1 Equations

1.1 Activator Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{1}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{2}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{3}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{4}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{5}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{6}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{7}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}V - \delta_{p,P_{TF}}[P_{TF}] \tag{8}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{9}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{[P_{TF}]^n}{(K_A)^n + [P_{TF}]^n}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{10}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{11}$$

1.2 Chain-Cre-TF Activator Cre-off Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat} V [C_{\mathrm{Cas},1}] \tag{12}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat} V [C_{\mathrm{Cas},1}] \tag{13}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}] H \tag{14}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}] H \tag{15}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat} V [C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{16}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{17}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H \tag{18}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}} \frac{V_C}{V} V - \delta_{p,P_{TF}}[P_{TF}] \tag{19}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}} V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{20}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{21}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{22}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{23}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1} \frac{[P_{TF}]^n}{(K_A)^n + [P_{TF}]^n} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{24}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2} V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{25}$$

1.3 Chain-Cre-TF Activator Cre-on Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat} V [C_{\mathrm{Cas},1}] \tag{26}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat} V [C_{\mathrm{Cas},1}] \tag{27}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}] H \tag{28}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}] H \tag{29}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat} V [C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{30}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{31}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H \tag{32}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}} \frac{{V_C}^*}{V} V - \delta_{p,P_{TF}}[P_{TF}] \tag{33}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}} V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{34}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{35}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{36}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{37}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1} \frac{[P_{TF}]^n}{(K_A)^n + [P_{TF}]^n} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{38}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2} V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{39}$$

1.4 Chain-Cre-TF Repressor Cre-off Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{40}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{41}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{42}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{43}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{44}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{45}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{46}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}\frac{V_C}{V}V - \delta_{p,P_{TF}}[P_{TF}] \tag{47}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}}V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{48}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{49}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{50}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{51}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{(K_R)^n}{(K_R)^n + [P_{TF}]^n}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{52}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{53}$$

1.5 Chain-Cre-TF Repressor Cre-on Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{54}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{55}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{56}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{57}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{58}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{59}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{60}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}\frac{{V_C}^*}{V}V - \delta_{p,P_{TF}}[P_{TF}] \tag{61}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}}V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{62}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{63}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{64}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{65}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{(K_R)^n}{(K_R)^n + [P_{TF}]^n}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{66}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{67}$$

1.6 Chain-TF-Cre Activator Cre-off Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{68}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{69}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{70}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{71}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{72}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{73}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{74}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}V - \delta_{p,P_{TF}}[P_{TF}] \tag{75}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}}\frac{[P_{TF}]^n}{(K_A)^n + [P_{TF}]^n}V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{76}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{77}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{78}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{79}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{V_C}{V}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{80}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{81}$$

1.7 Chain-TF-Cre Activator Cre-on Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{82}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{83}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{84}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{85}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{86}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{87}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{88}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}V - \delta_{p,P_{TF}}[P_{TF}] \tag{89}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}}\frac{[P_{TF}]^n}{(K_A)^n + [P_{TF}]^n}V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{90}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{91}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{92}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{93}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{{V_C}^*}{V}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{94}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{95}$$

1.8 Chain-TF-Cre Repressor Cre-off Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat} V [C_{\mathrm{Cas},1}] \tag{96}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat} V [C_{\mathrm{Cas},1}] \tag{97}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}] H \tag{98}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}] H \tag{99}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat} V [C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{100}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{101}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H \tag{102}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}} V - \delta_{p,P_{TF}}[P_{TF}] \tag{103}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}} \frac{(K_R)^n}{(K_R)^n + [P_{TF}]^n} V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{104}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{105}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{106}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{107}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{V_C}{V} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{108}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2} V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{109}$$

1.9 Chain-TF-Cre Repressor Cre-on Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{110}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{111}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{112}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{113}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{114}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{115}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{116}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}V - \delta_{p,P_{TF}}[P_{TF}] \tag{117}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}}\frac{(K_R)^n}{(K_R)^n + [P_{TF}]^n}V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{118}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{119}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{120}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{121}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{{V_C}^*}{V}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{122}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{123}$$

1.10 Cre-off Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat} V [C_{\mathrm{Cas},1}] \tag{124}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat} V [C_{\mathrm{Cas},1}] \tag{125}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}] H \tag{126}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}] H \tag{127}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat} V [C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{128}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{129}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H \tag{130}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}} V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{131}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{132}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{133}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{134}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{V_C}{V} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{135}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2} V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{136}$$

1.11 Cre-on Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat} V [C_{\mathrm{Cas},1}] \tag{137}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat} V [C_{\mathrm{Cas},1}] \tag{138}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}] H \tag{139}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}] H \tag{140}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat} V [C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{141}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{142}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H \tag{143}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}} V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{144}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{145}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{146}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{147}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{{V_C}^*}{V} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{148}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2} V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{149}$$

1.12 Joint Activator Cre-off Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat} V [C_{\mathrm{Cas},1}] \tag{150}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat} V [C_{\mathrm{Cas},1}] \tag{151}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}] H \tag{152}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}] H \tag{153}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat} V [C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{154}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{155}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H \tag{156}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}} V - \delta_{p,P_{TF}}[P_{TF}] \tag{157}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}} V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{158}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{159}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{160}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{161}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{[P_{TF}]^n}{(K_A)^n + [P_{TF}]^n}\frac{V_C}{V} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{162}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2} V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{163}$$

1.13 Joint Activator Cre-on Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{164}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{165}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{166}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{167}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{168}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{169}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{170}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}V - \delta_{p,P_{TF}}[P_{TF}] \tag{171}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}}V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{172}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{173}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{174}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{175}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{[P_{TF}]^n}{(K_A)^n + [P_{TF}]^n}\frac{{V_C}^*}{V}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{176}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{177}$$

1.14 Joint Repressor Cre-off Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{178}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{179}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{180}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{181}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{182}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{183}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{184}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}V - \delta_{p,P_{TF}}[P_{TF}] \tag{185}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}}V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{186}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{187}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{188}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{189}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{(K_R)^n}{(K_R)^n + [P_{TF}]^n}\frac{V_C}{V}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{190}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{191}$$

1.15 Joint Repressor Cre-on Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{192}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{193}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{194}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{195}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{196}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{197}$$

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{198}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}V - \delta_{p,P_{TF}}[P_{TF}] \tag{199}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}}V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{200}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{201}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{202}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{203}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{(K_R)^n}{(K_R)^n + [P_{TF}]^n}\frac{{V_C}^*}{V}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{204}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{205}$$

1.16 Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{206}$$
$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{207}$$
$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{208}$$
$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{209}$$
$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{210}$$
$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{211}$$
$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{212}$$
$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{213}$$
$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{214}$$
$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{215}$$

1.17 Repressor Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{216}$$
$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{217}$$
$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{218}$$
$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}]H \tag{219}$$
$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{220}$$
$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{221}$$
$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H \tag{222}$$
$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}V - \delta_{p,P_{TF}}[P_{TF}] \tag{223}$$
$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{224}$$
$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{(K_R)^n}{(K_R)^n + [P_{TF}]^n}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{225}$$
$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{226}$$