Supplementary Note 1 : The steady state intracellular leucine level is independent of most model parameters.

To see why the leucine level at steady state depends only on the upstream flux in our model, consider the following equations. which determine the steady state leucine value:

$$\frac{dI_1}{dt} = \frac{c_3 E_u K_5^2}{P^2 + K_5^2} - \frac{c_4 E_1 I_1}{I_1 + K_3} - d_3 I_1$$

$$\frac{dI_2}{dt} = \frac{c_4 E_1 I_1}{I_1 + K_3} - \frac{c_5 E_2 I_2}{I_2 + K_4} - d_4 I_2$$

$$\frac{dP}{dt} = \frac{c_5 E_2 I_2}{I_2 + K_4} + F_{ext} - d_5 P$$

Assuming the decay terms for the intermediates ($d_3 I_1$ and $d_4 I_2$) can be neglected, the flux terms for the intermediates cancel in the summation of these three equations, which leads to

$$\frac{c_3 E_u}{P^2 + K_5^2} + F_{ext} - d_5 P = 0$$

It follows that the solution for P depends only on the upstream enzyme E_u and the external flux F_{ext}, and not on the levels of the downstream enzymes.