

Table S1. *Parameters and variables for the dynamical model*

Name	Definition	MATLAB notation	Value	Unit	References	Etc.
κ	pMHC-TCR association rate	kappa	10^{-4}	s^{-1}	(Altan-Bonnet and Germain, 2005; François et al., 2013)	
ν	pMHC-TCR dissociation rate	nu	$0.1 \sim 1$	s^{-1}	(Altan-Bonnet and Germain, 2005; François et al., 2013)	$0.1 \sim 0.4$ for MAPPA
N	Number of phosphorylation steps	N	5		(François et al., 2013)	
ϕ_{max}	Phosphorylation rate	phi_max	0.09	s^{-1}	(François et al., 2013)	
b	Spontaneous dephosphorylation rate	b	0.04	s^{-1}	(François et al., 2013)	
γ	Phosphatase efficiency	gamma	1.2×10^{-6}	s^{-1}	(François et al., 2013)	
$S_{SHP1,T}$	Number of phosphatase (SHP-1) per cell	S_SHP1_t	60,000		(François et al., 2013)	
$C_{TCR,1}^*$	Half saturation level of $C_{TCR,1}$ for S_{SHP1} activation	C_TCR_1_star	500		(François et al., 2013)	
k_{costim}^{on}	Association rate of CD80/CD86 and CD28	k_on_costim	0.77 ± 0.06	$\mu m^2 s^{-1}$	(Collins et al., 2002)	Converted to 2D rate following (Jansson and Davis, 2011)
k_{costim}^{off}	dissociation rate of CD80/CD86 and CD28	k_off_costim	28 ± 2	s^{-1}	(Collins et al., 2002)	
k_{CTLA4}^{on}	Association rate of CD80/CD86 and CTLA $min^{-1}4$	k_on_CTLA4	1.09	$\mu m^2 s^{-1}$	(Collins et al., 2002)	Converted to 2D rate following (Jansson and Davis, 2011)
k_{CTLA4}^{off}	Dissociation rate of CD80/CD86 and CTLA4	k_off_CTLA4	5.1	s^{-1}	(Collins et al., 2002)	
k_{CTLA4}^{endo}	Rate of CTLA4 endocytosis	k_endo_CTLA4	0.291	m^{-1}	(Khailaie et al., 2017)	
$k_{mIL2R\alpha}^{transcription(basal)}$	Basal transcription rate of IL2R α	k_transc_basal_mIL2R_alpha	$0.03 \times k_{IL2\alpha}^{deg}$	h^{-1}	(Voisinne et al., 2015)	

$k_{mIL2R\alpha}^{transcription(TCR, costim)}$	Transcription rate of IL2R α downstream of TCR	k_transc_TCR_costim_mIL2R_alpha	$10 \times k_{IL2R\alpha}^{deg}$	h^{-1}	(Voisinne et al., 2015)	
$k_{mIL2R\alpha}^{transcription(pSTAT5)}$	Transcription rate of IL2R α downstream of pSTAT5	k_transc_pSTAT5_mIL2R_alpha	$4 \times 10^2 \times k_{IL2R\alpha}^{deg}$	h^{-1}	(Voisinne et al., 2015)	
$K_{TCR \rightarrow IL2R\alpha}$	Half saturation level of TCR activation for IL2R α production	K_TCR_IL2R_alpha	0.2 0.3		(François et al., 2013) (Voisinne et al., 2015)	0.1~1 for MAPPA
$n_{TCR \rightarrow IL2R\alpha}$	Hill coefficient of TCR activation for IL2R α production	n_TCR_IL2R_alpha	1		(Voisinne et al., 2015)	
$K_{costim \rightarrow IL2R\alpha}$	Half saturation level of costimulation for IL2R α production	K_costim_IL2R_alpha	10~100		This study	Varied for MAPPA
$n_{costim \rightarrow IL2R\alpha}$	Hill coefficient of costimulation for IL2R α production	n_costim_IL2R_alpha	1		This study	
$K_{JAK \rightarrow pSTAT5}$	Half saturation level of JAK activation for IL2R α production	K_JAK_pSTAT5	0.05		(Voisinne et al., 2015)	
$n_{JAK \rightarrow pSTAT5}$	Hill coefficient of JAK activation for IL2R α production	n_JAK_pSTAT5	2		(Busse et al., 2010; Feinerman et al., 2010; Voisinne et al., 2015)	For bistability of IL2R α
$K_{IL2 \rightarrow JAK}^{high}$	Half saturation level of IL2 for JAK activation (for high IL2R α level)	K_IL2_JAK_high	1	pM	(Voisinne et al., 2015)	
$K_{IL2 \rightarrow JAK}^{low}$	Half saturation level of IL2 for JAK activation (for low IL2R α level)	K_IL2_JAK_low	50	pM	(Voisinne et al., 2015)	
$R_{IL2R\alpha,0}$	Half saturation level of IL2R α for JAK activation	R_IL2R_alpha_0	2×10^4		(Voisinne et al., 2015)	
$k_{mIL2R\alpha}^{deg}$	Degradation rate of IL2R α mRNA	k_deg_mIL2R_alpha	0.2	h^{-1}	(Voisinne et al., 2015)	
$k_{IL2R\alpha}^{translation}$	Translation rate of IL2R α	k_transl_IL2R_alpha	$10^2 \times k_{mIL2R\alpha}^{deg}$	h^{-1}	(Voisinne et al., 2015)	
$k_{IL2R\alpha}^{deg}$	Rate of IL2R α endocytosis	k_deg_IL2R_alpha	$\ln(2)/5$ 0.05	h^{-1}	(Duprez et al., 1988; Tkach et al., 2014)	Set to 0.05 in this study

(Duprez and Dautry-Varsat, 1986; Voisinne et al., 2015)

$K_{IL2R\alpha;\beta\gamma,d}$	$k_{IL2\alpha;\beta\gamma}^{off}/k_{IL2\alpha;\beta\gamma}^{on}$	K_IL2R_a_bg	2700		(Cotari et al., 2013)	
$k_{IL2\alpha;\beta\gamma}^{on}$	Association rate of IL2R α and IL2R $\beta\gamma$		Not needed			
$k_{IL2\alpha;\beta\gamma}^{off}$	Dissociation rate of IL2R α -IL2R $\beta\gamma$ complexes		Not needed			
$k_{c_{IL2R}}^{endo}$	Rate of endocytosis of IL2-IL2R complexes	k_endo_C_IL2R	$\ln(2)/0.25$ 1.7	h^{-1}	(Duprez et al., 1988) (Busse et al., 2010)	Set to 2 in this study
k_{IL2R}^{on}	Association rate of IL2 and IL2R	k_on_IL2R	1.1×10^{11}	$M^{-1}h^{-1}$	(Wang and Smith, 1987)	
k_{IL2R}^{off}	Dissociation rate of IL2-IL2R complexes	k_off_IL2R	0.83	h^{-1}	(Wang and Smith, 1987)	
$K_{c_{IL2R},d}$	Equilibrium dissociation constant ($k_{IL2R}^{off}/k_{IL2R}^{on}$)	K_IL2_tr	1.0×10^{-11}	M	(Wang and Smith, 1987)	Used only for Tregs
$k_{mIL2}^{transcription(TCR)}$	Transcription rate of IL2 downstream of TCR and costimulation	k_transc_TCR_mIL2	162	h^{-1}	(Ferguson et al., 2001)	
$k_{mIL2}^{transcription(costim)}$	Transcription rate of IL2 downstream of costimulation	k_transc_costim_mIL2				
k_{mIL2}^{deg}	Degradation rate of IL-2 mRNA molecules	k_deg_mIL2	0.2	h^{-1}	(Shim et al., 2002)	
$k_{IL2}^{translation}$	Translation rate of IL-2	k_transl_IL2	266	h^{-1}	(Ferguson et al., 2001; Voisinne et al., 2015)	
k_{IL2}^{sec}	$\frac{k_{mIL2}^{transcription(TCR,costim)}k_{IL2}^{transl}}{k_{mIL2}^{deg}}$		60 7.5×3600 $1,200 \pm 500$	s^{-1} h^{-1} min^{-1}	(Voisinne et al., 2015) (Tkach et al., 2014) (Huang et al., 2013)	Dynamical variable in this study (q_{IL2})
$K_{TCR \rightarrow IL2}$	Half saturation level of TCR activation for IL2 production	K_TCR_IL2	0.2 0.8		(François et al., 2013) (Voisinne et al., 2015)	0.1~1 for MAPPA
$n_{TCR \rightarrow IL2}$	Hill coefficient of TCR activation for IL2 production	n_TCR_IL2	1		(Voisinne et al., 2015)	

$K_{costim \rightarrow IL2}$	Half saturation level of costimulation for IL2 production	K_costim_IL2	10~100		This study	
$n_{costim \rightarrow IL2}$	Hill coefficient of costimulation for IL2 production	n_costim_IL2	1		This study	
$K_{pSTAT5 \rightarrow IL2}$	Half saturation level of pSTAT5 for IL2 production	K_pSTAT5_IL2	$1/3 \cdot 10^5$		(Tkach et al., 2014)	0.1~1 for MAPPA
$n_{pSTAT5 \rightarrow IL2}$	Hill coefficient of pSTAT5 for IL2 production	n_pSTAT5_IL2	1		This study	
D_{IL2}	Diffusion constant of IL2	D_IL2	(aq) 100 (ext) 16 10 (T cell zone) 100	$\mu m^2 s^{-1}$	(Weidemann et al., 2011) (Höfer et al., 2012) (Busse et al., 2010) (Ross and Pompano, 2018)	aq: aqueous buffer ext: extracellular matrix 10~100 For MAPPA
$k_{IL2,extr}^{deg}$	Degradation rate of IL2 in the extracellular space of lymph nodes	k_deg	0.1	h^{-1}	(Busse et al., 2010)	
ρ	Radius of a T cell		4~10	μm		Set to 5 in this study
n_{tr}	Number density of regulatory T cells	n_tr, n_tr0	0.0001~0.001	μm^{-3}	This study	0.001: gastric lymph nodes
S_{DC}	Surface area of dendritic cells	S_DC	1,800~2,400	μm^2	(Miller et al., 2004)	Set to 2000 in this study
$S_{DC:T}$	Surface area of dendritic cell-T cell contacts	S_DC_TR	1~8 (avg)~70 12.6	μm^2	(Miller et al., 2004) (Jansson and Davis, 2011)	Set to 8 in this study
S_T	Surface area of T cells	S_T	314.16	μm^2		$4\pi\rho^2$
D_{tr}	Motility coefficient of Tregs	D_tr	0.83~1.76 0.17 (free Treg) 0.017 (Treg in contact with DC)	$\mu m^2 min$ $\mu m^2 s^{-1}$	(Wu et al., 2015) This study	JURKAT T-cells 3D In vivo Tregs
χ_0	Chemotactic constant	chi_0	0~100		This study	Set to 0 in this study
K_{cc}	Carrying capacity of Treg	K_cc	0.003	μm^{-3}	This study	
$k_{IL2 \rightarrow treg}^{prolif}$	Proliferation rate of Tregs induced by IL2	k_prolif_max	0.0385 1.07×10^{-5}	h^{-1} s^{-1}	This study	Doubling time: 18 hours

$K_{IL2 \rightarrow treg}^{prolif}$	Half maximum level of pSTAT5 for Treg proliferation	K_prolif_IL2	0.1		This study	
U_{min}	Minimum attractive potential between DCs and Tregs	U_min	0.05		This study	To simulate adhesive force between DCs and Tregs
n_U	Steepness of the potential	n_U	5		This study	
r_{half}	Distance leading to half U_{min}	r_half	15	μm	This study	
$K_{CD28, tr \rightarrow Umin}$	Half saturation CD28 signaling strength for adhesion	K_CD28_tr_U_min			This study	
$K_{pstat5, tr \rightarrow Umin}$	Half saturation pSTAT5 signaling strength for adhesion	K_pSTAT5_tr_U_min			This study	
f_{cont_low} f_{cont_high}	Contact efficiency between Tregs and DCs	f_contact_low f_contact_high	0.1~0.4 1~2.5		This study	Varied for MAPPA
$V_{neighbor}$	Volume of space encompassing the region where Tregs are in the engagement with DCs	V_neighbor	837.8	μm^3		$\frac{3}{4}\pi(15^2 - 5^2)$
$L_{antigen}$	Number of peptide-MHC per cell	L_antigen	1~10 ⁵		(Altan-Bonnet and Germain, 2005; François et al., 2013)	100~1000 for MAPPA
R_{TCR}	Number of TCR per cell	R_TCR	30,000		(Altan-Bonnet and Germain, 2005; François et al., 2013)	
$C_{TCR,j},$ $j = 0, \dots, N$		C_TCR_N			(François et al., 2013)	
S_{SHP1}	Number of activated phosphatase (SHP-1) per cell	S_SHP_1			(François et al., 2013)	
ϕ	Phosphorylation rate			s^{-1}	(François et al., 2013)	
R_{CD28}	Number of CD28 molecules per cell	R_CD28	30,000		(Sugár et al., 2017)	Similar to TCR

$L_{CD80 CD86}$	Number of CD80/CD86 molecules per cell	L_CD80_86, L_CD80_86_i	CD86: 400,000 CD80/CD86: 300,000	(Qureshi et al., 2011) (Khailaie et al., 2017)	100,000~1,000,000 for MAPPA
R_{CTLA4}	Number of CTLA-4 molecules on plasma membrane per cell	R_CTLA4	24500	(Khailaie et al., 2017)	
C_{CTLA4}	Number of CD80 CD86-CTLA-4 complexes per cell	C_CTLA4			
C_{costim}	Number of CD80 CD86-CD28 complexes per cell	C_costim			
$mR_{IL2R\alpha}$	Number of IL2R α mRNA	mR_IL2R_alpha			
$P_{TCR \rightarrow IL2R\alpha}^{on}$	Activation function of TCR for IL2R α production	P_on_TCR_IL2			
$P_{JAK \rightarrow pSTAT5}^{on}$	Activation function of JAK for pSTAT5 signaling	P_on_JAK_pSTAT5			
$P_{costim \rightarrow IL2R\alpha}^{on}$	Activation function of costimulation for IL2R α production	P_on_costim_IL2R_alpha			
S_{JAK}	Normalized level of activated JAK	S_JAK		(Voisinne et al., 2015)	
$R_{IL2R\alpha}$	Number of IL2R α molecules on plasma membrane per cell	R_IL2R_alpha	Tconv (basal): 3 Tconv (TCR): 1000 Tconv (IL2 max): 4×10^4 Treg (basal): 10^3 Treg (IL2 max): 4×10^4 Treg (constant): 10^4	(Voisinne et al., 2015) (Voisinne et al., 2015) (Voisinne et al., 2015) (Voisinne et al., 2015) (Voisinne et al., 2015) (Voisinne et al., 2015) (Feinerman et al., 2010)	
$R_{IL2R\beta\gamma}$	Number of IL2R $\beta\gamma$ molecules on plasma membrane per cell	R_IL2R_bg	Basal (w/o TCR activation): 1000 Max (with TCR activation): 10000	(Cotari et al., 2013) (Tkach et al., 2014)	w/o: without

R_{IL2R}	Number of IL2R molecules (IL2R α -IL2R $\beta\gamma$ complexes) on plasma membrane per cell	R_IL2R		
C_{IL2R}	Number of IL2-IL2R complexes on plasma membrane per cell	C_IL2R		
I_{mIL2}	Number of IL2 mRNA per cell	ml_IL2		
I_{IL2}	Concentration of IL2 in extracellular space in lymph node	I_IL2	μm^{-3} pM	
q_{IL2}	Secretion rate of IL2 to extracellular space	q_IL2	s^{-1}	$k_{IL2}^{translation} \cdot I_{mIL2}$
n_{tr}	Number density of Tregs in extracellular space surrounding a priming Tconv in lymph node	n_tr	μm^{-3}	

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