

Table S1. Parameter Values for Model 1

Most values are taken from the literature or derived from values in the literature. In a few instances values were derived by fitting to published experimental data as described in Methods.

Parameter	Description	Value Range	Reference
Ca²⁺ binding to CaM			
K_D^{1C}	Equilibrium binding of 1 st Ca ²⁺ to CaM C-terminus	7.3 - 12 uM	[1-3]
k_{off}^{1C}	Ca ²⁺ dissociation from CaM C-terminus	10 - 70 s ⁻¹	[4-6]
k_{on}^{1C}	Ca ²⁺ binding to CaM C-terminus	1.2 - 9.6 uM ⁻¹ s ⁻¹	[7]
K_D^{2C}	Equilibrium binding of 2 nd Ca ²⁺ to CaM C-terminus	0.4 - 1.7 uM	[1-3]
k_{off}^{2C}	2 nd Ca ²⁺ dissociation from CaM C-terminus	8.5 - 10 s ⁻¹	[4]
k_{on}^{2C}	2 nd Ca ²⁺ binding to CaM C-terminus	5 - 25 uM ⁻¹ s ⁻¹	[7]
K_D^{1N}	Equilibrium binding of 1 st Ca ²⁺ to CaM N-terminus	15 - 40 uM	[1-3]
k_{off}^{1N}	1 st Ca ²⁺ dissociation from CaM N-terminus	1000 - 4000 s ⁻¹	[4,6,8,9]
k_{on}^{1N}	1 st Ca ²⁺ binding to CaM N-terminus	25 - 260 uM ⁻¹ s ⁻¹	[7]
K_D^{2N}	Equilibrium binding of 2 nd Ca ²⁺ to CaM N-terminus	3.3 - 9 uM	[1-3]
k_{off}^{2N}	2 nd Ca ²⁺ dissociation from CaM N-terminus	500 - >1000 s ⁻¹	[4-6,8,9]
k_{on}^{2N}	2 nd Ca ²⁺ binding to CaM N-terminus	50 - 300 uM ⁻¹ s ⁻¹	[7]
CaM binding to CaMKII			
k_{on}^{CaM0}	CaM0 binding to CaMKII	3.8 mM ⁻¹ s ⁻¹	[10]
k_{off}^{CaM0}	CaM0 dissociating from CaMKII	5.5 s ⁻¹	[10]
k_{on}^{CaM1C}	CaM1C binding to CaMKII	59 mM ⁻¹ s ⁻¹	[10]
k_{off}^{CaM1C}	CaM1C dissociating from CaMKII	6.1 s ⁻¹	[10]
K_D^{CaM2C}	Equilibrium binding of CaM2C to CaMKII	1.6 - 8.4 uM	[2]
k_{on}^{CaM2C}	CaM2C binding to CaMKII	0.92 uM ⁻¹ s ⁻¹	[10]
k_{off}^{CaM2C}	CaM2C dissociating from CaMKII	6.8 s ⁻¹	[10]
$k_{on}^{CaM1N1C}$	CaM1N1C binding to CaMKII	0.33 uM ⁻¹ s ⁻¹	[10]
$k_{off}^{CaM1N1C}$	CaM1N1C dissociating from CaMKII	3.4 s ⁻¹	[10]
$k_{on}^{CaM1N2C}$	CaM1N2C binding to CaMKII	5.2 uM ⁻¹ s ⁻¹	[10]
$k_{off}^{CaM1N2C}$	CaM1N2C dissociating from CaMKII	3.8 s ⁻¹	[10]
k_{on}^{CaM1N}	CaM1N binding to CaMKII	22 mM ⁻¹ s ⁻¹	[10]
k_{off}^{CaM1N}	CaM1N dissociating from CaMKII	3.1 s ⁻¹	[10]
K_D^{CaM2N}	Equilibrium binding of CaM2N to CaMKII	16.5 - 23.5 uM	[2]
k_{on}^{CaM2N}	CaM2N binding to CaMKII	0.12 uM ⁻¹ s ⁻¹	[10]
k_{off}^{CaM2N}	CaM2N dissociating from CaMKII	1.7 s ⁻¹	[10]

$k_{on}^{CaM\ 2N1C}$	CaM2N1C binding to CaMKII	$1.9\ \mu M^{-1}s^{-1}$	[10]
$k_{off}^{CaM\ 2N1C}$	CaM2N1C dissociating from CaMKII	$1.9\ s^{-1}$	[10]
$K_D^{CaM\ 4}$	Equilibrium binding of CaM4 to CaMKII	0.04 - 0.08 μM	[2,4,11-13]
$k_{on}^{CaM\ 4}$	CaM4 binding to CaMKII	$14 - 60\ \mu M^{-1}s^{-1}$	[7]
$k_{off}^{CaM\ 4}$	CaM4 dissociating from CaMKII	$1.1 - 2.3\ s^{-1}$	[14]
Ca²⁺ binding to CaM-CaMKII			
k_{off}^{K1C}	1 st Ca ²⁺ dissociation from K•CaM C-terminus	$33\ s^{-1}$	[15]
k_{on}^{K1C}	1 st Ca ²⁺ binding to K•CaM C-terminus	$44\ \mu M^{-1}s^{-1}$	[15]
k_{off}^{K2C}	2 nd Ca ²⁺ dissociation from K•CaM C-terminus	$0.49 - 4.9\ s^{-1}$	[4,8,14,15]
k_{on}^{K2C}	2 nd Ca ²⁺ binding to K•CaM C-terminus	$44\ \mu M^{-1}s^{-1}$	[15]
k_{off}^{K1N}	1 st Ca ²⁺ dissociation from K•CaM N-terminus	$300\ s^{-1}$	[15]
k_{on}^{K1N}	1 st Ca ²⁺ binding to K•CaM N-terminus	$76\ \mu M^{-1}s^{-1}$	[15]
k_{off}^{K2N}	2 nd Ca ²⁺ dissociation from K•CaM N-terminus	$6 - 60\ s^{-1}$	[4,8,14,15]
k_{on}^{K2N}	2 nd Ca ²⁺ binding to K•CaM N-terminus	$76\ \mu M^{-1}s^{-1}$	[15]
CaMKII autophosphorylation			
K_D^{CaMKII}	Equilibrium binding of two CaMKII subunits	1.3 - 45 μM	[16,17]
k_{on}^{CaMKII}	K•CaM binding to KCaM	$10 - 100\ \mu M^{-1}s^{-1}$	[18,19]
k_{off}^{CaMKII}	K•CaM dissociation from KCaM	$13 - 4500\ s^{-1}$	[7]
$k_{on}^{CaMKIIP}$	K•CaM binding to pKCaM	$10 - 100\ \mu M^{-1}s^{-1}$	[18,19]
$k_{off}^{CaMKIIP}$	K•CaM dissociation from pKCaM	$13 - 4500\ s^{-1}$	[7]
$k_p^{CaM\ 0}$	Autophosphorylation of KCaM0	$0\ s^{-1}$	[20]
$k_p^{CaM\ 1C}$	Autophosphorylation of KCaM1C	$0.0 - 0.084\ s^{-1}$	[20]
$k_p^{CaM\ 2C}$	Autophosphorylation of KCaM2C	$0.044 - 0.084\ s^{-1}$	[2]
$k_p^{CaM\ 1N1C}$	Autophosphorylation of KCaM1N1C	$0.0 - 0.16\ s^{-1}$	[20]
$k_p^{CaM\ 1N2C}$	Autophosphorylation of KCaM1N2C	$0.044 - 1.25\ s^{-1}$	[20]
$k_p^{CaM\ 1N}$	Autophosphorylation of KCaM1N	$0.0 - 0.16\ s^{-1}$	[20]
$k_p^{CaM\ 2N}$	Autophosphorylation of KCaM2N	$0.079 - 0.16\ s^{-1}$	[2]
$k_p^{CaM\ 2N1C}$	Autophosphorylation of KCaM2N1C	$0.079 - 1.25\ s^{-1}$	[20]
$k_p^{CaM\ 4}$	Autophosphorylation of KCaM4	$0.5 - 1.25\ s^{-1}$	[2,21]

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