Goal

(italicized words identify optimization goals)

Wish to find W which has the *most* regular behavior over the *largest* contiguous subset of initial concentrations C_0, given gaussian disturbances of W. The contiguity may not be required, but seems to make sense (modelling a region which the cell can reliably keep the ambient concentrations within). We could take into account non-contiguous subsets, but that is not likely to be useful (it would be weird to have a motif which has similar behavior over different non-contiguous regions of ambient concentration).

Formulation

We define the norm over a matrix.

$$W - W' = W'', \text{ where } W''_{ij} = W_{ij} - W'_{ij} \ \forall \ i, j \tag{1}$$

$$|W| : \mathbb{R}_{n\times n} \to \mathbb{R} = \sqrt{\sum_{i,j\in[1,n]} W_{ij}} \tag{2}$$

Given fixed parameters $W \in \mathbb{R}_{n\times n}, \sigma_W \in \mathbb{R}$, define a Gaussian distribution of weights.

$$D(W'|W, \sigma_W) = (2\sigma_W^2\pi)^{-2} e^{\frac{-(|W'-W|)^2}{2\sigma_W^2}} \tag{3}$$

This says "mutations modify the weights of the matrix W' a Euclidean distance from the original weight matrix W with probability according to the gaussian distribution with parameter σ_W." This may not be realistic, but it captures the idea that if a mutation occurs, it is likely to modify multiple weights at once if it modifies any at all.

We define the "behavior" of a network (C_0, W) as the concentration vector $C(T)$ at some given time T. This assumes linear differential equations modelling activation and inhibition rates with no external input or output.

$$C_{C_0,W}(t) = C_0 + \int_0^t W \cdot C(t)dt \tag{4}$$

This may not be appropriate; some networks may have *very* reliable periodic behavior, where the period simply changes slightly in response to disturbance, which would lead to vastly different $C(T)$. However, if we restrict ourselves to networks which reach some sort of equilibrium (which need not be defined or used at this time), we can use just $C(T)$. We define networks that reach equilibrium over some region "centered" at C_0 as networks which have similar $C(T)$ for some large T over C'_0 normally distributed with mean C_0. $T > 0$

and must be "large enough to allow the system to get to equilibrium." We can accomplish this by simply choosing a timescale and picking networks which achieve equilibrium.

Variability

Variability V of a network is defined using variation v with an initial concentration (C_0, W) over some gaussian distribution of C'_0 is defined.

$$v(C_0, W', W) = \int_{C'_0 \in \mathbb{R}^n} D(C'_0 | C_0, \sigma_C) \cdot |C_{C'_0, W'}(T) - C_{C_0, W}(T)| \tag{5}$$

$$\begin{aligned} V(C_0, W) &= \int_{W' \in \mathbb{R}_{n \times n}} D(W' | W, \sigma_W) \cdot v(C_0, W', W) \\ &= \int_{W', C'_0} D(W' | W, \sigma_W) D(C'_0 | C_0, \sigma_C) \cdot |C_{C'_0, W'}(T) - C_{C_0, W}(T)| \end{aligned} \tag{6}$$

Finding stable networks X, then, is defined as an optimization problem. The most robust networks (the ones with the minimum variability) are (hopefully) likely to produce interesting network motifs.

$$X^* = \min_W \int_{C_0 \in \mathbb{R}^n} V(C_0, W) \tag{7}$$

Simulation of (C_0, W) seems possible by discretizing choices of C'_0 and W' normally distributed about C_0 and W.