Supplementary Material

Simulating dark expressions and interactions of *frq* and *wc-1* in the *Neurospora* circadian clock

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Rate equations of alternative WC-1$_n$ inhibitions

Rate equations for the mechanism shown in Fig. 1B:

$$\frac{d[frq\ mRNA]}{dt} = k_1 \frac{[WC-1_n]^2}{K+[WC-1_n]^2} - k_4[frq\ mRNA] + k_{01} \tag{S1a}$$

$$\frac{d[FRQ_c]}{dt} = k_2[frq\ mRNA] - (k_3+k_5)[FRQ_c] \tag{S1b}$$

$$\frac{d[FRQ_n]}{dt} = k_3[FRQ_c] + (k_{17}+k_{18})[FRQ_n : WC-1_n] - [FRQ_n](k_6 + k_{16}[WC-1_n]) \tag{S1c}$$

$$\frac{d[wc-1\ \ mRNA]}{dt} = k_7 - k_{10}[wc-1\ \ mRNA] \tag{S1d}$$

$$\frac{d[WC-1_c]}{dt} = \frac{k_8[FRQ_c][wc-1\ \ mRNA]}{K_2+[FRQ_c]} - (k_9+k_{11})[WC-1_c] \tag{S1e}$$

$$+k_{02}[wc-1\ \ mRNA]$$

$$\frac{d[WC-1_n]}{dt} = k_9[WC-1_c] - [WC-1_n](k_{12} + k_{16}[FRQ_n]) + k_{17}[FRQ_n : WC-1_n] \tag{S1f}$$

$$\frac{d[FRQ_n : WC-1_n]}{dt} = k_{16}[FRQ_n][WC-1_n] - (k_{17}+k_{18}+k_{20})[FRQ_n : WC-1_n] \tag{S1g}$$

$$\frac{d[WC-1_n^*]}{dt} = k_{18}[FRQ_n : WC-1_n] - k_{19}[WC-1_n^*] \tag{S1h}$$

Rate equations for the mechanism shown in Fig. 1C:

$$\frac{d[frq\ mRNA]}{dt} = k_1 \frac{[WC-1_n]^2}{K+[WC-1_n]^2} - k_4[frq\ mRNA] + k_{01} \tag{S2a}$$

$$\frac{d[FRQ_c]}{dt} = k_2[frq\ mRNA] - (k_3 + k_5)[FRQ_c] \tag{S2b}$$

$$\frac{d[FRQ_n]}{dt} = k_3[FRQ_c] + k_{17}[FRQ_n : WC-1_n] - [FRQ_n](k_6 + k_{16}[WC-1_n]) \tag{S2c}$$

$$\frac{d[wc-1\ \ mRNA]}{dt} = k_7 - k_{10}[wc-1\ \ mRNA] \tag{S2d}$$

$$\frac{d[WC-1_c]}{dt} = \frac{k_8[FRQ_c][wc-1\ \ mRNA]}{K_2 + [FRQ_c]} - (k_9 + k_{11})[WC-1_c] + k_{02}[wc-1\ \ mRNA] \tag{S2e}$$

$$\frac{d[WC-1_n]}{dt} = k_9[WC-1_c] - [WC-1_n](k_{12} + k_{16}[FRQ_n]) + k_{17}[FRQ_n : WC-1_n] \tag{S2f}$$

$$\frac{d[FRQ_n : WC-1_n]}{dt} = k_{16}[FRQ_n][WC-1_n] - (k_{17} + k_{18} + k_{20})[FRQ_n : WC-1_n] \tag{S2g}$$

$$\frac{d[WC-1_n^*]}{dt} = k_{18}[FRQ_n : WC-1_n] - k_{19}[WC-1_n^*] \tag{S2h}$$

$$\frac{d[FRQ_n^*]}{dt} = k_{18}[FRQ_n : WC-1_n] - k_{21}[FRQ_n^*] \tag{S2i}$$

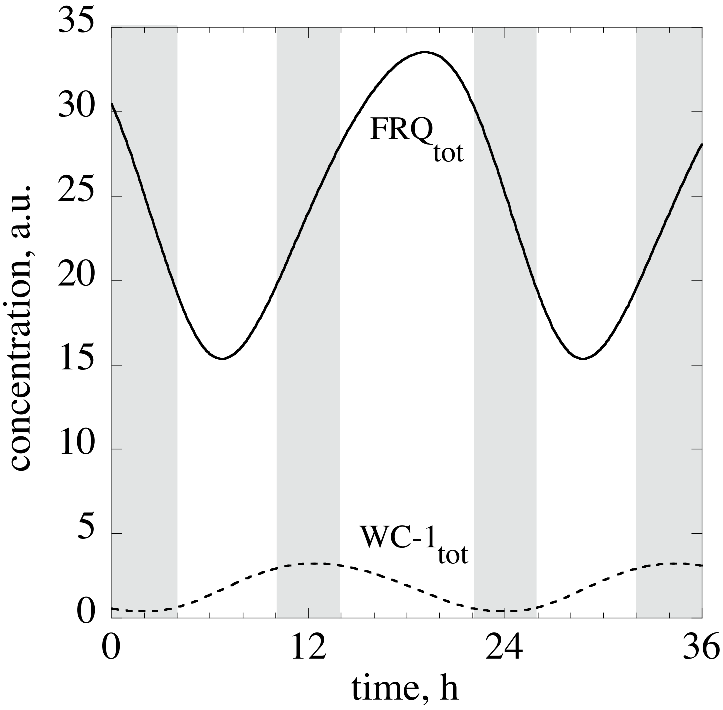
Figure S1. Predicted inverse variation relationship between total FRQ and total WC-1 rates. Maximum changes in FRQ concentration correspond to minimum changes in WC-1 and *vice versa*. Oscillations of FRQ_{tot} and WC-1_{tot} from Fig. 2A are shown where phases with maximum FRQ_{tot} variations are highlighted as grayed boxes.

Figure S2. Total FRQ and WC-1 levels as a function of the *wc-1* transcription rate k_7 in the oscillatory domain shown in Fig. 3C (A) k_7=0.1 a.u, (B) k_7=0.25 a.u, (C) k_7=0.35 a.u, (D)k_7=0.5 a.u.

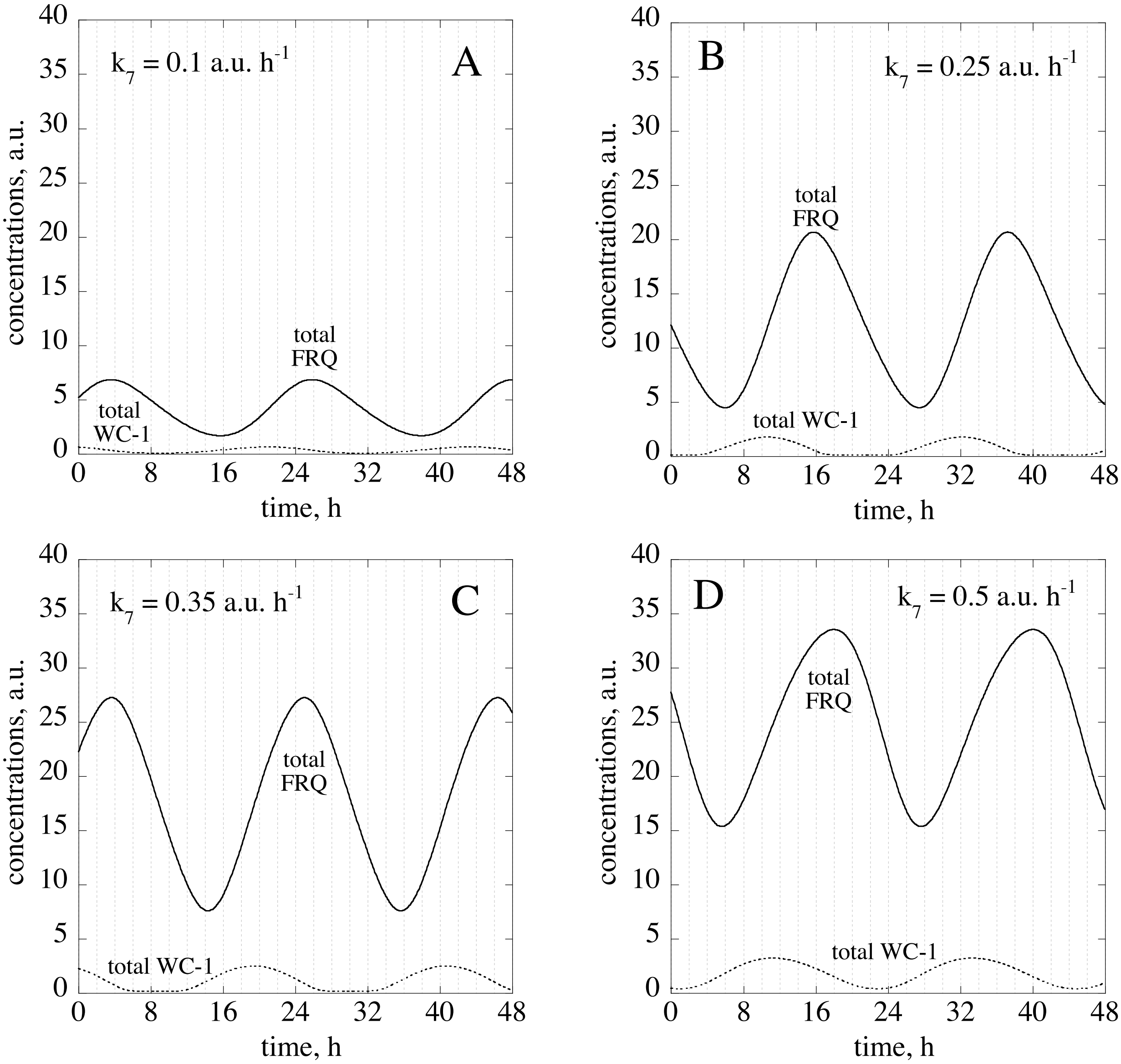
Figure S3. Modeling a 4h QA pulse in the inducible *frq*^{10} (*qa*-2FRQ) strain (compare with Fig. 2D in Ref 6. Same parameter sets as for *frq*$^{+}$ calculations (Table 1), but k_1=0, k_{01}=0.02 a.u.h^{-1}, and k_{02}=0.001 a.u. h^{-1}. Initial concentrations: [*frq* mRNA]=4.3E-06 a.u., [FRQ_c]=2.44E-05 a.u., [FRQ_n]=3.14E-07 a.u., [*wc-1* mRNA]=1.67 a.u., [WC-1_c]= 4.24E-05 a.u., [WC-1_n]=8.58E-02 a.u., [FRQ_n:WC-1_n]=1.50E-07 a.u.

Figure S4. (A) Temperature variation of *K* modeling ER24 behavior. (B) Curved Arrhenius plot leading to the period-temperature relationship shown in Fig. 4B (open squares). (C) Temperature variation of *K* modeling *frq*$^{+}$ behavior. (D) Curved Arrhenius plot leading to the *frq*$^{+}$ temperature compensation shown in Fig. 4B (open circles). (E) Temperature variation of k_5 used in the *frq*$^{+}$ and ER24 calculations. (F) Curved Arrhenius plot for k_5 used in *frq*$^{+}$ and ER24 calculations.

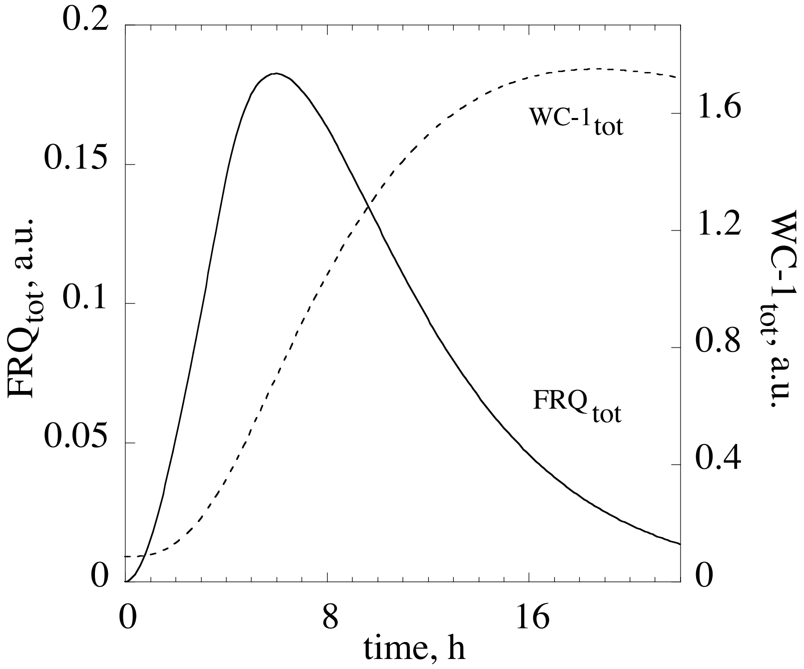
Figure S5. Total FRQ and WC-1 levels for 25°C parametrizations of (A) *frq*^{1}, (B) *frq*$^{+}$, (C) *frq*^{7}, and (D) *frq*^{S513I}, respectively.



Hong *et al.*: Simulating dark expressions... Fig. S1



Hong *et al.*: Simulating dark expressions..... Fig. S2



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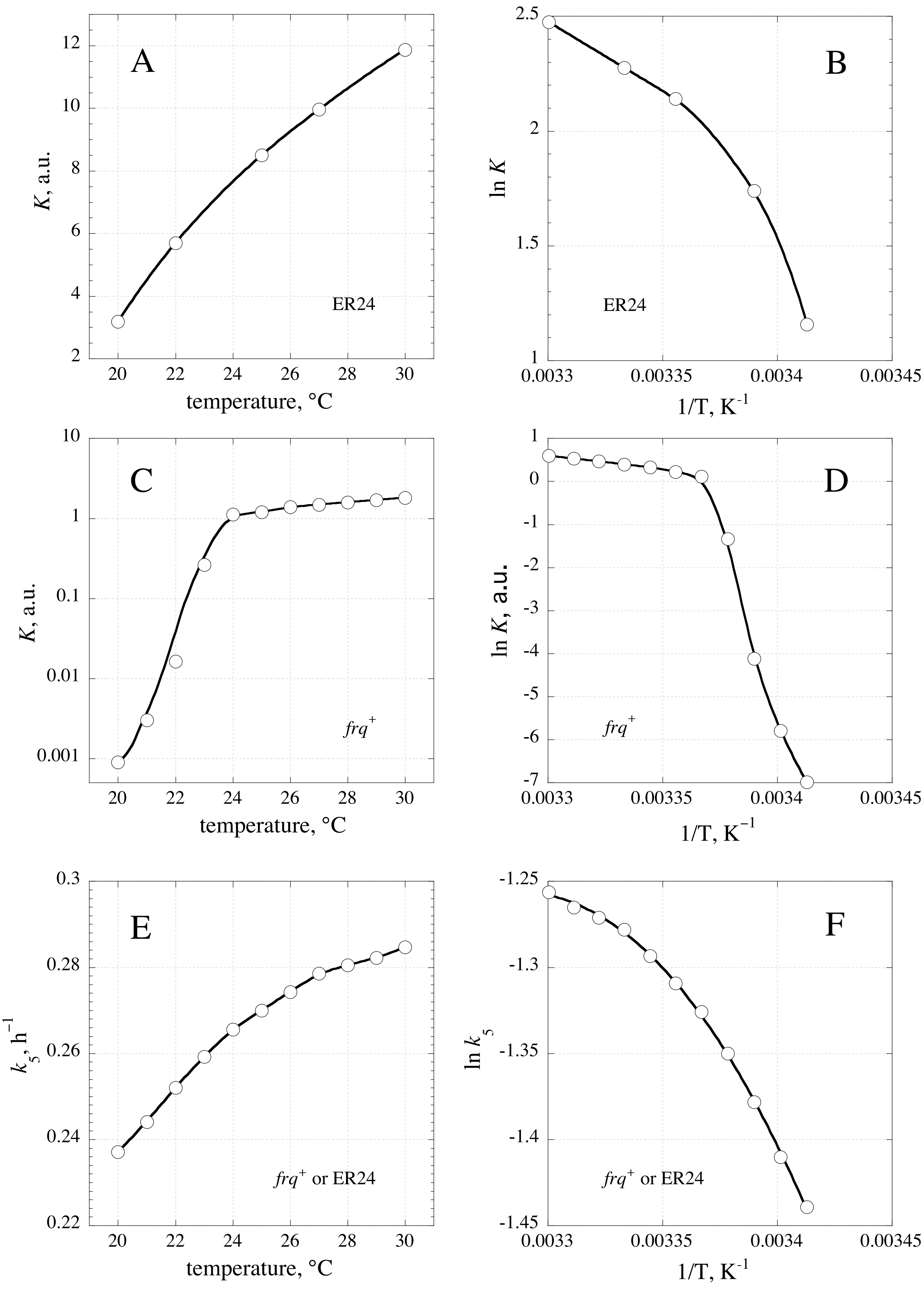

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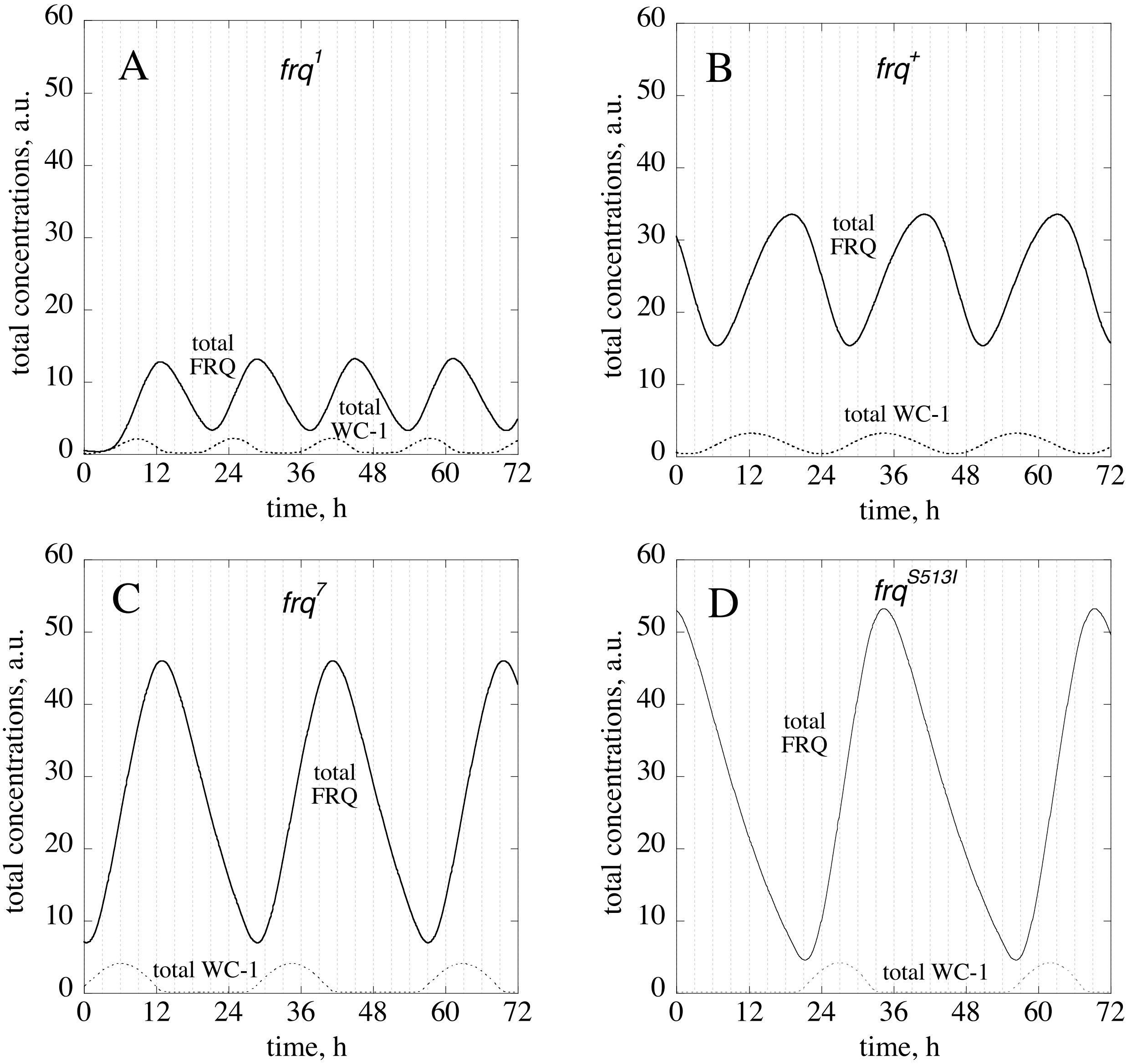

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