Supporting Result S1.
Theoretical Analyses of Gene Regulation in a Long Germ Network.

For a given regulatory networks without any FBL, “Gene Regulation Function[1-3]” (GRF) is useful to understand how the network generates stripe gene expressions in space. GRF is the function that plots the expression level of a regulated gene against its regulator. Here the regulator can be anywhere in the upstream of the regulation (i.e., indirect regulations are allowed). In this section, we give an example of the analysis by GRF on the network shown in Fig. 2A (see also Fig. S7).

Let us begin with the simplest case – a direct interaction between gene #5 and gene #0 in Fig. 2A. The GRF is given by

\[ P_5 = f_+ (P_0, K_{0\to5}) = \frac{P_0^a}{P_0^a + K_{0\to5}^a} \]

This function can be analytically derived from equation 1 at the steady state, i.e. when

\[ \frac{dP_5}{dt} = 0 \quad \text{and} \quad \frac{\partial^2 P_5}{\partial x^2} = 0 . \]

We shall hereafter refer to the positive and negative gene regulation functions in equation 1 as \( f_+ \) and \( f_- \), respectively.

If there are more than two regulatory connections to a gene, there could be multiple regulatory pathways from an upstream gene to the gene via FFLs. The “decomposed GRF” introduced below elucidates the role of multiple regulations. Let us consider a FFL (marked by + in Fig. 2A; also Fig. S7A) from #0 to # 30 as an example. First, following equation S1 in Methods S1, combinatorial regulation for gene #30 is decomposed into elementary regulation denoted by \( P_{30} = f_+ (P_{26}, K_{26\to30}) \) and \( P_{30} = f_- (P_{5}, K_{5\to30}) \). Next, the expression level of the gene #0 that regulates #26 and #5 is substituted into the decomposed GRFs. They are expressed by \( P_0 \) as

\[ P_{30} = f_+ (f_+ (P_0, K_{0\to26}); K_{26\to30}) \]
(red dotted line in Fig. S7A) and

\[ P_{30} = f_- \left( f_+ (P_0; K_{0 \rightarrow 5}); K_{3 \rightarrow 30} \right) \]

(blue dashed line in Fig. S7A), respectively. Finally, when combinatorial regulation (eq. S1) of gene #30 by #5 and #26 is taken into account, the steady state yields

\[ P_{30} = f_- (P_5; K_{5 \rightarrow 30}) \cdot f_+ (P_{26}; K_{26 \rightarrow 30}) \]

Furthermore the “integrated GRF” of \( P_{30} \) is expressed as a function of \( P_0 \) by

\[ P_{30} = f_- \left( f_+ (P_0; K_{0 \rightarrow 5}); K_{3 \rightarrow 30} \right) \cdot f_+ \left( f_+ (P_0; K_{0 \rightarrow 26}); K_{26 \rightarrow 30} \right) \]

(S4)

It follows that this function shows a bell-shaped concave curve (a solid line in Fig. S7A). For a spatial pattern, a GRF can also be numerically obtained from expression level of genes measured at each position [2,3] (a dotted line in Fig. S8). A GRF, that is measured from a single stripe pattern of gene #30 and a gradient pattern of gene #0 (Fig. S2A), agrees well with the integrated GRF analytically derived above (Fig. S8).

When the procedure is recursively applied to include the downstream genes, the final decomposed and integrated GRFs become functions of \( P_0 \). Regulation of gene #6 by gene #0 is assembled by three pathways (marked in violet, red, and light blue lines in Figure S7B). Since gene #30 negatively regulates #6, the decomposed GRF for a pathway via the above FFL shows a convex bell-shaped curve (a violet line in Figure S7B) denoted by

\[ P_6 = f_+ \left( f_+ (P_0; K_{0 \rightarrow 5}); K_{3 \rightarrow 30} \right) \cdot f_+ \left( f_+ (P_0; K_{0 \rightarrow 26}); K_{26 \rightarrow 30}; K_{30 \rightarrow 6} \right) \]

The other decomposed GRFs represent activation (a red line in Figure S7B),

\[ P_6 = f_+ \left( f_+ (P_0; K_{0 \rightarrow 26}); K_{26 \rightarrow 6} \right) \]
and repression (a light blue line in Figure S7B),

\[ P_6 = f_- \left( f_+ (P_6; K_{0\rightarrow10}); K_{10\rightarrow6} \right) \]

Combinatorial regulation (eq. S2 in Methods S1) of gene #6 by genes #30, #26, and #10 is given by

\[ P_6 = f_+ (P_{26}; K_{26\rightarrow6}) \cdot f_- (P_{30}; K_{30\rightarrow6}) + f_- (P_{10}; K_{10\rightarrow6}) \]

The integrated GRF of \( P_6 \) as a function of \( P_0 \) is therefore

\[
\begin{align*}
P_6 &= f_+ \left( f_+ (P_0; K_{0\rightarrow26}); K_{26\rightarrow6} \right) \\
&\quad \cdot f_- \left( f_- \left( f_+ (P_0; K_{0\rightarrow26}); K_{26\rightarrow6} \right) \right) \cdot f_+ \left( f_+ (P_0; K_{0\rightarrow26}); K_{26\rightarrow30}; K_{30\rightarrow6} \right) \\
&\quad + f_- \left( f_+ (P_0; K_{0\rightarrow10}); K_{10\rightarrow6} \right) \\
\end{align*}
\]

(S5)

This has two local minima (solid line in Fig. S7B) resulting in the spatial pattern with two local minima (gene #6 in Fig. S2A) because \( P_0(x) \) is monotonically decreasing function (eq. S3 in Methods S1 and Fig. S2A).

In Figure S7C, there are three regulatory connections to gene #14 from genes #17, #6, and #2. A decomposed GRF as a function of \( P_0 \) is calculated by successively substituting equation S4 integrated GRFs of \( P_{30} \) and to \( P_{17}=f_+ (P_{30}; K_{30\rightarrow17}) \), then \( P_{14}=f_+ (P_{17}; K_{17\rightarrow14}) \) (an orange line), and equation S5 to \( P_{14}=f_+ (P_6; K_{6\rightarrow14}) \) (a blue line) and \( P_4=f_+ (P_6; K_{6\rightarrow4}) \), \( P_2=f_+ (P_4; K_{4\rightarrow2}) \), then \( P_{14}=f_+ (P_2; K_{2\rightarrow14}) \) (a red line). The combinatorial regulation of #14 is given by

\[ P_{14} = f_+ \left( P_1; K_{1\rightarrow14} \right) \cdot f_- \left( P_6; K_{6\rightarrow14} \right) + f_- \left( P_2; K_{2\rightarrow14} \right) \]

(S6)

The integrated GRF of \( P_{14} \) plotted against \( P_0 \) shows five local minima (solid line) resulting in five stripes in the spatial pattern (Fig. S2A).

In Figure S7D, a FFL from #14 to #1 (marked by * in Fig. 2A) is decomposed into direct regulation and indirect regulation via #27. The corresponding GRF is calculated by recursively substituting equation S6 either to \( P_1=f_+ (P_{14}; K_{14\rightarrow1}) \) (a red line) or
\( P_{27} = f_s(P_{14}; K_{14 \rightarrow 27}) \), then \( P_1 = f_s(P_{27}; K_{27 \rightarrow 1}) \) (a blue line), respectively. Since the pathways to gene #1 directly from #14 and indirectly from #14 via #27 are competitive (eq. S1) in the present network.

\[
P_1 = f_s(P_{14}; K_{14 \rightarrow 1}) + f_s(P_{27}; K_{27 \rightarrow 1}) \tag{S6}
\]

The integrated GRF of \( P_1 \) plotted against \( P_0 \) shows ten local maxima (solid line) resulting in ten stripes in the spatial pattern (Fig. 1A).