Supplementary Material: Mathematical Model

1 Domain growth

In vivo, the domain of migration grows along the x axis, so that the length of the domain increases from 330μm initially to reach 1100μm at 24hrs into migration. This is a huge increase, and may have a large impact on the methods and success of migration. As such, domain growth is included in the model. The cells move with the underlying domain, and growth also impacts on the levels of chemoattractant. To solve numerically, it was necessary to rescale the equations by $z = x/L$, so that the equations are mapped onto a stationary domain. The solutions are then rescaled back to the moving domain for viewing.

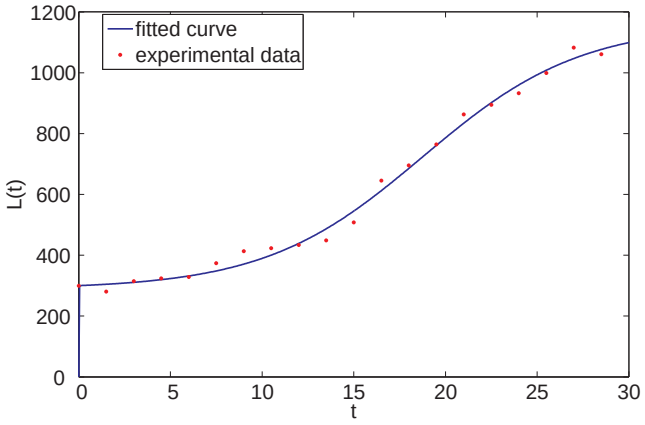

Figure 1: Experimental data (red dots) for domain length and the fitted logistic form (blue line).

The domain growth is found by fitting a logistic curve of the form

$$L(t) = \left(\frac{L_\infty e^{L_\infty \alpha (t-t_s)}}{L_\infty - 1 + e^{L_\infty \alpha (t-t_s)}} + 1 - \frac{L_\infty e^{L_\infty \alpha (-t_s)}}{L_\infty - 1 + e^{L_\infty \alpha (-t_s)}} \right) W, \tag{1}$$

where $L(t)$ is the length of the domain and W is the initial width of the domain, to experimental data. This gives $L_\infty = 960$, $\alpha = 0.0580$ and $t_s = -16$ (see Figure 1).

2 Chemoattractant

From data in the chick embryo, VEGF is expressed in the chick surface ectoderm directly overlying the NC cell migratory pathway and has been shown to be a NC cell chemoattractant (McLennan et al., 2010). We assume a constant production of VEGF by the ectoderm cells throughout the domain of invasion. To reconcile this constant production with our hypothesis of chemotaxis as a mechanism for invasion, we postulate that the cells may create their own gradient of chemoattractant through the internalization of VEGF. This would lead to lower levels of VEGF in areas where the cells have been present for longer periods, so that there is more VEGF further away from the neural tube. In our model, VEGF is produced logistically throughout the region (with linear proliferation rate, χ), and the internalization of VEGF by cells is modelled by weighted sink terms around the cells.

Hence the rate of change of VEGF concentration, c, is given by

$$\frac{\partial c}{\partial t} = \overbrace{D_c\left(\frac{1}{L^2}\frac{\partial^2 c}{\partial \xi^2} + \frac{\partial^2 c}{\partial y^2}\right)}^{\text{Diffusion}} \overbrace{-\lambda \sum_{i=1}^{n} c(x,y)\exp\left[-d\left((x-x_i)^2+(y-y_i)^2\right)\right]}^{\text{internalization}} \overbrace{-\frac{L'}{L}c}^{\text{Dilution}} + \overbrace{\chi c(1-c)}^{\text{Production}},$$

where D_c is the diffusion coefficient for the VEGF and λ and d are parameters governing the height and width of the weighting function used to describe the consumption of chemoattractant. We assume VEGF is produced logistically with a rate χ, however our results are not sensitive to this parameters as long as it is not large enough to overwhelm the consumption by cells (see Figure 2). There are n cells in the domain, which is $w\mu$m wide and $h\mu$m high, and the ith cell center is at (x_i, y_i).

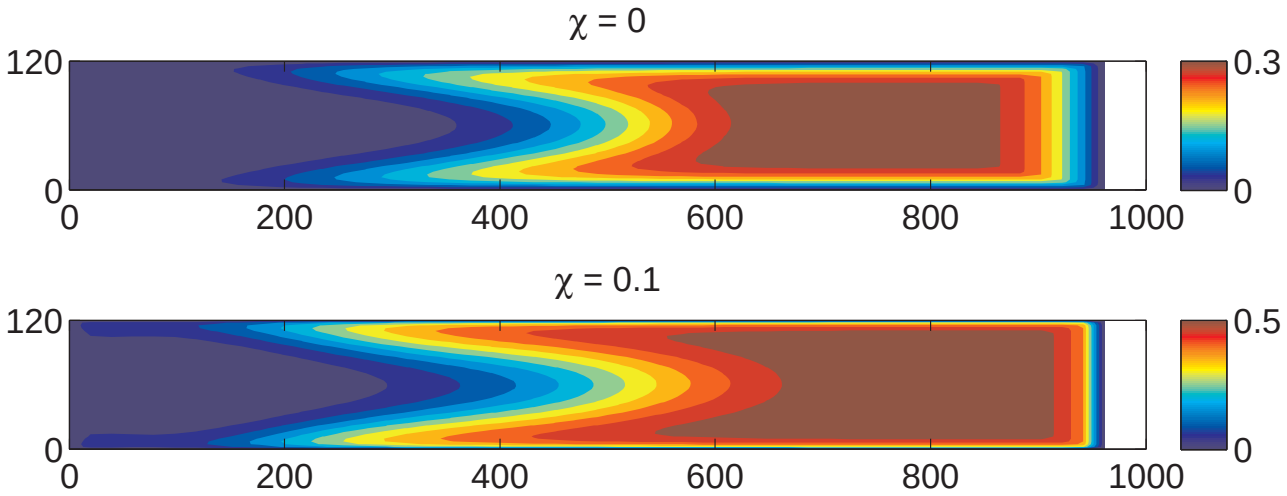

Figure 2: Simulated VEGF concentration with $\chi = 0$ and $\chi = 0.1$ after 24hrs.

We take as boundary conditions that the VEGF concentration is zero at each of the four boundaries of the region. This ensures that the concentration is not artificially high there due to the lower consumption of VEGF close to the edges of the domain (since there will be more overlapping regions of cell consumption in the interior of the domain). Hence the cells will not artificially cluster at the edge of the domain. We note in addition that this also provides a way of artificially simulating the exclusion zones between the migrating streams without explicitly including the inhibitory factors that may be present in these regions.

The concentration of VEGF may then be solved at each time step using the NAG solver d03ra. The zero boundary conditions require some care, however, to ensure that the initial conditions are sufficiently smooth to be able to solve the resultant equations.