

1 Symbols

Variable	Meaning
V_1	Construct vector, species 1
V_2	Construct vector, species 1
G_1	gRNA, species 1
G_2	gRNA, species 2
G_3	gRNA, species 3
G_4	gRNA, species 4
G_5	gRNA, species 5
G_6	gRNA, species 6
P_{dCas9}	dCas9 protein species
P_{GFP}	GFP protein species
$C_{dCas9,1}$	Complex of dCas9 protein and gRNA1
$C_{dCas9,2}$	Complex of dCas9 protein and gRNA2
$C_{dCas9,3}$	Complex of dCas9 protein and gRNA3
$C_{dCas9,4}$	Complex of dCas9 protein and gRNA4
$C_{dCas9,5}$	Complex of dCas9 protein and gRNA5
$C_{dCas9,6}$	Complex of dCas9 protein and gRNA6
$\alpha_{r,i}$	Transcription rate, species i
$\alpha_{p,i}$	Coupled transcription and translation rate, species i
δ_g	gRNA degradation rate
δ_p	Protein degradation rate
λ	Stable Molecule Dilution Rate
$\delta_{p,P_{dCas9}}$	dCas9 and dCas9-gRNA complex degradation rate
δ_{C_g}	dCas9-gRNA1 complex degradation rate
δ_{C_g}	dCas9-gRNA2 complex degradation rate
δ_{C_g}	dCas9-gRNA3 complex degradation rate
δ_{C_g}	dCas9-gRNA4 complex degradation rate
δ_{C_g}	dCas9-gRNA5 complex degradation rate
δ_{C_g}	dCas9-gRNA6 complex degradation rate
$\delta_{p,P_{GFP}}$	GFP protein degradation rate
k_{C_g}	dCas9 and gRNA binding rate
n	Hill coefficient
K_A	Hill Activation Constant
K_R	Hill Repression Constant
$I_{i,j}$	Interference Matrix entry at coordinates i, j

2 Equations

2.1 0 Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (1)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] \quad (2)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} V_2 - \lambda[P_{\text{GFP}}] \quad (3)$$

2.2 1 Target Site

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (4)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (5)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (6)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] \quad (7)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (8)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (9)$$

2.3 2 Heterogeneous Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (10)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (11)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (12)$$

$$\frac{d[G_2]}{dt} = \alpha_{r,G_2} V_1 - k_{C_g}[G_2][P_{\text{dCas9}}] - \delta_g[G_2] \quad (13)$$

$$\frac{d[C_{\text{dCas9},2}]}{dt} = k_{C_g}[G_2][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},2}] \quad (14)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] - k_{C_g}[G_2][P_{\text{dCas9}}] \quad (15)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},2}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (16)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (17)$$

2.4 2 Identical Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (18)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (19)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (20)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] \quad (21)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (22)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (23)$$

2.5 3 Heterogeneous Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (24)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (25)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (26)$$

$$\frac{d[G_2]}{dt} = \alpha_{r,G_2} V_1 - k_{C_g}[G_2][P_{\text{dCas9}}] - \delta_g[G_2] \quad (27)$$

$$\frac{d[C_{\text{dCas9},2}]}{dt} = k_{C_g}[G_2][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},2}] \quad (28)$$

$$\frac{d[G_3]}{dt} = \alpha_{r,G_3} V_1 - k_{C_g}[G_3][P_{\text{dCas9}}] - \delta_g[G_3] \quad (29)$$

$$\frac{d[C_{\text{dCas9},3}]}{dt} = k_{C_g}[G_3][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},3}] \quad (30)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] - k_{C_g}[G_2][P_{\text{dCas9}}] - k_{C_g}[G_3][P_{\text{dCas9}}] \quad (31)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},2}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},3}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (32)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (33)$$

2.6 3 Identical Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (34)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (35)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (36)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] \quad (37)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (38)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (39)$$

2.7 4 Heterogeneous Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (40)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (41)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (42)$$

$$\frac{d[G_2]}{dt} = \alpha_{r,G_2} V_1 - k_{C_g}[G_2][P_{\text{dCas9}}] - \delta_g[G_2] \quad (43)$$

$$\frac{d[C_{\text{dCas9},2}]}{dt} = k_{C_g}[G_2][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},2}] \quad (44)$$

$$\frac{d[G_3]}{dt} = \alpha_{r,G_3} V_1 - k_{C_g}[G_3][P_{\text{dCas9}}] - \delta_g[G_3] \quad (45)$$

$$\frac{d[C_{\text{dCas9},3}]}{dt} = k_{C_g}[G_3][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},3}] \quad (46)$$

$$\frac{d[G_4]}{dt} = \alpha_{r,G_4} V_1 - k_{C_g}[G_4][P_{\text{dCas9}}] - \delta_g[G_4] \quad (47)$$

$$\frac{d[C_{\text{dCas9},4}]}{dt} = k_{C_g}[G_4][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},4}] \quad (48)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] - k_{C_g}[G_2][P_{\text{dCas9}}] - k_{C_g}[G_3][P_{\text{dCas9}}] - k_{C_g}[G_4][P_{\text{dCas9}}] \quad (49)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},2}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},3}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},4}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (50)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (51)$$

2.8 4 Identical Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (52)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (53)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (54)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] \quad (55)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (56)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (57)$$

2.9 5 Heterogeneous Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (58)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (59)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (60)$$

$$\frac{d[G_2]}{dt} = \alpha_{r,G_2} V_1 - k_{C_g}[G_2][P_{\text{dCas9}}] - \delta_g[G_2] \quad (61)$$

$$\frac{d[C_{\text{dCas9},2}]}{dt} = k_{C_g}[G_2][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},2}] \quad (62)$$

$$\frac{d[G_3]}{dt} = \alpha_{r,G_3} V_1 - k_{C_g}[G_3][P_{\text{dCas9}}] - \delta_g[G_3] \quad (63)$$

$$\frac{d[C_{\text{dCas9},3}]}{dt} = k_{C_g}[G_3][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},3}] \quad (64)$$

$$\frac{d[G_4]}{dt} = \alpha_{r,G_4} V_1 - k_{C_g}[G_4][P_{\text{dCas9}}] - \delta_g[G_4] \quad (65)$$

$$\frac{d[C_{\text{dCas9},4}]}{dt} = k_{C_g}[G_4][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},4}] \quad (66)$$

$$\frac{d[G_5]}{dt} = \alpha_{r,G_5} V_1 - k_{C_g}[G_5][P_{\text{dCas9}}] - \delta_g[G_5] \quad (67)$$

$$\frac{d[C_{\text{dCas9},5}]}{dt} = k_{C_g}[G_5][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},5}] \quad (68)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] - k_{C_g}[G_2][P_{\text{dCas9}}] - k_{C_g}[G_3][P_{\text{dCas9}}] - k_{C_g}[G_4][P_{\text{dCas9}}] - k_{C_g}[G_5][P_{\text{dCas9}}] \quad (69)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},2}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},3}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},4}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},5}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (70)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (71)$$

2.10 5 Identical Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (72)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (73)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (74)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p, P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] \quad (75)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p, P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (76)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (77)$$

2.11 6 Heterogeneous Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (78)$$

$$\frac{d[G_1]}{dt} = \alpha_{r, G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (79)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (80)$$

$$\frac{d[G_2]}{dt} = \alpha_{r, G_2} V_1 - k_{C_g}[G_2][P_{\text{dCas9}}] - \delta_g[G_2] \quad (81)$$

$$\frac{d[C_{\text{dCas9},2}]}{dt} = k_{C_g}[G_2][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},2}] \quad (82)$$

$$\frac{d[G_3]}{dt} = \alpha_{r, G_3} V_1 - k_{C_g}[G_3][P_{\text{dCas9}}] - \delta_g[G_3] \quad (83)$$

$$\frac{d[C_{\text{dCas9},3}]}{dt} = k_{C_g}[G_3][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},3}] \quad (84)$$

$$\frac{d[G_4]}{dt} = \alpha_{r, G_4} V_1 - k_{C_g}[G_4][P_{\text{dCas9}}] - \delta_g[G_4] \quad (85)$$

$$\frac{d[C_{\text{dCas9},4}]}{dt} = k_{C_g}[G_4][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},4}] \quad (86)$$

$$\frac{d[G_5]}{dt} = \alpha_{r, G_5} V_1 - k_{C_g}[G_5][P_{\text{dCas9}}] - \delta_g[G_5] \quad (87)$$

$$\frac{d[C_{\text{dCas9},5}]}{dt} = k_{C_g}[G_5][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},5}] \quad (88)$$

$$\frac{d[G_6]}{dt} = \alpha_{r, G_6} V_1 - k_{C_g}[G_6][P_{\text{dCas9}}] - \delta_g[G_6] \quad (89)$$

$$\frac{d[C_{\text{dCas9},6}]}{dt} = k_{C_g}[G_6][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},6}] \quad (90)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p, P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] - k_{C_g}[G_2][P_{\text{dCas9}}] - k_{C_g}[G_3][P_{\text{dCas9}}] - k_{C_g}[G_4][P_{\text{dCas9}}] - k_{C_g}[G_5][P_{\text{dCas9}}] - k_{C_g}[G_6][P_{\text{dCas9}}] \quad (91)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p, P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},2}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},3}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},4}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},5}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},6}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (92)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (93)$$

2.12 6 Identical Target Sites

$$\frac{dV_2}{dt} = -\lambda V_2 \quad (94)$$

$$\frac{d[G_1]}{dt} = \alpha_{r,G_1} V_1 - k_{C_g}[G_1][P_{\text{dCas9}}] - \delta_g[G_1] \quad (95)$$

$$\frac{d[C_{\text{dCas9},1}]}{dt} = k_{C_g}[G_1][P_{\text{dCas9}}] - \lambda[C_{\text{dCas9},1}] \quad (96)$$

$$\frac{d[P_{\text{dCas9}}]}{dt} = \alpha_{p,P_{\text{dCas9}}} V_2 - \lambda[P_{\text{dCas9}}] - k_{C_g}[G_1][P_{\text{dCas9}}] \quad (97)$$

$$\frac{d[P_{\text{GFP}}]}{dt} = \alpha_{p,P_{\text{GFP}}} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} \frac{(K_R)^n}{(K_R)^n + [C_{\text{dCas9},1}]^n} V_2 - \lambda[P_{\text{GFP}}] \quad (98)$$

$$\frac{dV_1}{dt} = -\lambda V_1 \quad (99)$$