Synthases: A Surface Plasmon Resonance Study," *Biochem.*, vol. 35, pp. 8742-8747, 1996.*

[23] E.A. Sheta, K. McMillan, and B.S. Siler Masters, "Evidence for a Bidomain Structure of Constitutive Cerebellar Nitric Oxide Synthase," *J. Biol. Chem.*, vol. 269, no. 21, pp. 15147-15153, 1994.

[24] B.A. Weissman et al., "Activation and Inactivation of Neuronal Nitric Oxide Synthase: Characterization of Ca^{2+}-dependent [^{125}I]Calmodulin Binding," *Eur. J. Pharm.*, vol. 435, pp. 9-18, 2002.

[25] A. Persechini, H.D. White, and K.J. Gansz, "Different Mechanisms for Ca^{2+} Dissociation from Complexes of Calmodulin with Nitric Oxide Synthase or Myosin Light Chain Kinase," *J. Biol. Chem.*, vol. 271, no. 1, pp. 62-67, 1996.

[26] Romano DR, Pharris MC, Patel NM, Kinzer-Ursem TL. "Competitive tuning: Competition's role in setting the frequency-dependence of Ca2+-dependent proteins." PloS Comp Biol, vol. 13, 2017.

[27] Oliveira RF, Kim M, Blackwell KT. Subcellular Location of PKA Controls Striatal Plasticity: Stochastic Simulations in Spiny Dendrites. PLoS Comp Biol, vol. 8, 2012.

[28] Chay A, Zamparo I, Koschinski A, Zaccolo M, Blackwell KT. "Control of beta AR- and N-methyl-D-aspartate (NMDA) Receptor-Dependent cAMP Dynamics in Hippocampal Neurons." PloS Comp Biol, vol. 12, 2016.

[29] Hao HP, Zak DE, Sauter T, Schwaber J, Ogunnaike BA. Modeling the VPAC(2)-activated cAMP/PKA signaling pathway: From receptor to circadian clock gene induction. Biophysical Journal. 2006;90(5):1560-71. doi: 10.1529/biophysj.105.065250. PubMed PMID: WOS:000235235600010.

[30] Zhabotinsky AM, Camp RN, Epstein IR, Lisman JE. Role of the neurogranin concentrated in spines in the induction of long-term potentiation. Journal of Neuroscience. 2006;26(28):7337-47. doi: 10.1523/jneurosci.0729-06.2006. PubMed PMID: WOS:000238987700003

[31] Assume that CaM-dependent catalysis depends on Ca^{2+}/CaM state.

[32] Antunes G, Roque AC, de Souza FMS. Modelling intracellular competition for calcium: kinetic and thermodynamic control of different molecular modes of signal decoding. Scientific Reports. 2016;6:12. doi: 10.1038/srep23730. PubMed PMID: WOS:000373324800001.

*Not used in calculating average value because study used oligopeptide instead of protein
†Used to establish equivalence of smooth muscle and hippocampal MLCK

‡Used to select rates of MLCK association to and dissociation from $Ca^{2+}{}_4CaM$
§Used to select rates of Ca^{2+} dissociation from NOS-CaM

Model Equations

[AC1]`[t] ==

koffAC1CaM0 AC1CaM00[t] + koffAC1CaM2C AC1CaM2C[t] + koffAC1CaM2N AC1CaM2N[t] + koffAC1CaM4 AC1CaM2N2C[t] - konAC1CaM0 AC1[t] CaM00[t] - konAC1CaM2C AC1[t] CaM2C[t] - konAC1CaM2N AC1[t] CaM2N[t] - konAC1CaM4 AC1[t] CaM2N2C[t],

[AC1CaM00]`[t] ==

-koffAC1CaM0 AC1CaM00[t] + koffAC1C AC1CaM2C[t] + koffAC1N AC1CaM2N[t] - konAC1C AC1CaM00[t] Ca[t]^2 - konAC1N AC1CaM00[t] Ca[t]^2 + konAC1CaM0 AC1[t] CaM00[t],

[AC1CaM2C]`[t] ==

-koffAC1C AC1CaM2C[t] - koffAC1CaM2C AC1CaM2C[t] + koffAC1N AC1CaM2N2C[t] + konAC1C AC1CaM00[t] Ca[t]^2 - konAC1N AC1CaM2C[t] Ca[t]^2 + konAC1CaM2C AC1[t] CaM2C[t],

[AC1CaM2N]`[t] ==

-koffAC1CaM2N AC1CaM2N[t] - koffAC1N AC1CaM2N[t] + koffAC1C AC1CaM2N2C[t] + konAC1N AC1CaM00[t] Ca[t]^2 - konAC1C AC1CaM2N[t] Ca[t]^2 + konAC1CaM2N AC1[t] CaM2N[t],

[AC1CaM2N2C]`[t] ==

-koffAC1C AC1CaM2N2C[t] - koffAC1CaM4 AC1CaM2N2C[t] - koffAC1N AC1CaM2N2C[t] + konAC1N AC1CaM2C[t] Ca[t]^2 + konAC1C AC1CaM2N[t] Ca[t]^2 + konAC1CaM4 AC1[t] CaM2N2C[t],

[AC8ct]`[t] ==

koffAC8ctCaM0 AC8ctCaM00[t] + koffAC8ctCaM2C AC8ctCaM2C[t] + koffAC8ctCaM2N AC8ctCaM2N[t] + koffAC8ctCaM4 AC8ctCaM2N2C[t] - konAC8ctCaM0 AC8ct[t] CaM00[t] - konAC8ctCaM2C AC8ct[t] CaM2C[t] - konAC8ctCaM2N AC8ct[t] CaM2N[t] - konAC8ctCaM4 AC8ct[t] CaM2N2C[t],

[AC8ctCaM00]`[t] ==

-koffAC8ctCaM0 AC8ctCaM00[t] + koffAC8ctC AC8ctCaM2C[t] + koffAC8ctN AC8ctCaM2N[t] -

konAC8ctC AC8ctCaM00[t] Ca[t]^2 - konAC8ctN AC8ctCaM00[t] Ca[t]^2 + konAC8ctCaM0 AC8ct[t] CaM00[t],

[AC8ctCaM2C]`[t] == koffAC8ctC AC8ctCaM2C[t] - koffAC8ctCaM2C AC8ctCaM2C[t] + koffAC8ctN AC8ctCaM2N2C[t] +

konAC8ctC AC8ctCaM00[t] Ca[t]^2 - konAC8ctN AC8ctCaM2C[t] Ca[t]^2 + konAC8ctCaM2C AC8ct[t] CaM2C[t],

[AC8ctCaM2N]`[t] == -koffAC8ctCaM2N AC8ctCaM2N[t] - koffAC8ctN AC8ctCaM2N[t] + koffAC8ctC AC8ctCaM2N2C[t] +

konAC8ctN AC8ctCaM00[t] Ca[t]^2 - konAC8ctC AC8ctCaM2N[t] Ca[t]^2 + konAC8ctCaM2N AC8ct[t] CaM2N[t],

[AC8ctCaM2N2C]`[t] ==

-koffAC8ctC AC8ctCaM2N2C[t] - koffAC8ctCaM4 AC8ctCaM2N2C[t] - koffAC8ctN AC8ctCaM2N2C[t] + konAC8ctN AC8ctCaM2C[t] Ca[t]^2 + konAC8ctC AC8ctCaM2N[t] Ca[t]^2 + konAC8ctCaM4 AC8ct[t] CaM2N2C[t],

[AC8nt]`[t] ==

koffAC8ntCaM0 AC8ntCaM00[t] + koffAC8ntCaM2C AC8ntCaM2C[t] + koffAC8ntCaM2N AC8ntCaM2N[t] + koffAC8ntCaM4 AC8ntCaM2N2C[t] - konAC8ntCaM0 AC8nt[t] CaM00[t] - konAC8ntCaM2C AC8nt[t] CaM2C[t] -

konAC8ntCaM2N AC8nt[t] CaM2N[t] - konAC8ntCaM4 AC8nt[t] CaM2N2C[t],

[AC8ntCaM00]`[t] ==

-koffAC8ntCaM0 AC8ntCaM00[t] + koffAC8ntC AC8ntCaM2C[t] + koffAC8ntN AC8ntCaM2N[t] - konAC8ntC AC8ntCaM00[t] Ca[t]^2 - konAC8ntN AC8ntCaM00[t] Ca[t]^2 + konAC8ntCaM0 AC8nt[t] CaM00[t],

[AC8ntCaM2C]`[t] ==

-koffAC8ntC AC8ntCaM2C[t] - koffAC8ntCaM2C AC8ntCaM2C[t] + koffAC8ntN AC8ntCaM2N2C[t] +

konAC8ntC AC8ntCaM00[t] Ca[t]^2 - konAC8ntN AC8ntCaM2C[t] Ca[t]^2 + konAC8ntCaM2C AC8nt[t] CaM2C[t], [AC8ntCaM2N]`[t] ==

-koffAC8ntCaM2N AC8ntCaM2N[t] - koffAC8ntN AC8ntCaM2N[t] + koffAC8ntC AC8ntCaM2N2C[t] +

konAC8ntN AC8ntCaM00[t] Ca[t]^2 - konAC8ntC AC8ntCaM2N[t] Ca[t]^2 + konAC8ntCaM2N AC8nt[t] CaM2N[t],

[AC8ntCaM2N2C]`[t] ==

-koffAC8ntC AC8ntCaM2N2C[t] - koffAC8ntCaM4 AC8ntCaM2N2C[t] - koffAC8ntN AC8ntCaM2N2C[t] +

konAC8ntN AC8ntCaM2C[t] Ca[t]^2 + konAC8ntC AC8ntCaM2N[t] Ca[t]^2 + konAC8ntCaM4 AC8nt[t] CaM2N2C[t],

[AMP]`[t] == 4 koffR2cAMP R2cAMP4[t],

[CaM00]`[t] ==

koffAC1CaM0 AC1CaM00[t] + koffAC8ctCaM0 AC8ctCaM00[t] + koffAC8ntCaM0 AC8ntCaM00[t] - konAC1CaM0 AC1[t] CaM00[t] - konAC8ctCaM0 AC8ct[t] CaM00[t] - konAC8ntCaM0 AC8nt[t] CaM00[t] - konC Ca[t]^2 CaM00[t] - konN Ca[t]^2 CaM00[t] + koffC CaM2C[t] + koffN CaM2N[t] - konKCaM0 CaM00[t] CaMKII[t] + koffKCaM0 CaMKIICaM00[t] - konPPCaM0 CaM00[t] CaN[t] + koffPPCaM0 CaNCaM00[t] - konMKCaM0 CaM00[t] MLCK[t] + koffMKCaM0 MLCKCaM00[t] - konNgCaM0 CaM00[t] Ng[t] + koffNgCaM0 NgCaM00[t] - konNOSCaM0 CaM00[t] NOS[t] + koffNOSCaM0 NOSCaM00[t] - 100 konKCaM0 CaM00[t] pCaMKII[t] + koffKCaM0 pCaMKII00[t] - konPDE1CaM0 CaM00[t] PDE1[t] + koffPDE1CaM0 PDE1CaM00[t],

[CaM2C]`[t] ==

koffAC1CaM2C AC1CaM2C[t] + koffAC8ctCaM2C AC8ctCaM2C[t] + koffAC8ntCaM2C AC8ntCaM2C[t] + konC Ca[t]^2 CaM00[t] - koffC CaM2C[t] - konAC1CaM2C AC1[t] CaM2C[t] - konAC8ctCaM2C AC8ct[t] CaM2C[t] - konAC8ntCaM2C AC8nt[t] CaM2C[t] - konN Ca[t]^2 CaM2C[t] + koffN CaM2N2C[t] - konKCaM2C CaM2C[t] CaMKII[t] + koffKCaM2C CaMKIICaM2C[t] - konPPCaM2C CaM2C[t] CaN[t] + koffPPCaM2C CaNCaM2C[t] - konMKCaM2C CaM2C[t] MLCK[t] + koffMKCaM2C MLCKCaM2C[t] - konNgCaM2C CaM2C[t] Ng[t] + koffNgCaM2C NgCaM2C[t] - konNOSCaM2C CaM2C[t] NOS[t] + koffNOSCaM2C NOSCaM2C[t] - 100 konKCaM2C CaM2C[t] pCaMKII[t] + koffKCaM2C pCaMKII2C[t] -

konPDE1CaM2C CaM2C[t] PDE1[t] + koffPDE1CaM2C PDE1CaM2C[t],

[CaM2N]`[t] ==

koffAC1CaM2N AC1CaM2N[t] + koffAC8ctCaM2N AC8ctCaM2N[t] + koffAC8ntCaM2N AC8ntCaM2N[t] + konN Ca[t]^2 CaM00[t] - koffN CaM2N[t] - konAC1CaM2N AC1[t] CaM2N[t] - konAC8ctCaM2N AC8ct[t] CaM2N[t] - konAC8ntCaM2N AC8nt[t] CaM2N[t] - konC Ca[t]^2 CaM2N[t] + koffC CaM2N2C[t] - konKCaM2N CaM2N[t] CaMKII[t] + koffKCaM2N CaMKIICaM2N[t] - konPPCaM2N CaM2N[t] CaN[t] + koffPPCaM2N CaNCaM2N[t] - konMKCaM2N CaM2N[t] MLCK[t] + koffMKCaM2N MLCKCaM2N[t] - konNgCaM2N CaM2N[t] Ng[t] + koffNgCaM2N NgCaM2N[t] - konNOSCaM2N CaM2N[t] NOS[t] + koffNOSCaM2N NOSCaM2N[t] - 100 konKCaM2N CaM2N[t] pCaMKII[t] + koffKCaM2N pCaMKII2N[t] - konPDE1CaM2N CaM2N[t] PDE1[t] + koffPDE1CaM2N PDE1CaM2N[t],

[CaM2N2C]`[t] ==

koffAC1CaM4 AC1CaM2N2C[t] + koffAC8ctCaM4 AC8ctCaM2N2C[t] + koffAC8ntCaM4 AC8ntCaM2N2C[t] + konN Ca[t]^2 CaM2C[t] + konC Ca[t]^2 CaM2N[t] - koffC CaM2N2C[t] - koffN CaM2N2C[t] - konAC1CaM4 AC1[t] CaM2N2C[t] - konAC8ctCaM4 AC8ct[t] CaM2N2C[t] - konAC8ntCaM4 AC8nt[t] CaM2N2C[t] - konKCaM4 CaM2N2C[t] CaMKII[t] + koffKCaM4 CaMKIICaM2N2C[t] - konPPCaM4 CaM2N2C[t] CaN[t] + koffPPCaM4 CaNCaM2N2C[t] - konMKCaM4 CaM2N2C[t] MLCK[t] + koffMKCaM4 MLCKCaM2N2C[t] - konNgCaM4 CaM2N2C[t] Ng[t] + koffNgCaM4 NgCaM2N2C[t] - konNOSCaM4 CaM2N2C[t] NOS[t] + koffNOSCaM4 NOSCaM2N2C[t] - 100 konKCaM4 CaM2N2C[t] pCaMKII[t] + koffKCaM4 pCaMKII2N2C[t] - konPDE1CaM4 CaM2N2C[t] PDE1[t] + koffPDE1CaM4 PDE1CaM2N2C[t],

[CaMKII]`[t] ==

-konKCaM0 CaM00[t] CaMKII[t] - konKCaM2C CaM2C[t] CaMKII[t] - konKCaM2N CaM2N[t] CaMKII[t] - konKCaM4 CaM2N2C[t] CaMKII[t] + koffKCaM0 CaMKIICaM00[t] + koffKCaM2C CaMKIICaM2C[t] + koffKCaM2N CaMKIICaM2N[t] + koffKCaM4 CaMKIICaM2N2C[t] + kdpCaMKII PP1pCaMKII[t],

[CaMKIICaM00]`[t] ==

konKCaM0 CaM00[t] CaMKII[t] - koffKCaM0 CaMKIICaM00[t] - konKC Ca[t]^2 CaMKIICaM00[t] - konKN Ca[t]^2 CaMKIICaM00[t] - 2 konCaMKII CaMKIICaM00[t]^2 + koffKC CaMKIICaM2C[t] - 2 konCaMKII CaMKIICaM00[t] CaMKIICaM2C[t] + koffKN CaMKIICaM2N[t] - 2 konCaMKII CaMKIICaM00[t] CaMKIICaM2N[t] - 2 konCaMKII CaMKIICaM00[t] CaMKIICaM2N2C[t] + 2 koffCaMKII Dimer00w00[t] + kPCaM0 Dimer00w00[t] + koffCaMKII imer00w2C[t] + koffCaMKII Dimer00w2N[t] + koffCaMKII Dimer00w2N2C[t] + koffCaMKII Dimer2Cw00[t] + kPCaM2C

Dimer2Cw00[t] + koffCaMKII Dimer2N2Cw00[t] + kPCaM4 Dimer2N2Cw00[t] + koffCaMKII Dimer2Nw00[t] + kPCaM2N Dimer2Nw00[t] + koffCaMKIIP Dimerp00w00[t] + koffCaMKIIP Dimerp2Cw00[t] + koffCaMKIIP Dimerp2N2Cw00[t] + koffCaMKIIP Dimerp2Nw00[t] - konCaMKIIGluA1 CaMKIICaM00[t] GluA1[t] + kcatKCaM00GluA1p831 GluA1CaMKII00[t] + koffCaMKIIGluA1 GluA1CaMKII00[t] - konCaMKIIGluA1 CaMKIICaM00[t] GluA1p845[t] + kcatKCaM00GluA1p831 845CaMKII00[t] + koffCaMKIIGluA1 p845CaMKII00[t] - konCaMKIIP CaMKIICaM00[t] pCaMKII00[t] - konCaMKIIP CaMKIICaM00[t] pCaMKII2C[t] - konCaMKIIP CaMKIICaM00[t] pCaMKII2N[t] - konCaMKIIP CaMKIICaM00[t] CaMKII2N2C[t] + kdpCaMKII PP1pCaMKII00[t],

[CaMKIICaM2C]`[t] ==

konKCaM2C CaM2C[t] CaMKII[t] + konKC Ca[t]^2 CaMKIICaM00[t] - koffKC CaMKIICaM2C[t] - koffKCaM2C CaMKIICaM2C[t] - konKN Ca[t]^2 CaMKIICaM2C[t] - 2 konCaMKII CaMKIICaM00[t] CaMKIICaM2C[t] - 2 konCaMKII CaMKIICaM2C[t]^2 - 2 konCaMKII CaMKIICaM2C[t] CaMKIICaM2N[t] + koffKN CaMKIICaM2N2C[t] - 2 konCaMKII CaMKIICaM2C[t] CaMKIICaM2N2C[t] + koffCaMKII Dimer00w2C[t] + kPCaM0 Dimer00w2C[t] + koffCaMKII Dimer2Cw00[t] + 2 koffCaMKII Dimer2Cw2C[t] + kPCaM2C Dimer2Cw2C[t] + koffCaMKII Dimer2Cw2N[t] + koffCaMKII Dimer2Cw2N2C[t] + koffCaMKII Dimer2N2Cw2C[t] + kPCaM4 Dimer2N2Cw2C[t] + koffCaMKII Dimer2Nw2C[t] + kPCaM2N Dimer2Nw2C[t] + koffCaMKIIP Dimerp00w2C[t] + koffCaMKIIP Dimerp2Cw2C[t] + koffCaMKIIP Dimerp2N2Cw2C[t] + koffCaMKIIP Dimerp2Nw2C[t] - konCaMKIIGluA1 CaMKIICaM2C[t] GluA1[t] + kcatKCaM2CGluA1p831 GluA1CaMKII2C[t] + koffCaMKIIGluA1 GluA1CaMKII2C[t] - konCaMKIIGluA1 CaMKIICaM2C[t] GluA1p845[t] + kcatKCaM2CGluA1p831 p845CaMKII2C[t] + koffCaMKIIGluA1 p845CaMKII2C[t] - konCaMKIIP CaMKIICaM2C[t] pCaMKII00[t] -konCaMKIIP CaMKIICaM2C[t] pCaMKII2C[t] - konCaMKIIP CaMKIICaM2C[t] pCaMKII2N[t] - konCaMKIIP CaMKIICaM2C[t] pCaMKII2N2C[t] + kdpCaMKII P1pCaMKII2C[t],

[CaMKIICaM2N]`[t] ==

konKCaM2N CaM2N[t] CaMKII[t] + konKN Ca[t]^2 CaMKIICaM00[t] - koffKCaM2N CaMKIICaM2N[t] - koffKN CaMKIICaM2N[t] - konKC Ca[t]^2 CaMKIICaM2N[t] - 2 konCaMKII CaMKIICaM00[t] CaMKIICaM2N[t] - 2 konCaMKII CaMKIICaM2C[t] CaMKIICaM2N[t] - 2 konCaMKII CaMKIICaM2N[t]^2 + koffKC CaMKIICaM2N2C[t] - 2 konCaMKII CaMKIICaM2N[t] CaMKIICaM2N2C[t] + koffCaMKII Dimer00w2N[t] + kPCaM0 Dimer00w2N[t] + koffCaMKII Dimer2Cw2N[t] + kPCaM2C Dimer2Cw2N[t] + koffCaMKII Dimer2N2Cw2N[t] + kPCaM4 Dimer2N2Cw2N[t] + koffCaMKII Dimer2Nw00[t] + koffCaMKII Dimer2Nw2C[t] + 2 koffCaMKII Dimer2Nw2N[t] + kPCaM2N Dimer2Nw2N[t] + koffCaMKII Dimer2Nw2N2C[t] + koffCaMKIIP Dimerp00w2N[t] + koffCaMKIIP Dimerp2Cw2N[t] + koffCaMKIIP Dimerp2N2Cw2N[t] + koffCaMKIIP Dimerp2Nw2N[t] - konCaMKIIGluA1 CaMKIICaM2N[t] GluA1[t] + kcatKCaM2NGluA1p831 GluA1CaMKII2N[t] + koffCaMKIIGluA1 GluA1CaMKII2N[t] - konCaMKIIGluA1 CaMKIICaM2N[t] GluA1p845[t] + kcatKCaM2NGluA1p831 p845CaMKII2N[t] + koffCaMKIIGluA1 p845CaMKII2N[t] - konCaMKIIP CaMKIICaM2N[t] CaMKII00[t] - konCaMKIIP CaMKIICaM2N[t] pCaMKII2C[t] - konCaMKIIP CaMKIICaM2N[t] pCaMKII2N[t] - konCaMKIIP CaMKIICaM2N[t] pCaMKII2N2C[t] + kdpCaMKII PP1pCaMKII2N[t],

[CaMKIICaM2N2C]`[t] ==

konKCaM4 CaM2N2C[t] CaMKII[t] + konKN Ca[t]^2 CaMKIICaM2C[t] + konKC Ca[t]^2 CaMKIICaM2N[t] - koffKC CaMKIICaM2N2C[t] - koffKCaM4 CaMKIICaM2N2C[t] - koffKN CaMKIICaM2N2C[t] - 2 konCaMKII CaMKIICaM00[t] CaMKIICaM2N2C[t] - 2 konCaMKII CaMKIICaM2C[t] CaMKIICaM2N2C[t] - 2 konCaMKII CaMKIICaM2N[t] CaMKIICaM2N2C[t] - 2 konCaMKII CaMKIICaM2N2C[t]^2 + koffCaMKII Dimer00w2N2C[t] + kPCaM0 Dimer00w2N2C[t] + koffCaMKII Dimer2Cw2N2C[t] + kPCaM2C Dimer2Cw2N2C[t] + koffCaMKII Dimer2N2Cw00[t] + koffCaMKII imer2N2Cw2C[t] + koffCaMKII Dimer2N2Cw2N[t] + 2 koffCaMKII Dimer2N2Cw2N2C[t] + kPCaM4 Dimer2N2Cw2N2C[t] + koffCaMKII Dimer2Nw2N2C[t] + kPCaM2N Dimer2Nw2N2C[t] + koffCaMKIIP Dimerp00w2N2C[t] + koffCaMKIIP Dimerp2Cw2N2C[t] + koffCaMKIIP Dimerp2N2Cw2N2C[t] + koffCaMKIIP Dimerp2Nw2N2C[t] - konCaMKIIGluA1 aMKIICaM2N2C[t] GluA1[t] + kcatKCaM4GluA1p831 GluA1CaMKII2N2C[t] + koffCaMKIIGluA1 GluA1CaMKII2N2C[t] - konCaMKIIGluA1 CaMKIICaM2N2C[t] GluA1p845[t] + kcatKCaM4GluA1p831 p845CaMKII2N2C[t] + koffCaMKIIGluA1 p845CaMKII2N2C[t] - konCaMKIIP CaMKIICaM2N2C[t] pCaMKII00[t] - konCaMKIIP CaMKIICaM2N2C[t] pCaMKII2C[t] - konCaMKIIP CaMKIICaM2N2C[t] pCaMKII2N[t] - konCaMKIIP CaMKIICaM2N2C[t] pCaMKII2N2C[t] + kdpCaMKII PP1pCaMKII2N2C[t],

[CaN]`[t] ==

-konPPCaM0 CaM00[t] CaN[t] - konPPCaM2C CaM2C[t] CaN[t] - konPPCaM2N CaM2N[t] CaN[t] - konPPCaM4 CaM2N2C[t] CaN[t] + koffPPCaM0 CaNCaM00[t] + koffPPCaM2C CaNCaM2C[t] + koffPPCaM2N CaNCaM2N[t] + koffPPCaM4 CaNCaM2N2C[t],

[CaNCaM00]`[t] ==

konPPCaM0 CaM00[t] CaN[t] - koffPPCaM0 CaNCaM00[t] - konPPC Ca[t]^2 CaNCaM00[t] - konPPN Ca[t]^2 CaNCaM00[t] + koffPPC CaNCaM2C[t] + koffPPN CaNCaM2N[t] - konCaNp845 CaNCaM00[t] GluA1p845[t] -

konIp35CaN CaNCaM00[t] Ip35[t] + kdpIp35PP1CaNCaM00 Ip35CaN00[t] + koffIp35CaN Ip35CaN00[t] + kcatCaNCaM00p845 p845CaNCaM00[t] + koffCaNp845 p845CaNCaM00[t],

[CaNCaM2C]`[t] ==

konPPCaM2C CaM2C[t] CaN[t] + konPPC Ca[t]^2 CaNCaM00[t] - koffPPC CaNCaM2C[t] - koffPPCaM2C CaNCaM2C[t] - konPPN Ca[t]^2 CaNCaM2C[t] + koffPPN CaNCaM2N2C[t] - konCaNp845 CaNCaM2C[t] GluA1p845[t] - konIp35CaN CaNCaM2C[t] Ip35[t] + kdpIp35PP1CaNCaM2C Ip35CaN2C[t] + koffIp35CaN Ip35CaN2C[t] + kcatCaNCaM2Cp845 p845CaNCaM2C[t] + koffCaNp845 p845CaNCaM2C[t],

[CaNCaM2N]`[t] ==

konPPCaM2N CaM2N[t] CaN[t] + konPPN Ca[t]^2 CaNCaM00[t] - koffPPCaM2N CaNCaM2N[t] - koffPPN CaNCaM2N[t] - konPPC Ca[t]^2 CaNCaM2N[t] + koffPPC CaNCaM2N2C[t] - konCaNp845 CaNCaM2N[t] GluA1p845[t] - konIp35CaN CaNCaM2N[t] Ip35[t] + kdpIp35PP1CaNCaM2N Ip35CaN2N[t] + koffIp35CaN Ip35CaN2N[t] + kcatCaNCaM2Np845 p845CaNCaM2N[t] + koffCaNp845 p845CaNCaM2N[t],

[CaNCaM2N2C]`[t] ==

konPPCaM4 CaM2N2C[t] CaN[t] + konPPN Ca[t]^2 CaNCaM2C[t] + konPPC Ca[t]^2 CaNCaM2N[t] - koffPPC CaNCaM2N2C[t] - koffPPCaM4 CaNCaM2N2C[t] - koffPPN CaNCaM2N2C[t] - konCaNp845 CaNCaM2N2C[t] GluA1p845[t] - konIp35CaN CaNCaM2N2C[t] Ip35[t] + kdpIp35PP1CaNCaM4 Ip35CaN2N2C[t] + koffIp35CaN Ip35CaN2N2C[t] + kcatCaNCaM4p845 p845CaNCaM2N2C[t] + koffCaNp845 p845CaNCaM2N2C[t],

[cycAMP]`[t] ==

kATPcatAC1CaM00 AC1CaM00[t] + kATPcatAC1CaM2C AC1CaM2C[t] + kATPcatAC1CaM2N AC1CaM2N[t] + kATPcatAC1CaM4 AC1CaM2N2C[t] + kATPcatAC8ctCaM00 AC8ctCaM00[t] + kATPcatAC8ctCaM2C AC8ctCaM2C[t] + kATPcatAC8ctCaM2N AC8ctCaM2N[t] + kATPcatAC8ctCaM4 AC8ctCaM2N2C[t] - kcatPDE1CaM2C cycAMP[t] PDE1CaM2C[t] - kcatPDE1CaM2N cycAMP[t] PDE1CaM2N[t] - kcatPDE1CaM4 cycAMP[t] PDE1CaM2N2C[t] - kcatPDE4cAMP cycAMP[t] PDE4[t] - kcatpPDE4cAMP cycAMP[t] pPDE4[t] - koncAMP1 cycAMP[t] R2C2[t] + koffcAMP1 R2C2cAMP[t] - koncAMP2 cycAMP[t] R2C2cAMP[t] + koffcAMP2 R2C2cAMP2[t] - koncAMP3 cycAMP[t] R2C2cAMP2[t] + koffcAMP3 R2C2cAMP3[t] - koncAMP4 cycAMP[t] R2C2cAMP3[t] + koffcAMP4 R2C2cAMP4[t],

[Dimer00w00]`[t] ==

konCaMKII CaMKIICaM00[t]^2 - koffCaMKII Dimer00w00[t] - kPCaM0 Dimer00w00[t],

[Dimer00w2C]`[t] ==

konCaMKII CaMKIICaM00[t] CaMKIICaM2C[t] - koffCaMKII Dimer00w2C[t] - kPCaM0 Dimer00w2C[t],

[Dimer00w2N]`[t] ==

konCaMKII CaMKIICaM00[t] CaMKIICaM2N[t] - koffCaMKII Dimer00w2N[t] - kPCaM0 Dimer00w2N[t],

[Dimer00w2N2C]`[t] ==

konCaMKII CaMKIICaM00[t] CaMKIICaM2N2C[t] - koffCaMKII Dimer00w2N2C[t] - kPCaM0 Dimer00w2N2C[t],

[Dimer2Cw00]`[t] ==

konCaMKII CaMKIICaM00[t] CaMKIICaM2C[t] - koffCaMKII Dimer2Cw00[t] - kPCaM2C Dimer2Cw00[t],

[Dimer2Cw2C]`[t] ==

konCaMKII CaMKIICaM2C[t]^2 - koffCaMKII Dimer2Cw2C[t] - kPCaM2C Dimer2Cw2C[t],

[Dimer2Cw2N]`[t] ==

konCaMKII CaMKIICaM2C[t] CaMKIICaM2N[t] - koffCaMKII Dimer2Cw2N[t] - kPCaM2C Dimer2Cw2N[t],

[Dimer2Cw2N2C]`[t] ==

konCaMKII CaMKIICaM2C[t] CaMKIICaM2N2C[t] - koffCaMKII Dimer2Cw2N2C[t] - kPCaM2C Dimer2Cw2N2C[t],

[Dimer2N2Cw00]`[t] ==

konCaMKII CaMKIICaM00[t] CaMKIICaM2N2C[t] - koffCaMKII Dimer2N2Cw00[t] - kPCaM4 Dimer2N2Cw00[t],

[Dimer2N2Cw2C]`[t] ==
 konCaMKII CaMKIICaM2C[t] CaMKIICaM2N2C[t] -
  koffCaMKII Dimer2N2Cw2C[t] - kPCaM4 Dimer2N2Cw2C[t],
[Dimer2N2Cw2N]`[t] ==
 konCaMKII CaMKIICaM2N[t] CaMKIICaM2N2C[t] -
  koffCaMKII Dimer2N2Cw2N[t] - kPCaM4 Dimer2N2Cw2N[t],
[Dimer2N2Cw2N2C]`[t] ==
 konCaMKII CaMKIICaM2N2C[t]^2 - koffCaMKII Dimer2N2Cw2N2C[t] -
  kPCaM4 Dimer2N2Cw2N2C[t],
[Dimer2Nw00]`[t] ==
 konCaMKII CaMKIICaM00[t] CaMKIICaM2N[t] - koffCaMKII Dimer2Nw00[t] -
  kPCaM2N Dimer2Nw00[t],
[Dimer2Nw2C]`[t] ==
 konCaMKII CaMKIICaM2C[t] CaMKIICaM2N[t] - koffCaMKII Dimer2Nw2C[t] -
  kPCaM2N Dimer2Nw2C[t],
[Dimer2Nw2N]`[t] ==
 konCaMKII CaMKIICaM2N[t]^2 - koffCaMKII Dimer2Nw2N[t] -
  kPCaM2N Dimer2Nw2N[t],
[Dimer2Nw2N2C]`[t] ==
 konCaMKII CaMKIICaM2N[t] CaMKIICaM2N2C[t] -
  koffCaMKII Dimer2Nw2N2C[t] - kPCaM2N Dimer2Nw2N2C[t],
[Dimerp00w00]`[t] == -koffCaMKIIP Dimerp00w00[t] -
  kPCaM0 Dimerp00w00[t] + konCaMKIIP CaMKIICaM00[t] pCaMKII00[t],
[Dimerp00w2C]`[t] == -koffCaMKIIP Dimerp00w2C[t] -
  kPCaM2C Dimerp00w2C[t] + konCaMKIIP CaMKIICaM2C[t] pCaMKII00[t],
[Dimerp00w2N]`[t] == -koffCaMKIIP Dimerp00w2N[t] -
  kPCaM2N Dimerp00w2N[t] + konCaMKIIP CaMKIICaM2N[t] pCaMKII00[t],
[Dimerp00w2N2C]`[t] == -koffCaMKIIP Dimerp00w2N2C[t] -
  kPCaM4 Dimerp00w2N2C[t] + konCaMKIIP CaMKIICaM2N2C[t] pCaMKII00[t],
[Dimerp2Cw00]`[t] == -koffCaMKIIP Dimerp2Cw00[t] -
  kPCaM0 Dimerp2Cw00[t] + konCaMKIIP CaMKIICaM00[t] pCaMKII2C[t],
[Dimerp2Cw2C]`[t] == -koffCaMKIIP Dimerp2Cw2C[t] -
  kPCaM2C Dimerp2Cw2C[t] + konCaMKIIP CaMKIICaM2C[t] pCaMKII2C[t],
[Dimerp2Cw2N]`[t] == -koffCaMKIIP Dimerp2Cw2N[t] -
  kPCaM2N Dimerp2Cw2N[t] + konCaMKIIP CaMKIICaM2N[t] pCaMKII2C[t],
[Dimerp2Cw2N2C]`[t] == -koffCaMKIIP Dimerp2Cw2N2C[t] -
  kPCaM4 Dimerp2Cw2N2C[t] + konCaMKIIP CaMKIICaM2N2C[t] pCaMKII2C[t],

[Dimerp2N2Cw00]`[t] ==

-koffCaMKIIP Dimerp2N2Cw00[t] - kPCaM0 Dimerp2N2Cw00[t] + konCaMKIIP CaMKIICaM00[t] pCaMKII2N2C[t],

[Dimerp2N2Cw2C]`[t] ==

-koffCaMKIIP Dimerp2N2Cw2C[t] - kPCaM2C Dimerp2N2Cw2C[t] + konCaMKIIP CaMKIICaM2C[t] pCaMKII2N2C[t],

[Dimerp2N2Cw2N]`[t] ==

-koffCaMKIIP Dimerp2N2Cw2N[t] - kPCaM2N Dimerp2N2Cw2N[t] + konCaMKIIP CaMKIICaM2N[t] pCaMKII2N2C[t],

[Dimerp2N2Cw2N2C]`[t] ==

-koffCaMKIIP Dimerp2N2Cw2N2C[t] - kPCaM4 Dimerp2N2Cw2N2C[t] + konCaMKIIP CaMKIICaM2N2C[t] pCaMKII2N2C[t],

[Dimerp2Nw00]`[t] ==

-koffCaMKIIP Dimerp2Nw00[t] - kPCaM0 Dimerp2Nw00[t] + konCaMKIIP CaMKIICaM00[t] pCaMKII2N[t],

[Dimerp2Nw2C]`[t] ==

-koffCaMKIIP Dimerp2Nw2C[t] - kPCaM2C Dimerp2Nw2C[t] + konCaMKIIP CaMKIICaM2C[t] pCaMKII2N[t],

[Dimerp2Nw2N]`[t] ==

-koffCaMKIIP Dimerp2Nw2N[t] - kPCaM2N Dimerp2Nw2N[t] + konCaMKIIP CaMKIICaM2N[t] pCaMKII2N[t],

[Dimerp2Nw2N2C]`[t] ==

-koffCaMKIIP Dimerp2Nw2N2C[t] - kPCaM4 Dimerp2Nw2N2C[t] + konCaMKIIP CaMKIICaM2N2C[t] pCaMKII2N[t],

[GluA1]`[t] ==

-konCaMKIIGluA1 CaMKIICaM00[t] GluA1[t] - konCaMKIIGluA1 CaMKIICaM2C[t] GluA1[t] - konCaMKIIGluA1 CaMKIICaM2N[t] GluA1[t] - konCaMKIIGluA1 CaMKIICaM2N2C[t] GluA1[t] + koffCaMKIIGluA1 GluA1CaMKII00[t] + koffCaMKIIGluA1 GluA1CaMKII2C[t] + koffCaMKIIGluA1 GluA1CaMKII2N[t] + koffCaMKIIGluA1 GluA1CaMKII2N2C[t] + kcatp831PP1 GluA1p831PP1[t] + kcatp845PP1 GluA1p845PP1[t] + koffpCaMKIIGluA1 GluA1pCaMKII[t] + koffpCaMKIIGluA1 GluA1pCaMKII00[t] + koffpCaMKIIGluA1 GluA1pCaMKII2C[t] + koffpCaMKIIGluA1 GluA1pCaMKII2N[t] + koffpCaMKIIGluA1 GluA1pCaMKII2N2C[t] + koffPKA4GluA1 GluA1PKA4[t] + koffPKAcGluA1 GluA1PKAc[t] + kcatCaNCaM00p845 p845CaNCaM00[t] + kcatCaNCaM2Cp845 p845CaNCaM2C[t] + kcatCaNCaM2Np845 p845CaNCaM2N[t] + kcatCaNCaM4p845 p845CaNCaM2N2C[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII00[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII2C[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII2N[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII2N2C[t] - konPKAcGluA1 GluA1[t] PKAc[t] - konPKA4GluA1 GluA1[t] R2C2cAMP4[t],

[GluA1CaMKII00]`[t] ==

konCaMKIIGluA1 CaMKIICaM00[t] GluA1[t] - kcatKCaM00GluA1p831 GluA1CaMKII00[t] - koffCaMKIIGluA1 GluA1CaMKII00[t],

[GluA1CaMKII2C]`[t] ==

konCaMKIIGluA1 CaMKIICaM2C[t] GluA1[t] - kcatKCaM2CGluA1p831 GluA1CaMKII2C[t] - koffCaMKIIGluA1 GluA1CaMKII2C[t],

[GluA1CaMKII2N]`[t] ==

konCaMKIIGluA1 CaMKIICaM2N[t] GluA1[t] - kcatKCaM2NGluA1p831 GluA1CaMKII2N[t] - koffCaMKIIGluA1 GluA1CaMKII2N[t],

[GluA1CaMKII2N2C]`[t] ==

konCaMKIIGluA1 CaMKIICaM2N2C[t] GluA1[t] - kcatKCaM4GluA1p831 GluA1CaMKII2N2C[t] - koffCaMKIIGluA1 GluA1CaMKII2N2C[t],

[GluA1p831]`[t] ==

kcatKCaM00GluA1p831 GluA1CaMKII00[t] + kcatKCaM2CGluA1p831 GluA1CaMKII2C[t] + kcatKCaM2NGluA1p831 GluA1CaMKII2N[t] + kcatKCaM4GluA1p831 GluA1CaMKII2N2C[t] + koffp831PP1 GluA1p831PP1[t] + kcatPKCaM00GluA1p831 GluA1pCaMKII00[t] + kcatPKCaM2CGluA1p831 GluA1pCaMKII2C[t] + kcatPKCaM2NGluA1p831 GluA1pCaMKII2N[t] + kcatPKCaM4GluA1p831 GluA1pCaMKII2N2C[t] + koffPKA4GluA1 p831PKA4[t] + koffPKAcGluA1 p831PKAc[t] - konPKAcGluA1 GluA1p831[t] PKAc[t] - konp831PP1 GluA1p831[t] PP1[t] - konPKA4GluA1 GluA1p831[t] R2C2cAMP4[t],

[GluA1p831PP1]`[t] ==

-kcatp831PP1 GluA1p831PP1[t] - koffp831PP1 GluA1p831PP1[t] + konp831PP1 GluA1p831[t] PP1[t],

[GluA1p845][t] ==

-konCaMKIIGluA1 CaMKIICaM00[t] GluA1p845[t] - konCaMKIIGluA1 CaMKIICaM2C[t] GluA1p845[t] - konCaMKIIGluA1 CaMKIICaM2N[t] GluA1p845[t] - konCaMKIIGluA1 CaMKIICaM2N2C[t] GluA1p845[t] - konCaNp845 CaNCaM00[t] GluA1p845[t] - konCaNp845 CaNCaM2C[t] GluA1p845[t] - konCaNp845 CaNCaM2N[t] GluA1p845[t] - konCaNp845 CaNCaM2N2C[t] GluA1p845[t] + koffp845PP1 GluA1p845PP1[t] + kcatPKAcGluA1 GluA1PKAc[t] + kcatp831p845PP1 p831p845PP1[t] + koffCaMKIIGluA1 p845CaMKII00[t] + koffCaMKIIGluA1 p845CaMKII2C[t] + koffCaMKIIGluA1 p845CaMKII2N[t] + koffCaMKIIGluA1 p845CaMKII2N2C[t] + koffCaNp845 p845CaNCaM00[t] + koffCaNp845 p845CaNCaM2C[t] + koffCaNp845 p845CaNCaM2N[t] + koffCaNp845 p845CaNCaM2N2C[t] + koffpCaMKIIGluA1 p845pCaMKII[t] + koffpCaMKIIGluA1 p845pCaMKII00[t] + koffpCaMKIIGluA1 p845pCaMKII2C[t] + koffpCaMKIIGluA1 p845pCaMKII2N[t] + koffpCaMKIIGluA1 p845pCaMKII2N2C[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII00[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII2C[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII2N[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII2N2C[t] - konp845PP1 GluA1p845[t] PP1[t],

[GluA1p845PP1]`[t] ==

-kcatp845PP1 GluA1p845PP1[t] - koffp845PP1 GluA1p845PP1[t] + konp845PP1 GluA1p845[t] PP1[t],

[GluA1pCaMKII]`[t] ==

-koffpCaMKIIGluA1 GluA1pCaMKII[t] + konpCaMKIIGluA1 GluA1[t] pCaMKII[t],

[GluA1pCaMKII00][t] ==

-kcatPKCaM00GluA1p831 GluA1pCaMKII00[t] - koffpCaMKIIGluA1 GluA1pCaMKII00[t] + konpCaMKIIGluA1 GluA1[t] pCaMKII00[t],

[GluA1pCaMKII2C][t] ==

-kcatPKCaM2CGluA1p831 GluA1pCaMKII2C[t] - koffpCaMKIIGluA1 GluA1pCaMKII2C[t] + konpCaMKIIGluA1 GluA1[t] pCaMKII2C[t],

[GluA1pCaMKII2N][t] ==

-kcatPKCaM2NGluA1p831 GluA1pCaMKII2N[t] - koffpCaMKIIGluA1 GluA1pCaMKII2N[t] + konpCaMKIIGluA1 GluA1[t] pCaMKII2N[t],

[GluA1pCaMKII2N2C][t] ==

-kcatPKCaM4GluA1p831 GluA1pCaMKII2N2C[t] - koffpCaMKIIGluA1 GluA1pCaMKII2N2C[t] + konpCaMKIIGluA1 GluA1[t] pCaMKII2N2C[t],

[GluA1PKA4]`[t] ==

-koffPKA4GluA1 GluA1PKA4[t] + onPKA4GluA1 GluA1[t] R2C2cAMP4[t],

[GluA1PKAc]`[t] ==

-kcatPKAcGluA1 GluA1PKAc[t] - koffPKAcGluA1 GluA1PKAc[t] + konPKAcGluA1 GluA1[t] PKAc[t],

[I1]`[t] ==

koffI1PKAc I1PKAc[t] + kdpIp35PP1CaNCaM00 Ip35CaN00[t] + kdpIp35PP1CaNCaM2C Ip35CaN2C[t] + kdpIp35PP1CaNCaM2N Ip35CaN2N[t] + kdpIp35PP1CaNCaM4 Ip35CaN2N2C[t] - konI1PKAc I1[t] PKAc[t],

[I1PKAc]`[t] ==

-koffI1PKAc I1PKAc[t] - kpI1 I1PKAc[t] + konI1PKAc I1[t] PKAc[t],

[Ip35]`[t] ==

 kpI1 I1PKAc[t] - konIp35CaN CaNCaM00[t] Ip35[t] - konIp35CaN CaNCaM2C[t] Ip35[t] - konIp35CaN CaNCaM2N[t] Ip35[t] - konIp35CaN CaNCaM2N2C[t] Ip35[t] + koffIp35CaN Ip35CaN00[t] + koffIp35CaN Ip35CaN2C[t] + koffIp35CaN Ip35CaN2N[t] + koffIp35CaN Ip35CaN2N2C[t] + koffIp35PP1 Ip35PP1[t] - konIp35PP1 Ip35[t] PP1[t],

[Ip35CaN00]`[t] ==

 konIp35CaN CaNCaM00[t] Ip35[t] - kdpIp35PP1CaNCaM00 Ip35CaN00[t] - koffIp35CaN Ip35CaN00[t],

[Ip35CaN2C]`[t] ==

 konIp35CaN CaNCaM2C[t] Ip35[t] - kdpIp35PP1CaNCaM2C Ip35CaN2C[t] - koffIp35CaN Ip35CaN2C[t],

[Ip35CaN2N]`[t] ==

 konIp35CaN CaNCaM2N[t] Ip35[t] - kdpIp35PP1CaNCaM2N Ip35CaN2N[t] - koffIp35CaN Ip35CaN2N[t],

[Ip35CaN2N2C]`[t] ==

 konIp35CaN CaNCaM2N2C[t] Ip35[t] - kdpIp35PP1CaNCaM4 Ip35CaN2N2C[t] - koffIp35CaN Ip35CaN2N2C[t],

[Ip35PP1]`[t] ==

-koffIp35PP1 Ip35PP1[t] + konIp35PP1 Ip35[t] PP1[t],

[MLCK]`[t] ==

-konMKCaM0 CaM00[t] MLCK[t] - konMKCaM2C CaM2C[t] MLCK[t] - konMKCaM2N CaM2N[t] MLCK[t] - konMKCaM4 CaM2N2C[t] MLCK[t] + koffMKCaM0 MLCKCaM00[t] + koffMKCaM2C MLCKCaM2C[t] + koffMKCaM2N MLCKCaM2N[t] + koffMKCaM4 MLCKCaM2N2C[t],

[MLCKCaM00]`[t] ==

 konMKCaM0 CaM00[t] MLCK[t] - koffMKCaM0 MLCKCaM00[t] - konMKC Ca[t]^2 MLCKCaM00[t] - konMKN Ca[t]^2 MLCKCaM00[t] + koffMKC MLCKCaM2C[t] + koffMKN MLCKCaM2N[t],

[MLCKCaM2C]`[t] ==

 konMKCaM2C CaM2C[t] MLCK[t] + konMKC Ca[t]^2 MLCKCaM00[t] - koffMKC MLCKCaM2C[t] - koffMKCaM2C MLCKCaM2C[t] - konMKN Ca[t]^2 MLCKCaM2C[t] + koffMKN MLCKCaM2N2C[t],

[MLCKCaM2N]`[t] ==

 konMKCaM2N CaM2N[t] MLCK[t] + konMKN Ca[t]^2 MLCKCaM00[t] - koffMKCaM2N MLCKCaM2N[t] - koffMKN MLCKCaM2N[t] - konMKC Ca[t]^2 MLCKCaM2N[t] + koffMKC MLCKCaM2N2C[t],

[MLCKCaM2N2C]`[t] ==

 konMKCaM4 CaM2N2C[t] MLCK[t] + konMKN Ca[t]^2 MLCKCaM2C[t] + konMKC Ca[t]^2 MLCKCaM2N[t] - koffMKC MLCKCaM2N2C[t] - koffMKCaM4 MLCKCaM2N2C[t] - koffMKN MLCKCaM2N2C[t],

[Ng]`[t] == -konNgCaM0 CaM00[t] Ng[t] - konNgCaM2C CaM2C[t] Ng[t] - konNgCaM2N CaM2N[t] Ng[t] - konNgCaM4 CaM2N2C[t] Ng[t] + koffNgCaM0 NgCaM00[t] + koffNgCaM2C NgCaM2C[t] + koffNgCaM2N NgCaM2N[t] + koffNgCaM4 NgCaM2N2C[t],

[NgCaM00]`[t] ==

 konNgCaM0 CaM00[t] Ng[t] - koffNgCaM0 NgCaM00[t] - konNgC Ca[t]^2 NgCaM00[t] - konNgN Ca[t]^2 NgCaM00[t] + koffNgC NgCaM2C[t] + koffNgN NgCaM2N[t],

[NgCaM2C]`[t] ==

 konNgCaM2C CaM2C[t] Ng[t] + konNgC Ca[t]^2 NgCaM00[t] - koffNgC NgCaM2C[t] - koffNgCaM2C NgCaM2C[t] - konNgN Ca[t]^2 NgCaM2C[t] + koffNgN NgCaM2N2C[t],

[NgCaM2N]`[t] ==

 konNgCaM2N CaM2N[t] Ng[t] + konNgN Ca[t]^2 NgCaM00[t] - koffNgCaM2N NgCaM2N[t] - koffNgN NgCaM2N[t] - konNgC Ca[t]^2 NgCaM2N[t] + koffNgC NgCaM2N2C[t], [NgCaM2N2C]`[t] ==

konNgCaM4 CaM2N2C[t] Ng[t] + konNgN Ca[t]^2 NgCaM2C[t] + konNgC Ca[t]^2 NgCaM2N[t] - koffNgC NgCaM2N2C[t] - koffNgCaM4 NgCaM2N2C[t] - koffNgN NgCaM2N2C[t],

[NOS]`[t] ==

-konNOSCaM0 CaM00[t] NOS[t] - konNOSCaM2C CaM2C[t] NOS[t] - konNOSCaM2N CaM2N[t] NOS[t] - konNOSCaM4 CaM2N2C[t] NOS[t] + koffNOSCaM0 NOSCaM00[t] + koffNOSCaM2C NOSCaM2C[t] + koffNOSCaM2N NOSCaM2N[t] + koffNOSCaM4 NOSCaM2N2C[t],

[NOSCaM00]`[t] ==

konNOSCaM0 CaM00[t] NOS[t] - koffNOSCaM0 NOSCaM00[t] - konNOSC Ca[t]^2 NOSCaM00[t] - konNOSN Ca[t]^2 NOSCaM00[t] + koffNOSC NOSCaM2C[t] + koffNOSN NOSCaM2N[t],

[NOSCaM2C]`[t] ==

konNOSCaM2C CaM2C[t] NOS[t] + konNOSC Ca[t]^2 NOSCaM00[t] - koffNOSC NOSCaM2C[t] - koffNOSCaM2C NOSCaM2C[t] - konNOSN Ca[t]^2 NOSCaM2C[t] + koffNOSN NOSCaM2N2C[t],

[NOSCaM2N]`[t] ==

konNOSCaM2N CaM2N[t] NOS[t] + konNOSN Ca[t]^2 NOSCaM00[t] - koffNOSCaM2N NOSCaM2N[t] - koffNOSN NOSCaM2N[t] - konNOSC Ca[t]^2 NOSCaM2N[t] + koffNOSC NOSCaM2N2C[t],

[NOSCaM2N2C]`[t] ==

konNOSCaM4 CaM2N2C[t] NOS[t] + konNOSN Ca[t]^2 NOSCaM2C[t] + konNOSC Ca[t]^2 NOSCaM2N[t] - koffNOSC NOSCaM2N2C[t] - koffNOSCaM4 NOSCaM2N2C[t] - koffNOSN NOSCaM2N2C[t],

[p831p845]`[t] ==

koffp831p845PP1 p831p845PP1[t] + kcatPKAcGluA1 p831PKAc[t] + kcatKCaM00GluA1p831 p845CaMKII00[t] + kcatKCaM2CGluA1p831 p845CaMKII2C[t] + kcatKCaM2NGluA1p831 p845CaMKII2N[t] + kcatKCaM4GluA1p831 p845CaMKII2N2C[t] + kcatPKCaM00GluA1p831 p845pCaMKII00[t] + kcatPKCaM2CGluA1p831 p845pCaMKII2C[t] + kcatPKCaM2NGluA1p831 p845pCaMKII2N[t] + kcatPKCaM4GluA1p831 p845pCaMKII2N2C[t] - konp831p845PP1 p831p845[t] PP1[t],

[p831p845PP1]`[t] ==

-kcatp831p845PP1 p831p845PP1[t] - koffp831p845PP1 p831p845PP1[t] + konp831p845PP1 p831p845[t] PP1[t],

[p831PKA4]`[t] ==

-koffPKA4GluA1 p831PKA4[t] + konPKA4GluA1 GluA1p831[t] R2C2cAMP4[t],

[p831PKAc]`[t] ==

-kcatPKAcGluA1 p831PKAc[t] - koffPKAcGluA1 p831PKAc[t] + konPKAcGluA1 GluA1p831[t] PKAc[t],

[p845CaMKII00]`[t] ==

konCaMKIIGluA1 CaMKIICaM00[t] GluA1p845[t] - kcatKCaM00GluA1p831 p845CaMKII00[t] - koffCaMKIIGluA1 p845CaMKII00[t],

[p845CaMKII2C]`[t] ==

konCaMKIIGluA1 CaMKIICaM2C[t] GluA1p845[t] - kcatKCaM2CGluA1p831 p845CaMKII2C[t] - koffCaMKIIGluA1 p845CaMKII2C[t],

[p845CaMKII2N]`[t] ==

konCaMKIIGluA1 CaMKIICaM2N[t] GluA1p845[t] - kcatKCaM2NGluA1p831 p845CaMKII2N[t] - koffCaMKIIGluA1 p845CaMKII2N[t],

[p845CaMKII2N2C]`[t] ==

konCaMKIIGluA1 CaMKIICaM2N2C[t] GluA1p845[t] - kcatKCaM4GluA1p831 p845CaMKII2N2C[t] - koffCaMKIIGluA1 p845CaMKII2N2C[t], [p845CaNCaM00]`[t] ==

konCaNp845 CaNCaM00[t] GluA1p845[t] - kcatCaNCaM00p845 p845CaNCaM00[t] - koffCaNp845 p845CaNCaM00[t] - konPPC Ca[t]^2 p845CaNCaM00[t] - konPPN Ca[t]^2 p845CaNCaM00[t] + koffPPC p845CaNCaM2C[t] + koffPPN p845CaNCaM2N[t],

[p845CaNCaM2C]`[t] ==

konCaNp845 CaNCaM2C[t] GluA1p845[t] + konPPC Ca[t]^2 p845CaNCaM00[t] - kcatCaNCaM2Cp845 p845CaNCaM2C[t] - koffCaNp845 p845CaNCaM2C[t] - koffPPC p845CaNCaM2C[t] - konPPN Ca[t]^2 p845CaNCaM2C[t] + koffPPN p845CaNCaM2N2C[t],

[p845CaNCaM2N]`[t] ==

konCaNp845 CaNCaM2N[t] GluA1p845[t] + konPPN Ca[t]^2 p845CaNCaM00[t] - kcatCaNCaM2Np845 p845CaNCaM2N[t] - koffCaNp845 p845CaNCaM2N[t] - koffPPN p845CaNCaM2N[t] - konPPC Ca[t]^2 p845CaNCaM2N[t] + koffPPC p845CaNCaM2N2C[t],

[p845CaNCaM2N2C]`[t] ==

konCaNp845 CaNCaM2N2C[t] GluA1p845[t] + konPPN Ca[t]^2 p845CaNCaM2C[t] + konPPC Ca[t]^2 p845CaNCaM2N[t] - kcatCaNCaM4p845 p845CaNCaM2N2C[t] - koffCaNp845 p845CaNCaM2N2C[t] - koffPPC p845CaNCaM2N2C[t] - koffPPN p845CaNCaM2N2C[t],

[p845pCaMKII]`[t] == -koffpCaMKIIGluA1 p845pCaMKII[t] + konpCaMKIIGluA1 GluA1p845[t] pCaMKII[t],

[p845pCaMKII00][t] ==

-kcatPKCaM00GluA1p831 p845pCaMKII00[t] - koffpCaMKIIGluA1 p845pCaMKII00[t] + konpCaMKIIGluA1 GluA1p845[t] pCaMKII00[t],

[p845pCaMKII2C][t] ==

-kcatPKCaM2CGluA1p831 p845pCaMKII2C[t] -koffpCaMKIIGluA1 p845pCaMKII2C[t] + konpCaMKIIGluA1 GluA1p845[t] pCaMKII2C[t],

[p845pCaMKII2N][t] ==

-kcatPKCaM2NGluA1p831 p845pCaMKII2N[t] - koffpCaMKIIGluA1 p845pCaMKII2N[t] + konpCaMKIIGluA1 GluA1p845[t] pCaMKII2N[t],

[p845pCaMKII2N2C][t] ==

-kcatPKCaM4GluA1p831 p845pCaMKII2N2C[t] - koffpCaMKIIGluA1 p845pCaMKII2N2C[t] + konpCaMKIIGluA1 GluA1p845[t] pCaMKII2N2C[t],

[pCaMKII]`[t] ==

kPCaM4 Dimerp2N2Cw2N2C[t] + koffpCaMKIIGluA1 GluA1pCaMKII[t] + koffpCaMKIIGluA1 p845pCaMKII[t] - 100 konKCaM0 CaM00[t] pCaMKII[t] - 100 konKCaM2C CaM2C[t] pCaMKII[t] - 100 konKCaM2N CaM2N[t] pCaMKII[t] - 100 konKCaM4 CaM2N2C[t] pCaMKII[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII[t] + koffKCaM0 pCaMKII00[t] + koffKCaM2C pCaMKII2C[t] + koffKCaM2N pCaMKII2N[t] + koffKCaM4 pCaMKII2N2C[t] - konPP1CaMKII pCaMKII[t] PP1[t] + offPP1CaMKII PP1pCaMKII[t],

[pCaMKII00]`[t] ==

kPCaM0 Dimer00w00[t] + kPCaM0 Dimer00w2C[t] + kPCaM0 Dimer00w2N[t] + kPCaM0 Dimer00w2N2C[t] + koffCaMKIIP Dimerp00w00[t] + 2 kPCaM0 Dimerp00w00[t] + koffCaMKIIP Dimerp00w2C[t] + kPCaM2C Dimerp00w2C[t] + koffCaMKIIP Dimerp00w2N[t] + kPCaM2N Dimerp00w2N[t] + koffCaMKIIP Dimerp00w2N2C[t] + kPCaM4 Dimerp00w2N2C[t] + kPCaM0 Dimerp2Cw00[t] + kPCaM0 Dimerp2N2Cw00[t] + kPCaM0 Dimerp2Nw00[t] + kcatPKCaM00GluA1p831 GluA1pCaMKII00[t] + koffpCaMKIIGluA1 GluA1pCaMKII00[t] + kcatPKCaM00GluA1p831 p845pCaMKII00[t] + koffpCaMKIIGluA1 p845pCaMKII00[t] + 100 konKCaM0 CaM00[t] pCaMKII[t] - koffKCaM0 pCaMKII00[t] - konKC Ca[t]^2 pCaMKII00[t] - konKN Ca[t]^2 pCaMKII00[t] - konCaMKIIP CaMKIICaM00[t] pCaMKII00[t] - konCaMKIIP CaMKIICaM2C[t] pCaMKII00[t] - konCaMKIIP CaMKIICaM2N[t] pCaMKII00[t] - konCaMKIIP CaMKIICaM2N2C[t] pCaMKII00[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII00[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII00[t] + koffKC pCaMKII2C[t] + koffKN pCaMKII2N[t] - konPP1CaMKII pCaMKII00[t] PP1[t] + koffPP1CaMKII PP1pCaMKII00[t],

[pCaMKII2C]`[t] ==

kPCaM2C Dimer2Cw00[t] + kPCaM2C Dimer2Cw2C[t] + kPCaM2C Dimer2Cw2N[t] + kPCaM2C Dimer2Cw2N2C[t] + kPCaM2C Dimerp00w2C[t] + koffCaMKIIP Dimerp2Cw00[t] + kPCaM0 Dimerp2Cw00[t] + koffCaMKIIP Dimerp2Cw2C[t] + 2 kPCaM2C Dimerp2Cw2C[t] + koffCaMKIIP Dimerp2Cw2N[t] + kPCaM2N Dimerp2Cw2N[t] + koffCaMKIIP Dimerp2Cw2N2C[t] + kPCaM4 Dimerp2Cw2N2C[t] + kPCaM2C Dimerp2N2Cw2C[t] + kPCaM2C Dimerp2Nw2C[t] + kcatPKCaM2CGluA1p831 GluA1pCaMKII2C[t] + koffpCaMKIIGluA1 GluA1pCaMKII2C[t] + kcatPKCaM2CGluA1p831 p845pCaMKII2C[t] + koffpCaMKIIGluA1 p845pCaMKII2C[t] + 100 konKCaM2C CaM2C[t] pCaMKII[t] + konKC Ca[t]^2 pCaMKII00[t] - koffKC pCaMKII2C[t] - koffKCaM2C pCaMKII2C[t] - konKN Ca[t]^2 pCaMKII2C[t] - konCaMKIIP CaMKIICaM00[t] pCaMKII2C[t] - konCaMKIIP CaMKIICaM2C[t] pCaMKII2C[t] - konCaMKIIP CaMKIICaM2N[t] pCaMKII2C[t] - konCaMKIIP CaMKIICaM2N2C[t] pCaMKII2C[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII2C[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII2C[t] + koffKN pCaMKII2N2C[t] - konPP1CaMKII pCaMKII2C[t] PP1[t] + koffPP1CaMKII PP1pCaMKII2C[t],

[pCaMKII2N]`[t] ==

kPCaM2N Dimer2Nw00[t] + kPCaM2N Dimer2Nw2C[t] + kPCaM2N Dimer2Nw2N[t] + kPCaM2N Dimer2Nw2N2C[t] + kPCaM2N Dimerp00w2N[t] + kPCaM2N Dimerp2Cw2N[t] + kPCaM2N Dimerp2N2Cw2N[t] + koffCaMKIIP Dimerp2Nw00[t] +kPCaM0 Dimerp2Nw00[t] + koffCaMKIIP Dimerp2Nw2C[t] + kPCaM2C Dimerp2Nw2C[t] + koffCaMKIIP Dimerp2Nw2N[t] + 2 kPCaM2N Dimerp2Nw2N[t] + koffCaMKIIP Dimerp2Nw2N2C[t] + kPCaM4 Dimerp2Nw2N2C[t] + kcatPKCaM2NGluA1p831 GluA1pCaMKII2N[t] + koffpCaMKIIGluA1 GluA1pCaMKII2N[t] + kcatPKCaM2NGluA1p831 p845pCaMKII2N[t] + koffpCaMKIIGluA1 p845pCaMKII2N[t] + 100 konKCaM2N CaM2N[t] pCaMKII[t] + konKN Ca[t]^2 pCaMKII00[t] - koffKCaM2N pCaMKII2N[t] - koffKN pCaMKII2N[t] - konKC Ca[t]^2 pCaMKII2N[t] - konCaMKIIP CaMKIICaM00[t] pCaMKII2N[t] - konCaMKIIP CaMKIICaM2C[t] pCaMKII2N[t] - konCaMKIIP CaMKIICaM2N[t] pCaMKII2N[t] - konCaMKIIP CaMKIICaM2N2C[t] pCaMKII2N[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII2N[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII2N[t] + koffKC pCaMKII2N2C[t] - konPP1CaMKII pCaMKII2N[t] PP1[t] + koffPP1CaMKII PP1pCaMKII2N[t],

[pCaMKII2N2C]`[t] ==

kPCaM4 Dimer2N2Cw00[t] + kPCaM4 Dimer2N2Cw2C[t] + kPCaM4 Dimer2N2Cw2N[t] + kPCaM4 Dimer2N2Cw2N2C[t] + kPCaM4 Dimerp00w2N2C[t] + kPCaM4 Dimerp2Cw2N2C[t] + koffCaMKIIP Dimerp2N2Cw00[t] + kPCaM0 Dimerp2N2Cw00[t] + koffCaMKIIP Dimerp2N2Cw2C[t] + kPCaM2C Dimerp2N2Cw2C[t] + koffCaMKIIP Dimerp2N2Cw2N[t] + kPCaM2N Dimerp2N2Cw2N[t] + koffCaMKIIP Dimerp2N2Cw2N2C[t] + kPCaM4 Dimerp2N2Cw2N2C[t] + kPCaM4 Dimerp2Nw2N2C[t] + kcatPKCaM4GluA1p831 GluA1pCaMKII2N2C[t] + koffpCaMKIIGluA1 GluA1pCaMKII2N2C[t] + kcatPKCaM4GluA1p831 p845pCaMKII2N2C[t] + koffpCaMKIIGluA1 p845pCaMKII2N2C[t] + 100 konKCaM4 CaM2N2C[t] pCaMKII[t] + konKN Ca[t]^2 pCaMKII2C[t] + konKC Ca[t]^2 pCaMKII2N[t] - koffKC pCaMKII2N2C[t] - koffKCaM4 pCaMKII2N2C[t] - koffKN pCaMKII2N2C[t] - konCaMKIIP CaMKIICaM00[t] pCaMKII2N2C[t] - konCaMKIIP CaMKIICaM2C[t] pCaMKII2N2C[t] - konCaMKIIP CaMKIICaM2N[t] pCaMKII2N2C[t] - konCaMKIIP CaMKIICaM2N2C[t] pCaMKII2N2C[t] - konpCaMKIIGluA1 GluA1[t] pCaMKII2N2C[t] - konpCaMKIIGluA1 GluA1p845[t] pCaMKII2N2C[t] - konPP1CaMKII pCaMKII2N2C[t] PP1[t] + koffPP1CaMKII PP1pCaMKII2N2C[t],

[PDE1]`[t] ==

-konPDE1CaM0 CaM00[t] PDE1[t] - konPDE1CaM2C CaM2C[t] PDE1[t] - konPDE1CaM2N CaM2N[t] PDE1[t] - konPDE1CaM4 CaM2N2C[t] PDE1[t] + koffPDE1CaM0 PDE1CaM00[t] + koffPDE1CaM2C PDE1CaM2C[t] + koffPDE1CaM2N PDE1CaM2N[t] + koffPDE1CaM4 PDE1CaM2N2C[t],

[PDE1CaM00]`[t] ==

konPDE1CaM0 CaM00[t] PDE1[t] - koffPDE1CaM0 PDE1CaM00[t] - konPDE1C Ca[t]^2 PDE1CaM00[t] - konPDE1N Ca[t]^2 PDE1CaM00[t] + koffPDE1C PDE1CaM2C[t] + koffPDE1N PDE1CaM2N[t],

[PDE1CaM2C]`[t] ==

konPDE1CaM2C CaM2C[t] PDE1[t] + konPDE1C Ca[t]^2 PDE1CaM00[t] - koffPDE1C PDE1CaM2C[t] - koffPDE1CaM2C PDE1CaM2C[t] - konPDE1N Ca[t]^2 PDE1CaM2C[t] + koffPDE1N PDE1CaM2N2C[t],

[PDE1CaM2N]`[t] ==

konPDE1CaM2N CaM2N[t] PDE1[t] + konPDE1N Ca[t]^2 PDE1CaM00[t] - koffPDE1CaM2N PDE1CaM2N[t] - koffPDE1N PDE1CaM2N[t] - konPDE1C Ca[t]^2 PDE1CaM2N[t] + koffPDE1C PDE1CaM2N2C[t],

[PDE1CaM2N2C]`[t] ==

konPDE1CaM4 CaM2N2C[t] PDE1[t] + konPDE1N Ca[t]^2 PDE1CaM2C[t] + konPDE1C Ca[t]^2 PDE1CaM2N[t] - koffPDE1C PDE1CaM2N2C[t] - koffPDE1CaM4 PDE1CaM2N2C[t] - koffPDE1N PDE1CaM2N2C[t],

[PDE4]`[t] ==
 koffPKAPDE4 PDE4PKAc[t] - konPKAPDE4 PDE4[t] PKAc[t],
[PDE4PKAc]`[t] == -kcatPKAPDE4 PDE4PKAc[t] -
  koffPKAPDE4 PDE4PKAc[t] + konPKAPDE4 PDE4[t] PKAc[t],
[PKAc]`[t] ==
 kcatPKAcGluA1 GluA1PKAc[t] + koffPKAcGluA1 GluA1PKAc[t] +
  koffI1PKAc I1PKAc[t] + kpI1 I1PKAc[t] + kcatPKAcGluA1 p831PKAc[t] +
  koffPKAcGluA1 p831PKAc[t] + kcatPKAPDE4 PDE4PKAc[t] +
  koffPKAPDE4 PDE4PKAc[t] - konPKAcGluA1 GluA1[t] PKAc[t] -
  konPKAcGluA1 GluA1p831[t] PKAc[t] - konI1PKAc I1[t] PKAc[t] -
  konPKAPDE4 PDE4[t] PKAc[t] + koffPKAinhib PKAi[t] -
  konPKAinhib PKAc[t] PKAinhibitor[t] + ksplitPKAc R2C2cAMP4[t] -
  kjoinPKAc PKAc[t] R2cAMP4[t] + ksplitPKAc R2CcAMP4[t] -
  kjoinPKAc PKAc[t] R2CcAMP4[t],
[PKAi]`[t] == -koffPKAinhib PKAi[t] +
  konPKAinhib PKAc[t] PKAinhibitor[t] - konR2C PKAi[t] R2[t] -
  konR2C2 PKAi[t] R2C[t] + koffR2C PKAinhibitor[t] R2C[t] +
  koffR2C2 PKAinhibitor[t] R2C2[t],
[PKAinhibitor]`[t] ==
 koffPKAinhib PKAi[t] - konPKAinhib PKAc[t] PKAinhibitor[t] +
  konR2C PKAi[t] R2[t] + konR2C2 PKAi[t] R2C[t] -
  koffR2C PKAinhibitor[t] R2C[t] - koffR2C2 PKAinhibitor[t] R2C2[t],
[PP1]`[t] ==
 kcatp831PP1 GluA1p831PP1[t] + koffp831PP1 GluA1p831PP1[t] +
  kcatp845PP1 GluA1p845PP1[t] + koffp845PP1 GluA1p845PP1[t] +
  koffIp35PP1 Ip35PP1[t] + kcatp831p845PP1 p831p845PP1[t] +
  koffp831p845PP1 p831p845PP1[t] - konp831PP1 GluA1p831[t] PP1[t] -
  konp845PP1 GluA1p845[t] PP1[t] - konIp35PP1 Ip35[t] PP1[t] -
  konp831p845PP1 p831p845[t] PP1[t] - konPP1CaMKII pCaMKII[t] PP1[t] -
   konPP1CaMKII pCaMKII00[t] PP1[t] -
  konPP1CaMKII pCaMKII2C[t] PP1[t] -
  konPP1CaMKII pCaMKII2N[t] PP1[t] -
  konPP1CaMKII pCaMKII2N2C[t] PP1[t] + kdpCaMKII PP1pCaMKII[t] +
  koffPP1CaMKII PP1pCaMKII[t] + kdpCaMKII PP1pCaMKII00[t] +
  koffPP1CaMKII PP1pCaMKII00[t] + kdpCaMKII PP1pCaMKII2C[t] +
  koffPP1CaMKII PP1pCaMKII2C[t] + kdpCaMKII PP1pCaMKII2N[t] +
  koffPP1CaMKII PP1pCaMKII2N[t] + kdpCaMKII PP1pCaMKII2N2C[t] +

koffPP1CaMKII PP1pCaMKII2N2C[t],
[PP1pCaMKII]`[t] ==
konPP1CaMKII pCaMKII[t] PP1[t] - kdpCaMKII PP1pCaMKII[t] -
koffPP1CaMKII PP1pCaMKII[t],
[PP1pCaMKII00]`[t] ==
konPP1CaMKII pCaMKII00[t] PP1[t] - kdpCaMKII PP1pCaMKII00[t] -
koffPP1CaMKII PP1pCaMKII00[t] - konKC Ca[t]^2 PP1pCaMKII00[t] -
konKN Ca[t]^2 PP1pCaMKII00[t] + koffKC PP1pCaMKII2C[t] +
koffKN PP1pCaMKII2N[t],
[PP1pCaMKII2C]`[t] ==
konPP1CaMKII pCaMKII2C[t] PP1[t] + konKC Ca[t]^2 PP1pCaMKII00[t] -
kdpCaMKII PP1pCaMKII2C[t] - koffKC PP1pCaMKII2C[t] -
koffPP1CaMKII PP1pCaMKII2C[t] - konKN Ca[t]^2 PP1pCaMKII2C[t] +
koffKN PP1pCaMKII2N2C[t],
[PP1pCaMKII2N]`[t] ==
konPP1CaMKII pCaMKII2N[t] PP1[t] + konKN Ca[t]^2 PP1pCaMKII00[t] -
kdpCaMKII PP1pCaMKII2N[t] - koffKN PP1pCaMKII2N[t] -
koffPP1CaMKII PP1pCaMKII2N[t] - konKC Ca[t]^2 PP1pCaMKII2N[t] +
koffKC PP1pCaMKII2N2C[t],
[PP1pCaMKII2N2C]`[t] ==
konPP1CaMKII pCaMKII2N2C[t] PP1[t] + konKN Ca[t]^2 PP1pCaMKII2C[t] +
konKC Ca[t]^2 PP1pCaMKII2N[t] - kdpCaMKII PP1pCaMKII2N2C[t] -
koffKC PP1pCaMKII2N2C[t] - koffKN PP1pCaMKII2N2C[t] -
koffPP1CaMKII PP1pCaMKII2N2C[t],
[pPDE4]`[t] == kcatPKAPDE4 PDE4PKAc[t],
[R2]`[t] == -konR2C PKAi[t] R2[t] +
koffR2C PKAinhibitor[t] R2C[t] + koffR2cAMP R2cAMP4[t],
[R2C]`[t] ==
konR2C PKAi[t] R2[t] - konR2C2 PKAi[t] R2C[t] -
koffR2C PKAinhibitor[t] R2C[t] + koffR2C2 PKAinhibitor[t] R2C2[t],
[R2C2]`[t] ==
konR2C2 PKAi[t] R2C[t] - koncAMP1 cycAMP[t] R2C2[t] -
koffR2C2 PKAinhibitor[t] R2C2[t] + koffcAMP1 R2C2cAMP[t],
[R2C2cAMP]`[t] ==
koncAMP1 cycAMP[t] R2C2[t] - koffcAMP1 R2C2cAMP[t] -
koncAMP2 cycAMP[t] R2C2cAMP[t] + koffcAMP2 R2C2cAMP2[t],
[R2C2cAMP2]`[t] ==

koncAMP2 cycAMP[t] R2C2cAMP[t] - koffcAMP2 R2C2cAMP2[t] -
koncAMP3 cycAMP[t] R2C2cAMP2[t] + koffcAMP3 R2C2cAMP3[t],
[R2C2cAMP3]`[t] ==
koncAMP3 cycAMP[t] R2C2cAMP2[t] - koffcAMP3 R2C2cAMP3[t] -
koncAMP4 cycAMP[t] R2C2cAMP3[t] + koffcAMP4 R2C2cAMP4[t],
[R2C2cAMP4]`[t] ==
koffPKA4GluA1 GluA1PKA4[t] + koffPKA4GluA1 p831PKA4[t] +
koncAMP4 cycAMP[t] R2C2cAMP3[t] - koffcAMP4 R2C2cAMP4[t] -
ksplitPKAc R2C2cAMP4[t] - konPKA4GluA1 GluA1[t] R2C2cAMP4[t] -
konPKA4GluA1 GluA1p831[t] R2C2cAMP4[t] +
kjoinPKAc PKAc[t] R2CcAMP4[t],
[R2cAMP4]`[t] == -koffR2cAMP R2cAMP4[t] -
kjoinPKAc PKAc[t] R2cAMP4[t] + ksplitPKAc R2CcAMP4[t],
[R2CcAMP4]`[t] ==
ksplitPKAc R2C2cAMP4[t] + kjoinPKAc PKAc[t] R2cAMP4[t] -
ksplitPKAc R2CcAMP4[t] - kjoinPKAc PKAc[t] R2CcAMP4[t]