## Supplementary Material

System of ordinary differential equations of the genetic regulatory network of Figure 4.

$$\begin{split} HB'[t] &= -HB[t]d_{HB} + \left(p_0^{BCD8}\right)_{HB}HB_0^{BCD8}[t] + \left(p_{KNI}^{BCD8}\right)_{HB}HB_{KNI}^{BCD8}[t] \\ &- HB[t]kni_{hb}KNI_{0,0}^0[t] - HB[t]kni_{hb}KNI_{0,0}^{BCD8}[t] \\ &- HB[t]kni_{hb}KNI_{0,TLL8}^0[t] - HB[t]kni_{hb}KNI_{0,TLL8}^{BCD8}[t] \\ &+ kni_{-hb}KNI_{HB,0}^0[t] + kni_{-hb}KNI_{HB,0}^{BCD8}[t] + kni_{-hb}KNI_{HB,TLL8}^0[t] \\ &+ kni_{-hb}KNI_{HB,TLL8}^0[t] + kni_{-hb}KNI_{HB,0}^0[t] - KNI[t]hb_{kni}HB_0^{BCD8}[t] \\ &+ kni_{-hb}KNI_{HB,TLL8}^0[t] + kni_{-hb}KNI_{HB,0}^0[t] - KNI[t]hb_{kni}HB_0^{BCD8}[t] \\ &+ kni_{-hb}KNI_{HB,TLL8}^0[t] + hb_{-kni}HB_{KNI}^0[t] + \left(p_{0,0}^{BCD8}\right)_{KNI}KNI_{0,0}^{BCD8}[t] \\ &+ \left(p_{0,TL8}^{BCD8}\right)_{KNI}KNI_{0,0}^{BCD8}[t] + \left(p_{HB,0}^{BCD8}\right)_{KNI}KNI_{0,0}^{BCD8}[t] \\ &+ \left(p_{0,TL8}^{BCD8}\right)_{KNI}KNI_{0,0}^{BCD8}[t] + \left(p_{HB,0}^{BCD8}\right)_{KNI}KNI_{HB,0}^{BCD8}[t] \\ &+ \left(p_{HB,TLL8}^{BCD8}\right)_{KNI}KNI_{BCD8}^{BCD8}[t] \\ &+ \left(p_{HB,TL8}^{BCD8}[t] + hb_{-kni}HB_{KNI}^0[t] \\ \left(HB_0^0\right)'[t] &= -BCD8hb_{bcd8}HB_0^0[t] - KNI[t]hb_{kni}HB_0^0[t] \\ &+ hb_{-bcd8}HB_0^{BCD8}[t] + hb_{-kni}HB_{KNI}^{BCD8}[t] \\ \left(HB_{0}^{BCD8}\right)'[t] &= BCD8hb_{bcd8}HB_0^0[t] - BCD8hb_{bcd8}HB_0^{BCD8}[t] \\ &- hb_{-kni}HB_{0}^{BCD8}[t] + hb_{-kni}HB_{KNI}^{BCD8}[t] \\ \left(HB_{KNI}^0\right)'[t] &= KNI[t]hb_{kni}HB_0^{BCD8}[t] + BCD8hb_{bcd8}HB_{KNI}^0[t] \\ &- hb_{-kni}HB_{KNI}^0[t] - BCD8hb_{bcd8}HB_{KNI}^0[t] \\ &- hb_{-kni}HB_{KNI}^0[t] - BCD8hb_{bcd8}HB_{KNI}^0[t] \\ &- hb_{-kni}HB_{KNI}^0[t] + hb_{-bcd8}HB_{KNI}^{BCD8}[t] \\ \left(HB_{KNI}^0\right)'[t] &= KNI[t]hb_{kni}HB_0^{BCD8}[t] + BCD8hb_{bcd8}HB_{KNI}^0[t] \\ &- hb_{-kni}HB_{KNI}^0[t] - hb_{-kni}HB_{KNI}^{BCD8}[t] \\ \left(KNI_{0,0}^0\right)'[t] &= -BCD8kni_{bcd8}KNI_{0,0}^0[t] - HB[t]kni_{hb}KNI_{0,0}^0[t] \\ &- TLL8kni_{kl8}KNI_{0,0}^0[t] + kni_{-bcd8}KNI_{0,0}^{BCD8}[t] \\ \left(KNI_{0,0}^0\right)'[t] &= -BCD8kni_{bcd8}KNI_{0,0}^0[t] - HB[t]kni_{hb}KNI_{0,0}^0[t] \\ &- TLL8kni_{kl8}KNI_{0,0}^0[t] + kni_{-bcd8}KNI_{0,0}^{BCD8}[t] \\ \left(KNI_{0,0}^0[t] + kni_{-hb}KNI_{0,0}^0[t] + kni_{-hb}KNI_{0,0}^0[t] \\ &+ kni_{-ull8}KNI_{0,0}^0[t] + kni_{-bcd8}KNI_{0,0}^{BCD8}[t] \\ \right\}$$

$$\begin{split} & \left( KNI_{0,0}^{BCD\$} \right)'[t] &= BCD\$kni_{bcd\$}KNI_{0,0}^{0}[t] - kni_{-bcd\$}KNI_{0,0}^{BCD\$}[t] \\ &\quad - HB[t]kni_{hb}KNI_{0,0}^{BCD\$}[t] \\ &\quad - TLL\$kni_{tt}KNI_{0,0}^{BCD\$}[t] + kni_{-ttt}KNI_{0,TLL\$}^{BCD\$}[t] \\ &\quad + kni_{-hb}KNI_{HB,0}^{BCD\$}[t] + kni_{-ttt}KNI_{0,TLL\$}^{BCD\$}[t] \\ &\quad + kni_{-hb}KNI_{HB,0}^{BCD\$}[t] \\ &\quad - HB[t]kni_{hb}KNI_{0,0}^{0}[t] - BCD\$kni_{bcd\$}KNI_{0,TLL\$}^{0}[t] \\ &\quad - HB[t]kni_{hb}KNI_{0,TLL\$}^{0}[t] - kni_{-ttt}KNI_{0,TLL\$}^{0}[t] \\ &\quad + kni_{-bcd}KNI_{0,TLL\$}^{BCD\$}[t] + kni_{-hb}KNI_{0,TLL\$}^{0}[t] \\ &\quad + kni_{-bcd}KNI_{0,TLL\$}^{BCD\$}[t] + kni_{-hb}KNI_{0,TLL\$}^{0}[t] \\ &\quad - kni_{-bcd}KNI_{0,TLL\$}^{BCD\$}[t] - HB[t]kni_{hb}KNI_{0,TLL\$}^{0}[t] \\ &\quad - kni_{-bcd}KNI_{0,TLL\$}^{BCD\$}[t] - HB[t]kni_{hb}KNI_{0,TLL\$}^{0}[t] \\ &\quad - kni_{-bcd}KNI_{0,TLL\$}^{BCD\$}[t] + kni_{-hb}KNI_{0,TLL\$}^{BCD\$}[t] \\ &\quad - kni_{-bcd}KNI_{0,TLL\$}^{BCD\$}[t] + kni_{-hb}KNI_{BD,TL\$}^{BCD\$}[t] \\ &\quad - kni_{-bcd}KNI_{0,TLL\$}^{BCD\$}[t] + kni_{-hb}KNI_{BD,0}^{BcD\$}[t] \\ &\quad - kni_{-bcd}KNI_{HB,0}^{BCD\$}[t] + kni_{-hb}KNI_{HB,0}^{BcD\$}[t] \\ &\quad - kni_{-bcd}KNI_{HB,0}^{BcD\$}[t] + kni_{-ttt}KNI_{HB,0}^{0}[t] \\ &\quad - kni_{-bcd}KNI_{HB,0}^{BcD\$}[t] + kni_{-ttt}KNI_{BB,0}^{BcD\$}[t] \\ &\quad - kni_{-bcd}KNI_{BD,0}^{BcD\$}[t] + kni_{-ttt}KNI_{BB,0}^{BcD\$}[t] \\ &\quad - kni_{-bcd}KNI_{BD,0}^{BcD\$}[t] + kni_{-ttt}KNI_{BB,0}^{BcD\$}[t] \\ &\quad - kni_{-bcd}KNI_{BB,0}^{BcD\$}[t] + kni_{-ttt}KNI_{BB,0}^{BcD\$}[t] \\ &\quad - kni_{-bcd}KNI_{BB,0}^{BcD\$}[t] + kni_{-ttt}KNI_{BB,0}^{BcD\$}[t] \\ &\quad - kni_{-bcd}KNI_{BB,0}^{BcD\$}[t] + kni_{-ttt}KNI_{BB,0}^{BcD\$}[t] \\ &\quad - kni_{-ttt}KNI_{BB,0}^{BcD\$}[t] + kni_{-ttt}KNI_{BB,0}^{BcD\$}[t] \\ &\quad$$

The conservation laws of the system of ordinary differential equations (1) are,

$$GC_{KNI} = KNI_{HB,TLL\$}^{BCD\$}[t] + KNI_{HB,0}^{BCD\$}[t] + KNI_{0,TLL\$}^{BCD\$}[t] + KNI_{0,0}^{0}[t] + HB_{KNI}^{0}[t] + HB_{0}^{BCD\$}[t] + HB_{0}^{0}[t]$$

$$GC_{HB} = HB_{KNI}^{BCD\$}[t] + HB_{0}^{BCD\$}[t] + HB_{0}^{0}[t] + HB_{0}^{0}[t]$$

$$(2)$$

The symbols TLL and BCD represent the concentration of TLL and BCD. In fact, TLL  $\equiv TLL$  (x) and BCD  $\equiv BCD$  (x), where x is the coordinate along the antero-posterior axis of the *Drosophila* embryo.

The parameter values of the system of equations (1) for the fits in Figure 5, obtained by multi-objective optimization technique, and are shown in the table below.

$hb_{bcd} = 1.141$	$hb_{kni} = 0.035$	$kni_{bcd} = 0.706$
$kni_{hb} = 1.956$	$kni_{tll} = 0.087$	$hb_{-bcd} = 1.000$
$hb_{-kni} = 0.001$	$kni_{-bcd} = 0.100$	$kni_{-hb} = 0.003$
$kni_{-tll} = 0.265$	$(p_0^{BCD\$})_{HB} = 1.954$	$(p_{KNI}^{BCD\$})_{HB} = 0.000$
$(p_{0,0}^{BCD\$})_{KNI} = 2.351$	$(p_{HB,0}^{BCD\$})_{KNI} = 0.004$	$(p_{0,TLL\$}^{BCD\$})_{KNI} = 2.065$
$(p_{HB,TLL\$}^{BCD\$})_{KNI} = 0.0196$	$d_{HB} = 0.000$	$d_{KNI} = 0.136$
$\alpha_{hb} = 0.100$	$\alpha_{kni} = 2.000$	Time = 10.000
$GC_{HB} = 273.236$	$GC_{KNI} = 325.558$	

Table 1: Parameter values of the fits shown in Figure 5. The first 18 parameters are the free parameters of the differential equation model 1. The parameter  $t^*$  is the total integration time of the system of differential equations. The parameters  $\alpha_{hb}$  and  $\alpha_{kni}$  are scale factors that multiply the differential equation solutions  $HB(t^*)$  and  $KNI(t^*)$ , in order to avoid biasing of data. Note that experimental data obtained by fluorescent methods indicate a concentration that is proportional to the actual concentration of HB and KNIproteins, and these scaling factors are unknown and are different for each protein. The constants  $GC_{HB}$  and  $GC_{KNI}$  are the total gene concentrations that are responsible for the transcription and translation of proteins HB and KNI (conservation laws (2)).

System of ordinary differential equations of the genetic regulatory network of Figure 6.

$$\begin{split} HB'[t] &= -HB[t]kni_{hb}KNI_{0,CTLS}^{BCDS}[t] + kni_{-hb}KNI_{B,CTLS}^{BCDS}[t] \\ &- HB(t)kni_{hb}KNI_{0,CTLS}^{BCDS}[t] + kni_{-hb}KNI_{B,CTLS}^{BCDS}[t] \\ &+ (P_{KNI,KBS}^{BCDS}) + BHBB_{KNI,HKBS}^{BCDS}[t] + (P_{0,0}^{BCDS}) + BBHB_{0,0}^{BCDS}[t] \\ &+ (P_{KNI,0}^{BCDS}) + BHBB_{KNI,0}^{BCDS}[t] + (P_{0,0}^{DCDS}) + BBHB_{0,0}^{BCDS}[t] \\ &- HB[t]kni_{hb}KNI_{0,0}^{0}t] + kni_{-hb}KNI_{B,0}^{0}t] - d_{HB}HB[t] \\ &- HB[t]kni_{hb}KNI_{0,0}^{0}t] + kni_{-hb}KNI_{B,0}^{0}t] - d_{HB}HB[t] \\ &- HB[t]kni_{hb}KNI_{0,0}^{0}t] + kni_{-hb}KNI_{B,0}^{0}t] - d_{HB}HB[t] \\ &- KNI[t]hb_{kni}HB_{0,0}^{DOS}[t] + hb_{-kni}HB_{KNI,0}^{BCDS}[t] \\ &- KNI[t]hb_{kni}HB_{0,0}^{DOS}[t] + hb_{-kni}HB_{KNI,0}^{BCDS}[t] \\ &+ (P_{B,0}^{BCDS}) K_{NI}KNI_{B,0}^{BCDS}[t] + (P_{B,0}^{BCDS}) K_{NI}KNI_{B,0}^{BCDS}[t] \\ &+ (P_{0,0}^{BCDS}) K_{NI}KNI_{B,0}^{BCDS}[t] + hb_{-kni}HB_{KNI,0}^{CN}[t] \\ &- KNI[t]hb_{kni}HB_{0,0}^{0}t] + hb_{-kni}HB_{KNI,0}^{0}t] - d_{KNI}KNI_{B,0}^{BCDS}[t] \\ &- KNI[t]hb_{kni}HB_{0,0}^{0}t] + hb_{-kni}HB_{KNI,0}^{BCDS}[t] \\ &- KNI[t]hb_{kni}HB_{0,0}^{0}t] + hb_{-kni}HB_{KNI,0}^{BCDS}[t] \\ &- KNI[t]hb_{kni}HB_{0,0}^{0}t] + hb_{-kni}HB_{0,0}^{BCDS}[t] - HKB$hb_{hkb}HB_{0,0}^{0}[t] \\ &+ hb_{-hkb8}HB_{0,0}^{0}t] + hb_{-bcd}$HB_{0,0}^{BCDS}[t] - HKB$hb_{hkb}HB_{0,0}^{BCDS}[t] \\ &+ hb_{-hkb8}HB_{0,HKB8}^{BCDS}[t] - KNI[t]hb_{kni}HB_{0,0}^{BCDS}[t] + hb_{-kni}HB_{KNI,0}^{BCDS}[t] \\ &+ hb_{-hkb8}HB_{0,HKB8}^{BCDS}[t] - KNI[t]hb_{kni}HB_{0,0}^{BCDS}[t] + hb_{-kni}HB_{KNI,0}^{BCDS}[t] \\ &+ hb_{-hkb8}HB_{0,HKB8}^{BCDS}[t] - hb_{-bcd8}HB_{0,HKB8}^{BCDS}[t] \\ &+ hKB$hb_{hkb8}HB_{0,0}^{BCDS}[t] - hb_{-hkb8}HB_{0,HKB8}^{BCDS}[t] \\ &+ KNI[t]hb_{kni}HB_{0,0}^{0}t] - hb_{-hkb}HB_{0,HKB8}^{BCDS}[t] \\ &+ KNI[t]hb_{kni}HB_{0,0}^{0}t] - hb_{-hkb}HB_{0,HKB8}^{BCDS}[t] \\ &+ KNI[t]hb_{kni}HB_{0,0}^{0}t] + hb_{-hkm}HB_{KNI,0}^{BCDS}[t] \\ &- KNI[t]hb_{kni}HB_{0,0}^{0}t] + hb_{-hkb}HB_{KNI,0}^{BCDS}[t] \\ &- KNI[t]hb_{kni}HB_{0,0}^{0}t] + hb_{-hkb}HB_{KNI,0}^{BCDS}[t] \\ &- KNI[t]hb_{kni}HB_{0,0}^{0}t] + hb_{-hkb}HB_{KNI,0}^{BCDS}[t] \\ &-$$

Equations (1) and (3) differ by the HKB\$ terms and the associated operon forms. The HKB\$ terms are represented in bold.

The conservation laws of the system of ordinary differential equations (3) are,

$$GC_{KNI} = KNI_{HB,TLL}^{BCD}[t] + KNI_{HB,0}^{BCD}[t] + KNI_{0,TLL}^{BCD}[t] + KNI_{0,0}^{BCD}[t] + KNI_{HB,TLL}^{0}[t] + KNI_{HB,0}^{0}[t] + KNI_{0,TLL}^{0}[t] + KNI_{0,0}^{0}[t] GC_{HB} = HB_{KNI,HKB}^{BCD}[t] + HB_{0,HKB}^{BCD}[t] + HB_{KNI,0}^{BCD}[t] + HB_{0,0}^{BCD}[t] + HB_{KNI,HKB}^{0}[t] + HB_{0,HKB}^{0}[t] + HB_{KNI,0}^{0}[t] + HB_{0,0}^{0}[t]$$
(4)

The parameter values of the system of equations (3) for the fits in Figure 7, obtained by multi-objective optimization technique, are shown in the table below.

$a_1 = 121.870$	$a_2 = 296.738$	$L_1 = 0.856$
$L_2 = 0.874$	$hb_{bcd} = 0.984$	$hb_{kni} = 1.558$
$hb_{hkb} = 1.015$	$kni_{bcd} = 4.870$	$kni_{hb} = 2.866$
$kni_{tll} = 0.994$	$hb_{-bcd} = 1.000$	$hb_{-kni} = 0.127$
$hb_{-hkb} = 0.413$	$kni_{-bcd} = 0.001$	$kni_{-hb} = 0.350$
$kni_{-tll} = 0.324$	$(p_{0,0}^{BCD\$})_{HB} = 81.868$	$(p_{KNI,0}^{BCD\$})_{HB} = 0.000$
$(p_{0,HKB\$}^{BCD\$})_{HB} = 71.838$	$(p_{HB,HKB\$}^{BCD\$})_{HB} = 6.679$	$(p_{0,0}^{BCD\$})_{KNI} = 98.934$
$(p_{HB,0}^{BCD\$})_{KNI} = 0.054$	$(p_{0,TLL\$}^{BCD\$})_{KNI} = 23.722$	$(p_{HB,TLL\$}^{BCD\$})_{KNI} = 0.055$
$d_{HB} = 0.354$	$d_{KNI} = 0.191$	$\alpha_{HB} = 0.109$
$\alpha_{KNI} = 0.654$	$t^* = 29.107$	$GC_{HB} = 43.979$
$GC_{KNI} = 21.399$		

Table 2: Parameter values of the fits shown in Figure 7. The first 26 parameters are the free parameters of the differential equation model 3. The parameter  $t^*$  is the total integration time of the system of differential equations. The parameters  $\alpha_{HB}$  and  $\alpha_{KNI}$  are scale factors that multiply the differential equation solutions  $HB(t^*)$  and  $KNI(t^*)$ , in order to avoid biasing of data. Note that experimental data obtained by fluorescent methods indicate a concentration that is proportional to the actual concentration of HB and KNI proteins, and these scaling factors are unknown and are different for each protein. The constants  $GC_{HB}$  and  $GC_{KNI}$  are the total gene concentrations that are responsible for the transcription and translation of proteins HB and KNI.

$hb_{bcd} = 1.142$	$hb_{kni} = 0.034$	$kni_{bcd} = 0.709$
$kni_{hb} = 1.954$	$kni_{tll} = 0.088$	$hb_{-bcd} = 1.000$
$hb_{-kni} = 0.002$	$kni_{-bcd} = 0.998$	$kni_{-hb} = 0.002$
$kni_{-tll} = 0.265$	$(p_0^{BCD\$})_{HB} = 1.938$	$(p_{KNI}^{BCD\$})_{HB} = 0.005$
$(p_{0,0}^{BCD\$})_{KNI} = 2.374$	$(p_{HB,0}^{BCD\$})_{KNI} = 0.002$	$(p_{0,TLL\$}^{BCD\$})_{KNI} = 2.051$
$(p_{HB,TLL\$}^{BCD\$})_{KNI} = 0.014$	$d_{HB} = 0.004$	$d_{KNI} = 0.138$
$\alpha_{hb} = 0.100$	$\alpha_{kni} = 2.000$	$t^* = 10.000$
$GC_{HB} = 273.219$	$GC_{KNI} = 325.652$	

Parameter values for the fits in Figure 9 a):

Table 3: Parameter values of the fits shown in Figure 9 a) and system of equations (1).

Parameter values for the fits in Figure 9 b):

$hb_{bcd} = 1.141$	$hb_{kni} = 0.035$	$kni_{bcd} = 0.706$
$kni_{hb} = 1.956$	$kni_{tll} = 0.087$	$hb_{-bcd} = 1.000$
$hb_{-kni} = 0.001$	$kni_{-bcd} = 1.000$	$kni_{-hb} = 0.003$
$kni_{-tll} = 0.265$	$(p_0^{BCD\$})_{HB} = 1.954$	$(p_{KNI}^{BCD\$})_{HB} = 0.000$
$(p_{0,0}^{BCD\$})_{KNI} = 2.351$	$(p_{HB,0}^{BCD\$})_{KNI} = 0.003$	$(p_{0,TLL\$}^{BCD\$})_{KNI} = 2.065$
$(p_{HB,TLL\$}^{BCD\$})_{KNI} = 0.020$	$d_{HB} = 0.000$	$d_{KNI} = 0.136$
$\alpha_{hb} = 0.100$	$\alpha_{kni} = 2.000$	$t^* = 10.000$
$GC_{HB} = 273.235$	$GC_{KNI} = 325.558$	

Table 4: Parameter values of the fits shown in Figure 9 b) and system of equations (1).