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Accelerated tumor invasion under non-isotropic cell dispersal in glioblastomas

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1. Biological experiments.– Glioblastoma (GLB) U87 cells were cultured by Stein and co-workers [1–3]. In Ref. [3], they tracked the paths of individual cells during 2 days. To the best of our knowledge, these are the only data available making it possible to estimate the values of the dispersal parameters used in our model (namely $D_x = \frac{<\triangle_x^2>}{2T} = 0.9 \cdot 10^{-4}$ cm^2/day and $U_x = \frac{<\triangle_x>}{T} = 0.012$ cm/day, as explained in our paper). In those experiments [3] mutant cells (U87ΔEGFR) were used, but Stein et al. believe that the results are also valid for wild-type cells (U87WT). Indeed, Stein et al. applied the same experimental data from Ref. [3] to wild-type cells (U87WT) in Ref. [2], p. 360. For this reason, we have taken into account the observed invasion speeds *in vitro* from both cell lines (Ref. [2], Fig. 2A) to determine the experimental speed range (shaded regions in Figs. 2-3 in our paper). The range thus obtained ($0.0067 < c < 0.0133$ cm/day) is also consistent with an independent experimental value (0.008 cm/day) obtained by other authors [4]. In this way, we have followed a conservative approach by including all of the experimental data available.

2. Numerical methods.– For the Dirac delta model we have derived the following implicit equation for the GLB invasion speed (see Eq. (14) in the main paper)

$$e^{\lambda cT} - e^{gT} = p\ e^{\lambda d} + (1-p)\ e^{-\lambda d} - 1, \tag{1}$$

where $c > 0$ and $\lambda > 0$. We use the same experimental values already applied in Sec. II of the main paper for the reproductive and dispersal parameters (namely $g = 0.1$ day^{-1}, $T = 1$ day and $D_x = 0.9 \cdot 10^{-4}$ cm^2/day, i.e. $d = \sqrt{2D_xT} = 0.0134$ cm, see Eq. (6) in the main paper).

For each value of p, the GLB invasion speed c has to be found numerically from Eq. (1). One way to do this is to plot the left- and right-hand sides of Eq. (1) (LHS and RHS, respectively) as a function of λ. Since the LHS of Eq. (1) is < 0 for $c = 0$, whereas the RHS is always ≥ 0, it is clear that for low enough values of c Eq. (1) is not satisfied for any value of λ. Thus, we can begin by plotting the LHS and RHS of Eq. (1) as a function of λ, for a value of c low enough so that both curves do not cross. By gradually increasing the value of c, at some point both curves will eventually cross (this will happen for sure, because the LHS grows with increasing c without bound, whereas the RHS is independent of c). Clearly, this procedure yields the minimum value of c for which Eq. (1) has a solution such that $c > 0$ and $\lambda > 0$. Note that this corresponds to the marginal stability criterion, already applied to the second-order or reaction-diffusion-advection (RDA) model in our main paper (Sec. II).

We have followed a procedure that is equivalent to that explained above, but leads to somewhat clearer figures. For example, consider the case $p = 0.5$. We have defined $f(\lambda)$ as the RHS minus the LHS of Eq. (1). We have plotted $f(\lambda)$ for a value of c low enough so that this difference is positive for all values of λ. We have then increased the value of c until the curve almost crosses the horizontal axis (Fig. S1, obtained for $c = 0.00561$ cm/day). A slight further increase in the value of c makes the curve cross the horizontal axis (Fig. S2, $c = 0.00562$ cm/day), i.e. front solutions to Eq. (1) now exist. Thus, for $p = 0.5$ (Figs. S1 and S2) the GLB invasion speed is $c = 0.0056$ cm/day. This is the leftmost value of the curve c_1 in Fig. 3 in the main paper. The rest of the values for the Dirac delta model (curve c_1 in Fig. 3 in the main paper) have been obtained in the same way, by considering other values of p.

Also for the Dirac delta model, we can check the validity of our approach by considering the special case $p = 1$. This corresponds to all cells moving radially outwards the same distance d. Then the front speed predicted by Eq. (1) should be simply $d/T = 0.0134$ cm/day. This is indeed the result found by the procedure above (see Fig. 3 in the main paper, rightmost value of the curve c_1).

For the Gaussian and Laplacian models, we have applied exactly the same numerical procedure, by simply replacing Eq. (1) above (i.e., Eq. (14) in the main paper) by the corresponding equations for the Gaussian and Laplacian models (Eqs. (17) and (20) in the main paper, respectively).

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Fig. S1. The dimensionless function $f(\lambda)$ for $p = 0.5$ and a value of c low enough so that there is no real solution to the equation $f(\lambda) = 0$, i.e. to Eq. (1). Compare to Fig. S2.

Fig. S2. The dimensionless function $f(\lambda)$ for $p = 0.5$ and a value of c high enough so that there are real solutions to the equation $f(\lambda) = 0$, i.e. to Eq. (1). Compare to Fig. S1.

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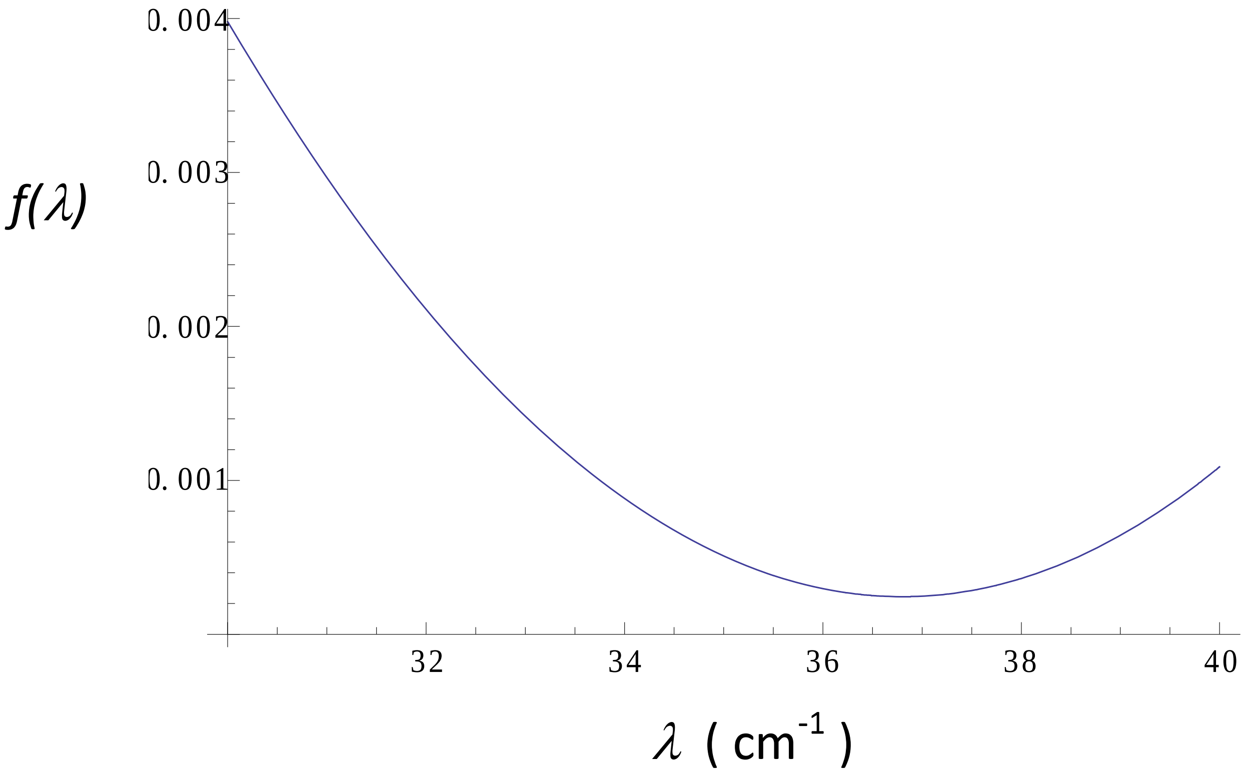
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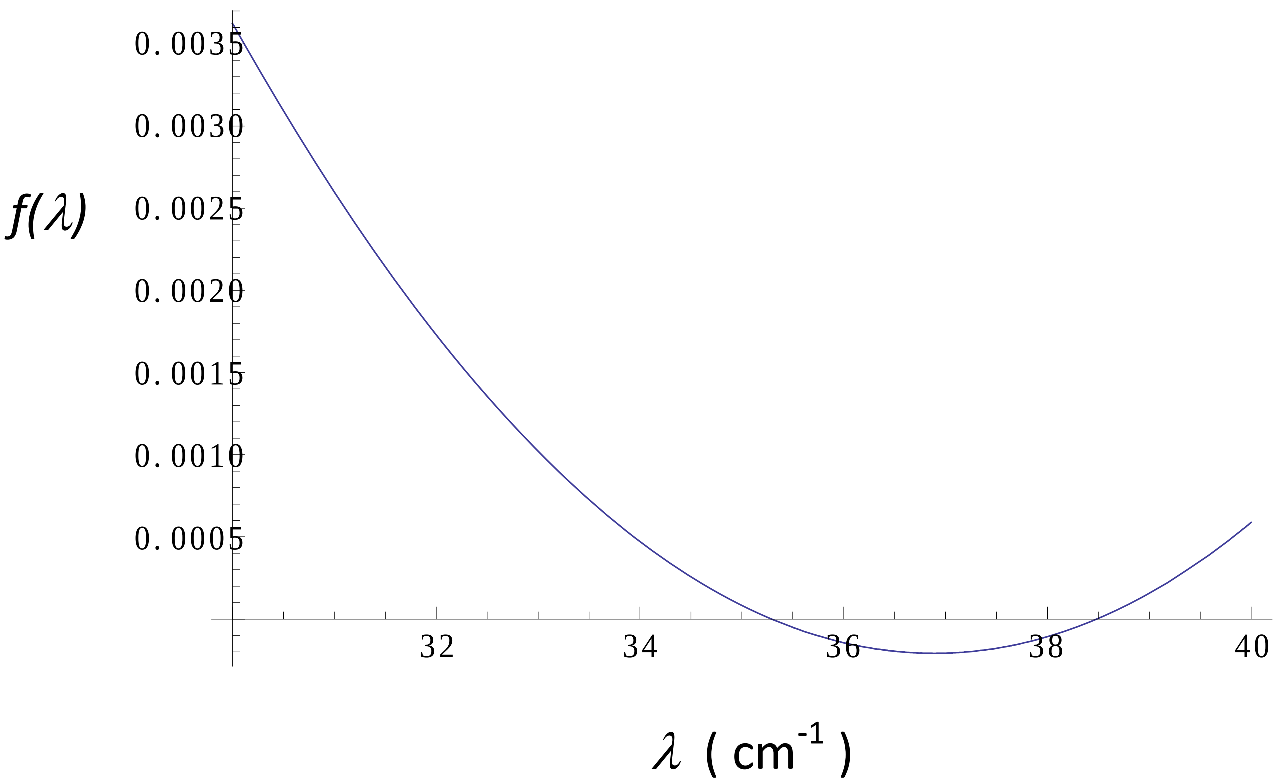
0.002
0.001
$f(\lambda)$
32
34
36
38
40
λ (cm^{-1})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0.0030
0.0025
0.0020
0.0015
0.0010
0.0005
32
34
36
38
40
λ (cm-1)