1 Equations

1.1 Basic Kill Switch

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

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

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

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

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

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

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

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{8}$$

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

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{10}$$

1.2 Repression of Cre-activated Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat}V[C_{\mathrm{Cas},1}] \tag{11}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat}V[C_{\mathrm{Cas},1}] \tag{12}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}]H \tag{13}$$

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

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat}V[C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{15}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}]H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{16}$$

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

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}}\frac{(K_R)^n}{(K_R)^n + [P_{TF}]^n}V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{18}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{19}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre}V_C[P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{20}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}}V - \delta_{p,P_{TF}}[P_{TF}] \tag{21}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{22}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{{V_C}^*}{V}V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{23}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2}V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{24}$$

1.3 Cre-activated Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat} V [C_{\mathrm{Cas},1}] \tag{25}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat} V [C_{\mathrm{Cas},1}] \tag{26}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}] H \tag{27}$$

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

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat} V [C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{29}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},2}}^*]}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H - \delta_{C_g}[{C_{\mathrm{Cas},2}}^*] \tag{30}$$

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

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}} V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{32}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{33}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{34}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{35}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{{V_C}^*}{V} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{36}$$

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

1.4 Dual-activated Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat} V [C_{\mathrm{Cas},1}] \tag{38}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat} V [C_{\mathrm{Cas},1}] \tag{39}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}] H \tag{40}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}] H \tag{41}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat} V [C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{42}$$

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

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H \tag{44}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}} V - \delta_{p,P_{TF}}[P_{TF}] \tag{45}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cre}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cre}}} V - \delta_{p,P_{\mathrm{Cre}}}[P_{\mathrm{Cre}}] \tag{46}$$

$$\frac{\mathrm{d}V_C}{\mathrm{d}t} = -k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{V_C}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{47}$$

$$\frac{\mathrm{d}{V_C}^*}{\mathrm{d}t} = k_{cre} V_C [P_{\mathrm{Cre}}]^4 + \frac{{V_C}^*}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \tag{48}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{49}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1}\frac{[P_{TF}]^n}{(K_A)^n + [P_{TF}]^n}\frac{{V_C}^*}{V} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{50}$$

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

1.5 Activator on Kill Switch

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -k_{cat} V [C_{\mathrm{Cas},1}] \tag{52}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},1}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_{C_g}[C_{\mathrm{Cas},1}] - k_{cat} V [C_{\mathrm{Cas},1}] \tag{53}$$

$$\frac{\mathrm{d}[C_{\mathrm{Cas},2}]}{\mathrm{d}t} = k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{C_g}[C_{\mathrm{Cas},2}] - k_{cat}[C_{\mathrm{Cas},2}] H \tag{54}$$

$$\frac{\mathrm{d}H}{\mathrm{d}t} = -k_{cat}[C_{\mathrm{Cas},2}] H \tag{55}$$

$$\frac{\mathrm{d}[{C_{\mathrm{Cas},1}}^*]}{\mathrm{d}t} = k_{cat} V [C_{\mathrm{Cas},1}] - \delta_{C_g}[{C_{\mathrm{Cas},1}}^*] \tag{56}$$

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

$$\frac{\mathrm{d}H^*}{\mathrm{d}t} = k_{cat}[C_{\mathrm{Cas},2}] H \tag{58}$$

$$\frac{\mathrm{d}[P_{TF}]}{\mathrm{d}t} = \alpha_{p,P_{TF}} V - \delta_{p,P_{TF}}[P_{TF}] \tag{59}$$

$$\frac{\mathrm{d}[P_{\mathrm{Cas}}]}{\mathrm{d}t} = \alpha_{p,P_{\mathrm{Cas}}} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_{p,P_{\mathrm{Cas}}}[P_{\mathrm{Cas}}] \tag{60}$$

$$\frac{\mathrm{d}[G_1]}{\mathrm{d}t} = \alpha_{r,G_1} \frac{[P_{TF}]^n}{(K_A)^n + [P_{TF}]^n} V - k_{C_g}[P_{\mathrm{Cas}}][G_1] - \delta_g[G_1] \tag{61}$$

$$\frac{\mathrm{d}[G_2]}{\mathrm{d}t} = \alpha_{r,G_2} V - k_{C_g}[P_{\mathrm{Cas}}][G_2] - \delta_g[G_2] \tag{62}$$