Supplementary Table 1

Sensitivity of the model to alteration of individual parameters at the baseline period of 23.8 hours

parameter	description	classification	relative sensitivity of period*
umPt	degradation rate constant for Per2	Degradation	-0.254
unbin	normalized binding rate constant for BMAL-CLOCK/NPAS2 to Per1/2/Cry1 E-box	Association	-0.223
Ct	total CK1 concentration	Phosphorylation	-0.152
ac	binding rate constant for PER1/2 to CKIε/δ	Phosphorylation	-0.125
hto	CKIε/δ phosphorylation rate constant for PER2	Phosphorylation	-0.103
ubc	degradation rate constant for BMAL-CLOCK/NPAS2	Degradation	-0.096
nl	nuclear localization rate constant for proteins bound to PER	Translocation	-0.096
umRt	degradation rate constant for Cry2	Degradation	0.089
up	degradation rate constant for CKI phosphorylated PER	Degradation	0.082
trRt	transcription rate constant for Cry2	Production	-0.05
tlr	translation rate constant for CRY1 and CRY2	Production	-0.047
umB	degradation rate constant for Bmal1	Degradation	-0.047
dr	unbinding rate constant for PER1/2 to CRY1/2	Association	-0.044
trgto	increase rate of GSK3β activity	Phosphorylation	0.044
urt	degradation rate constant for Cry2	Degradation	0.044
ugto	decrease rate of GSK3β activity	Phosphorylation	-0.043
tlc	translation rate constant for CLOCK	Production	-0.043
ar	binding rate constant for PER1/2 to CRY1/2	Association	-0.041
tmc	rate constant for folding and nuclear export of Per1/2, Cry1/2, Bmal and Npas2 mRNA	Translocation	-0.037
hoo	CKIε/δ phosphorylation rate constant for PER1	Phosphorylation	-0.03
uro	degradation rate constant for CRY1	Degradation	-0.028
Nf	ratio of nuclear to cytoplasmic compartment volume	Translocation	-0.026
phos	phosphorylation rate constant for BMAL-CLOCK/NPAS2	Phosphorylation	-0.022
trPt	transcription rate constant for of Per2	Production	0.021
tlp	translation rate constant for PER1 and PER2	Production	0.021
us	clearance rate of cAMP and activated CREB	Degradation	-0.021
umPo	degradation rate constant for Per1	Degradation	-0.018
unbinrev	normalized unbinding rate constant for REV-ERBs to Cry1/Npas2 RORE	Association	0.016
tlrev	translation rate constant for REV-ERBs	Production	-0.016
urev	degradation rate constant for unphosphorylated REV-ERBs	Degradation	0.016
cbin	binding rate constant for BMAL to CLOCK/NPAS2	Association	-0.015
binrev	normalized binding rate constant for REV-ERBs to Cry1/Npas2 RORE	Association	-0.015

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umRev	degradation rate constant for Rev-Erbs	Degradation	0.015
uncbin	unbinding rate constant for BMAL to CLOCK/NPAS2	Association	0.015
trRev	transcription rate constant for Rev-Erbs	Production	-0.014
uc	degradation rate constant for CLOCK/NPAS2	Degradation	0.013
ag	binding rate constant for REV-ERBs to GSK3β	Phosphorylation	0.012
cbbin	binding rate constant for CRY1/2 to BMAL-CLOCK/NPAS2 in the nucleus	Association	-0.012
tlb	translation rate constant for BMAL	Production	0.011
Ek	potassium reversal potential	Voltage Dynamics	-0.011
trB	transcription rate constant for Bmal	Production	0.01
dc	unbinding rate constant for PER1/2 to CKIε/δ	Phosphorylation	0.01
ts	clearance time constant for shell calcium	Calcium Dynamics	-0.009
lne	nuclear export rate constant for unbound kinases GSK3β and CKI	Translocation	0.008
trPo	transcription rate constant for Per1	Production	-0.007
CtrPt	transcription rate of Per2 from CRE activation	Production	0.007
ks	conversion factor between calcium current and shell calcium concentration	Calcium Dynamics	-0.007
tc	clearance time constant for cytosolic calcium	Calcium Dynamics	0.007
upu	degradation rate constant for unphosphorylated PER	Degradation	-0.007
dg	unbinding rate constant for PER2/REV-ERBs to GSK3β	Phosphorylation	-0.006
unsbin	rate constant for activated CREB unbinding from CRE site	Coupling	-0.006
bbin	binding rate constant for PER1/2 to BMAL-CLOCK/NPAS2 in the nucleus	Association	-0.006
binrevb	normalized binding rate constant for REV-ERBs to Bmal RORE	Association	-0.006
trRo	transcription rate constant for of Cry1	Production	0.005
clk	the strength of the influence of the molecular clock on the electrical activity of SCN neurons	Voltage Dynamics	0.005
uncbbin	unbinding rate constant for CRY1/2 to BMAL-CLOCK/NPAS2 in the nucleus	Association	0.005
unbinrevb	normalized unbinding rate constant for REV-ERBs to Bmal RORE	Association	0.005
unbinc	normalized unbinding rate constant for BMAL-CLOCK/NPAS2 to Cry2 E-box	Association	-0.004
umNp	degradation rate constant for Npas2	Degradation	0.004
Eca	calcium reversal potential	Voltage Dynamics	-0.004
sbin	rate constant for activated CREB binding to CRE site on DNA	Coupling	0.003
kc	conversion factor between calcium current and cytosolic calcium concentration	Calcium Dynamics	0.003
nlrev	nuclear localization rate constant for REV-ERBs as well as GSK3β if bound	Translocation	-0.003
Ena	sodium reversal potential	Voltage Dynamics	0.003
K2	sigmoid parameter for inactivation of L-type calcium channels	Calcium Dynamics	0.003
uprev	degradation rate constant for GSK3β phosphorylated REV-ERBs	Degradation	0.002
ub	degradation rate constant for Bmal	Degradation	-0.002
umRo	degradation rate constant for Cry1	Degradation	-0.002
bs	basal release rate of shell calcium	Calcium Dynamics	-0.002

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gna	maximum sodium conductance	Voltage Dynamics	-0.002
taurl	time constant of L-type calcium channels	Calcium Dynamics	-0.002
gcanl	maximum conductance of non-L-type calcium channels	Voltage Dynamics	-0.002
nlbc	nuclear localization rate constant for BMAL-CLOCK/NPAS2	Translocation	-0.002
tmcrev	rate constant for folding and nuclear export of Rev-Erbs mRNA	Translocation	-0.001
trNp	transcription rate constant for Npas2	Production	-0.001
K1	sigmoid parameter for inactivation of L-type calcium channels	Calcium Dynamics	0.001
uv	degradation rate of VIP	Degradation	-0.001
CtrPo	transcription rate of Per1 from CRE activation	Production	-0.001
uncvbin	rate constant for CRY1/CRY2 unbinding from VPAC2R	Coupling	-0.001
gk	maximum potassium conductance	Voltage Dynamics	0.001
unbbin	unbinding rate constant for PER1/2 to BMAL-CLOCK/NPAS2 in the nucleus	Association	-0.001
cvbin	rate constant for CRY1/CRY2 binding to VPAC2R	Coupling	-0.001
vbin	rate constant for VIP binding to VPAC2R	Coupling	0.001
unbinr	normalized unbinding rate constant for BMAL-CLOCK/NPAS2 to Rev-erbs E-box	Association	-0.001
Vt	VPAC2R expression level	Production	-0.001
binc	normalized binding rate constant for BMAL-CLOCK/NPAS2 to Cry2 E-box	Association	0.001
tlnp	translation rate constant for NPAS2	Production	-0.001
ne	nuclear export rate constant for protein bound to PER	Translocation	-0.001
gcal	maximum conductance of L-type calcium channels	Voltage Dynamics	0.001
nerev	nuclear export rate constant for REV-ERBs as well as GSK3β if bound	Translocation	-0.001
Gt	total GSK3β concentration	Phosphorylation	0.001
agp	binding rate constant for PER2 to GSK3β	Phosphorylation	0
c	membrane capacitance	Voltage Dynamics	0
binr	normalized binding rate constant for BMAL-CLOCK/NPAS2 to Rev-erbs E-box	Association	0
vs	cAMP production rate (when VPAC2R bound by VIP & not inhibited by CRY) (= activation rate of CREB by cAMP)	Coupling	0
bin	normalized binding rate constant for BMAL-CLOCK/NPAS2 to Per1/2/Cry1 E-box	Association	0
taurnl	time constant of non-L-type calcium channels	Calcium Dynamics	0
unvbin	rate constant for VIP unbinding from VPAC2R	Coupling	0
bc	basal release rate of cytosolic calcium	Calcium Dynamics	0
gnaleak	sodium leak channel conductance	Voltage Dynamics	0
vpr	VIP release rate	Association	0
gkca	maximal conductance of calcium-dependent potassium channels	Voltage Dynamics	0
gkleak	potassium leak channel conductance	Voltage Dynamics	0
aR	rate of GABA synapic channel opening	Voltage Dynamics	0
aD	rate of GABA synapic channel closing	Voltage Dynamics	0

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Tmax	maximum released GABA neurotransmitter concentration	Voltage Dynamics	0
VT	GABA synapse release threshold	Voltage Dynamics	0
Kp	GABA synapse release sensitivity	Voltage Dynamics	0
Egaba	GABA synaptic current reversal potential	Voltage Dynamics	0
ggaba	maximum conductance of the GABA synaptic current	Voltage Dynamics	0
Iglut	strength of the current caused by glutamate input (irrelevant in DD)	Voltage Dynamics	0

**** Positive values occur when increasing the parameter value increases period.***

Highlighted parameters increase period from wild type to mPer2(Luc) with a <25% change from baseline