

Table S1. The Rb-E2f bistable switch model with fluid-flow effects (adapted from (Yao et al., 2008), with modifications marked with •)

$\frac{d[M]}{dt} = k_M \left(\frac{[S]}{K_S + [S]} + FR \right)_{ss} \bullet - d_M[M]$
$\frac{d[CD]}{dt} = \frac{k_{CD}[M]}{K_M + [M]} + k_{CDS} \left(\frac{[S]}{K_S + [S]} + FR \right)_{ss} \bullet - d_{CD}[CD]$
$\frac{d[R]}{dt} = k_R + \frac{k_{DP}[RP]}{K_{RP} + [RP]} - k_{RE}[R][E] - \frac{k_{P1}[CD][R]}{K_{CD} + [R]} - \frac{k_{P2}[CE][R]}{K_{CE} + [R]} - d_R[R]$
$\frac{d[CE]}{dt} = \frac{k_{CE}[E]}{K_E + [E]} - d_{CE}[CE]$
$\frac{d[E]}{dt} = k_E \left(\frac{[M]}{K_M + [M]} \right) \left(\frac{[E]}{K_E + [E]} \right) + \frac{k_b[M]}{K_M + [M]} + \frac{k_{P1}[CD][RE]}{K_{CD} + [RE]} + \frac{k_{P2}[CE][RE]}{K_{CE} + [RE]} - k_{RE}[R][E] - d_E[E]$
$\frac{d[RP]}{dt} = \frac{k_{P1}[CD][R]}{K_{CD} + [R]} + \frac{k_{P2}[CE][R]}{K_{CE} + [R]} + \frac{k_{P1}[CD][RE]}{K_{CD} + [RE]} + \frac{k_{P2}[CE][RE]}{K_{CE} + [RE]} - \frac{k_{DP}[RP]}{K_{RP} + [RP]} - d_{RP}[RP]$
$\frac{d[RE]}{dt} = k_{RE}[R][E] - \frac{k_{P1}[CD][RE]}{K_{CD} + [RE]} - \frac{k_{P2}[CE][RE]}{K_{CE} + [RE]} - d_{RE}[RE]$
$FR = w * \frac{f_0}{K_f + f_0} \bullet$

Variables:

S: serum concentration; *M*: Myc; *E*: E2F; *CD*: Cyclin D/Cdk4,6; *CE*: Cyclin E/Cdk2; *R*: Rb family proteins; *RP*: Phosphorylated Rb; *RE*: Rb-E2F complex; *f*₀: extracellular fluid flow rate •

Initial condition:

$[M] = [E] = [CD] = [CE] = [R] = [RP] = 0$ nM; $[RE] = 0.55$ nM;
 $f_0 = 0, 5, 20$ $\mu\text{l hr}^{-1}$ •

Note: Model parameters are adapted from (Yao et al., 2008) and defined in Table S2, including newly added parameters.

Table S2. Model parameters (adapted from (Yao *et al.*, 2008), with modifications marked with •)

Symbol	Values	Description
k_M	1.0 nM hr ⁻¹	Rate constant of Myc synthesis driven by growth factors
k_E	0.4 nM hr ⁻¹	Rate constant of E2F synthesis driven by Myc and E2F
k_b	0.003 nM hr ⁻¹	Rate constant of E2F synthesis driven by Myc alone
k_{CD}	0.03 nM hr ⁻¹	Rate constant of CycD synthesis driven by Myc
k_{CDS}	0.45 nM hr ⁻¹	Rate constant of CycD synthesis driven by growth factors
k_{CE}	0.35 nM hr ⁻¹	Rate constant of CycE synthesis driven by E2F
k_R	0.18 nM hr ⁻¹	Rate constant of Rb constitutive synthesis
k_{P1}	18 hr ⁻¹	Phosphorylation rate constant of Rb by CycD/Cdk4,6
k_{P2}	18 hr ⁻¹	Phosphorylation rate constant of Rb by CycE/Cdk2
k_{DP}	3.6 nM hr ⁻¹	Dephosphorylation rate constant of Rb by phosphatases
k_{RE}	180 nM ⁻¹ hr ⁻¹	Association rate constant of Rb and E2F
K_S	2.5 nM	Michaelis-Menten parameter for CycD and Myc synthesis by growth factors
K_E	0.15 nM	Michaelis-Menten parameter for CycE and E2F synthesis by E2F
K_M	0.15 nM	Michaelis-Menten parameter for CycD and E2F synthesis by Myc
K_{RP}	0.01 nM	Michaelis-Menten parameter for Rb dephosphorylation
K_{CD}	0.92 nM	Michaelis-Menten parameter for Rb phosphorylation by CycD/Cdk4,6
K_{CE}	0.92 nM	Michaelis-Menten parameter for Rb phosphorylation by CycE/Cdk2
d_M	0.7 hr ⁻¹	Degradation rate constant of Myc
d_E	0.25 hr ⁻¹	Degradation rate constant of E2F
d_{CD}	1.5 hr ⁻¹	Degradation rate constant of CycD
d_{CE}	1.5 hr ⁻¹	Degradation rate constant of CycE
d_R	0.06 hr ⁻¹	Degradation rate constant of Rb
d_{RP}	0.06 hr ⁻¹	Degradation rate constant of phosphorylated Rb
d_{RE}	0.03 hr ⁻¹	Degradation rate constant of Rb-E2F complex
K_f	2.5-15.0 μ l hr ⁻¹	•Michaelis-Menten parameter for the effects of fluid flow*
w	0.2-0.3	•Scaling factor for the effects of fluid flow*
ss	0.80 (or as noted)	•Scaling factor reflecting the batch variations of individual experiments

*Serum concentration-dependent as follows:

$$[S] = 0.02 \text{ or } 1: w = 0.3, K_f = 2.5$$

$$[S] = 2: w = 0.3, K_f = 13$$

$$[S] = 4: w = 0.2, K_f = 15$$

Supplementary References

Yao, G., Lee, T.J., Mori, S., Nevins, J.R., and You, L. (2008). A bistable Rb-E2F switch underlies the restriction point. *Nat Cell Biol* *10*, 476-482. [10.1038/ncb1711](https://doi.org/10.1038/ncb1711).