

Electronic Supplementary Material

Size matters: tissue size as a marker for a transition between reaction–diffusion regimes in spatio-temporal distribution of morphogens

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1.1. Analytical solution of the 1D Reaction Diffusion model assuming a finite domain, a source and a sink boundary conditions at $\varepsilon = 0$ and $\varepsilon = R$, respectively.

We considered a 1D tissue of length L where a morphogen is produced at $x = 0$, it diffuses to the tissue tip with a diffusion constant D and degrades linearly at a rate k . We assumed that at the tip of the tissue in $x = L$ there is a sink. At $t = 0$ there is no morphogen in the tissue. The changes in the morphogen distribution C_1 in time and space are expressed mathematically as the reaction diffusion equation:

$$\frac{\partial C_1}{\partial t} = D \frac{\partial^2 C_1}{\partial x^2} - kC_1 \quad (\text{Eq. S.1.})$$

With the following conditions:

No morphogen at initial time:

$$C_1(x, t = 0) = 0$$

Morphogen production at $x = 0$:

$$\frac{dC_1}{dx}(x = 0, t) = -\frac{q}{D}$$

Where q is the morphogen production rate at $x = 0$.

And a sink at the tip of the tissue $x = L$:

$$C_1(x = L, t) = 0$$

We rewrote Eq. S.1. in terms of the dimensionless variables $\varepsilon = \frac{x}{\sqrt{\frac{D}{k}}}$ and $\tau = kt$. We defined the

quantities R and S as $R = \frac{L}{\sqrt{\frac{D}{k}}}$ and $S = \frac{q}{\sqrt{Dk}}$ and we rewrote the concentration as $(\varepsilon, \tau) = \frac{C_1(\varepsilon, \tau)}{S}$:

$$\frac{\partial C}{\partial \tau} = \frac{\partial^2 C}{\partial \varepsilon^2} - C \quad (\text{Eq. S.2.})$$

With the following conditions. No morphogen at initial time:

$$C(\varepsilon, \tau = 0) = 0$$

Morphogen production at $\varepsilon = 0$:

$$\frac{dC}{d\varepsilon}(\varepsilon = 0, \tau) = -1$$

And a sink at the tip of the tissue $\varepsilon = R$:

$$C(\varepsilon = R, \tau) = 0$$

To solve this equation we redefined C in terms of an auxiliary function C_2 defined as:

$$C = C_2 e^{-\tau}$$

We calculated the derivatives of C_2 in terms of the derivatives of C . The second spatial derivative is:

$$\frac{\partial^2 C}{\partial \varepsilon^2} = e^{-\tau} \frac{\partial^2 C_2}{\partial \varepsilon^2}$$

And the time derivative is:

$$\frac{\partial C}{\partial \tau} = e^{-\tau} \frac{\partial C_2}{\partial \tau} - C_2 e^{-\tau}$$

This leads to the following equation:

$$\frac{\partial C_2}{\partial \tau} = \frac{\partial^2 C_2}{\partial \varepsilon^2} \quad (\text{Eq. S.3.})$$

With the following boundary conditions:

$$C_2(\varepsilon, \tau = 0) = 0$$

$$\frac{\partial C_2(\varepsilon = 0, \tau)}{\partial \varepsilon} = -e^\tau$$

$$C_2(\varepsilon = R, \tau) = 0$$

To solve Eq. S.3., solely performing a separation of variables would not suffice with this particular initial condition. Doing so, would yield the only solution as the trivial one, $C_2(\varepsilon, \tau) = 0$. To overcome this difficulty, we redefined C_2 using the auxiliary functions $C_3(\varepsilon, \tau)$, $f(\tau)$ and $g(\varepsilon)$. The explicit definition of the auxiliary functions $g(\varepsilon)$ and $f(\tau)$ will be defined later.

$$C_2(\varepsilon, \tau) = C_3(\varepsilon, \tau) + g(\varepsilon)f(\tau)$$

The derivative with respect to τ is:

$$\frac{\partial C_2(\varepsilon, \tau)}{\partial \tau} = \frac{\partial C_3(\varepsilon, \tau)}{\partial \tau} + g(\varepsilon) \frac{\partial f(\tau)}{\partial \tau}$$

And derivative with respect to ε is:

$$\frac{\partial^2 C_2(\varepsilon, \tau)}{\partial \varepsilon^2} = \frac{\partial^2 C_3(\varepsilon, \tau)}{\partial \varepsilon^2} + \frac{\partial^2 g(\varepsilon)}{\partial \varepsilon^2} f(\tau)$$

We rewrote the reaction diffusion equation in C_3 as:

$$\frac{\partial C_3(\varepsilon, \tau)}{\partial \tau} = \frac{\partial^2 C_3(\varepsilon, \tau)}{\partial \varepsilon^2} + \frac{\partial^2 g(\varepsilon)}{\partial \varepsilon^2} f(\tau) - g(\varepsilon) \frac{\partial f(\tau)}{\partial \tau}$$

The initial condition:

$$C_3(\varepsilon, \tau = 0) = -g(\varepsilon)f(\tau = 0)$$

With the following boundary conditions:

The source:

$$\frac{\partial C_3(\varepsilon = 0, \tau)}{\partial \varepsilon} = -e^\tau - \frac{\partial g(\varepsilon = 0)}{\partial \varepsilon} f(\tau)$$

And the sink:

$$C_3(\varepsilon = R, \tau) = -g(\varepsilon = R)f(\tau)$$

It is desirable that the initial condition is different from 0 and the boundary conditions are equal to

0. We defined $f(\tau)$ and $g(\varepsilon)$ as:

$$f(\tau) = -e^\tau, g(\varepsilon) = \varepsilon - R$$

With this choice Eq. S.3. turns out to be:

$$\frac{\partial C_3(\varepsilon, \tau)}{\partial \tau} = \frac{\partial^2 C_3(\varepsilon, \tau)}{\partial \varepsilon^2} + (\varepsilon - R)e^\tau \quad (\text{Eq. S.4.})$$

The initial condition:

$$C_3(\varepsilon, \tau = 0) = (\varepsilon - R)$$

With the following boundary conditions:

The source:

$$\frac{\partial C_3(\varepsilon = 0, \tau)}{\partial \varepsilon} = 0$$

And the sink:

$$C_3(\varepsilon = R, \tau) = 0$$

The solution to systems of the type of Eq. S.4. can be found in [1]. In this reference, the authors

defined a method to find the solution for systems with the following aspect:

$$r(x)m(t) \frac{\partial u(x, t)}{\partial t} - \left[\frac{\partial \left(p(x) \frac{\partial u(x, t)}{\partial x} \right)}{\partial x} + q(x)u(x, t) \right] = F(x, t)$$

$$\alpha u(x = a, t) + \beta \frac{\partial u(x = a, t)}{\partial x} = 0$$

$$\gamma u(x = b, t) + \delta \frac{\partial u(x = b, t)}{\partial x} = 0$$

$$u(x, t = 0) = f(x)$$

Where $u(x, t)$, $r(x)$, $m(t)$, $p(x)$, $q(x)$, $F(x, t)$ and $f(x)$ are functions and a , b , α , β , γ and δ are constants.

The authors defined the following quantities:

$$f_j = \int_a^b f(x) v_j(x) r(x) dx$$

$$F_j(t) = \int_a^b F(x, t) v_j(x) dx$$

Where $v_j(x)$ and λ_j are obtained from the solution of the following problem:

$$\frac{\partial \left(p(x) \frac{\partial v_j(x)}{\partial x} \right)}{\partial x} + q(x)v_j(x) + \lambda_j v_j(x) = 0$$

With the conditions:

$$\alpha v(x = a, t) + \beta \frac{\partial v(x = a, t)}{\partial x} = 0$$

$$\gamma v(x = b, t) + \delta \frac{\partial v(x = b, t)}{\partial x} = 0$$

The solution to the problem is:

$$u(x, t) = \sum_{j=0}^{\infty} f_j v_j(x) e^{-\lambda_j \int_0^t \frac{1}{m(s)} ds} + \sum_{j=0}^{\infty} v_j(x) e^{-\lambda_j \int_0^t \frac{1}{m(s)} ds} \int_0^t \frac{F_j(s)}{m(s)} e^{\lambda_j \int_0^s \frac{1}{m(w)} dw} ds$$

In our problem, we solved Eq. S.4. by identifying the following quantities:

$$m(\tau) = 1, r(\varepsilon) = 1, q(\varepsilon) = 0, p(\varepsilon) = 1, F(\varepsilon, \tau) = (\varepsilon - R)e^\tau$$

$$f(\varepsilon) = (\varepsilon - R), a = 0, b = R, \alpha = 0, \beta = 1, \gamma = 1, \delta = 0$$

First we solved the associated homogeneous problem:

$$\frac{\partial^2 v_j(\varepsilon)}{\partial \varepsilon^2} + \lambda_j v_j(\varepsilon) = 0$$

$$\frac{\partial v_j(\varepsilon = 0)}{\partial \varepsilon} = 0$$

$$v_j(\varepsilon = R) = 0$$

The solution to this problem is:

$$v_j(\varepsilon) = \sqrt{\frac{2}{R}} \cos\left(\frac{\left(j + \frac{1}{2}\right)\pi\varepsilon}{R}\right)$$

And:

$$\sqrt{\lambda_j} = \frac{\left(j + \frac{1}{2}\right)\pi}{R}$$

It is important to notice that since $v_j(\varepsilon)$ are the elements of a base of the space of functions, they

need to be normalized. This means that $\int_0^R v_j(\varepsilon)^2 d\varepsilon = 1$.

We calculated f_j :

$$f_j = -\frac{\sqrt{\frac{2}{R}}}{\left[\frac{(j + \frac{1}{2})\pi}{R}\right]^2}$$

We also calculated $F_j(\tau)$:

$$F_j(\tau) = -\frac{\sqrt{\frac{2}{R}} e^\tau}{\left[\frac{(j + \frac{1}{2})\pi}{R}\right]^2}$$

The solution to the equation is:

$$C_3(\varepsilon, \tau) = \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right) e^\tau}{\left[\frac{(j+\frac{1}{2})\pi}{R}\right]^2} \left[\frac{\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)^2 e^{-\left[\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)^2 + 1\right]\tau}}{\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)^2 + 1} \right]_{+1} \quad (\text{Eq. S.5.})$$

We obtained the original function:

$$C(\varepsilon, \tau) = [C_3(\varepsilon, \tau) - (\varepsilon - R)e^\tau] e^{-\tau}$$

$$C(\varepsilon, \tau) = [C_3(\varepsilon, \tau)e^{-\tau} - (\varepsilon - R)]$$

$$C(\varepsilon, \tau) = \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{(j + \frac{1}{2})\pi\varepsilon}{R}\right)}{\left[\frac{(j + \frac{1}{2})\pi}{R}\right]^2} \left[\frac{\left(\frac{(j + \frac{1}{2})\pi\varepsilon}{R}\right)^2 e^{-\left[\left(\frac{(j + \frac{1}{2})\pi\varepsilon}{R}\right)^2 + 1\right]\tau}}{\left(\frac{(j + \frac{1}{2})\pi\varepsilon}{R}\right)^2 + 1} \right]_{+1} - (\varepsilon - R)$$

$$\begin{aligned}
C(\varepsilon, \tau) = & \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)}{\left[\frac{(j+\frac{1}{2})\pi}{R}\right]^2} \frac{1}{\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)^2 + 1} - (\varepsilon - R) \\
& + \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)}{\left[\frac{(j+\frac{1}{2})\pi}{R}\right]^2} e^{-\left[\left(\frac{(j+\frac{1}{2})\pi}{R}\right)^2 + 1\right]\tau}
\end{aligned}$$

We rewrote $(\varepsilon - R)$ in the base of $\sqrt{\frac{2}{R}} \cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)$ in the interval $\varepsilon \in (0, R)$ as:

$$(\varepsilon - R) = \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)}{\left[\frac{(j+\frac{1}{2})\pi}{R}\right]^2}$$

To do this calculation, we wrote $(\varepsilon - R)$ as:

$$(\varepsilon - R) = \sum_{j=0}^{\infty} \alpha_j \sqrt{\frac{2}{R}} \cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)$$

And we obtained α_j by taking the inner product as the integral:

$$\alpha_j = \int_0^R (\varepsilon - R) \sqrt{\frac{2}{R}} \cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right) d\varepsilon$$

$$\alpha_j = -\sqrt{\frac{2}{R}} \frac{1}{\left[\frac{(j+\frac{1}{2})\pi}{R}\right]^2}$$

We wrote $C(\varepsilon, \tau)$ as:

$$C(\varepsilon, \tau) = \sum_{j=0}^{\infty} \frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)}{\left[\frac{(j+\frac{1}{2})\pi}{R}\right]^2 + 1} + \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)}{\left[\frac{(j+\frac{1}{2})\pi}{R}\right]^2 + 1} e^{-\left[\left(\frac{(j+\frac{1}{2})\pi}{R}\right)^2 + 1\right]\tau}$$

We wrote $\frac{e^{-\varepsilon}}{1+e^{-2R}} - \frac{e^{\varepsilon}}{1+e^{2R}}$ in the base of $\sqrt{\frac{2}{R}} \cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)$ in the interval $\varepsilon \in (0, R)$ as:

$$\frac{e^{-\varepsilon}}{1+e^{-2R}} - \frac{e^{\varepsilon}}{1+e^{2R}} = \sum_{j=0}^{\infty} \frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)}{\left[\frac{(j+\frac{1}{2})\pi}{R}\right]^2 + 1}$$

To do this calculation, we wrote $\left(\frac{e^{-\varepsilon}}{1+e^{-2R}} - \frac{e^{\varepsilon}}{1+e^{2R}}\right)$ as:

$$\frac{e^{-\varepsilon}}{1+e^{-2R}} - \frac{e^{\varepsilon}}{1+e^{2R}} = \sum_{j=0}^{\infty} \alpha_j \sqrt{\frac{2}{R}} \cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)$$

And we obtained α_j by taking the inner product as the integral:

$$\alpha_j = \int_0^R \left(\frac{e^{-\varepsilon}}{1+e^{-2R}} - \frac{e^{\varepsilon}}{1+e^{2R}}\right) \sqrt{\frac{2}{R}} \cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right) d\varepsilon$$

$$\alpha_j = \sqrt{\frac{2}{R} \frac{1}{\left[\frac{(j+\frac{1}{2})\pi}{R}\right]^2 + 1}}$$

Finally, we wrote $C(\varepsilon, \tau)$ as:

$$C(\varepsilon, \tau) = \left(\frac{e^{-\varepsilon}}{1+e^{-2R}} - \frac{e^{\varepsilon}}{1+e^{2R}} \right) + \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)}{\left(\frac{(j+\frac{1}{2})\pi}{R}\right)^2 + 1} e^{-\left[\left(\frac{(j+\frac{1}{2})\pi}{R}\right)^2 + 1\right]\tau} \quad (\text{Eq. S.6.})$$

1.2. Analytical solution of the 1D Reaction Diffusion model assuming a finite domain, a source and no flux boundary conditions at $\varepsilon = 0$ and $\varepsilon = R$, respectively.

We considered a 1D tissue of length L where a morphogen is produced at $x = 0$, it diffuses to the tissue tip with a diffusion constant D and degrades linearly at a rate k . We assumed that at the tip of the tissue in $x = L$ there is a no flux boundary condition. At $t = 0$ there is no morphogen in the tissue. The changes in the morphogen distribution C_1 in time and space are expressed mathematically as the reaction diffusion equation (Eq. S.1.):

$$\frac{\partial C_1}{\partial t} = D \frac{\partial^2 C_1}{\partial x^2} - kC_1$$

With the following conditions:

No morphogen at initial time:

$$C_1(x, t = 0) = 0$$

Morphogen production at $x = 0$:

$$\frac{dC_1}{dx}(x = 0, t) = -\frac{q}{D}$$

Where q is the morphogen production rate at $x = 0$.

And no flux boundary conditions at the tip of the tissue $x = L$:

$$\frac{dC_1}{dx}(x = L, t) = 0$$

We followed the same procedure that was used in section S.1.1.. We rewrote Eq. S.1. in terms of

the dimensionless variables $\varepsilon = \frac{x}{\sqrt{\frac{D}{k}}}$ and $\tau = kt$. We defined the quantities R and S as $R = \frac{L}{\sqrt{\frac{D}{k}}}$ and

$S = \frac{q}{\sqrt{Dk}}$ and we defined the concentration as $C(\varepsilon, \tau) = \frac{C_1(\varepsilon, \tau)}{S}$. We obtained the following equation (Eq. S.2.):

$$\frac{\partial C}{\partial \tau} = \frac{\partial^2 C}{\partial \varepsilon^2} - C$$

With the following conditions:

No morphogen at initial time:

$$C(\varepsilon, \tau = 0) = 0$$

Morphogen production at $\varepsilon = 0$:

$$\frac{dC}{d\varepsilon}(\varepsilon = 0, \tau) = -1$$

And no flux boundary condition at the tip of the tissue $\varepsilon = R$:

$$\frac{dC}{d\varepsilon}(\varepsilon = R, \tau) = 0$$

We used an auxiliary function to solve Eq. S.2. following the same procedure as in section S.1. In that section, we used three auxiliary functions and combined them into only one auxiliary function C_4 :

$$C(\varepsilon, \tau) = \left[C_4(\varepsilon, \tau) e^{-\tau} - \left(\varepsilon - \frac{\varepsilon^2}{2R} \right) \right]$$

With this choice, we obtained for Eq. S.2.:

$$\frac{\partial C_4(\varepsilon, \tau)}{\partial \tau} = \frac{\partial^2 C_4(\varepsilon, \tau)}{\partial \varepsilon^2} + \frac{e^\tau}{R} \left(1 + R\varepsilon - \frac{\varepsilon^2}{2} \right) \quad (\text{Eq. S.7.})$$

With the following boundary conditions:

The initial condition:

$$C_4(\varepsilon, \tau = 0) = \left(\varepsilon - \frac{\varepsilon^2}{2R} \right)$$

The source:

$$\frac{\partial C_4(\varepsilon = 0, \tau)}{\partial \varepsilon} = 0$$

And the tip:

$$\frac{\partial C_4(\varepsilon = R, \tau)}{\partial \varepsilon} = 0$$

We used the method presented in [1] as defined on section S.1.1. We identified the following quantities:

$$m(\tau) = 1, r(\varepsilon) = 1, q(\varepsilon) = 0, p(\varepsilon) = 1, F(\varepsilon, \tau) = \frac{e^\tau}{R} \left(1 + R\varepsilon - \frac{\varepsilon^2}{2} \right)$$

$$f(\varepsilon) = \left(\varepsilon - \frac{\varepsilon^2}{2R} \right), a = 0, b = R, \alpha = 0, \beta = 1, \gamma = 1, \delta = 0$$

First, we solved the associated homogeneous problem:

$$\frac{\partial^2 v_j(\varepsilon)}{\partial \varepsilon^2} + \lambda_j v_j(\varepsilon) = 0$$

$$\frac{\partial v_j(\varepsilon = 0)}{\partial \varepsilon} = 0$$

$$\frac{\partial v_j(\varepsilon = R)}{\partial \varepsilon} = 0$$

The solution to this problem is:

If $\lambda_j \neq 0$:

$$v_j(\varepsilon) = \sqrt{\frac{2}{R}} \cos\left(\frac{j\pi\varepsilon}{R}\right)$$

And:

$$\sqrt{\lambda_j} = \frac{j\pi}{R}$$

And if $\lambda_j = 0$:

$$v_0(\varepsilon) = \sqrt{\frac{1}{R}}$$

We calculated f_j :

If $\lambda_j \neq 0$:

$$f_j = -\sqrt{\frac{2}{R}} \frac{1}{\left(\frac{j\pi}{R}\right)^2}$$

And if $\lambda_j = 0$:

$$f_j = \sqrt{\frac{1}{R}} \frac{R^2}{3}$$

We calculated $F_j(t)$:

If $\lambda_j \neq 0$:

$$F_j(\tau) = -\frac{e^\tau}{\left(\frac{j\pi}{R}\right)^2} \sqrt{\frac{2}{R}}$$

And if $\lambda_j = 0$:

$$F_j(\tau) = \sqrt{\frac{1}{R}} e^{\tau} \left(\frac{R^2}{3} + 1 \right)$$

The solution to Eq. S.7. is:

$$C_4(\varepsilon, \tau) = \frac{R}{3} + \frac{1}{R} (e^{\tau} - 1) \left(\frac{R^2}{3} + 1 \right) + \sum_{j=1}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left(\frac{j\pi}{R}\right)^2} e^{-\left(\frac{j\pi}{R}\right)^2 \tau} \left[1 + \int_0^{\tau} e^{\tau} e^{\left(\frac{j\pi}{R}\right)^2 \tau} d\tau \right]$$

$$C_4(\varepsilon, \tau) = -\frac{1}{R} + \frac{1}{R} e^{\tau} \left(\frac{R^2}{3} + 1 \right) + \sum_{j=1}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left(\frac{j\pi}{R}\right)^2} e^{-\left(\frac{j\pi}{R}\right)^2 \tau} \left[1 + \frac{e^{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} - 1}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} \right] \quad (\text{Eq. S.8.})$$

We obtained the original function:

$$C(\varepsilon, \tau) = \left[C_4(\varepsilon, \tau) - \left(\varepsilon - \frac{\varepsilon^2}{2R} \right) e^{\tau} \right] e^{-\tau}$$

$$C(\varepsilon, \tau) = \left[C_4(\varepsilon, \tau) e^{-\tau} - \left(\varepsilon - \frac{\varepsilon^2}{2R} \right) \right]$$

$$C(\varepsilon, \tau) = -\frac{1}{R} e^{-\tau} + \frac{1}{R} \left(\frac{R^2}{3} + 1 \right) + \sum_{j=1}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left(\frac{j\pi}{R}\right)^2} \left[e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} + \frac{1 - e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau}}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} \right]$$

$$- \left(\varepsilon - \frac{\varepsilon^2}{2R} \right)$$

$$C(\varepsilon, \tau) = -\frac{1}{R} e^{-\tau} + \left(\frac{R}{3} + \frac{1}{R} \right) + \sum_{j=1}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau}$$

$$+ \sum_{j=1}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left[\left(\frac{j\pi}{R}\right)^2\right]} \left[\frac{1}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} \right] - \left(\varepsilon - \frac{\varepsilon^2}{2R} \right)$$

We wrote $\left(\varepsilon - \frac{\varepsilon^2}{2R}\right)$ in the base of $\sqrt{\frac{2}{R}} \cos\left(\frac{j\pi\varepsilon}{R}\right)$ and $\sqrt{\frac{1}{R}}$ as:

$$\left(\varepsilon - \frac{\varepsilon^2}{2R}\right) = \frac{R}{3} + \sum_{j=1}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left[\frac{j\pi}{R}\right]^2}$$

So we wrote $C(\varepsilon, \tau)$ as:

$$C(\varepsilon, \tau) = -\frac{1}{R}e^{-\tau} + \frac{1}{R} + \sum_{j=1}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left[\frac{j\pi}{R}\right]^2 + 1} e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} + \sum_{j=1}^{\infty} \frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left[\frac{j\pi}{R}\right]^2 + 1}$$

We wrote $\frac{e^\varepsilon}{1-e^{2R}} + \frac{e^{-\varepsilon}}{e^{-2R}-1}$ in the base of $\sqrt{\frac{2}{R}} \cos\left(\frac{j\pi\varepsilon}{R}\right)$ and $\sqrt{\frac{1}{R}}$ as:

$$\frac{e^\varepsilon}{1-e^{2R}} + \frac{e^{-\varepsilon}}{e^{-2R}-1} = -\frac{1}{R} - \sum_{j=1}^{\infty} \frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left[\frac{j\pi}{R}\right]^2 + 1}$$

Finally, we wrote $C(\varepsilon, \tau)$ as:

$$C(\varepsilon, \tau) = -\left(\frac{e^\varepsilon}{1-e^{2R}} + \frac{e^{-\varepsilon}}{e^{-2R}-1}\right) - \frac{e^{-\tau}}{R} + \sum_{j=1}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left[\frac{j\pi}{R}\right]^2 + 1} e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} \quad (\text{Eq. S.9.})$$

From $C(\varepsilon, \tau)$, we calculated its steady state by taking in Eq. S.9. the limit of τ to infinite:

$$C_{ss}(\varepsilon) = -\left(\frac{e^\varepsilon}{1-e^{2R}} + \frac{e^{-\varepsilon}}{e^{-2R}-1}\right) \quad (\text{Eq. S.10.})$$

This previous result can also be obtained from the original differential equation by solving for C

when $\frac{\partial C}{\partial \tau} = 0$.

1.3. Analytical solution of the 1D Reaction Diffusion model assuming a finite domain a fixed concentration and a sink boundary conditions at $\varepsilon = 0$ and $\varepsilon = R$, respectively.

Similarly, as in sections S.1.1. and S.1.2., we considered a 1D tissue of length L . Now we assumed the morphogen concentration is fixed at $x = 0$, it diffuses to the tissue tip with a diffusion constant D and degrades linearly at a rate k . We assumed that at the tip of the tissue in $x = L$ there is a sink. At $t = 0$ there is no morphogen in the tissue. The changes in the morphogen distribution C_1 in time and space are expressed mathematically as the reaction diffusion equation (Eq. S.1.):

$$\frac{\partial C_1}{\partial t} = D \frac{\partial^2 C_1}{\partial x^2} - k C_1$$

With the following conditions:

No morphogen at initial time:

$$C_1(x, t = 0) = 0$$

Fixed morphogen concentration at $x = 0$:

$$C_1(x = 0, t) = C_0$$

Where C_0 is a constant.

And sink at the tip of the tissue $x = L$:

$$C_1(x = L, t) = 0$$

We followed the same procedure that was used in sections S.1. and S.2.. We rewrote this equation

in terms of the dimensionless variables $\varepsilon = \frac{x}{\sqrt{\frac{D}{k}}}$ and $\tau = kt$. We defined the quantity R as $R = \frac{L}{\sqrt{\frac{D}{k}}}$

and we defined the concentration as $C(\varepsilon, \tau) = \frac{C_1(\varepsilon, \tau)}{C_0}$. We obtained the following equation (Eq. S.2.):

$$\frac{\partial C}{\partial t} = \frac{\partial^2 C}{\partial \varepsilon^2} - C$$

With the following conditions:

No morphogen at initial time:

$$C(\varepsilon, \tau = 0) = 0$$

Fixed morphogen at $\varepsilon = 0$:

$$C(\varepsilon = 0, \tau) = 1$$

And a sink at the tip of the tissue = R :

$$C(\varepsilon = R, \tau) = 0$$

We used an auxiliary function to solve Eq. S.2. following the same idea as in section S.1.1. In that section, we used three auxiliary functions and combined them into only one auxiliary function C_4 :

$$C(\varepsilon, \tau) = \left[C_4(\varepsilon, \tau) e^{-\tau} + \left(1 - \frac{\varepsilon}{R} \right) \right]$$

With this election Eq. S.2. is:

$$\frac{\partial C_4(\varepsilon, \tau)}{\partial \tau} = \frac{\partial^2 C_4(\varepsilon, \tau)}{\partial \varepsilon^2} + e^{\tau} \left(1 - \frac{\varepsilon}{R} \right) \quad (\text{Eq. S.11.})$$

With the following boundary conditions:

The initial condition:

$$C_4(\varepsilon, \tau = 0) = \left(\frac{\varepsilon}{R} - 1\right)$$

The source:

$$C_4(\varepsilon = 0, \tau) = 0$$

And the tip:

$$C_4(\varepsilon = R, \tau) = 0$$

We used the method presented in [1] as defined on section S.1.1. We identified the following quantities:

$$m(\tau) = 1, r(\varepsilon) = 1, q(\varepsilon) = 0, p(\varepsilon) = 1, F(\varepsilon, \tau) = e^\tau \left(\frac{\varepsilon}{R} - 1\right)$$

$$f(\varepsilon) = \left(\frac{\varepsilon}{R} - 1\right), a = 0, b = R, \alpha = 0, \beta = 1, \gamma = 1, \delta = 0$$

First, we solved the associated homogeneous problem:

$$\frac{\partial^2 v_j(\varepsilon)}{\partial \varepsilon^2} + \lambda_j v_j(\varepsilon) = 0$$

$$v_j(\varepsilon = 0) = 0$$

$$v_j(\varepsilon = R) = 0$$

The solution to this problem is:

$$v_j(\varepsilon) = \sqrt{\frac{2}{R}} \sin\left(\frac{j\pi\varepsilon}{R}\right)$$

And:

$$\sqrt{\lambda_j} = \frac{j\pi}{R}$$

We calculated f_j :

$$f_j = -\sqrt{\frac{2}{R}} \frac{1}{j\pi}$$

We calculated $F_j(t)$:

$$F_j(\tau) = -\sqrt{\frac{2}{R}} \frac{e^\tau}{j\pi}$$

The solution to Eq. S.11. is:

$$C_4(\varepsilon, \tau) = \sum_{j=0}^{\infty} \sqrt{\frac{2}{R}} \sin\left(\frac{j\pi\varepsilon}{R}\right) e^{-\left(\frac{j\pi}{R}\right)^2 \tau} \left[-\sqrt{\frac{2}{R}} \frac{1}{j\pi} + \int_0^t -\sqrt{\frac{2}{R}} \frac{e^\tau}{j\pi} e^{\left(\frac{j\pi}{R}\right)^2 \tau} d\tau \right]$$

$$C_4(\varepsilon, \tau) = \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\sin\left(\frac{j\pi\varepsilon}{R}\right)}{\frac{j\pi}{R}} e^{-\left(\frac{j\pi}{R}\right)^2 \tau} \left[1 + \frac{e^{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} - 1}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} \right] \quad (\text{Eq. S.12.})$$

We obtained the original function:

$$C(\varepsilon, \tau) = \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\sin\left(\frac{j\pi\varepsilon}{R}\right)}{\frac{j\pi}{R}} \left[e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} + \frac{1 - e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau}}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} \right] + \left(1 - \frac{\varepsilon}{R}\right)$$

$$C(\varepsilon, \tau) = \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\sin\left(\frac{j\pi\varepsilon}{R}\right)}{\frac{j\pi}{R}} \left[\frac{\left(\frac{j\pi}{R}\right)^2 e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} + 1}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} \right] + \left(1 - \frac{\varepsilon}{R}\right)$$

We wrote $\left(1 - \frac{\varepsilon}{R}\right)$ in the base of $\sqrt{\frac{2}{R}} \sin\left(\frac{j\pi\varepsilon}{R}\right)$ as:

$$\left(1 - \frac{\varepsilon}{R}\right) = \sum_{j=0}^{\infty} \frac{2}{R} \frac{\sin\left(\frac{j\pi\varepsilon}{R}\right)}{\frac{j\pi}{R}}$$

We wrote $C(\varepsilon, \tau)$ as:

$$C(\varepsilon, \tau) = \sum_{j=0}^{\infty} \frac{2}{R} \frac{\sin\left(\frac{j\pi\varepsilon}{R}\right)}{\frac{j\pi}{R}} \left[\frac{\left(\frac{j\pi}{R}\right)^2 e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} + 1}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} - 1 \right]$$

$$C(\varepsilon, \tau) = \sum_{j=0}^{\infty} \frac{2}{R} \frac{\sin\left(\frac{j\pi\varepsilon}{R}\right)}{\frac{j\pi}{R}} \left[\frac{\left(\frac{j\pi}{R}\right)^2 e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} - \left(\frac{j\pi}{R}\right)^2}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} \right]$$

We wrote $\frac{e^{\varepsilon-R} - e^{-\varepsilon+R}}{e^{-R} - e^R}$ in the base of $\sqrt{\frac{2}{R}} \sin\left(\frac{j\pi\varepsilon}{R}\right)$ as:

$$\frac{e^{\varepsilon-R} - e^{-\varepsilon+R}}{e^{-R} - e^R} = \sum_{j=0}^{\infty} \frac{2}{R} \frac{\sin\left(\frac{j\pi\varepsilon}{R}\right) \frac{j\pi}{R}}{\left[\frac{j\pi}{R}\right]^2 + 1}$$

Finally, we wrote $C(\varepsilon, \tau)$ as:

$$C(\varepsilon, \tau) = \frac{e^{\varepsilon-R} - e^{-\varepsilon+R}}{e^{-R} - e^R} + \sum_{j=0}^{\infty} \frac{2}{R} \sin\left(\frac{j\pi\varepsilon}{R}\right) \left[\frac{\frac{j\pi}{R} e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau}}{\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]} \right] \quad (\text{Eq. S.13.})$$

From $C(\varepsilon, \tau)$ we calculated its steady state by taking in Eq. S.13. the limit of τ to infinite:

$$C_{SS}(\varepsilon) = \frac{e^{\varepsilon-R} - e^{-\varepsilon+R}}{e^{-R} - e^R} \quad (\text{Eq. S.14.})$$

This previous result can also be obtained from the original differential equation by solving for C

when $\frac{\partial C}{\partial \tau} = 0$.

1.4 Analytical solution of the finite-domain model in simple 2D geometries

We considered a 2D tissue of length L_1 and L_2 where a morphogen is produced at $x = 0$, it diffuses to the tissue tip with a diffusion constant D and degrades linearly at a rate k . We assumed that at the tip of the tissue in $x = L_1$ there is a sink and we have no fluxes on $y = 0$ and $y = L_2$. At $t = 0$ the tissue has $C(x, y, t = 0) = f(x, y)$ and we solved for the particular case in which $f(x, y) = 0$. The changes in the morphogen distribution C in time and space are expressed mathematically as the reaction diffusion equation:

We have:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} + D \frac{\partial^2 C}{\partial y^2} - kC$$

With the following conditions:

At initial time:

$$C(x, y, t = 0) = f(x, y)$$

And:

$$\frac{dC}{dx}(x = 0, y, t) = -Q$$

$$C(x = L_1, y, t) = 0$$

$$\frac{dC}{dy}(x, y = 0, t) = 0$$

$$\frac{dC}{dy}(x, y = L_2, t) = 0$$

In normalized units ($\tau = kt$, $\varepsilon = \frac{x}{\sqrt{\frac{D}{k}}}$ and $\rho = \frac{y}{\sqrt{\frac{D}{k}}}$):

$$\frac{\partial C}{\partial \tau} = \frac{\partial^2 C}{\partial \varepsilon^2} + \frac{\partial^2 C}{\partial \rho^2} - C$$

With the following conditions:

At initial time:

$$C(\varepsilon, \rho, \tau = 0) = f(x, y)$$

And:

$$\frac{dC}{d\varepsilon}(\varepsilon = 0, \rho, \tau) = -1$$

$$C(\varepsilon = R_1, \rho, \tau) = 0$$

$$\frac{dC}{d\rho}(\varepsilon, \rho = 0, \tau) = 0$$

$$\frac{dC}{d\rho}(\varepsilon, \rho = R_2, \tau) = 0$$

We can write C as:

$$C(\varepsilon, \rho, \tau) = C_1(\varepsilon, \rho, \tau) + C_{ss}(\varepsilon, \rho)$$

And $C_{ss}(\varepsilon, \rho)$ is the steady state solution.

$$0 = \frac{\partial^2 C_{ss}(\varepsilon, \rho)}{\partial \varepsilon^2} + \frac{\partial^2 C_{ss}(\varepsilon, \rho)}{\partial \rho^2} - C_{ss}(\varepsilon, \rho)$$

And:

$$\frac{dC_{ss}}{d\varepsilon}(\varepsilon = 0, \rho) = -1$$

$$C_{ss}(\varepsilon = R_1, \rho) = 0$$

$$\frac{dC_{ss}}{d\rho}(\varepsilon, \rho = 0) = 0$$

$$\frac{dC_{ss}}{d\rho}(\varepsilon, \rho = R_2) = 0$$

The original equation now is:

$$\frac{\partial C_1}{\partial \tau} = \frac{\partial^2 C_1}{\partial \varepsilon^2} + \frac{\partial^2 C_1}{\partial \rho^2} - C_1$$

With the following conditions:

At initial time:

$$C(\varepsilon, \rho, \tau = 0) = f(\varepsilon, \rho)$$

$$C_1((\varepsilon, \rho, \tau = 0)) = f(\varepsilon, \rho) - C_{ss}(\varepsilon, \rho)$$

And:

$$\frac{dC}{d\varepsilon}(\varepsilon = 0, \rho, \tau) = -1$$

$$C(\varepsilon = R_1, \rho, \tau) = 0$$

$$\frac{dC}{d\rho}(\varepsilon, \rho = 0, \tau) = 0$$

$$\frac{dC}{d\rho}(\varepsilon, \rho = R_2, \tau) = 0$$

Goes to:

$$\frac{dC_1}{d\varepsilon}(\varepsilon = 0, \rho, \tau) = 0$$

$$C_1(\varepsilon = R_1, \rho, \tau) = 0$$

$$\frac{dC_1}{d\rho}(\varepsilon, \rho = 0, \tau) = 0$$

$$\frac{dC_1}{d\rho}(\varepsilon, \rho = R_2, \tau) = 0$$

We can choose:

$$C_1 = X(\varepsilon)Y(\rho)T(\tau)$$

Thus:

$$\frac{1}{T(\tau)} \frac{\partial T(\tau)}{\partial \tau} - \frac{1}{X(\varepsilon)} \frac{\partial^2 X(\varepsilon)}{\partial \varepsilon^2} - \frac{1}{Y(\rho)} \frac{\partial^2 Y(\rho)}{\partial \rho^2} = -1$$

We ask:

$$\frac{1}{T(\tau)} \frac{\partial T(\tau)}{\partial \tau} = j_t$$

$$\frac{1}{X(\varepsilon)} \frac{\partial^2 X(\varepsilon)}{\partial \varepsilon^2} = -j_x$$

$$\frac{1}{Y(\rho)} \frac{\partial^2 Y(\rho)}{\partial \rho^2} = -j_y$$

And:

$$j_t + j_x + j_y = -1$$

So:

$$T(\tau) = a_t e^{j_t \tau}$$

$$X(\varepsilon) = a_{x1} \cos(\sqrt{j_x} \varepsilon) + a_{x2} \sin(\sqrt{j_x} \varepsilon)$$

$$Y(\rho) = a_{y1} \cos(\sqrt{j_y} \rho) + a_{y2} \sin(\sqrt{j_y} \rho)$$

The boundary conditions give us:

$$X(\varepsilon) = \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j + \frac{1}{2})\pi}{R_1} \varepsilon\right)$$

And for $j_y \neq 0$:

$$Y(\rho) = \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right)$$

And for $j_y = 0$:

$$Y(\rho) = \sqrt{\frac{1}{R_2}}$$

The solution is:

$$C_1(\varepsilon, \rho, \tau) = \sum_{j,n} \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j + \frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) a_{jn} e^{\left(-1 - \left(\frac{(j + \frac{1}{2})\pi}{R_1}\right)^2 - \left(\frac{n\pi}{R_2}\right)^2\right) \tau}$$

At $\tau=0$:

$$C_1(\varepsilon, \rho, \tau = 0) = \sum_{j,n} \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j + \frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) a_{jn}$$

And we knew:

$$C_1(\varepsilon, \rho, \tau = 0) = f(\varepsilon, \rho) - C_{ss}(\varepsilon, \rho)$$

Thus, a_{jn} can be obtained by asking:

$$a_{jn} = \iint [f(\varepsilon, \rho) - C_{ss}(\varepsilon, \rho)] \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j + \frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) d\varepsilon d\rho$$

The general solution is:

$$C_1(\varepsilon, \rho, \tau) = \sum_{j,n} \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j+\frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) e^{\left(-1 - \left(\frac{(j+\frac{1}{2})\pi}{R_1}\right)^2 - \left(\frac{n\pi}{R_2}\right)^2\right)\tau}$$

$$\iint [f(\varepsilon, \rho) - C_{ss}(\varepsilon, \rho)] \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j+\frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) d\varepsilon d\rho$$

Of note, there is an abuse of notation in the previous result. For $n=0$ the prefactor is $\sqrt{\frac{1}{R_2}}$ instead of $\sqrt{\frac{2}{R_2}}$.

Finally, we need to calculate the steady state:

$$0 = \frac{\partial^2 C_{ss}(\varepsilon, \rho)}{\partial \varepsilon^2} + \frac{\partial^2 C_{ss}(\varepsilon, \rho)}{\partial \rho^2} - C_{ss}(\varepsilon, \rho)$$

And:

$$\frac{dC_{ss}(\varepsilon = 0, \rho)}{d\varepsilon} = -1$$

$$C_{ss}(\varepsilon = R_1, \rho) = 0$$

$$\frac{dC_{ss}(\varepsilon, \rho = 0)}{d\rho} = 0$$

$$\frac{dC_{ss}(\varepsilon, \rho = R_2)}{d\rho} = 0$$

We propose:

$$C_{ss}(\varepsilon, \rho) = \alpha(\varepsilon)$$

Thus, we obtain:

$$0 = \frac{\partial^2 \alpha(\varepsilon)}{\partial \varepsilon^2} - \alpha(\varepsilon)$$

And:

$$\frac{d\alpha(\varepsilon = 0)}{d\varepsilon} = -1$$

$$\alpha(\varepsilon = R_1) = 0$$

We choose:

$$\alpha(\varepsilon) = ae^\varepsilon + b e^{-\varepsilon}$$

$$\frac{d\alpha(\varepsilon = 0)}{d\varepsilon} = a - b = -1$$

$$a = -1 + b$$

$$\alpha(\varepsilon = R_1) = (-1 + b)e^{R_1} + b e^{-R_1} = 0$$

$$b(e^{R_1} + e^{-R_1}) = e^{R_1}$$

$$b = \frac{e^{R_1}}{e^{R_1} + e^{-R_1}}$$

$$a = -1 + \frac{e^{R_1}}{e^{R_1} + e^{-R_1}} = -\frac{e^{-R_1}}{e^{R_1} + e^{-R_1}}$$

So:

$$\alpha(\varepsilon) = -\frac{e^{-R_1}}{e^{R_1} + e^{-R_1}} e^\varepsilon + \frac{e^{R_1}}{e^{R_1} + e^{-R_1}} e^{-\varepsilon}$$

$$\alpha(\varepsilon) = \frac{-e^{\varepsilon-R_1} + e^{R_1-\varepsilon}}{e^{R_1} + e^{-R_1}} = \frac{\sinh(R_1 - \varepsilon)}{\cosh(R_1)}$$

So:

$$C_{ss}(\varepsilon, \rho) = \frac{\sinh(R_1 - \varepsilon)}{\cosh(R_1)}$$

Thus, the original solution is:

$$C(\varepsilon, \rho, \tau) = C_1(\varepsilon, \rho, \tau) + C_{ss}(\varepsilon, \rho)$$

With:

$$C_1(\varepsilon, \rho, \tau) = \sum_{j,n} \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j+\frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) e^{\left(-1 - \left(\frac{(j+\frac{1}{2})\pi}{R_1}\right)^2 - \left(\frac{n\pi}{R_2}\right)^2\right)\tau} \iint \left[f(\varepsilon, \rho) - \frac{\sinh(R_1 - \varepsilon)}{\cosh(R_1)} \right] \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j+\frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) d\varepsilon d\rho$$

For $f(\varepsilon, \rho) = 0$:

$$\iint \left[-\frac{\sinh(R_1 - \varepsilon)}{\cosh(R_1)} \right] \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j+\frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) d\varepsilon d\rho$$

As $f(\varepsilon, \rho) = \frac{\sinh(R_1 - \varepsilon)}{\cosh(R_1)}$ does not depend on ρ , the integral on ρ is 0 except for $n=0$, therefore:

$$\begin{aligned} & \iint \left[-\frac{\sinh(R_1 - \varepsilon)}{\cosh(R_1)} \right] \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j + \frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) d\varepsilon d\rho = \\ & \sqrt{R_2} \int_0^{R_1} \left[-\frac{\sinh(R_1 - \varepsilon)}{\cosh(R_1)} \right] \sqrt{\frac{2}{R_1}} \cos\left(\frac{(j + \frac{1}{2})\pi}{R_1} \varepsilon\right) d\varepsilon = \\ & -\sqrt{\frac{2}{R_1}} \frac{\sqrt{R_2}}{\left(\frac{(j + \frac{1}{2})\pi}{R_1}\right)^2 + 1} \end{aligned}$$

Hence:

$$C_1(\varepsilon, \rho, \tau) = \sum_{j,n} -\sqrt{\frac{2}{R_1}} \cos\left(\frac{(j + \frac{1}{2})\pi}{R_1} \varepsilon\right) \sqrt{\frac{1}{R_2}} e^{\left(-1 - \left(\frac{(j + \frac{1}{2})\pi}{R_1}\right)^2\right)\tau} \sqrt{\frac{2}{R_1}} \frac{\sqrt{R_2}}{\left(\frac{(j + \frac{1}{2})\pi}{R_1}\right)^2 + 1}$$

Thus, we obtain:

$$C(\varepsilon, \rho, \tau) = \frac{\sinh(R_1 - \varepsilon)}{\cosh(R_1)} + \sum_{j,n} -\frac{2}{R_1} \frac{\cos\left(\frac{(j + \frac{1}{2})\pi}{R_1} \varepsilon\right)}{\left(\frac{(j + \frac{1}{2})\pi}{R_1}\right)^2 + 1} e^{\left(-1 - \left(\frac{(j + \frac{1}{2})\pi}{R_1}\right)^2\right)\tau} \quad (\text{Eq. S.15.})$$

Next, we considered a 2D tissue of length L_1 and L_2 where a morphogen is produced at $x = 0$ and $y = 0$, it diffuses towards the tissue tip with a diffusion constant D and linearly degrades at a rate k . We assumed that at the tip of the tissue in $x = L_1$ and $y = L_2$ we have no fluxes going out of the tissue. At $t = 0$ the tissue has $C(x, y, t = 0) = f(x, y)$ and we solved for the particular case in which $f(x, y) = 0$. The changes in the morphogen distribution C_1 in time and space are expressed mathematically as the reaction diffusion equation:

We have:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} + D \frac{\partial^2 C}{\partial y^2} - kC$$

With the following conditions:

At initial time:

$$C(x, y, t = 0) = f(x, y)$$

And:

$$\frac{dC}{dx}(x = 0, y, t) = -Q$$

$$\frac{dC}{dx}(x = L_1, y, t) = 0$$

$$\frac{dC}{dy}(x, y = 0, t) = -Q$$

$$\frac{dC}{dy}(x, y = L_2, t) = 0$$

We followed the same procedure as in the previous example and we obtained (in normalized units ε , ρ and τ):

$$C_1(\varepsilon, \rho, \tau) = \sum_{j,n} \sqrt{\frac{2}{R_1}} \cos\left(\frac{j\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) a_{jn} e^{\left(-1 - \left(\frac{j\pi}{R_1}\right)^2 - \left(\frac{n\pi}{R_2}\right)^2\right)\tau} \iint [f(\varepsilon, \rho) - C_{ss}(\varepsilon, \rho)] \sqrt{\frac{2}{R_1}} \cos\left(\frac{j\pi}{R_1} \varepsilon\right) \sqrt{\frac{2}{R_2}} \cos\left(\frac{n\pi}{R_2} \rho\right) d\varepsilon d\rho$$

Here there is an abuse of notation. For $j=0$ the prefactor is $\sqrt{\frac{1}{R_1}}$ instead of $\sqrt{\frac{2}{R_1}}$ and for $n=0$ the prefactor is $\sqrt{\frac{1}{R_2}}$ instead of $\sqrt{\frac{2}{R_2}}$.

For the steady state we obtained:

$$C_{ss}(\varepsilon, \rho) = \frac{\cosh(R_1 - \varepsilon)}{\sinh(R_1)} + \frac{\cosh(R_2 - \rho)}{\sinh(R_2)}$$

And for $f(\varepsilon, \rho) = 0$ we calculated the integrals and finally obtained:

$$C(\varepsilon, \rho, \tau) = \frac{\cosh(R_1 - \varepsilon)}{\sinh(R_1)} - \frac{e^{-\tau}}{R_1} - \sum_{j=1} \frac{2}{R_1} \frac{\cos\left(\frac{j\pi}{R_1} \varepsilon\right)}{\left(\frac{j\pi}{R_1}\right)^2 + 1} e^{\left(-1 - \left(\frac{j\pi}{R_1}\right)^2\right)\tau} + \frac{\cosh(R_2 - \rho)}{\sinh(R_2)} - \frac{e^{-\tau}}{R_2} - \sum_{n=1} \frac{2}{R_2} \frac{\cos\left(\frac{n\pi}{R_2} \rho\right)}{\left(\frac{n\pi}{R_2}\right)^2 + 1} e^{\left(-1 - \left(\frac{n\pi}{R_2}\right)^2\right)\tau}$$

(Eq. S.16.)

2. Comparison between analytical and numerical solutions of the 1D Reaction Diffusion model assuming a finite domain.

We tested the analytical solutions in 1D for the finite model with a sink and with no flux at $\varepsilon = 0$ by a numerical integration of Eq. S.6. for different values of R (see Fig. S1). We used a finite differences scheme by using Euler method with a fixed spatial step of $\Delta x = \frac{R}{100}$ and a time step of $\Delta t = \frac{\Delta x^2}{3}$, which guaranties the numerical stability of the method. Furthermore, we numerically tested the analytical solutions in 2D (see Fig. S2).

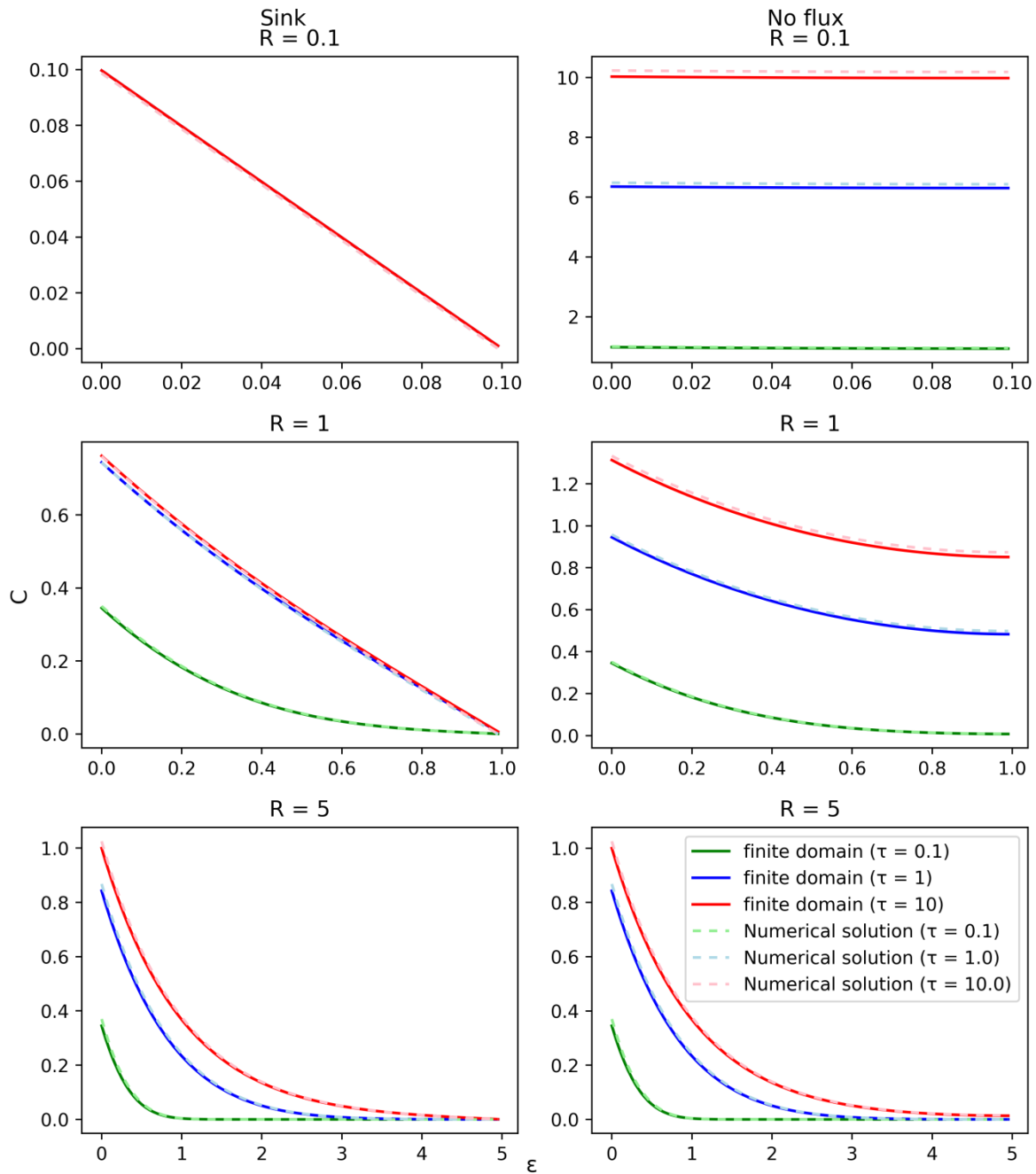


Figure S1. Comparison between the numerical and analytical solution for the concentration as a function of the spatial position in 1D for different times. A), C) and E) show the morphogen distribution for the model with a sink at $\varepsilon = R$ for R equal to 0.1, 1 and 5, respectively. B), D) and F) show the morphogen distribution for the model with no flux at $\varepsilon = R$ for R equal to 0.1, 1 and 5, respectively. The straight lines in these panels are the analytical solutions at time equal to 0.1, 1 and 10. The dotted lines are the numerical solution at those times.

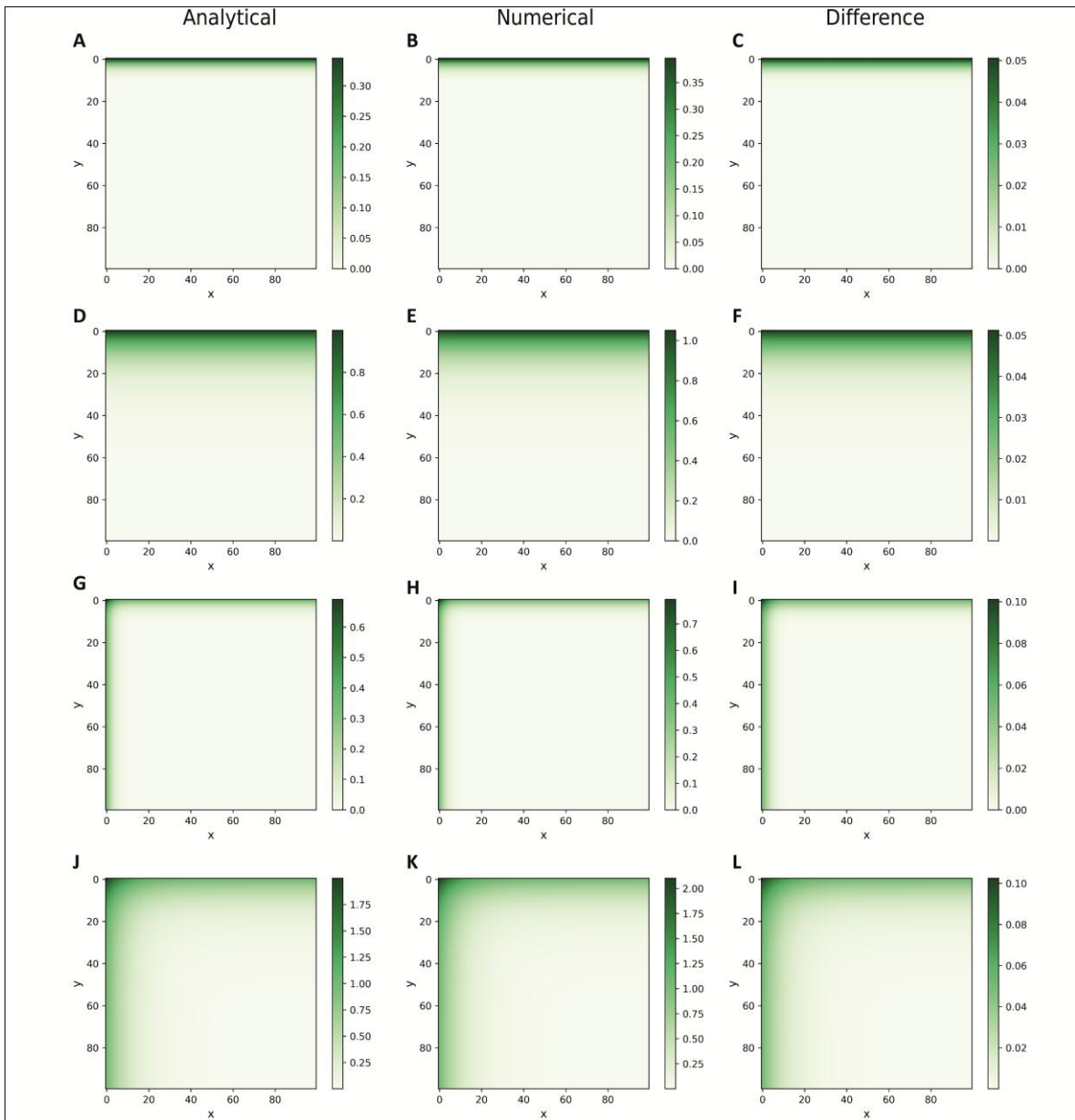


Figure S2. Comparison between the numerical and analytical solution for the concentration as a function of the spatial position in 2D for different times. A) to F) show the morphogen distribution for the 2D model with one source, one sink and two no fluxes. A) and D) are the analytical solution at time 0.1 and 10, respectively. B) and E) show the numerical solution at time 0.1 and 10, respectively. C) and F) show the absolute value of the difference between the analytical and the numerical solutions at time 0.1 and 10, respectively. G) to L) show the morphogen distribution for the 2D model with two sources and two no fluxes. G) and J) show the analytical solution at time 0.1 and 10, respectively. H) and K) show the numerical solution at time 0.1 and 10, respectively. I) and L) show the absolute value of the difference between the analytical and the numerical solutions at time 0.1 and 10, respectively.

3. Steady state of the 1D Reaction Diffusion model assuming a finite domain.

We already calculated in Eq. S.6., that the morphogen concentration depends on ε and τ for the model assuming a finite domain with a sink at $\varepsilon = R$ as follows:

$$C(\varepsilon, \tau) = \left(\frac{e^{-\varepsilon}}{1 + e^{-2R}} - \frac{e^{\varepsilon}}{1 + e^{2R}} \right) + \sum_{j=0}^{\infty} -\frac{2}{R} \frac{\cos\left(\frac{(j + \frac{1}{2})\pi\varepsilon}{R}\right)}{\left(\frac{(j + \frac{1}{2})\pi}{R}\right)^2 + 1} e^{-\left[\left(\frac{(j + \frac{1}{2})\pi}{R}\right)^2 + 1\right]\tau}$$

From $C(\varepsilon, \tau)$ we calculated its steady state by taking in Eq. S.6. the limit of τ to infinite:

$$C_{ss}(\varepsilon) = \left(\frac{e^{-\varepsilon}}{1 + e^{-2R}} - \frac{e^{\varepsilon}}{1 + e^{2R}} \right) \quad (\text{Eq. S.}$$

16.)

Following the same procedure for the no flux boundary condition at $\varepsilon = R$ be obtain:

$$C_{ss}(\varepsilon) = -\left(\frac{e^{\varepsilon}}{1 - e^{2R}} + \frac{e^{-\varepsilon}}{e^{-2R} - 1} \right)$$

We calculated the total amount of morphogen in the tissue $N_{ss}(\varepsilon)$:

$$N_{ss}(\varepsilon) = \int_0^R C_{ss}^{finite}(\varepsilon) d\varepsilon$$

To achieve that it is useful to integrate directly from the differential equation:

$$\frac{d^2 C}{d\varepsilon^2} - C = 0$$

$$\int_0^R \frac{d^2 C_{ss}^{finite}(\varepsilon)}{d\varepsilon^2} d\varepsilon - \int_0^R C_{ss}^{finite}(\varepsilon) d\varepsilon = 0$$

$$\frac{dC_{ss}^{finite}(\varepsilon = R)}{d\varepsilon} - \frac{dC_{ss}^{finite}(\varepsilon = 0)}{d\varepsilon} - N_{ss}(\varepsilon) = 0$$

$$N_{ss}(\varepsilon) = 1 \quad (\text{Eq. S.17.})$$

To continue our analysis, we expanded using Laurent series $C_{ss}^{finite}(\varepsilon)$ for R in $R=0$:

$$C_{ss}^{finite}(\varepsilon) = \frac{\cosh(\varepsilon)}{R} - \sinh(\varepsilon) + \frac{1}{3}R\cosh(\varepsilon) + O(R^3)$$

If we look for small values of R , we can see that we also have small values of ε . In this case:

$$\sinh(\varepsilon) \sim 0$$

$$\cosh(\varepsilon) \sim 1$$

Thus, we obtain:

$$C_{ss}^{finite}(\varepsilon) \sim \frac{1}{R} \quad (\text{Eq. S.18.})$$

4. ε_{10} calculation.

We defined ε_{10} as the position in space in which the concentration is 10 % of the concentration at the source. We calculated this value analytically for the steady state. For an infinite domain, the steady state is:

$$C_{ss}(\varepsilon) = e^{-\varepsilon} \quad (\text{Eq. S.19.})$$

We found ε_{10} by solving the following equation:

$$C_{ss}(\varepsilon_{10}) = \frac{C_{ss}(0)}{10}$$

$$e^{-\varepsilon_{10}} = \frac{1}{10}$$

$$\varepsilon_{10} = \ln(10) \sim 2.3 \quad (\text{Eq. S.20.})$$

Where $\ln(x)$ is the natural logarithm of x .

We also calculated ε_{10} analytically for the steady state in a finite domain with a sink at $\varepsilon = R$.

First, we rewrote the steady state (Eq. S.16.) as:

$$C_{ss}(\varepsilon) = \left(\frac{e^{-\varepsilon}}{1 + e^{-2R}} - \frac{e^{\varepsilon}}{1 + e^{2R}} \right) = \frac{\sinh(R - \varepsilon)}{\cosh(R)}$$

Where $\sinh(\varepsilon)$ and $\cosh(\varepsilon)$ are the hyperbolic sine and hyperbolic cosine of ε , respectively.

We found ε_{10} by solving the following equation:

$$C_{ss}(\varepsilon_{10}) = \frac{C_{ss}(0)}{10}$$

$$\frac{\sinh(R - \varepsilon_{10})}{\cosh(R)} = \frac{1}{10} \frac{\sinh(R)}{\cosh(R)}$$

$$\varepsilon_{10} = R - \operatorname{arcsinh}\left(\frac{\sinh(R)}{10}\right) \quad (\text{Eq. S.21.})$$

In the limit of R going to infinity in the previous equation, we obtained:

$$\lim_{R \rightarrow \infty} \varepsilon_{10} = \lim_{R \rightarrow \infty} \left[R - \operatorname{arcsinh}\left(\frac{\sinh(R)}{10}\right) \right] = \ln(10) \sim 2.3$$

This is in agreement with the solution obtained before.

We followed the same procedure with the model assuming a finite domain with no flux at $\varepsilon = R$ and obtained:

$$\varepsilon_{10} = R - \operatorname{arccosh}\left(\frac{\cosh(R)}{10}\right) \quad (\text{Eq. S.22.})$$

5. R_c calculation.

From ε_{10} in the steady state of the model assuming a finite domain with a sink at $\varepsilon = R$ as a function of R (Eq. S. 21.) we identified two regimes: while for large values of R , ε_{10} reaches a plateau, for small values of R , ε_{10} has a line-like behavior. To characterize the transition between both regimes, we Taylor-expanded ε_{10} and arbitrarily looked for the $R = R_c$ upon which the second non-zero term of the series would be about 20 % of the first linear term. First, we calculated the Taylor series of ε_{10} around $R = 0$:

$$\varepsilon_{10}(R) = \varepsilon_{10}(0) + \frac{d\varepsilon_{10}(0)}{dR}R + \frac{d^2\varepsilon_{10}(0)}{dR^2}\frac{R^2}{2} + \frac{d^3\varepsilon_{10}(0)}{dR^3}\frac{R^3}{6} + O(R^4)$$

Where the coefficients are:

$$\varepsilon_{10}(0) = 0, \frac{d\varepsilon_{10}(0)}{dR} = 0.9, \frac{d^2\varepsilon_{10}(0)}{dR^2} = 0, \frac{d^3\varepsilon_{10}(0)}{dR^3} = -0.099$$

We looked for a R_{crit} value such that $\frac{d\varepsilon_{10}(0)}{dR}R_{crit}$ is not much bigger in module than the first non-vanishing term of higher order than R . We arbitrarily defined “not much bigger” in this context as one term being one fifth of the other. This means:

$$\frac{1}{5} \left| \frac{d\varepsilon_{10}(0)}{dR} \right| R_c = \left| \frac{d^3\varepsilon_{10}(0)}{dR^3} \right| \frac{R_c^3}{6}$$

$$R_c = \sqrt{\frac{6 \left| \frac{d\varepsilon_{10}(0)}{dR} \right|}{5 \left| \frac{d^3\varepsilon_{10}(0)}{dR^3} \right|}} = \sqrt{\frac{6*0.9}{5*0.099}} \approx 3.3 \quad (\text{Eq. S.23.})$$

With the finite model with a no flux boundary condition at $\varepsilon = R$ we followed the same procedure but we expanded Eq. S.22 around $R = 3$:

$$\varepsilon_{10}(R) = \varepsilon_{10}(3) + \frac{d\varepsilon_{10}(3)}{dR}(R - 3) + \frac{d^2\varepsilon_{10}(3)}{dR^2}\frac{(R - 3)^2}{2} + O((R - 3)^3)$$

Where the coefficients are:

$$\varepsilon_{10}(0) = 2.88, \frac{d\varepsilon_{10}(0)}{dR} = -7.6, \frac{d^2\varepsilon_{10}(0)}{dR^2} = 629.9$$

So:

$$\frac{1}{5} \left| \varepsilon_{10}(3) + \frac{d\varepsilon_{10}(3)}{dR} (R_c - 3) \right| = \left| \frac{d^2\varepsilon_{10}(3)}{dR^2} \right| \frac{(R_c - 3)^2}{2}$$

$$R_c \approx 3.04$$

6. $\mu_\tau(\epsilon)$ and $\sigma_\tau(\epsilon)$ calculation.

Berezhkovskii *et al.* have developed a method to estimate the mean time it takes a morphogen to reach its steady state [2].

They defined the local relaxation function $\alpha(x, t)$ as:

$$\alpha(x, t) = 1 - \frac{C(x, t)}{C_{ss}(x)}$$

Where $C(x, t)$ is the concentration of morphogen at the position x at time t and $C_{ss}(x)$ is the concentration of the morphogen at its steady state at position x . It is important to note that in the above mentioned article $\alpha(x, t)$ is defined as $R(x, t)$.

From the relaxation function, they obtained the probability density:

$$\varphi(t|x) = -\frac{\partial \alpha(x, t)}{\partial t}$$

From the probability density, they obtained the mean time it takes it to establish a morphogen gradient as:

$$\tau(x) = \int_0^\infty t \varphi(t|x) dt = \int_0^\infty \alpha(x, t) dt$$

We used this definition to estimate how long it takes to establish a morphogen gradient in a finite tissue with a sink at $\epsilon = R$ by using the analytic solution presented in this work (Eq. S.6.).

$$\alpha(\epsilon, t) = \sum_{j=0}^{\infty} \frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\epsilon}{R}\right)}{\left(\frac{(j+\frac{1}{2})\pi}{R}\right)^2 + 1} \frac{e^{-\left[\left(\frac{(j+\frac{1}{2})\pi}{R}\right)^2 + 1\right]t}}{\left(\frac{e^{-\epsilon}}{1+e^{-2R}} - \frac{e^\epsilon}{1+e^{2R}}\right)}$$

With the model assuming a finite domain with no flux at $\varepsilon = R$:

$$\alpha(\varepsilon, t) = \frac{1}{-\left(\frac{e^\varepsilon}{1-e^{2R}} + \frac{e^{-\varepsilon}}{e^{-2R}-1}\right)} \left[\frac{e^{-\tau}}{R} + \sum_{j=1}^{\infty} \frac{2 \cos\left(\frac{j\pi\varepsilon}{R}\right)}{R \left(\left(\frac{j\pi}{R}\right)^2 + 1\right)} e^{-\left[\left(\frac{j\pi}{R}\right)^2 + 1\right]\tau} \right]$$

The mean time of the model assuming a finite domain with a sink at $\varepsilon = R$ is:

$$\mu_\tau(\varepsilon) = \sum_{j=0}^{\infty} \frac{2}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\varepsilon}{R}\right)}{\left[\left(\frac{(j+\frac{1}{2})\pi}{R}\right)^2 + 1\right]^2} \frac{1}{\left(\frac{e^{-\varepsilon}}{1+e^{-2R}} - \frac{e^\varepsilon}{1+e^{2R}}\right)} \quad (\text{Eq. S.24.})$$

And for the model assuming a finite domain with no flux at $\varepsilon = R$:

$$\mu_\tau(\varepsilon) = \frac{1}{-\left(\frac{e^\varepsilon}{1-e^{2R}} + \frac{e^{-\varepsilon}}{e^{-2R}-1}\right)} \left[\frac{1}{R} + \sum_{j=1}^{\infty} \frac{2}{R} \frac{\cos\left(\frac{j\pi\varepsilon}{R}\right)}{\left(\left(\frac{j\pi}{R}\right)^2 + 1\right)^2} \right] \quad (\text{Eq. S. 25.})$$

It is important to know how good this estimate obtained previously is. To achieve that, we calculated the standard deviation:

$$\sigma_\tau(\varepsilon) = \sqrt{E[\tau^2] - \mu_\tau(\varepsilon)^2}$$

Where $E[\tau^2]$ is defined as:

$$E[\tau^2] = \int_0^{\infty} t^2 \varphi(t|x) dt = 2t \int \alpha(x, t) dt \Big|_{t=0}^{\infty} - 2 \int_0^{\infty} \left(\int \alpha(x, t) dt \right) dt$$

For the model assuming a finite domain with a sink at $\varepsilon = R$, we obtained:

$$E[\epsilon\tau^2] = \sum_{j=0}^{\infty} \frac{4}{R} \frac{\cos\left(\frac{(j+\frac{1}{2})\pi\epsilon}{R}\right)}{\left[\left(\frac{(j+\frac{1}{2})\pi}{R}\right)^2 + 1\right]^3} \frac{1}{\left(\frac{e^{-\epsilon}}{1+e^{-2R}} - \frac{e^{\epsilon}}{1+e^{2R}}\right)}$$

And for of the model assuming a finite domain with no flux at $\epsilon = R$, we obtained:

$$E[\tau^2] = \frac{2}{-\left(\frac{e^{\epsilon}}{1-e^{2R}} + \frac{e^{-\epsilon}}{e^{-2R}-1}\right)} \left[\frac{1}{R} + \sum_{j=1}^{\infty} \frac{2}{R} \frac{\cos\left(\frac{j\pi\epsilon}{R}\right)}{\left(\frac{j\pi}{R}\right)^2 + 1} \right]$$

And for the infinite domain, we obtained:

$$\sigma(\epsilon) = \frac{\sqrt{\epsilon+2}}{2} \tag{Eq. S.26.}$$

7. Finite *versus* infinite domains in the reaction-diffusion model used in the FRAP-based determination of diffusion parameters

We considered a 1D tissue of length L where a morphogen is produced at $x = 0$, it diffuses to the tissue tip with a diffusion constant D and degrades linearly at a rate k . We assumed that at the tip of the tissue in $x = L$ there is a sink or a no flux. At $t = 0$ the tissue is at steady state except between $x = d$ and $x = d + h$ where it is bleached and it has b times the concentration at steady state. The changes in the morphogen distribution C_1 in time and space are expressed mathematically as the reaction diffusion equation:

$$\frac{\partial C_1}{\partial t} = D \frac{\partial^2 C_1}{\partial x^2} - kC_1 \quad (\text{Eq. S.27.})$$

With the following conditions:

Morphogen at initial time:

Initial time for x between d and $d+h$:

$$C_1(x, t = 0) = bC_{ss}(x)$$

Initial time for x elsewhere:

$$C_1(x, t = 0) = C_{ss}(x)$$

Or:

$$C_1(x, t = 0) = C_{ss}(x) + (b - 1)C_{ss}(x)\theta(x - d)\theta(-x + d)$$

Morphogen production at $x = 0$:

$$\frac{dC_1}{dx}(x = 0, t) = -\frac{q}{D}$$

Where q is the morphogen production rate at $x = 0$.

And a sink at the tip of the tissue $x = L$:

$$C_1(x = L, t) = 0$$

Or a no flux boundary condition at $x = L$:

$$\frac{dC_1}{dx}(x = L, t) = 0$$

We rewrote Eq. S.27. in terms of the dimensionless variables $\varepsilon = \frac{x}{\sqrt{\frac{D}{k}}}$ and $\tau = kt$. We defined the

quantities R and S as $R = \frac{L}{\sqrt{\frac{D}{k}}}$ and $S = \frac{q}{\sqrt{Dk}}$ and we rewrote the concentration as $(\varepsilon, \tau) = \frac{C_1(\varepsilon, \tau)}{S}$:

$$\frac{\partial C}{\partial \tau} = \frac{\partial^2 C}{\partial \varepsilon^2} - C$$

With the following conditions. No morphogen at initial time:

$$C_1(\varepsilon, t = 0) = C_{ss}(\varepsilon) + (b - 1)C_{ss}(\varepsilon)\theta\left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}}\right)\theta\left(-\varepsilon + \frac{d + h}{\sqrt{\frac{D}{k}}}\right)$$

Morphogen production at $\tau = 0$:

$$\frac{dC}{d\varepsilon}(\varepsilon = 0, \tau) = -1$$

And a sink at the tip of the tissue $\varepsilon = R$:

$$C(\varepsilon = R, \tau) = 0$$

Or a no flux at $\varepsilon = R$:

$$\frac{dC}{d\varepsilon}(\varepsilon = R, \tau) = 0$$

We calculated $C_{ss}(x)$ for the model assuming a finite domain with a sink at $\varepsilon = R$:

$$C_{ss}(x) = \frac{\sinh(R - \varepsilon)}{\cosh(R)}$$

For the model assuming a finite domain with no flux at $\varepsilon = R$:

$$C_{ss}(x) = \frac{\cosh(R - \varepsilon)}{\sinh(R)}$$

To solve this equation we redefined C in terms of an auxiliary function C_2 defined as:

$$C = C_2 e^{-\tau}$$

We calculated the derivatives of C_2 in terms of the derivatives of C . The second spatial derivative

is:

$$\frac{\partial^2 C}{\partial \varepsilon^2} = e^{-\tau} \frac{\partial^2 C_2}{\partial \varepsilon^2}$$

And the time derivative is:

$$\frac{\partial C}{\partial \tau} = e^{-\tau} \frac{\partial C_2}{\partial \tau} - C_2 e^{-\tau}$$

This leads to the following equation:

$$\frac{\partial C_2}{\partial \tau} = \frac{\partial^2 C_2}{\partial \varepsilon^2}$$

With the following boundary conditions:

$$C_2(\varepsilon, \tau = 0) = C_{ss}(\varepsilon) + (b - 1)C_{ss}(\varepsilon) \theta \left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}} \right) \theta \left(-\varepsilon + \frac{d + h}{\sqrt{\frac{D}{k}}} \right)$$

$$\frac{\partial C_2(\varepsilon = 0, \tau)}{\partial \varepsilon} = -e^\tau$$

$$C_2(\varepsilon = R, \tau) = 0$$

Or a no flux:

$$\frac{dC_2}{d\varepsilon}(\varepsilon = R, \tau) = 0$$

We redefined C_2 using the auxiliary functions $C_3(\varepsilon, \tau)$, $f(\tau)$ and $g(\varepsilon)$. The explicit definition of the auxiliary functions $g(\varepsilon)$ and $f(\tau)$ will be defined later.

$$C_2(\varepsilon, \tau) = C_3(\varepsilon, \tau) + g(\varepsilon)f(\tau)$$

The derivative with respect to τ is:

$$\frac{\partial C_2(\varepsilon, \tau)}{\partial \tau} = \frac{\partial C_3(\varepsilon, \tau)}{\partial \tau} + g(\varepsilon) \frac{\partial f(\tau)}{\partial \tau}$$

And derivative with respect to ε is:

$$\frac{\partial^2 C_2(\varepsilon, \tau)}{\partial \varepsilon^2} = \frac{\partial^2 C_3(\varepsilon, \tau)}{\partial \varepsilon^2} + \frac{\partial^2 g(\varepsilon)}{\partial \varepsilon^2} f(\tau)$$

We rewrote the reaction diffusion equation in C_3 as:

$$\frac{\partial C_3(\varepsilon, \tau)}{\partial \tau} = \frac{\partial^2 C_3(\varepsilon, \tau)}{\partial \varepsilon^2} + \frac{\partial^2 g(\varepsilon)}{\partial \varepsilon^2} f(\tau) - g(\varepsilon) \frac{\partial f(\tau)}{\partial \tau}$$

The initial condition:

$$C_3(\varepsilon, \tau = 0) = C_{ss}(\varepsilon) + (b - 1)C_{ss}(\varepsilon) \theta \left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}} \right) \theta \left(-\varepsilon + \frac{d+h}{\sqrt{\frac{D}{k}}} \right) - g(\varepsilon)f(\tau = 0)$$

With the following boundary conditions:

The source:

$$\frac{\partial C_3(\varepsilon = 0, \tau)}{\partial \varepsilon} = -e^\tau - \frac{\partial g(\varepsilon = 0)}{\partial \varepsilon} f(\tau)$$

And the sink:

$$C_3(\varepsilon = R, \tau) = -g(\varepsilon = R)f(\tau)$$

Or no flux:

$$\frac{\partial C_3(\varepsilon = R, \tau)}{\partial \varepsilon} = -\frac{\partial g(\varepsilon = R)}{\partial \varepsilon}f(\tau)$$

It is desirable that the initial condition is different from 0 and the boundary conditions are equal to

0. We defined $f(\tau)$ and $g(\varepsilon)$ as:

For the model assuming a finite domain with a sink at $\varepsilon = R$:

$$f(\tau) = -e^\tau, g(\varepsilon) = \varepsilon - R$$

For the model assuming a finite domain with no flux at $\varepsilon = R$:

$$f(\tau) = -e^\tau, g(\varepsilon) = \left(\varepsilon - \frac{\varepsilon^2}{2R}\right)$$

With this choice:

For the model assuming a finite domain with a sink at $\varepsilon = R$:

$$\frac{\partial C_3(\varepsilon, \tau)}{\partial \tau} = \frac{\partial^2 C_3(\varepsilon, \tau)}{\partial \varepsilon^2} + (\varepsilon - R)$$

For the model assuming a finite domain with no flux at $\varepsilon = R$:

$$\frac{\partial C_3(\varepsilon, \tau)}{\partial \tau} = \frac{\partial^2 C_3(\varepsilon, \tau)}{\partial \varepsilon^2} + \frac{e^\tau}{R} + \left(\varepsilon - \frac{\varepsilon^2}{2R}\right)e^\tau$$

With the following boundary conditions:

The initial condition:

For the model assuming a finite domain with a sink at $\varepsilon = R$:

$$C_3(\varepsilon, \tau = 0) = C_{ss}(\varepsilon) + (b - 1)C_{ss}(\varepsilon)\theta\left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}}\right)\theta\left(-\varepsilon + \frac{d+h}{\sqrt{\frac{D}{k}}}\right) + (\varepsilon - R)$$

For the model assuming a finite domain with no flux at $\varepsilon = R$:

$$C_3(\varepsilon, \tau = 0) = C_{ss}(\varepsilon) + (b - 1)C_{ss}(\varepsilon)\theta\left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}}\right)\theta\left(-\varepsilon + \frac{d+h}{\sqrt{\frac{D}{k}}}\right) + \left(\varepsilon - \frac{\varepsilon^2}{2R}\right)$$

The source:

$$\frac{\partial C_3(\varepsilon = 0, \tau)}{\partial \varepsilon} = 0$$

And the sink:

$$C_3(\varepsilon = R, \tau) = 0$$

Or no flux:

The source:

$$\frac{\partial C_3(\varepsilon = R, \tau)}{\partial \varepsilon} = 0$$

The solution to systems of this type can be found in [1]. In this reference, the authors defined a method to find the solution for systems with the following aspect:

$$r(x)m(t)\frac{\partial u(x,t)}{\partial t} - \left[\frac{\partial \left(p(x)\frac{\partial u(x,t)}{\partial x} \right)}{\partial x} + q(x)u(x,t) \right] = F(x,t)$$

$$\alpha u(x = a, t) + \beta \frac{\partial u(x = a, t)}{\partial x} = 0$$

$$\gamma u(x = b, t) + \delta \frac{\partial u(x = b, t)}{\partial x} = 0$$

$$u(x, t = 0) = f(x)$$

Where $u(x, t)$, $r(x)$, $m(t)$, $p(x)$, $q(x)$, $F(x, t)$ and $f(x)$ are functions and a , b , α , β , γ and δ are constants.

They defined the following quantities:

$$f_j = \int_a^b f(x) v_j(x) r(x) dx$$

$$F_j(t) = \int_a^b F(x, t) v_j(x) dx$$

Where $v_j(x)$ and λ_j are obtained from the solution of the following problem:

$$\frac{\partial \left(p(x) \frac{\partial v_j(x)}{\partial x} \right)}{\partial x} + q(x) v_j(x) + \lambda_j v_j(x) = 0$$

With the conditions:

$$\alpha v(x = a, t) + \beta \frac{\partial v(x = a, t)}{\partial x} = 0$$

$$\gamma v(x = b, t) + \delta \frac{\partial v(x = b, t)}{\partial x} = 0$$

The solution to the problem is:

$$u(x, t) = \sum_{j=0}^{\infty} f_j v_j(x) e^{-\lambda_j \int_0^t \frac{1}{m(s)} ds} + \sum_{j=0}^{\infty} v_j(x) e^{-\lambda_j \int_0^t \frac{1}{m(s)} ds} \int_0^t \frac{F_j(s)}{m(s)} e^{\lambda_j \int_0^s \frac{1}{m(w)} dw} ds$$

In our problem, $u(\varepsilon, \tau) = C_3(\varepsilon, \tau)$ and we identified the following quantities:

For the model assuming a finite domain with a sink at $\varepsilon = R$:

$$m(\tau) = 1, r(\varepsilon) = 1, q(\varepsilon) = 0, p(\varepsilon) = 1, F(\varepsilon, \tau) = (\varepsilon - R)e^\tau$$

$$f(\varepsilon) = C_{ss}(\varepsilon) + (b - 1)C_{ss}(\varepsilon)\theta\left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}}\right)\theta\left(-\varepsilon + \frac{d+h}{\sqrt{\frac{D}{k}}}\right) + (\varepsilon - R), a = 0, b = R, \alpha = 0, \beta = 1,$$

$$\gamma = 1, \delta = 0$$

For the model assuming a finite domain with no flux at $\varepsilon = R$:

$$m(\tau) = 1, r(\varepsilon) = 1, q(\varepsilon) = 0, p(\varepsilon) = 1, F(\varepsilon, \tau) = \frac{e^\tau}{R} + \left(\varepsilon - \frac{\varepsilon^2}{2R}\right)e^\tau$$

$$f(\varepsilon) = C_{ss}(\varepsilon) + (b - 1)C_{ss}(\varepsilon)\theta\left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}}\right)\theta\left(-\varepsilon + \frac{d+h}{\sqrt{\frac{D}{k}}}\right) + \left(\varepsilon - \frac{\varepsilon^2}{2R}\right), a = 0, b = R, \alpha = 0, \beta =$$

$$1, \gamma = 0, \delta = 1$$

First we solved the associated homogeneous problem:

$$\frac{\partial^2 v_j(\varepsilon)}{\partial \varepsilon^2} + \lambda_j v_j(\varepsilon) = 0$$

$$\frac{\partial v_j(\varepsilon = 0)}{\partial \varepsilon} = 0$$

$$v_j(\varepsilon = R) = 0$$

Here λ_j is the eigenvalue associated to $v_j(\varepsilon)$, it should not be confused with the characteristic length of the morphogen λ .

The solution to this problem is:

For the model assuming a finite domain with a sink at $\varepsilon = R$:

$$v_j(\varepsilon) = \sqrt{\frac{2}{R}} \cos\left(\frac{\left(j + \frac{1}{2}\right)\pi\varepsilon}{R}\right)$$

And:

$$\sqrt{\lambda_j} = \frac{\left(j + \frac{1}{2}\right)\pi}{R}$$

For the model assuming a finite domain with no flux at $\varepsilon = R$:

$$v_j(\varepsilon) = \sqrt{\frac{2}{R}} \cos\left(\frac{j\pi\varepsilon}{R}\right)$$

And:

$$\sqrt{\lambda_j} = \frac{j\pi}{R}$$

Or if $j=0$:

$$v_j(\varepsilon) = \sqrt{\frac{1}{R}}$$

It is important to notice that since $v_j(\varepsilon)$ are the elements of a base of the space of functions, they need to be normalized. This means that $\int_0^R v_j(\varepsilon)^2 d\varepsilon = 1$.

We calculated f_j :

For the model assuming a finite domain with a sink at $\varepsilon = R$:

$$f_j = \int_0^R \sqrt{\frac{2}{R}} \cos\left(\frac{\left(j + \frac{1}{2}\right)\pi\varepsilon}{R}\right) \left[\frac{\sinh(R - \varepsilon)}{\cosh(R)} + (b - 1) \frac{\sinh(R - \varepsilon)}{\cosh(R)} \theta\left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}}\right) \theta\left(-\varepsilon + \frac{d+h}{\sqrt{\frac{D}{k}}}\right) + (\varepsilon - R) \right] d\varepsilon$$

$$f_j = \int_0^R \sqrt{\frac{2}{R}} \cos\left(\frac{\left(j + \frac{1}{2}\right)\pi\varepsilon}{R}\right) \frac{\sinh(R - \varepsilon)}{\cosh(R)} d\varepsilon + (b - 1) \int_{\frac{d}{\sqrt{\frac{D}{k}}}}^{\frac{d+h}{\sqrt{\frac{D}{k}}}} \sqrt{\frac{2}{R}} \cos\left(\frac{\left(j + \frac{1}{2}\right)\pi\varepsilon}{R}\right) b \frac{\sinh(R - \varepsilon)}{\cosh(R)} d\varepsilon - \frac{\sqrt{\frac{2}{R}}}{\left[\frac{\left(j + \frac{1}{2}\right)\pi}{R}\right]^2}$$

$$f_j = \frac{\sqrt{\frac{2}{R}}}{\left[\frac{\left(j + \frac{1}{2}\right)\pi}{R}\right]^2 + 1} - \frac{\sqrt{\frac{2}{R}}}{\left[\frac{\left(j + \frac{1}{2}\right)\pi}{R}\right]^2}$$

$$+ (b - 1) \frac{\sqrt{\frac{2}{R}}}{\left[\frac{\left(j + \frac{1}{2}\right)\pi}{R}\right]^2 + 1} \left(\frac{-\frac{\left(j + \frac{1}{2}\right)\pi}{R} \sin\left(\frac{\left(j + \frac{1}{2}\right)\pi \frac{d}{\sqrt{\frac{D}{k}}}\right) \sinh\left(R - \frac{d}{\sqrt{\frac{D}{k}}}\right)}{\cosh(R)} + \frac{\cos\left(\frac{\left(j + \frac{1}{2}\right)\pi \frac{d}{\sqrt{\frac{D}{k}}}\right) \cosh\left(R - \frac{d}{\sqrt{\frac{D}{k}}}\right)}{\cosh(R)} - \frac{-\frac{\left(j + \frac{1}{2}\right)\pi}{R} \sin\left(\frac{\left(j + \frac{1}{2}\right)\pi \frac{d+h}{\sqrt{\frac{D}{k}}}\right) \sinh\left(R - \frac{d+h}{\sqrt{\frac{D}{k}}}\right)}{\cosh(R)} - \frac{\cos\left(\frac{\left(j + \frac{1}{2}\right)\pi \frac{d+h}{\sqrt{\frac{D}{k}}}\right) \cosh\left(R - \frac{d+h}{\sqrt{\frac{D}{k}}}\right)}{\cosh(R)} \right) \quad (\text{Eq. S.28.})$$

For the model assuming a finite domain with no flux at $\varepsilon = R$:

If $\lambda_j \neq 0$:

$$f_j = \int_0^R \sqrt{\frac{2}{R}} \cos\left(\frac{j\pi\varepsilon}{R}\right) \left[\frac{\cosh(R-\varepsilon)}{\sinh(R)} + (b-1) \frac{\cosh(R-\varepsilon)}{\sinh(R)} \theta\left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}}\right) \theta\left(-\varepsilon + \frac{d+h}{\sqrt{\frac{D}{k}}}\right) + \left(\varepsilon - \frac{\varepsilon^2}{2R}\right) \right] d\varepsilon$$

$$f_j = \int_0^R \sqrt{\frac{2}{R}} \cos\left(\frac{j\pi\varepsilon}{R}\right) \frac{\cosh(R-\varepsilon)}{\sinh(R)} d\varepsilon +$$

$$\int_{\frac{d}{\sqrt{\frac{D}{k}}}}^{\frac{d+h}{\sqrt{\frac{D}{k}}}} (b-1) \sqrt{\frac{2}{R}} \cos\left(\frac{j\pi\varepsilon}{R}\right) \frac{\cosh(R-\varepsilon)}{\sinh(R)} d\varepsilon$$

$$- \sqrt{\frac{2}{R}} \frac{1}{\left(\frac{j\pi}{R}\right)^2}$$

$$f_j = \frac{\sqrt{\frac{2}{R}}}{\left[\frac{j\pi}{R}\right]^2 + 1} - \frac{\sqrt{\frac{2}{R}}}{\left[\frac{j\pi}{R}\right]^2}$$

$$(b-1) \frac{\sqrt{\frac{2}{R}}}{\left[\frac{j\pi}{R}\right]^2 + 1} \left(\frac{\cos\left(\frac{j\pi d}{R\sqrt{\frac{D}{k}}}\right) \sinh\left(R - \frac{d}{\sqrt{\frac{D}{k}}}\right)}{\sinh(R)} - \frac{\frac{j\pi}{R} \sin\left(\frac{j\pi d}{R\sqrt{\frac{D}{k}}}\right) \cosh\left(R - \frac{d}{\sqrt{\frac{D}{k}}}\right)}{\sinh(R)} - \frac{\cos\left(\frac{j\pi(d+h)}{R\sqrt{\frac{D}{k}}}\right) \sinh\left(R - \frac{d+h}{\sqrt{\frac{D}{k}}}\right)}{\sinh(R)} + \right.$$

$$\left. \frac{\frac{j\pi}{R} \sin\left(\frac{j\pi(d+h)}{R\sqrt{\frac{D}{k}}}\right) \cosh\left(R - \frac{d+h}{\sqrt{\frac{D}{k}}}\right)}{\sinh(R)} \right) \quad (\text{Eq. S.29.})$$

And if $\lambda_j = 0$:

$$f_j = \int_0^R \sqrt{\frac{1}{R}} \left[\frac{\cosh(R-\varepsilon)}{\sinh(R)} + (b-1) \frac{\cosh(R-\varepsilon)}{\sinh(R)} \theta\left(\varepsilon - \frac{d}{\sqrt{\frac{D}{k}}}\right) \theta\left(-\varepsilon + \frac{d+h}{\sqrt{\frac{D}{k}}}\right) + \left(\varepsilon - \frac{\varepsilon^2}{2R}\right) \right] d\varepsilon$$

$$f_j = \sqrt{\frac{1}{R}} \int_0^R \frac{\cosh(R - \varepsilon)}{\sinh(R)} d\varepsilon +$$

$$\int_{\frac{d}{\sqrt{k}}}^{\frac{d+h}{\sqrt{k}}} (b-1) \sqrt{\frac{1}{R}} \frac{\cosh(R - \varepsilon)}{\sinh(R)} d\varepsilon$$

$$+ \sqrt{\frac{1}{R}} \frac{R^2}{3}$$

$$f_j = \sqrt{\frac{1}{R}} + \sqrt{\frac{1}{R}} \frac{R^2}{3}$$

$$+(b-1) \sqrt{\frac{1}{R}} \left(\frac{\cosh(R)}{\sinh(R)} \left(\sinh\left(\frac{d+h}{\sqrt{k}}\right) - \sinh\left(\frac{d}{\sqrt{k}}\right) \right) + \cosh\left(\frac{d}{\sqrt{k}}\right) - \cosh\left(\frac{d+h}{\sqrt{k}}\right) \right) \quad (\text{Eq.}$$

S.30.)

We also calculated $F_j(\tau)$:

For the model assuming a finite domain with a sink at $\varepsilon = R$:

$$F_j(\tau) = - \frac{\sqrt{\frac{2}{R}} e^{\tau}}{\left[\frac{(j + \frac{1}{2}) \pi}{R} \right]^2}$$

For the model assuming a finite domain with no flux at $\varepsilon = R$:

If $\lambda_j \neq 0$:

$$F_j(\tau) = -\frac{e^\tau}{\left(\frac{j\pi}{R}\right)^2} \sqrt{\frac{2}{R}}$$

And if $\lambda_j = 0$:

$$F_j(\tau) = \sqrt{\frac{1}{R}} e^\tau \left(\frac{R^2}{3} + 1 \right)$$

We obtained the original function:

For the model assuming a finite domain with a sink at $\varepsilon = R$:

$$C(\varepsilon, \tau) = [C_3(\varepsilon, \tau) - (\varepsilon - R)e^\tau] e^{-\tau}$$

$$C(\varepsilon, \tau) = [C_3(\varepsilon, \tau)e^{-\tau} - (\varepsilon - R)]$$

For the model assuming a finite domain with no flux at $\varepsilon = R$:

$$C(\varepsilon, \tau) = \left[C_3(\varepsilon, \tau) - \left(\varepsilon - \frac{\varepsilon^2}{2R} \right) e^\tau \right] e^{-\tau}$$

$$C(\varepsilon, \tau) = \left[C_3(\varepsilon, \tau)e^{-\tau} - \left(\varepsilon - \frac{\varepsilon^2}{2R} \right) \right]$$

We calculated the recovery of the average concentration $f(t)$ in the bleached region. To achieve that we used the original coordinates x and t instead of the normalized ones ε and τ :

$$f(t) = \frac{1}{h} \int_d^{d+h} C(x, t) dx$$

For the model assuming a finite domain with a sink at $\varepsilon = R$:

$$f(t) = \frac{\sqrt{D}}{h} \int_{\frac{d}{\sqrt{k}}}^{\frac{d+h}{\sqrt{k}}} C(\varepsilon, t) d\varepsilon$$

$$f(t) = \frac{\sqrt{D}}{h} \int_{\frac{d}{\sqrt{k}}}^{\frac{d+h}{\sqrt{k}}} \left[\sum_{j=0}^{\infty} f_j v_j(x) e^{-\lambda_j \int_0^{kt} \frac{1}{m(s)} ds} + \sum_{j=0}^{\infty} v_j(x) e^{-\lambda_j \int_0^t \frac{1}{m(s)} ds} \int_0^{kt} \frac{F_j(s)}{m(s)} e^{\lambda_j \int_0^s \frac{1}{m(w)} dw} ds e^{-kt} - \left(\varepsilon - \frac{\varepsilon^2}{2R} \right) \right] d\varepsilon$$

$f(t)$

$$= \frac{\sqrt{D}}{h} \left[\sum_{j=0}^{\infty} f_j \sqrt{\frac{2}{R}} \frac{\sin\left(\frac{(j+\frac{1}{2})\pi d+h}{R} \frac{D}{\sqrt{k}}\right) - \sin\left(\frac{(j+\frac{1}{2})\pi d}{R} \frac{D}{\sqrt{k}}\right)}{\frac{(j+\frac{1}{2})\pi}{R}} e^{-\lambda_j \int_0^{kt} \frac{1}{m(s)} ds} + \sum_{j=0}^{\infty} \sqrt{\frac{2}{R}} \frac{\sin\left(\frac{(j+\frac{1}{2})\pi d+h}{R} \frac{D}{\sqrt{k}}\right) - \sin\left(\frac{(j+\frac{1}{2})\pi d}{R} \frac{D}{\sqrt{k}}\right)}{\frac{(j+\frac{1}{2})\pi}{R}} e^{-\lambda_j \int_0^{kt} \frac{1}{m(s)} ds} \int_0^{kt} \frac{F_j(s)}{m(s)} e^{\lambda_j \int_0^s \frac{1}{m(w)} dw} ds e^{-kt} - \left(\varepsilon - \frac{\varepsilon^2}{2R} \right) \right]$$

Thus, the expression of the recovery curve ($f(t)$) for the model assuming a sink boundary condition

at $\varepsilon = R$ is as follows:

$$\begin{aligned}
f(t) = & \\
& \left[\frac{\sqrt{\frac{D}{k}}}{h} \sum_{j=0}^{\infty} f_j \sqrt{\frac{2}{R}} \frac{\sin\left(\left(j+\frac{1}{2}\right)\pi \frac{d+h}{L}\right) - \sin\left(\left(j+\frac{1}{2}\right)\pi \frac{d}{L}\right)}{\frac{\left(j+\frac{1}{2}\right)\pi}{\frac{L}{\sqrt{\frac{D}{k}}}}} e^{-\left(\left(\frac{\left(j+\frac{1}{2}\right)\pi}{\frac{L}{\sqrt{\frac{D}{k}}}\right)+1\right)kt} + \right. \\
& \sum_{j=0}^{\infty} \sqrt{\frac{2}{R}} \frac{\sin\left(\left(j+\frac{1}{2}\right)\pi \frac{d+h}{L}\right) - \sin\left(\left(j+\frac{1}{2}\right)\pi \frac{d}{L}\right)}{\frac{\left(j+\frac{1}{2}\right)\pi}{\frac{L}{\sqrt{\frac{D}{k}}}}} e^{-\left(\left(\frac{\left(j+\frac{1}{2}\right)\pi}{\frac{L}{\sqrt{\frac{D}{k}}}\right)+1\right)kt} \int_0^{kt} F_j(s) e^{\left(\left(\frac{\left(j+\frac{1}{2}\right)\pi}{\frac{L}{\sqrt{\frac{D}{k}}}\right)+1\right)s} ds - \\
& \left. \frac{-3\frac{L}{\sqrt{\frac{D}{k}}}\left(\frac{d}{\sqrt{\frac{D}{k}}}\right)^2 + 3\frac{L}{\sqrt{\frac{D}{k}}}\left(\frac{d+h}{\sqrt{\frac{D}{k}}}\right)^2 + \left(\frac{d}{\sqrt{\frac{D}{k}}}\right)^3 - \left(\frac{d+h}{\sqrt{\frac{D}{k}}}\right)^3}{6\frac{L}{\sqrt{\frac{D}{k}}}} \right] \quad (\text{Eq. S.31.})
\end{aligned}$$

With f_j defined in Eq. S.28.

For the model assuming a finite domain with no flux at $\varepsilon = R$:

$$\begin{aligned}
f(t) &= \frac{\sqrt{\frac{D}{k}}}{h} \int_{\frac{d}{\sqrt{\frac{D}{k}}}}^{\frac{d+h}{\sqrt{\frac{D}{k}}}} C(\varepsilon, t) d\varepsilon \\
f(t) &= \frac{\sqrt{\frac{D}{k}}}{h} \int_{\frac{d}{\sqrt{\frac{D}{k}}}}^{\frac{d+h}{\sqrt{\frac{D}{k}}}} \left[\sum_{j=0}^{\infty} f_j v_j(x) e^{-\lambda_j \int_0^{kt} \frac{1}{m(s)} ds} \right. \\
& \quad \left. + \sum_{j=0}^{\infty} v_j(x) e^{-\lambda_j \int_0^{kt} \frac{1}{m(s)} ds} \int_0^{kt} \frac{F_j(s)}{m(s)} e^{\lambda_j \int_0^s \frac{1}{m(w)} dw} ds e^{-kt} - \left(\varepsilon - \frac{\varepsilon^2}{2R} \right) \right] d\varepsilon
\end{aligned}$$

$f(t)$

$$\begin{aligned}
 &= \frac{\sqrt{\frac{D}{k}}}{h} \left[e^{-kt} f_0 e^{-\lambda_0 \int_0^{kt} \frac{1}{m(s)} ds} \frac{h}{\sqrt{\frac{D}{k}}} \sqrt{\frac{1}{R}} + \sqrt{\frac{1}{R}} \frac{h}{\sqrt{\frac{D}{k}}} e^{-\lambda_0 \int_0^{kt} \frac{1}{m(s)} ds} \int_0^{kt} \frac{F_0(s)}{m(s)} e^{\lambda_j \int_0^s \frac{1}{m(w)} dw} ds e^{-kt} \right. \\
 &+ \sum_{j=1}^{\infty} f_j \sqrt{\frac{2}{R}} \frac{\sin\left(\frac{j\pi d+h}{R \sqrt{\frac{D}{k}}}\right) - \sin\left(\frac{j\pi d}{R \sqrt{\frac{D}{k}}}\right)}{\frac{j\pi}{R}} e^{-\lambda_j \int_0^{kt} \frac{1}{m(s)} ds} e^{-kt} \\
 &+ \sum_{j=1}^{\infty} \sqrt{\frac{2}{R}} \frac{\sin\left(\frac{j\pi d+h}{R \sqrt{\frac{D}{k}}}\right) - \sin\left(\frac{j\pi d}{R \sqrt{\frac{D}{k}}}\right)}{\frac{j\pi}{R}} e^{-\lambda_j \int_0^{kt} \frac{1}{m(s)} ds} \int_0^{kt} \frac{F_j(s)}{m(s)} e^{\lambda_j \int_0^s \frac{1}{m(w)} dw} ds e^{-kt} \\
 &\left. - \left(\frac{\left(\frac{d+h}{\sqrt{\frac{D}{k}}}\right)^2}{2} - \frac{\left(\frac{d}{\sqrt{\frac{D}{k}}}\right)^2}{2} - R \frac{h}{\sqrt{\frac{D}{k}}} \right) \right]
 \end{aligned}$$

$$\begin{aligned}
& f(t) \\
&= \frac{\sqrt{\frac{D}{k}}}{h} \left[e^{-kt} f_0 \frac{h}{\sqrt{\frac{D}{k}}} \sqrt{\frac{1}{R}} + \sqrt{\frac{1}{R}} \frac{h}{\sqrt{\frac{D}{k}}} e^{-kt} \int_0^{kt} F_0(s) ds \right. \\
&+ \sum_{j=1}^{\infty} f_j \sqrt{\frac{2}{R}} \frac{\sin\left(\frac{j\pi d+h}{R\sqrt{\frac{D}{k}}}\right) - \sin\left(\frac{j\pi d}{R\sqrt{\frac{D}{k}}}\right) - \left(\left(\frac{j\pi}{L\sqrt{\frac{D}{k}}}\right)^2 + 1\right) kt}{\frac{j\pi}{R}} e^{-\left(\left(\frac{j\pi}{L\sqrt{\frac{D}{k}}}\right)^2 + 1\right) kt} \\
&+ \sum_{j=1}^{\infty} \sqrt{\frac{2}{R}} \frac{\sin\left(\frac{j\pi d+h}{R\sqrt{\frac{D}{k}}}\right) - \sin\left(\frac{j\pi d}{R\sqrt{\frac{D}{k}}}\right) - \left(\left(\frac{j\pi}{L\sqrt{\frac{D}{k}}}\right)^2 + 1\right) kt}{\frac{j\pi}{R}} \int_0^{kt} F_j(s) e^{-\left(\left(\frac{j\pi}{L\sqrt{\frac{D}{k}}}\right)^2 + 1\right) s} ds \\
&\left. - \left(\frac{\left(\frac{d+h}{\sqrt{\frac{D}{k}}}\right)^2}{2} - \frac{\left(\frac{d}{\sqrt{\frac{D}{k}}}\right)^2}{2} - R \frac{h}{\sqrt{\frac{D}{k}}} \right) \right]
\end{aligned}$$

Thus, the expression of the recovery curve ($f(t)$) for the model assuming a no flux boundary condition at $\varepsilon = R$ is as follows:

$$f(t) =$$

$$\left[\frac{\sqrt{\frac{D}{k}}}{h} e^{-kt} f_0 \frac{h}{\sqrt{\frac{D}{k}}} \sqrt{\frac{1}{R}} + \frac{1}{R} \left(\frac{R^2}{3} + 1 \right) \frac{h}{\sqrt{\frac{D}{k}}} (1 - e^{-kt}) + \sum_{j=1}^{\infty} f_j \sqrt{\frac{2}{R}} \frac{\sin\left(\frac{j\pi d+h}{R \sqrt{\frac{D}{k}}}\right) - \sin\left(\frac{j\pi d}{R \sqrt{\frac{D}{k}}}\right)}{\frac{j\pi}{R}} e^{-\left(\left(\frac{j\pi}{L \sqrt{\frac{D}{k}}}\right)^2 + 1\right) kt} + \right.$$

$$\left. \sum_{j=1}^{\infty} \frac{2}{\sqrt{\frac{D}{k}}} \frac{\sin\left(\frac{j\pi d+h}{L \sqrt{\frac{D}{k}}}\right) - \sin\left(\frac{j\pi d}{L \sqrt{\frac{D}{k}}}\right)}{\frac{j\pi}{L}} \frac{1 - e^{-\left(\left(\frac{j\pi}{L \sqrt{\frac{D}{k}}}\right)^2 + 1\right) kt}}{\left(\frac{j\pi}{L \sqrt{\frac{D}{k}}}\right)^4} - \left(\frac{\left(\frac{d+h}{\sqrt{\frac{D}{k}}}\right)^2}{2} - \frac{\left(\frac{d}{\sqrt{\frac{D}{k}}}\right)^2}{2} - \frac{L}{\sqrt{\frac{D}{k}}} \frac{h}{\sqrt{\frac{D}{k}}} \right) \right] \quad (\text{Eq. S.32.})$$

With f_0 defined in Eq. S.30. and f_j defined in Eq. S.29.

Finally, the expression or the recovery curve ($f(t)$) predicted by the infinite-domain model as calculated by Kicheva and collaborators (3) is as follows:

$$f(t) =$$

$$\frac{q \sqrt{\frac{D}{k}}}{2h} \left\{ e^{-\frac{d+h}{\sqrt{\frac{D}{k}}}} \left[e^{\frac{h}{\sqrt{\frac{D}{k}}}} \sqrt{\frac{D}{k}} (b + (b-1)\varphi + 1) - 2 \sqrt{\frac{D}{k}} ((b-1)\varphi + 1) \right] + (b-1) e^{-\frac{Dt+(d+h)\sqrt{\frac{D}{k}}}{k}} \sqrt{\frac{D}{k}} (\varphi -$$

$$\begin{aligned}
1) & \left[e^{\frac{h}{\sqrt{D}} \operatorname{erf}\left(\frac{d}{\sqrt{Dt}}\right)} + e^{\frac{Dt+h\sqrt{D}}{Dk}} - e^{\frac{h}{\sqrt{D}} \operatorname{erf}\left(\frac{h}{2\sqrt{Dt}}\right)} + \operatorname{erf}\left(\frac{h}{2\sqrt{Dt}}\right) + \operatorname{erf}\left(\frac{d+h}{\sqrt{Dt}}\right) - e^{\frac{h}{\sqrt{D}} \operatorname{erf}\left(\frac{2d+h}{2\sqrt{Dt}}\right)} + \right. \\
& e^{\frac{Dt}{Dk}} \operatorname{erf}\left(\frac{\sqrt{Dt}}{\sqrt{Dk}}\right) + e^{\frac{Dt+h\sqrt{D}}{Dk}} \operatorname{erf}\left(\frac{\sqrt{Dt}}{\sqrt{Dk}}\right) + e^{\frac{Dt}{Dk}} \operatorname{erf}\left(\frac{h\sqrt{D}-2Dt}{2\sqrt{Dt}\sqrt{Dk}}\right) - e^{\frac{Dt+h\sqrt{D}}{Dk}} \operatorname{erf}\left(\frac{h\sqrt{D}+2Dt}{2\sqrt{Dt}\sqrt{Dk}}\right) + \\
& \left. e^{\frac{Dt+h\sqrt{D}+2d\sqrt{D}}{Dk}} \left(-\operatorname{erf}\left(\frac{d\sqrt{D}+Dt}{\sqrt{Dt}\sqrt{Dk}}\right) - e^{\frac{h}{\sqrt{D}} \operatorname{erf}\left(\frac{(d+h)\sqrt{D}+Dt}{\sqrt{Dt}\sqrt{Dk}}\right)} + \left(1 + e^{\frac{h}{\sqrt{D}}}\right) \operatorname{erf}\left(\frac{(2d+h)\sqrt{D}+2Dt}{2\sqrt{Dt}\sqrt{Dk}}\right) \right) - \right. \\
& \left. \left. \operatorname{erf}\left(\frac{2d+h}{2\sqrt{Dt}}\right) \right\} \quad (\text{Eq. S.33.})
\end{aligned}$$

Where $\operatorname{erf}(x)$ is the error function of x and φ is the immobile fraction. In this work we have obtained the solution for a finite tissue when $\varphi = 0$ (no immobile particles).

8. Error of assuming an infinite domain instead of finite one in the steady state calculations.

We defined the error of using the infinite model in the steady state (E) as:

$$E(\varepsilon) = \left| C_{ss\text{infinite}}(\varepsilon) - C_{ss\text{finite}}(\varepsilon) \right| = \left| e^{-\varepsilon} - \left(\frac{e^{-\varepsilon}}{1+e^{-2R}} - \frac{e^{\varepsilon}}{1+e^{2R}} \right) \right| \quad (\text{Eq. S.34.})$$

We defined the accumulated error of using the infinite model in steady state (E_{acc}) as the integral over the tissue of the error of using the infinite model in steady state (Eq. S.35.) divided by the length of the tissue. For the model assuming a finite domain with a sink at $\varepsilon = R$ we obtained:

$$E_{acc}(R) = \frac{1}{R} \int_0^R E(\varepsilon) d\varepsilon = \frac{(1-\tanh(R)) * \sinh(R)}{R} \quad (\text{Eq. S.35.})$$

Where $\tanh(R)$ is the hyperbolic tangent function of R and $\sinh(R)$ is the hyperbolic sine of R .

For the model assuming a finite domain with a no flux at $\varepsilon = R$ we obtained:

$$E(\varepsilon) = \left| C_{ss\text{infinite}}(\varepsilon) - C_{ss\text{finite}}(\varepsilon) \right| = \left| e^{-\varepsilon} - \frac{\cosh(R-\varepsilon)}{\sinh(R)} \right| \quad (\text{Eq. S.22.})$$

And:

$$E_{acc}(R) = \frac{1}{R} \int_0^R E(\varepsilon) d\varepsilon = \frac{\sinh(R) - \cosh(R)}{R} \quad (\text{Eq. S.23.})$$

Where $\cosh(R)$ is the hyperbolic cosine function of R and $\sinh(R)$ is the hyperbolic sine of R .

9. Comparison between the computational efficiency between numerical and analytical solutions.

Multiscale computational models that involve morphogen gradients, encoded in a reaction diffusion scheme [4,5,6], combine different coupled scales, which may lead to long simulation times. Typically, this scheme is numerically implemented. Therefore, we wondered if our new analytical solution could improve the efficiency, compared to a numerical approach. To achieve that goal, we compared the computational time needed to obtain the morphogen concentration using the analytical solution with respect of the numerical solution.

We used domains of lengths $R = 0.1$, $R = 1$ and $R = 10$ and calculated the concentration of morphogen at each position in the tissue at times $\tau = 0.1$, $\tau = 1$ and $\tau = 10$. We discretized the domain in 100 equal parts of length $\frac{R}{100}$.

For the analytical solution, we first determined the optimum number of terms in the sum. To that end, we asked that:

$$\frac{\sum_{j=0}^{j^{max}+1} a_j(\varepsilon, \tau) - \sum_{j=0}^{j^{max}} a_j(\varepsilon, \tau)}{\sum_{j=0}^{j^{max}} a_j(\varepsilon, \tau)} < \varphi \quad (\text{Eq. S.36.})$$

With $a_j(\varepsilon, \tau)$ obtained from $C(\varepsilon, \tau) = \sum_{j=0}^{\infty} a_j(\varepsilon, \tau)$. In this way, adding more terms above j^{max} has little impact on the solution. We chose φ equal to 0.00001.

For the numerical solution, we performed a finite difference simulation. We chose the length of

the time step as $\Delta t = \frac{\Delta x^2}{3} = \frac{\left(\frac{R}{100}\right)^2}{3}$ to avoid oscillations in the solution [7].

Our calculation of the analytical solution is faster than the numerical implementation (Table S1).

We observed that, for small values of R , the time needed to run the numerical simulations is

larger. The time step Δt must meet the condition that $\Delta t < \frac{\Delta x^2}{2}$. Thus, for small values of R , Δx is small and consequently Δt is even smaller. This leads to an increase in the number of time steps needed to perform the simulation.

	Analytical solution			Numerical Solution		
	$R = 0.1$	$R = 1$	$R = 10$	$R = 0.1$	$R = 1$	$R = 10$
$\tau = 0.1$	0.002 sec	0.003 sec	0.002 sec	81.454 sec	0.831 sec	0.010 sec
$\tau = 1$	0.004 sec	0.005 sec	0.005 sec	815.204 sec	8.355 sec	0.084 sec
$\tau = 10$	0.007 sec	0.008 sec	0.007 sec	8150.534 sec	81.688 sec	0.822 sec

Table S1. Comparison between the computational time needed to perform the simulation using the numerical and analytical solution for the concentration as a function of space for different times with different domain length (R).

The simulations were performed in python in an Intel Core i7-7700k with 16 GB of RAM and can be found in [8].

10. Supplementary references

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