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Supporting Online Material for

Feedback Loops Shape Cellular Signals in Space and Time

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This PDF file includes:

Table S1

Other Supporting Online Material for this manuscript includes the following:
available at www.sciencemag.org/cgi/content/full/322/5900/390/DC1

Table S2 as zipped archive

Equations for "Feedback loops shape cellular signals in space and time"

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For all equations, in is the input and α is the output.

Figure 1A homeostat

$$\frac{d\alpha}{dt} = in - k_1 * \frac{\alpha^n}{\alpha^n + EC50^n} - \alpha$$

where $n = 6$, $EC50 = 0.1$, $k_1 = 0.2$

Figure 1A signal limiter

$$\frac{d\alpha}{dt} = in - k_2 * \alpha^n - \alpha$$

where $n = 5$, $k_2 = 0.8$

Figure 1A adaptive system

$$\frac{d\alpha}{dt} = in * (1 - \beta) - \alpha$$
$$\frac{d\beta}{dt} = \tau_\beta * (\alpha - k_1 * \beta)$$

where $k_1 = 0.5$, $\tau_\beta = 0.01$

Figure 1A transient generator

$$\frac{d\alpha}{dt} = in - \alpha * \beta^n - \alpha$$
$$\frac{d\beta}{dt} = \tau_\beta * (\alpha - k_1 * \beta)$$

where $n = 5$, $k_1 = 0.05$, $\tau_\beta = 0.01$

Figure 1B amplifier

$$\frac{d\alpha}{dt} = in + k_1 * \frac{\alpha^n}{\alpha^n + EC50^n} - \alpha$$

where $k_1 = 0$ (no feedback) or 1 (feedback), $n = 1$, $EC50 = 2$

Figure 1B accelerator or delay

$$\frac{d\alpha}{dt} = in + k_1 * \frac{\alpha^n}{\alpha^n + EC50^n} - \alpha - \alpha^n$$

where $k_1 = 0$ (no feedback) or 1 (delay) or 8 (accelerator), $n = 5$, $EC50 = 0.56$

Figure 1B bistable switch

$$\frac{d\alpha}{dt} = in + \frac{\alpha^n}{\alpha^n + EC50^n} - k_1 * \alpha$$

where $n = 5$, $EC50 = 0.8$, $k_1 = 0.1$

Figure 1C bistable pulse generator

$$\frac{d\alpha}{dt} = in + \frac{\alpha^n}{\alpha^n + EC50^n} - \alpha - \alpha * \beta$$
$$\frac{d\beta}{dt} = \tau_\beta * (\alpha - k_1 * \beta)$$

where $n = 4$, $\tau_\beta = 0.01$, $k_1 = 0.01$

Figure 1C oscillator

$$\frac{d\alpha}{dt} = in + \frac{\alpha^n}{\alpha^n + EC50^n} - \alpha - k_1 * \alpha * \beta^n$$
$$\frac{d\beta}{dt} = \tau_\beta * (\alpha - \beta)$$

where $n = 4$, $k_1 = 10$, $\tau_\beta = 0.01$

Figure 2A combined limiter and homeostat

$$\frac{d\alpha}{dt} = in - k_1 * \frac{\alpha^{n1}}{\alpha^{n1} + EC50^{n1}} - k_2 * \alpha^{n2} - \alpha$$

where $n1 = 6$, $EC50 = 0.1$, $k_1 = 0.2$, $k_2 = 0.8$, $n2 = 5$

Figure 2B robust oscillator

$$\frac{d\alpha}{dt} = in * (1 - k_2 * \gamma) + \frac{\alpha^n}{EC50^n + \alpha^n} - \alpha - k_1 * \alpha * \beta^n$$
$$\frac{d\beta}{dt} = \tau_\beta * (\alpha - \beta)$$
$$\frac{d\gamma}{dt} = \tau_\gamma * (\alpha - \gamma)$$

where $n = 4$, $k_1 = 10$, $\tau_\beta = 0.01$, $k_2 = 0.6$, $\tau_\gamma = 0.005$

Figure 2C robust switch

$$\frac{d\alpha}{dt} = \frac{\beta + \gamma}{(\beta + \gamma) + 1} - \alpha$$
$$\frac{d\beta}{dt} = \tau_\beta * (\frac{(in + \alpha)^n}{EC50^n + (in + \alpha)^n} - \beta)$$
$$\frac{d\gamma}{dt} = \tau_\gamma * (\frac{\alpha^n}{\alpha^n + EC50^n} - \gamma)$$

where $n = 6$, $EC50 = 0.5$, $\tau_\beta = 1$, $\tau_\gamma = 0.05$

Figure 1C all spatial panels

We modeled arrays of pixels by using 2-dimensional convolution to simulate spatial spreading.

Figure 1C local pulse

For a single pixel:

$$\frac{d\alpha}{dt} = in + \frac{\alpha_{g\alpha}^n}{EC50^n + \alpha_{g\alpha}^n} - \beta * \alpha + k_1 * \alpha$$
$$\frac{d\beta}{dt} = \tau_\beta * (\alpha_{g\beta} - k_2 * \beta)$$

where $\alpha_{g\alpha}$ and $\alpha_{g\beta}$ are the values for the pixels after 2-dimensional convolution with a Gaussian filter with standard deviation of 2 and 4 pixels, repectively, $\tau_\beta = 5$, $k_1 = 0.1$, $k_2 = 0.01$, $n = 4$, $EC50 = 0.2$

Figure 1C traveling wave

For a single pixel:

$$\frac{d\alpha}{dt} = in + \frac{\alpha_g^n}{EC50^n + \alpha_g^n} - (\beta + k_{\alpha off}) * \alpha$$
$$\frac{d\beta}{dt} = \tau_\beta * (\alpha_g - k_{\beta off} * \beta)$$

where α_g is the value for the pixel after 2-dimensional convolution with a Gaussian filter with standard deviation of 2 pixels, $\tau_\beta = 0.8$, $k_{\alpha off} = 0.1$, $k_{\beta off} = 0.1$, $n = 4$, $EC50 = 0.2$

Figure 1C polarity

A membrane recruitment model was used, where the total amount of signaling component is fixed and α represents the amount of signaling component bound to a single pixel of membrane.

$$\frac{d\alpha}{dt} = (in + \frac{\alpha_g^n}{EC50^n + \alpha_g^n}) * (\alpha_{total} - \alpha_{bound}) - k_{off} * \alpha$$

where α_g is the value for the pixel after 2-dimensional convolution with a Gaussian filter with standard deviation of 2 pixels, $\alpha_{total} = 10$, $\alpha_{bound} = \sum_{allpixels} \alpha$, $k_{off} = 0.05$, $n = 2$, $EC50 = 0.2$