

Early Cell Cycle Model - ODEs

Anthony Hart

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1 State Variables

$$\frac{d[\text{IR}]}{dt} = -R1$$

$$\frac{d[\text{pIR}]}{dt} = +R1$$

$$\frac{d[\text{PI3K}]}{dt} = -R2$$

$$\frac{d[\text{pPI3K}]}{dt} = +R2$$

$$\frac{d[\text{PIP2}]}{dt} = -R3$$

$$\frac{d[\text{PIP3}]}{dt} = +R3$$

$$\frac{d[\text{PDK1}]}{dt} = -R4$$

$$\frac{d[\text{aPDK1}]}{dt} = +R4$$

$$\frac{d[\text{mTORC2}]}{dt} = -R5$$

$$\frac{d[\text{amTORC2}]}{dt} = +R5$$

$$\frac{d[\text{AKT}]}{dt} = -R6$$

$$\frac{d[\text{pAKT308}]}{dt} = +R6 - R7$$

$$\frac{d[\text{ppAKT308473}]}{dt} = +R7$$

$$\frac{d[\text{mTORC1}]}{dt} = -R8$$

$$\frac{d[\text{amTORC1}]}{dt} = +R8$$

$$\frac{d[\text{S6K}]}{dt} = -R9$$

$$\frac{d[\text{pS6K}]}{dt} = +R9$$

$$\frac{d[\text{FGFR}]}{dt} = -R10$$

$$\frac{d[\text{pFGFR}]}{dt} = +R10$$

$$\begin{aligned}
\frac{d[\text{Ras}]}{dt} &= -R11 \\
\frac{d[\text{aRas}]}{dt} &= +R11 \\
\frac{d[\text{Raf}]}{dt} &= -R12 \\
\frac{d[\text{aRaf}]}{dt} &= +R12 \\
\frac{d[\text{MEK}]}{dt} &= -R13 \\
\frac{d[\text{pMEK}]}{dt} &= +R13 \\
\frac{d[\text{ERK}]}{dt} &= -R14 \\
\frac{d[\text{pERK}]}{dt} &= +R14 \\
\frac{d[\text{ERa}]}{dt} &= -R15 \\
\frac{d[\text{aERa}]}{dt} &= +R15 \\
\frac{d[\text{Myc}]}{dt} &= +R16 - R17 - R18 \\
\frac{d[\text{pMyc}]}{dt} &= +R18 \\
\frac{d[\text{GSK3b}]}{dt} &= -R19 \\
\frac{d[\text{pGSK3b}]}{dt} &= +R19 \\
\frac{d[\text{FOXO3}]}{dt} &= -R20 \\
\frac{d[\text{pFOXO3}]}{dt} &= +R20 \\
\frac{d[\text{cycD}]}{dt} &= +R21 - R22 - R27 \\
\frac{d[\text{cycE}]}{dt} &= +R23 - R24 - R28 \\
\frac{d[\text{cycA}]}{dt} &= +R25 - R26 - R29 \\
\frac{d[\text{CDK46}]}{dt} &= -R27 \\
\frac{d[\text{CDK2}]}{dt} &= -R28 - R29 \\
\frac{d[\text{CDK46cycD}]}{dt} &= +R27 \\
\frac{d[\text{CDK2cycE}]}{dt} &= +R28 \\
\frac{d[\text{CDK2cycA}]}{dt} &= +R29
\end{aligned}$$

$$\frac{d[p21_27]}{dt} = -R30$$

$$\frac{d[pp21_27]}{dt} = +R30$$

$$\frac{d[E2F]}{dt} = +R31 - R32 - R33$$

$$\frac{d[RbE2F]}{dt} = +R33$$

$$\frac{d[Rb]}{dt} = -R33 - R34$$

$$\frac{d[pRb]}{dt} = +R34 - R35$$

$$\frac{d[pppRb]}{dt} = +R35$$

2 ODEs

$$\begin{aligned}
R1 &= (k_{c1f1} \text{Ins IR}) - (V_{\max,1r1} p\text{IR}) && \{\text{reversible}\} \\
R2 &= \left(\frac{k_{c2f1} p\text{IR PI3K}}{1 + (p\text{S6K}/K_{i2})} + k_{c2f2} p\text{FGFR PI3K} \right) - (V_{\max,2r1} p\text{PI3K}) && \{\text{reversible}\} \\
R3 &= (k_{c3f1} p\text{PI3K PIP2}) - ((V_{\max,3r1} + k_{c3r1} \text{PTEN}) \text{PIP3}) && \{\text{reversible}\} \\
R4 &= (k_{c4f1} \text{PIP3 PDK1}) - (V_{\max,4r1} a\text{PDK1}) && \{\text{reversible}\} \\
R5 &= \left(\frac{k_{c5f1} \text{PIP3 mTORC2}}{1 + (ppp\text{Rb}/K_{i5})} \right) - (V_{\max,5r1} a\text{mTORC2}) && \{\text{reversible}\} \\
R6 &= (k_{c6f1} a\text{PDK1 AKT}) - (V_{\max,6r1} p\text{AKT308}) && \{\text{reversible}\} \\
R7 &= (k_{c7f1} a\text{mTORC2 pAKT308} (1 + \alpha_7 \text{CDK2cycA})) - (V_{\max,7r1} pp\text{AKT308473}) && \{\text{reversible}\} \\
R8 &= ((k_{c8f1} p\text{AKT308} + \text{AKTscale } k_{c8f1} pp\text{AKT308473}) \text{mTORC1}) - (V_{\max,8r1} a\text{mTORC1}) && \{\text{reversible}\} \\
R9 &= (k_{c9f1} a\text{mTORC1 S6K}) - (V_{\max,9r1} p\text{S6K}) && \{\text{reversible}\} \\
R10 &= (k_{c10f1} \text{FGF FGFR})(1 + \alpha_{10} \text{E2F}) - (V_{\max,10r1} p\text{FGFR}) && \{\text{reversible}\} \\
R11 &= \left(\frac{k_{c11f1} p\text{FGFR} + k_{c11f2} p\text{IR}}{1 + (p\text{ERK}/K_{i11})} \text{Ras} \right) - (V_{\max,11r1} a\text{Ras}) && \{\text{reversible}\} \\
R12 &= \left(\frac{k_{c12f1} a\text{Ras Raf}}{1 + (p\text{AKT308}/K_{i12}) + (pp\text{AKT308473}/(\text{AKTscale } K_{i12}))} \right) - (V_{\max,12r1} a\text{Raf}) && \{\text{reversible}\} \\
R13 &= (k_{c13f1} a\text{Raf MEK}) - (V_{\max,13r1} p\text{MEK}) && \{\text{reversible}\} \\
R14 &= (k_{c14f1} p\text{MEK ERK}) - (V_{\max,14r1} p\text{ERK}) && \{\text{reversible}\} \\
R15 &= \left(\frac{k_{c15f1} \text{Est ERa}(1 + \alpha_{15} \text{FOXO3})}{1 + (E_{i0}/K_{i15})} \right) - (V_{\max,15r1} a\text{ERa}) && \{\text{reversible}\} \\
R16 &= k_{c16f1} a\text{ERa}(1 + \alpha_{16a} p\text{ERK} + \alpha_{16b} \text{cycD}) + k_{c16f2} \text{E2F} \\
R17 &= k_{\text{deg}17f1} \text{Myc}(1 + \alpha_{17} \text{GSK3b}) \\
R18 &= (k_{c18f1} p\text{ERK Myc}) - (V_{\max,18r1} p\text{Myc}) && \{\text{reversible}\} \\
R19 &= ((k_{c19f1} p\text{AKT308} + \text{AKTscale } k_{c19f1} pp\text{AKT308473}) \text{GSK3b}) - (V_{\max,19r1} p\text{GSK3b}) && \{\text{reversible}\} \\
R20 &= ((k_{c20f1} p\text{AKT308} + \text{AKTscale } k_{c20f1} pp\text{AKT308473}) \text{FOXO3}) - (V_{\max,20r1} p\text{FOXO3}) && \{\text{reversible}\} \\
R21 &= k_{c21f1} a\text{mTORC1} + k_{c21f2} p\text{ERK} + k_{c21f3} (\text{Myc} + p\text{Myc}) + k_{c21f4} a\text{ERa}(1 + \alpha_{21a} p\text{ERK} + \alpha_{21b} \text{cycD}) \\
R22 &= k_{\text{deg}22f1} \text{cycD}(1 + \alpha_{22} \text{GSK3b}) \\
R23 &= k_{c23f1} \text{E2F}(1 + \alpha_{23} (\text{Myc} + p\text{Myc})) + k_{c23f2} (\text{Myc} + p\text{Myc}) \\
R24 &= k_{\text{deg}24f1} \text{cycE}(1 + \alpha_{24} \text{GSK3b}) \\
R25 &= k_{c25f1} \text{E2F}(1 + \alpha_{25} (\text{Myc} + p\text{Myc})) + k_{c25f2} (\text{Myc} + p\text{Myc}) \\
R26 &= k_{\text{deg}26f1} \text{cycA} \\
R27 &= \left(\frac{k_{a27f1} \text{CDK46 cycD}(1 + \alpha_{27} pp21_{27})}{1 + (\text{CDK46}_{i0}/K_{i27})} \right) - (k_{d27r1} \text{CDK46cycD}) && \{\text{reversible}\}
\end{aligned}$$

$$R28 = \left(\frac{k_{a28f1} \text{CDK2 cycE}}{1 + (p21_27/K_{i28})} \right) - (k_{d28r1} \text{CDK2cycE}) \quad \{\text{reversible}\}$$

$$R29 = k_{a29f1} \text{CDK2 cycA} (1 + \alpha_{29} p\text{AKT308} + \text{AKTscale} \alpha_{29} pp\text{AKT308473}) - (k_{d29r1} \text{CDK2cycA}) \quad \{\text{reversible}\}$$

$$R30 = ((k_{c30f1} p\text{AKT308} + \text{AKTscale} k_{c30f1} pp\text{AKT308473}) p21_27 (1 + \alpha_{30} (\text{Myc} + p\text{Myc}))) \\ - (V_{\max,30r1} pp21_27) \quad \{\text{reversible}\}$$

$$R31 = k_{c31f1} (\text{Myc} + p\text{Myc}) + k_{c31f2} \text{E2F}$$

$$R32 = k_{\text{deg}32f1} \text{E2F}$$

$$R33 = k_{a33f1} \text{E2FRb} - (k_{d33r1} \text{RbE2F}) \quad \{\text{reversible}\}$$

$$R34 = k_{c34f1} \text{CDK46cycD Rb} - (V_{\max,34r1} p\text{Rb}) \quad \{\text{reversible}\}$$

$$R35 = k_{c35f1} \text{CDK2cycE} p\text{Rb} - (V_{\max,35r1} ppp\text{Rb}) \quad \{\text{reversible}\}$$