A multiscale model of complex endothelial cell dynamics in early angiogenesis

Daria Stepanova[1,2 *], Helen M. Byrne[3], Philip K. Maini[3], Tomás Alarcón[4,1,2,5]

1 Centre de Recerca Matemàtica, Bellaterra (Barcelona), Spain
2 Departament de Matemàtiques, Universitat Autònoma de Barcelona, Bellaterra (Barcelona), Spain
3 Wolfson Centre for Mathematical Biology, Mathematical Institute, University of Oxford, Oxford, UK
4 Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain
5 Barcelona Graduate School of Mathematics (BGSMath), Barcelona, Spain

* dstepanova@crm.cat

Variable	**Indexes**	**Description**
$E_i = 1$ $E_i = 0$	$i \in \mathcal{I}_{init}$ $i \in \mathcal{I} \setminus \mathcal{I}_{init}$	Initial distribution of cell nuclei.
$N_i = \text{Unif}[(1-\xi)b_N, (1+\xi)b_N]$ $D_i = \text{DUnif}[(1-\xi)b_D, (1+\xi)b_D]$ $I_i = \text{DUnif}[(1-\xi)I_0, (1+\xi)I_0]$ $R2_i = \text{DUnif}[(1-\xi)b_{R2}, (1+\xi)b_{R2}]$ $R2_i^* = \text{DUnif}[(1-\xi)R2_0^*, (1+\xi)R2_0^*]$ $N_i = D_i = I_i = R2_i = R2_i^* = 0$	$i \in \mathcal{I}_{init}$ $i \in \mathcal{I} \setminus \mathcal{I}_{init}$	Cells are initialised with ligand/receptor numbers corresponding to their baseline gene expression with a correction for random fluctuations included via the parameter ξ. At the voxels where there is no cell nucleus, subcellular variables are initialised with the value zero.
$l_i^{s_{init}} = 2\Delta_{init}$	$i \in \mathcal{I}_{init}$	The alignment of ECM fibrils for voxels where cells were initially placed in the direction $s_{init} \in \mathcal{S}$.
$l_i^s = \text{Unif}[0, \Delta_{init}]$ $l_i^s = \text{Unif}[0, \Delta_{init}]$	$i \in \mathcal{I} \setminus \mathcal{I}_{init}$, $\forall s \in \mathcal{S}$ $i \in \mathcal{I}_{init}$, $\forall s \neq s_{init} \in \mathcal{S}$	The alignment of ECM fibrils for the rest of the voxels is initialised with a small random value in a given range, $[0, \Delta_{init}]$, imitating random orientation of fibrils prior to their realignment due to cell migration.
$c_i = c_{init}$ $c_i = c_{max}$	$i \in \mathcal{I}_{init}$ $i \in \mathcal{I} \setminus \mathcal{I}_{init}$	The ECM concentration at the voxels with cells is equal to $c_{init} \in [0, c_{max}]$ (specified for each numerical experiment). For other voxels, the ECM is assumed to be unchanged, thus equal to the maximum ECM concentration, c_{max}.
$m_i = m_{init}$ $m_i = 0$	$i \in \mathcal{I}_{init}$ $i \in \mathcal{I} \setminus \mathcal{I}_{init}$	The concentration of BM components at the voxels with cells is equal to $m_{init} \in [0, 1]$ (specified for each numerical experiment). For other voxels, no BM components have been deposited, thus the concentration is set to zero.

S3 Table. Initial conditions for numerical simulations. Here $\mathcal{I}$ is the set of all voxels; $\mathcal{S}$ is the set of all possible migration directions. $\text{DUnif}[a, b]$ is a discrete uniform distribution over all integer numbers lying within the interval $[a, b]$; $\text{Unif}[a, b]$ is the uniform distribution on the interval $[a, b]$. Baseline gene expression parameters for the VEGF-Delta-Notch signalling are listed in S1 Table. $\Delta_{init} = 1.0$ for all numerical simulations (this value, as, in general, for the value of the OL variable, is non-dimensional). The fluctuation parameter, ξ, is set to 0.1 in all numerical simulations. The exact values for c_{init} and m_{init} are given for each numerical experiment in S4 Table, as well as the set of initial cell positions, $\mathcal{I}_{init}$. For the description of model variables see Table 1 in the main text.