**Suppl. Table S1. Model Parameter Values.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| parameter | WT  | Par\_I | Par\_II | Par\_III |  **Parameter description** |
| **Degradation rates for nuclear proteins or nuclear protein complexes [h−1]** |
| *dx1* | 0.08 | 0.064 | 0.099 | 0.073 | CLOCK/BMAL |
| *dx2* | 0.06 | 0.057 | 0.055 | 0.048 | PER\*N/CRYN |
| *dx3* | 0.09 | 0.079 | 0.111 | 0.089 | PERN/CRYN |
| *dx5* | 0.17 | 0.185 | 0.187 | 0.171 | REV-ERBN |
| *dx6* | 0.12 | 0.076 | 0.104 | 0.109 | RORN |
| *dx7* | 0.15 | 0.11 | 0.176 | 0.12 | BMALN |
| **Degradation rates for mRNAs [h−1]** |
| *dy1* | 0.3 | 0.358 | 0.338 | 0.29 | *Per* |
| *dy2* | 0.2 | 0.17 | 0.214 | 0.162 | *Cry* |
| *dy3* | 2 | 1.836 | 1.586 | 1.792 | *Rev-Erb* |
| *dy4* | 0.2 | 0.13 | 0.169 | 0.149 | *Ror* |
| *dy5* | 1.6 | 1.353 | 1.234 | 1.663 | *Bmal* |
| **Degradation rates for cytoplasmic proteins [h−1]** |
| *dz1* | 0.23 | 0.208 | 0.22 | 0.236 | CRYC |
| *dz2* | 0.25 | 0.194 | 0.293 | 0.22 | PERC |
| *dz3* | 0.6 | 0.442 | 0.663 | 0.551 | PERC\* |
| *dz4* | 0.2 | 0.184 | 0.182 | 0.17 | PERC\*/CRYC |
| *dz5* | 0.2 | 0.207 | 0.254 | 0.151 | PERC/CRYC |
| *dz6* | 0.31 | 0.274 | 0.35 | 0.274 | REV-ERBC |
| *dz7* | 0.3 | 0.392 | 0.34 | 0.286 | RORC |
| *dz8* | 0.73 | 0.769 | 0.897 | 0.815 | BMALC |
| **Reaction rates for complex formation/dissociation** |
| *kfx1* | 2.3 | 2.27 | 2.727 | 2.524 | CLOCK/BMAL formation **[h−1]**CLOCK is assumed to be maintained at a constant (large) concentration in the nucleus. |
| *kdx1* | 0.01 | 0.009 | 0.011 | 0.01 | CLOCK/BMAL dissociation **[h−1]** |
| *kfz4* | 1 | 1.023 | 1.203 | 0.96 | PERC\*/CRYC formation **[(a.u.· h)−1]** |
| *kdz4* | 1 | 1.12 | 1.008 | 0.865 | PERC\*/CRYC dissociation **[h−1]** |
| *kfz5* | 1 | 1.162 | 1.054 | 0.919 | PERC/CRYC formation **[(a.u.·h)−1]** |
| *kdz5* | 1 | 0.853 | 1.458 | 0.877 | PERC/CRYC dissociation **[h−1]** |
| **Phosphorylation/dephosphorylation reaction rates [h−1]** |
| *kphz2* | 2 | 1.768 | 2.132 | 2.199 | PERC-phosphorylation rate |
| *kdphz3* | 0.05 | 0.047 | 0.048 | 0.046 | PERC\*-dephosphorylation rate |
| **Transcription rates [a.u.·h−1]** |
| *V1max*  | 1 | 0.943 | 0.978 | 0.913 | *Per* |
| *V2max* | 2.92 | 4.485 | 3.552 | 2.511 | *Cry* |
| *V3max* | 1.9 | 3.589 | 1.954 | 1.78 | *Rev-Erb* |
| *V4max* | 10.9 | 9.026 | 13.002 | 8.994 | *Ror* |
| *V5max* | 1 | 1.145 | 0.882 | 1.004 | *Bmal* |
| **Dissociation constants of transcription factors from gene loci [a.u.]** |
| *kt1* | 3 | 3.639 | 3.594 | 2.403 | CLOCK/BMALactivation of *PER2* transcription |
| *ki1* | 0.9 | 0.825 | 0.801 | 0.921 | PER/CRYinhibition of *PER2* transcription |
| *kt2* | 2.4 | 1.733 | 2.893 | 2.146 | CLOCK/BMALactivation of *CRY* transcription |
| *ki2* | 0.7 | 0.538 | 0.68 | 0.684 | PER/CRYinhibition of *CRY* transcription |
| *ki21* | 5.2 | 6.979 | 4.494 | 3.801 | REV-ERBinhibition of *CRY* transcription |
| *kt3* | 2.07 | 1.818 | 2.246 | 1.796 | CLOCK/BMALactivation of *REV-ERB* transcription |
| *ki3* | 3.3 | 4.628 | 3.293 | 3.216 | PER/CRYinhibition of *REV-ERB* transcription |
| *kt4* | 0.9 | 0.851 | 0.987 | 1.015 | CLOCK/BMALactivation of *ROR* transcription |
| *ki4* | 0.4 | 0.548 | 0.447 | 0.393 | PER/CRYinhibition of *ROR* transcription |
| *kt5* | 8.35 | 9.256 | 7.775 | 6.677 | RORactivation of *BMAL* transcription |
| *ki5* | 1.94 | 1.908 | 1.487 | 1.893 | REV-ERBinhibition of *BMAL* transcription |
| **Transcription fold activation (dimensionless)** |
| *a* | 12 | 17.508 | 10.877 | 14.77 | *Per* |
| *d* | 12 | 9.451 | 15.357 | 10.999 | *Cry* |
| *g* | 5 | 4.996 | 4.553 | 4.894 | *Rev-Erb* |
| *h* | 5 | 6.099 | 4.758 | 6.491 | *Ror* |
| *i* | 12 | 24.292 | 11.232 | 14.438 | *Bmal* |
| **Production rates of protein from mRNA [h−1]**  |
| *kp1* | 0.4 | 0.4 | 0.355 | 0.332 | PERC |
| *kp2* | 0.26 | 0.287 | 0.288 | 0.3 | CRYC |
| *kp3* | 0.37 | 0.568 | 0.327 | 0.4 | REV-ERBC |
| *kp4* | 0.76 | 1.487 | 0.762 | 0.738 | RORC |
| *kp5* | 1.21 | 1.295 | 1.099 | 1.081 | BMALC |
|  **Nuclear Import/Export rates [h−1]** |
| *kiz4* | 0.2 | 0.385 | 0.226 | 0.192 | PERC\*/CRYC into nucleus |
| *kiz5* | 0.1 | 0.08 | 0.105 | 0.114 | PERC/CRYC into nucleus |
| *kiz6* | 0.5 | 0.577 | 0.511 | 0.508 | REV-ERBC into nucleus |
| *kiz7* | 0.1 | 0.106 | 0.092 | 0.101 | RORC into nucleus |
| *kiz8* | 0.1 | 0.098 | 0.1 | 0.102 | BMALC into nucleus |
| *kex2* | 0.02 | 0.021 | 0.017 | 0.023 | PER\*N/CRYN into cytoplasm |
| *kex3* | 0.02 | 0.026 | 0.016 | 0.024 | PERN/CRYN into cytoplasm |
|  **Hill exponents of transcription (dimensionless)** |
| *b* | 5 | 4 | 6 | 8 | *Per*-activation by CLOCK/BMAL |
| *c* | 7 | 6 | 7 | 9 | *Per*-inhibition by PER/CRY |
| *e* | 6 | 1 | 14 | 7 | *Cry*-activation by CLOCK/BMAL  |
| *f* | 4 | 2 | 8 | 4 | *Cry*-inhibition by PER/CRY |
| *f1* | 1 | 2 | 0 | 3 | *Cry*-inhibition by REV-ERB |
| *v* | 6 | 6 | 11 | 16 | *Rev-Erb*-activation by CLOCK/BMAL |
| *w* | 2 | 1 | 1 | 1 | *Rev-Erb*-inhibition by PER/CRY |
| *p* | 6 | 5 | 12 | 1 | *Ror*-activation by CLOCK/BMAL |
| *q* | 3 | 3 | 2 | 4 | *Ror*-inhibition by PER/CRY |
| *n* | 2 | 1 | 1 | 1 | *Bmal*-activation by ROR |
| *m* | 5 | 4 | 4 | 3 | *Bmal*-inhibition by REV-ERB |
|  **Exogenous RNA levels [a.u.]** |
| *y10* | 0 | 0 | 0 | 0 | *Per* |
| *y20* | 0 | 0 | 0 | 0 | *Cry* |
| *y30* | 0 | 0 | 0 | 0 | *Rev-Erb* |
| *y40* | 0 | 0 | 0 | 0 | *Ror* |
| *y50* | 0 | 0 | 0 | 0 | *Bmal* |
| **Sense-antisense RNA interactions** |
| *λ* | 1 | 1.005 | 0.774 | 0.862 | Maximum rate of synthesis of *Per2AS* **[a.u.** **h−1]** |
| *KAS* | 1 | 1.063 | 1.109 | 1.086 | *Per2AS* inhibition of *Per2* synthesis **[a.u.]** |
| ** | 1 | 1 | 1 | 1 | Magnitude of *Per2AS* effect on *Per2* synthesis (dimensionless) |
| *KS* | 0.1 | 0.101 | 0.1 | 0.077 | *Per2* inhibition of *Per2AS* synthesis **[a.u.]** |
| *dAS* | 2 | 1.669 | 2.126 | 1.409 | Degradation rate constant for *Per2AS* **[h−1]** |

\*WT refers to the parameter values assigned in Relogio *et al.* [1], whereas ‘Par\_I, \_II, \_III’ are sets of parameter values chosen by us, as described in Suppl. Text S4.

[1]. Relógio A, Westermark PO, Wallach T, Schellenberg K, Kramer A, Herzel H. Tuning the Mammalian Circadian Clock: Robust Synergy of Two Loops. *PLOS Comput. Biol.* **7**:e1002309 (2011).