Parameter Description	Symbol	Value
Initial free plasma concentration of CK1 inhibitor (32 mg/kg)	**prodi**	**2562.61 nM**
Transfer rate from plasma to brain for CK1 inhibitor	**nlpin**	**6.33/hr**
Transfer rate from brain to plasma for CK1 inhibitor	**nepin**	**15.35/hr**
Transfer rate from brain to cell for CK1 inhibitor	**nlbin**	**0.486/hr**
Transfer rate from cell to brain for CK1 inhibitor	**nebin**	**19.2/hr**
Nuclear localization rate constant for CK1 inhibitor	**nlin**	**0.533/hr**
Nuclear export rate constant for CK1 inhibitor	**nein**	**0.192/hr**
Nuclear export rate constant for CK1 and CK1 inhibitor complex	**lnei**	**0.047/hr**
Binding rate constant for CK1 inhibitor to CK1	**inbin**	**0.421/nMhr**
Unbinding rate constant for CK1 inhibitor to CK1	**inubin**	**3.38/hr**
Clearance rate constant for free CK1 inhibitor in plasma	**uinp**	**1.653/hr**
Ratio of cytoplasmic to nuclearcompartment volume	Nf*	3.351
Transcription rate constant for Per1	trPo	25.92nM/hr
Transcription rate constant for Per2	trPt	44.85nM/hr
Transcription rate constant for Cry1	trRo	23.07nM/hr
Transcription rate constant for Cry2	trRt	39.94nM/hr
Transcription rate constant for Bmal (1)	trB	46.10nM/hr
Transcription rate constant for Npas2 (1)	trNp	0.33nM/hr
Transcription rate constant for Rev-Erbs	trRev	102.9nM/hr
Translation rate constant for PER1 and PER2	tlp	1.81/hr
Translation rate constant for CRY1 and CRY2	tlr	5.038/hr
Translation rate constant for BMAL (1)	tlb	0.53/hr
Translation rate constant for CLOCK (1)	tlc	4.645/hr
Translation rate constant for NPAS2 (1)	tlnp	1.251/hr
Translation rate constant for REV-ERBs	tlrev	8.907/hr
Binding rate constant for PER2 to GSK3β (4)	agp	1.396/nMhr
Binding rate constant for REV-ERBs to GSK3β (4)	ag	0.162/nMhr
Unbinding rate constant for PER2/REV-ERBs to GSK3β (4)	dg	2.935/hr
Binding rate constant for PER1/2 to CKIε/δ	ac	0.046/nMhr

Unbinding rate constant for PER1/2 to CKIε/δ	dc	0.108/hr
Binding rate constant for PER1/2 to CRY1/2	ar	0.024/nMhr
Unbinding rate constant for PER1/2 to CRY1/2	dr	0.605/hr
Binding rate constant for PER1/2 to BMAL-CLOCK/NPAS2 in the nucleus (2)	bbin	6.926/nMhr
Unbinding rate constant for PER1/2 to BMAL-CLOCK/NPAS2 in the nucleus (2)	unbbin	0.13/hr
Binding rate constant for CRY1/2 to BMAL-CLOCK/NPAS2 in the nucleus (2)	cbbin	6.599/nMhr
Unbinding rate constant for CRY1/2 to BMAL-CLOCK/NPAS2 in the nucleus (2)	uncbbin	0.304/hr
Binding rate constant for BMAL to CLOCK/NPAS2 (1)	cbin	0.045/nMhr
Unbinding rate constant for BMAL to CLOCK/NPAS2 (1)	uncbin	7.272/hr
Binding rate constant for REV-ERBs to GSK3β (4)	ag	0.162/nMhr
Normalized binding rate constant for BMAL-CLOCK/NPAS2 to Per1/2/Cry1 E-box (3)	bin	6.972/hr
Normalized unbinding rate constant for BMAL-CLOCK/NPAS2 to Per1/2/Cry1 E-box (3)	unbin	0.255/hr
Normalized binding rate constant for BMAL-CLOCK/NPAS2 to Cry2 E-box (3)	binc	0.280/hr
Normalized unbinding rate constant for BMAL-CLOCK/NPAS2 to Cry2 E-box (3)	unbinc	0.009/hr
Normalized binding rate constant for BMAL-CLOCK/NPAS2 to Rev-erbs E-box (3)	binr	6.154/hr
Normalized unbinding rate constant for BMAL-CLOCK/NPAS2 to Rev-erbs E-box (3)	unbinr	2.91/hr
Normalized binding rate constant for REV-ERBs to Bmal RORE (1)	binrevb	0.006/hr
Normalized unbinding rate constant for REV-ERBs to Bmal RORE (1)	unbinrevb	5.305/hr
Normalized binding rate constant for REV-ERBs to Cry1/Npas2 RORE (1)	binrev	0.012/hr
Normalized unbinding rate constant for REV-ERBs to Cry1/Npas2 RORE (1)	unbinrev	10.97/hr
Rate constant for folding and nuclear export of Per1/2, Cry1/2, Bmal and Npas2 mRNA	tmc	0.164/hr
Rate constant for folding and nuclear export of Rev-Erbs mRNA	tmcrev	9.263/hr
Nuclear localization rate constant for proteins bound to PER	nl	0.643/hr
Nuclear export rate constant for protein bound to PER	ne	0.026/hr
Nuclear localization rate constant for REV-ERBs as well as GSK3β if bound (4)	nlrev	9.637/hr
Nuclear export rate constant for REV-ERBs as well as GSK3β if bound (4)	nerve	0.015/hr
Nuclear localization rate constant for BMAL-CLOCK/NPAS2 (1)	nlbc	5.265/hr

Nuclear export rate constant for unbound kinases GSK3β and CKI (4)	lne*	0.595/hr
Total CK1 concentration	Ct	57.61nM
Total GSK3β concentration (4)	Gt	79.73nM
CKIε/δ phosphorylation rate constant for PER1	hoo	0.527/hr
CKIε/δ phosphorylation rate constant for PER2	hto	2.456/hr
Phosphorylation rate constant for BMAL-CLOCK/NPAS2 (1)	phos	0.291/hr
Increase rate of GSK3β activity (4)	trgto	0.644/hr
Decrease rate of GSK3β activity (4)	ugto	0.063/hr
Degradation rate constant for Per1	umPo	0.765/hr
Degradation rate constant for Per2	umPt	0.589/hr
Degradation rate constant for Cry1	umRo	0.403/hr
Degradation rate constant for Cry2	umRt	0.456/hr
Degradation rate constant for Bmal (1)	umB	0.795/hr
Degradation rate constant for Npas2 (1)	umNp	0.369/hr
Degradation rate constant for Rev-Erbs	umRev	1.51/hr
Degradation rate constant for unphosphorylated PER	upu	0.07/hr
Degradation rate constant for CKI phosphorylated PER	up	3.537/hr
Degradation rate constant for CRY1	uro	0.174/hr
Degradation rate constant for CRY2	urt	0.482/hr
Degradation rate constant for BMAL (1)	ub	0.019/hr
Degradation rate constant for CLOCK/NPAS2 (1)	uc	0.025/hr
Degradation rate constant for BMAL-CLOCK/NPAS2 (1)	ubc	0.349/hr
Degradation rate constant for unphosphorylated REV-ERBs (4)	urev	1.649/hr
Degradation rate constant for GSK3β phosphorylated REV-ERBs (4)	uprev	0.517/hr
Additional Per1 transcription rate in the presence of light(5)	lono	0.206
Additional Per2 transcription rate in the presence of light (5)	lont	0.396
Light level (5)	ltI	500 lux
Rate of activation of pho (5)	lta	0.607
Light effect decrease (backward) rate (5)	ltb	0.013

Table S5. Parameters of the mathematical model.11 new parameters that describe dynamics of CK1 inhibitor (PF-670462) are highlighted in bold. * indicates two parameters of the original Kim-Forger model, which are also used to describe dynamics

of CK1 inhibitor (Figure S2b). Presented value of prodi represents the initial free plasma concentration of CK1 inhibitor corresponding to 32 mg/kg dosing. The value of prodi is scaled according to the amount of dosing. For the *in vitro* simulations, presented value of prodi represents the initial free CK1 inhibitor concentration in medium after 5.2 μM dose, which is scaled according to the amount of dosing. See Materials and methods for details of parameter estimation. Parameters of original model are adopted from Supplementary Table S3 in Kim and Forger, MSB (2012).