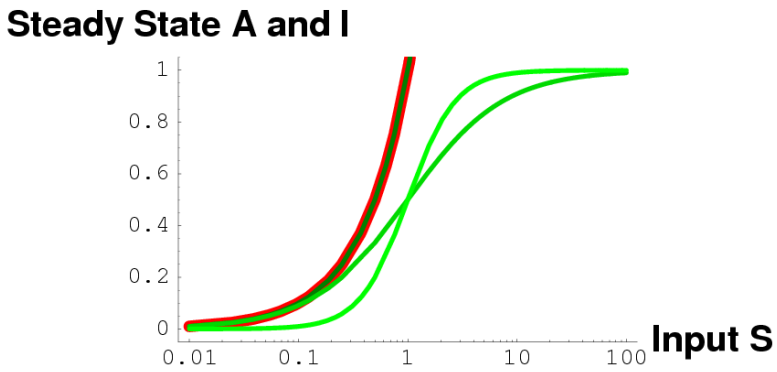

Figure 1: Steady state activator, nonconserved (dark green), saturating (green), sigmoidal (lime) and steady state, nonconserved inhibitor (red).

1 Saturating Activator

We initially modify LEGI by adding a saturating term to the production of activator, eq. (1). This produces a steady state activation profile that is bounded, fig. 1. The resulting response (fig. 2) becomes dependent on input strength and activator nonlinearity.

$$a'[t] = \frac{S^n}{Km^n + S^n} - a(t) \tag{1}$$

$$i'(t) = \alpha * (S - i(t)) \tag{2}$$

$$r'(t) = \beta * (a(t)(R_{tot} - r(t)) - i(t)r(t)) \tag{3}$$

- for $Km \ll S$, it's the original LEGI model. a and i are equal for all inputs, therefore the response is flat.
- for $Km \approx S$ and $n = 1$, saturated activator. The inhibitor gradually outproduces the activator, leading to a monotonically decreasing response.
- for $Km \approx S$ and $n > 1$, sigmoidal activator. The activator initially lags the inhibitor before attempting to catch up, producing a biphasic response.

Looking at the response curves fig. 2, one can infer the gradient response in a purely local model (no diffusion of inhibitor).

- the LEGI model (cyan flat) cannot sense gradients
- the saturated activator (blue decreasing) can only model repulsion
- the sigmoidal activator (navy bell) is capable of attraction and repulsion

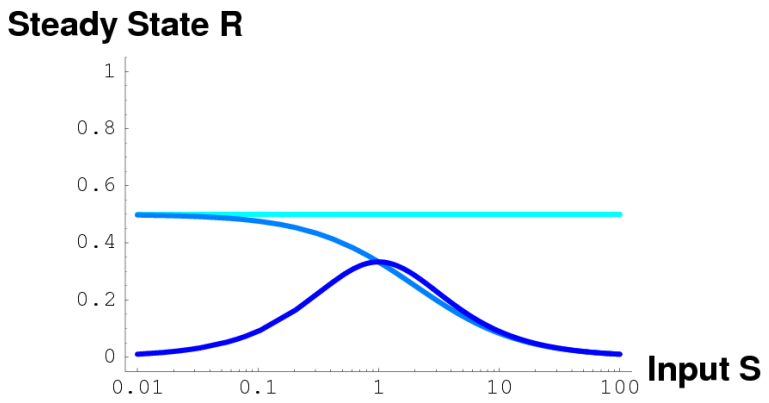

Figure 2: Steady state response for LEGI (cyan), saturating activator (blue), sigmoidal activator (navy).

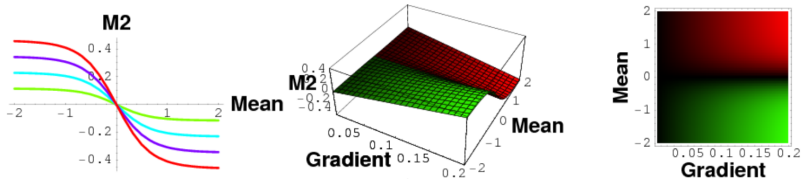

Figure 3: Chemotaxis metric

Many metrics were then derived in an attempt to quantify "attraction" and "repulsion". The M_2 metric (eq. (4)) offered the best anti-symmetrical curve (fig. 3) given the symmetrical response (fig. 2: navy, bell curve). It reveals a "stopping point" where attraction becomes repulsion, regardless of external gradient.

$$M_2 = \frac{r_{front} - r_{back}}{Mean[r]} \tag{4}$$

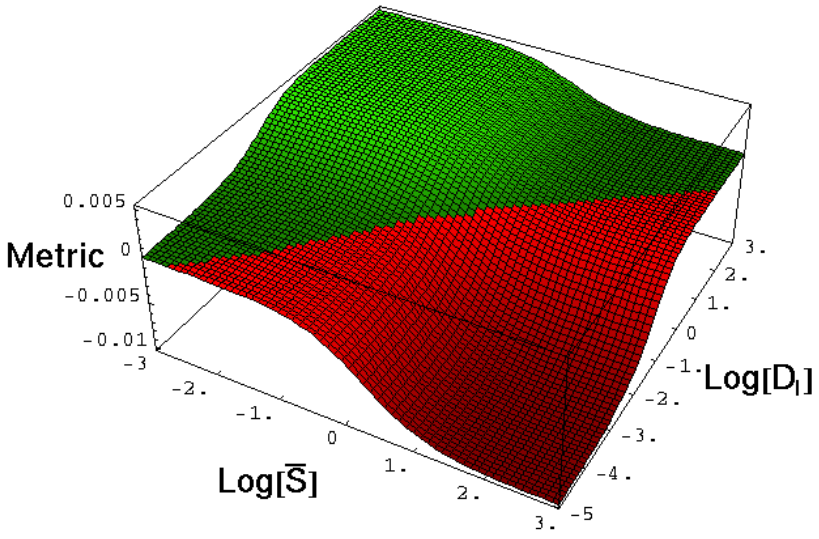

Figure 4: M_2 chemoattraction (green) and chemorepulsion (red)

2 Saturating Activator, diffusible inhibitor

Here we modify LEGI by adding a saturating term to the production of activator, eq. (5) and allowing for the diffusion of inhibitor, eq. (6).

$$\frac{\partial a(t,x)}{\partial t} = S * (A_{tot} - a) - a \tag{5}$$

$$\frac{\partial i(t,x)}{\partial t} = \alpha * (S - i) + D_i \frac{\partial^2 i}{\partial x^2} \tag{6}$$

$$\frac{\partial r(t,x)}{\partial t} = \beta * (a(R_{tot} - r) - i * r) \tag{7}$$

Modifying the diffusion of the inhibitor D_i transitions the model between a purely local one to a purely global model. Applying the metric from eq. (4) yields the response in fig. 4 as a function in input and inhibitor diffusion.

- when $D_i \approx 0$, we have a monotonically decreasing response, similar to the blue curve in fig. 2 and thus only repulsion for all inputs (all red in fig. 4, for $D_i = 10^{-5}$)
- when $D_i \approx 1$, we interestingly achieve the same biphasic behavior of the purely local model with sigmoidal activation.
- when $D_i \gg 1$, we almost get the original LEGI, modeling only attraction until the activator saturates.

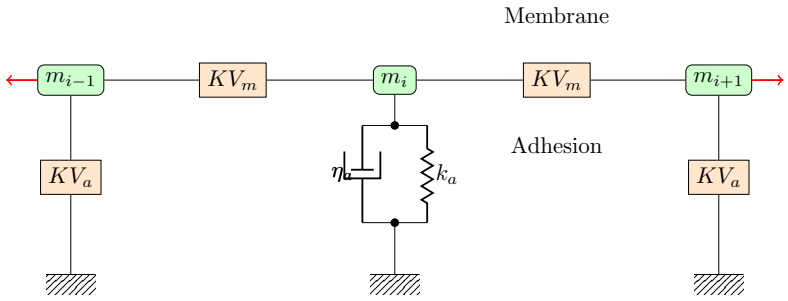

Figure 5: Membrane model

3 Mechanical model

The mechanical model of the cell is modeled as a series of Kelvin-Voigt elements. fig. 5 A Kelvin-Voigt element is a spring and damper connected in parallel that models a visco-elastic material. Adhesion is modeled as a set of K-V elements anchored in parallel to the ground while the cytoskeleton is modeled as a set of K-V elements connected in series across adhesion sites. Upon applying a protrusive force on the edge elements the internal stresses can be computed fig. 6. This internal stress can be used as feedback to the chemical signalling.

$$s_i = L * \frac{i-1}{n-1} \tag{8}$$

$$x_i(0) = s_i \tag{9}$$

$$x_i'(0) = 0 \tag{10}$$

$$\begin{aligned} m_i * x_i''(t) = {} & k_a(s_i - x_i(t)) - \eta_a * x_i'(t) \\ & + Fm_i(t) + Fm_{i-1}(t) \end{aligned} \tag{11}$$

$$\begin{aligned} Fm_i(t) = {} & k_m \left(\frac{x_{i+1}(t) - x_i(t)}{dL} - 1 \right) \\ & - \eta_m \left(x_i(t) - x_{i+1}(t) \right) \end{aligned} \tag{12}$$

4 Notes

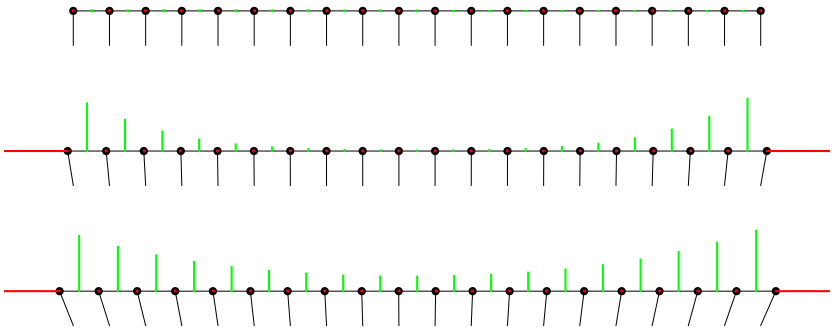

Figure 6: Mechanical model of membrane undergoing stretching. Black lines, Kelvin-Voigt elements, vertical ones are adhesive elements, horizontal ones are cytoskeletal. Red lines, force of protrusion. Green lines, force of stress on spring in K-V element (modeling cytoskeletal elastic stretch along cell).