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| **Restriction Point Module** |
| **cMyc** |
| $$w\_{Myc}=R\_{0}^{Myc}+R\_{HP}^{Myc}∙HP$$ | $$F\_{Myc}=\frac{1}{1+e^{-σ∙wMyc}}$$ | $$\frac{dMyc}{dt}=ts\_{Myc}∙(F\_{Myc}-Myc)$$ |
| **cMyc parameters** |
| $$R\_{0}^{Myc}= -0.5$$ | $$R\_{HP}^{Myc}=1$$ | $$ts\_{Myc}=0.1$$ |
| **P21** |
| $$w\_{p21}=R\_{0}^{p21}+R\_{HP}^{p21}∙HP+R\_{Myc}^{p21}∙Myc$$ | $$F\_{p21}= \frac{1}{1+ e^{-σ∙w\_{p21}}}$$ | $$\frac{dp21}{dt}=ts\_{p21}∙(F\_{p21}-p21)$$ |
| **P21 parameters** |
| $$R\_{0}^{p21}= -0.5$$ | $$R\_{HP}^{p21}=1$$ | $$R\_{Myc}^{p21}= -2$$ | $$ts\_{p21}=0.1$$ |
| **CyclinD** |
| $$w\_{CycD}=R\_{0}^{CycD}+R\_{HP}^{CycD}∙HP+R\_{Myc}^{CycD}∙Myc$$ | $$F\_{CycD}= \frac{1}{1+e^{-σ∙w\_{CycD}}}$$ | $$\frac{dCycD}{dt}=ts\_{CycD}∙(F\_{CycD}-CycD)$$ |
| **CyclinD parameters** |
| $$R\_{0}^{CycD}= -0.33$$ | $$R\_{HP}^{CycD}=1$$ | $$R\_{Myc}^{CycD}=1$$ | $$ts\_{CycD}=0.1$$ |
| **RB** |
| $$w\_{Rb}=R\_{0}^{Rb}+R\_{Cdk}^{Rb}∙Cdk2+R\_{CycD}^{Rb}∙CycD$$ | $$F\_{Rb}= \frac{1}{1+e^{-σ∙w\_{Rb}}}$$ | $$\frac{dRb}{dt}=ts\_{Rb}∙(F\_{Rb}-Rb)$$ |
| **RB parameters** |
| $$R\_{0}^{Rb}=1.2$$ | $$R\_{Cdk}^{Rb}= -1.4$$ | $$ts\_{Rb}=1$$ | $$R\_{CycD}^{Rb}= -1.5$$ |
| **CdK** |
| $$w\_{Cdk}=R\_{0}^{Cdk}+R\_{Rb}^{Cdk}∙Rb+R\_{p21}^{Cdk}∙p21$$ | $$F\_{Cdk}= \frac{1}{1+e^{-σ∙w\_{Cdk}}}$$ | $$\frac{dCdk2}{dt}=ts\_{Cdk}∙(F\_{Cdk}-Cdk2)$$ |
| **CdK parameters** |
| $$R\_{0}^{Cdk}= 1$$ | $$R\_{Rb}^{Cdk}= -2$$ | $$R\_{p21}^{Cdk}= -2$$ | $$ts\_{Cdk}=0.5$$ |
| **Global Parameters** |
| $$σ=5$$ | $$HP=1$$ |

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| **Transcriptional Response Module** |
| **NfKb** |
| $$W\_{NFkB}=R\_{0}^{NFkB}+R\_{IkB}^{NF}∙IkB$$ | $$F\_{NFkB}= \frac{1}{1+e^{-σ∙W\_{NFkB}}}$$ | $$\frac{dNFkB}{dt}=ts\_{NFkB}∙(F\_{NFkB}-NFkB)$$ |
| **NfKb parameters** |
| $$R\_{0}^{NFkB}=0.4$$ | $$R\_{IkB}^{NF}= -1.2$$ | $$ts\_{NFkB}=2$$ | $$σ=5$$ |
| **ImR** |
| $$W\_{ImR}=R\_{0}^{ImR}+R\_{NFkB}^{ImR}∙NFkB$$ | $$F\_{ImR}= \frac{1}{1+e^{-σ∙W\_{ImR}}}$$ | $$\frac{dImR}{dt}=ts\_{ImR}\*(F\_{ImR}-ImR)$$ |
| **ImR parameters** |
| $$R\_{0}^{ImR}=-0.4$$ | $$R\_{NFkB}^{ImR}=1.5$$ | $$ts\_{ImR}=0.1$$ |
| **IKB** |
| $$W\_{IkB}=R\_{0}^{IkB}+R\_{HP}^{IkB}∙HP+R\_{ImR}^{IkB}∙ImR$$ | $$F\_{IkB}= \frac{1}{1+e^{-σ∙W\_{IkB}}}$$ | $$\frac{dIkB}{dt}=ts\_{IkB}∙(F\_{IkB}-IkB)$$ |
| **IKB parameters** |
| $$R\_{0}^{IkB}=0.3$$ | $$R\_{HP}^{IkB}= -1$$ | $$R\_{ImR}^{IkB}=2.4$$ | $$ts\_{IkB}=2$$ |
| **NfKB- Downstream Genes** |
| $$W\_{IL8}=R\_{0}^{IL8}+R\_{NFkB}^{IL8}∙NFkB$$ | $$F\_{IL8}= \frac{1}{1+e^{-σ∙W\_{IL8}}}$$ | $$\frac{dIL8}{dt}=ts\_{IL8}∙(F\_{IL8}-IL8)$$ |
| **Downstream Gene Parameters** |
| $$R\_{0}^{IL8}=-0.4$$ | $$R\_{NFkB}^{IL8}=1.5$$ | $$ts\_{IL8}=1$$ |
| **Beta\_Catenin** |
| $$W\_{Bet}=R\_{0}^{Bet}+R\_{HP}^{Bet}∙HP$$ | $$F\_{Bet}=\frac{1}{1+e^{-σ∙W\_{Bet}}}$$ | $$\frac{dBet}{dt}=ts\_{Bet}∙(F\_{Bet}-Bet)$$ |
| **Beta-Catenin Parameters** |
| $$R\_{0}^{Bet}=-0.4$$ | $$R\_{HP}^{Bet}=1$$ | $$ts\_{Bet}=0.2$$ |

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| **HH Response Module** |
| **Wnt Equations** |
| $$W\_{Wnt}=R\_{0}^{Wnt}+ R\_{Gas}^{Wnt} ∙Gas+ R\_{Ihh}^{Wnt} ∙Ihh$$ | $$F\_{Wnt}=\frac{1}{1+ e^{-σ∙W\_{Wnt}}}$$ | $$\frac{dWnt}{dt}= ts\_{Wnt}∙(F\_{Wnt}-Wnt)$$ |
| Wnt Parameters |
| $R\_{0}^{Wnt}$ = -1 | $$R\_{Ihh}^{Wnt}= 2$$ | $$R\_{Gas}^{Wnt}=1$$ | $$ts\_{Wnt}=1$$ |
| **Ihh Equations** |
| $$W\_{Ihh}=R\_{0}^{Ihh}+ R\_{Wnt}^{Ihh} ∙Wnt$$ | $$F\_{Ihh}=\frac{1}{1+ e^{-σ∙W\_{Ihh}}}$$ | $$\frac{dIhh}{dt}= ts\_{Ihh}∙(F\_{Ihh}-Ihh)$$ |
| Ihh Parameters |
| $R\_{0}^{Ihh}$ = - 0.9 | $R\_{Wnt}^{Ihh}$ = -1 | $$ts\_{Ihh}=1$$ |
| **Shh Equations** |
| $$W\_{Shh}= R\_{0}^{Shh}+ (R\_{Acid}^{Shh}∙Acid)+ (R\_{BMMSC}^{Shh}∙ BMMSC)+(R\_{IL1}^{Shh} ∙ IL1)$$ | $$F\_{Acid}= \frac{1}{1+ e^{-σ∙W\_{Shh}}}$$ | $$\frac{dShh}{dt}= ts\_{Shh}∙(F\_{Shh}-Shh)$$ |
| Shh Parameters |
| $$R\_{0}^{Shh}= -0.9$$ | $$R\_{Acid}^{Shh}=1.8$$ | $R\_{BMMSC}^{Shh}$ = 2.3 | $$R\_{IL1}^{Shh}= -1$$ | $$ts\_{Shh}=1$$ |
| **TGF Equations** |
| $$W\_{TGF}= R\_{0}^{TGF}+ R\_{HP}^{TGF}∙HP$$ | $$F\_{TGF}= \frac{1}{1+ e^{-σ∙W\_{TGF}}}$$ | $$\frac{dTGF}{dt}= ts\_{TGF}∙(F\_{TGF}-TGF)$$ |
| TGF Parameters |
| $$R\_{0}^{TGF}= -0.5$$ | $$R\_{HP}^{TGF}=1$$ | $$ts\_{TGF}=0.005$$ |
| **BMMSC Equations** |
| $$W\_{BMMSC}= R\_{0}^{BMMSC}+ R\_{TGF}^{BMMSC}∙TGF+ R\_{Shh}^{BMMSC}∙Shh$$ | $$F\_{BMMSC}= \frac{1}{1+e^{-σ∙W\_{BMMSC}}}$$ | $$\frac{dBMMSC}{dt}= ts\_{BMMSC}∙(F\_{BMMSC}-BMMSC)$$ |
| BMMSC Parameters |
| $$R\_{0}^{BMMSC}= -1.5$$ | $$R\_{Shh}^{BMMSC}=1$$ | $$R\_{TGF}^{BMMSC}=5$$ | $$ts\_{BMMSC}=0.01$$ |
| **Gas Equations** |
| $$W\_{Gas}= R\_{0}^{Gas}+ R\_{HP}^{Gas}∙Shh$$ | $$F\_{Gas}= \frac{1}{1+ e^{-σ∙W\_{Gas}}}$$ | $$\frac{dGas}{dt}= ts\_{Gas}∙(F\_{Gas}-Gas)$$ |
| Gas Parameters |
| $$R\_{0}^{Gas}=0.5$$ | $$R\_{HP}^{Gas}= -1$$ | $$ts\_{Gas}=0.01$$ |
| **Atrophy Module** |
| **IL-1 Equations** |
| $$W\_{IL1}= R\_{0}^{IL1}+ R\_{HP}^{IL1}∙HP$$ | $$F\_{IL1}= \frac{1}{1+ e^{-σ∙W\_{IL1}}}$$ | $$\frac{dIL1}{dt}= ts\_{IL1}∙(F\_{IL1}-IL1)$$ |
| IL-1 Parameters |
| $$R\_{0}^{IL1}= -1$$ | $$R\_{HP}^{IL1}=1$$ | $$ts\_{IL1}=2$$ |
| **Acid Equations** |
| $$W\_{Acid}= R\_{0}^{Acid}+ (R\_{IL1}^{Acid}∙IL1)+ (R\_{Shh}^{Acid}∙ Shh)$$ | $$F\_{Acid}= \frac{1}{1+e^{-σ∙W\_{Acid}} }$$ | $$\frac{dAcid}{dt}= ts\_{Acid}∙(F\_{Acid}-Acid)$$ |
| Acid Parameters |
| $$R\_{0}^{Acid}= -1$$ | $$R\_{Shh}^{Acid}=2$$ | $$R\_{IL1}^{Acid}= -1.8$$ | $$ts\_{Acid}=1$$ |