Analytical approximation for the range of action: minimal model (section 2.1)

In this Appendix we provide some details on the derivation of eq. (6), which expresses the range of action (ROA) of a donor cell via miRNA propagation in the case of the minimal model (eqs. (1)-(4)). Adding eqs. (1) and (2) leads to the steady-state condition

$$v_{\text{smiRNA}}(x) - k_{\text{dmiRNA}} \cdot \text{miRNA}(x) + D \frac{\partial^2}{\partial x^2} \text{miRNA}(x) = 0.$$  (A)

This equation can be solved analytically. We incorporate the fact that $v_{\text{smiRNA}}$ must take a different value in $x = 0$ as compared to the rest of the system by using a combination of Heaviside functions such that $v_{\text{smiRNA}}(x) = v_{\text{smiRNA}}^0$ whenever $-dx/2 < x < dx/2$ and that $v_{\text{smiRNA}}(x) = v_{\text{smiRNA}}$ otherwise. In these expressions, $v_{\text{smiRNA}}^0$ and $v_{\text{smiRNA}}$ are the rate of miRNA production at the origin ($x = 0$) and anywhere else in the tissue, respectively. Using the no-flux boundary conditions,

$$\frac{d}{dx} \text{miRNA}(L) = \frac{d}{dx} \text{miRNA}(-L) = 0,$$  (B)

an exact solution can be obtained. It consists in a rather intricate superposition of products of exponentials and Heaviside functions, the exact form of which is not relevant for our purpose. Indeed, the information we need here is an expression for $\text{miRNA}(x)$ for large systems ($L \gg dx$). In this limit, we find that

$$\text{miRNA}(x) \approx \frac{e^{\frac{x-dx/2}{\lambda}}}{2 k_{\text{dmiRNA}}} \left[ v_{\text{smiRNA}}^0 \left( e^{-2 \frac{x}{\lambda}} - e^{-2 \frac{x-dx/2}{\lambda}} \right) + v_{\text{smiRNA}} \left( e^{-2 \frac{x}{\lambda}} + 2 e^{-\frac{(x-dx/2)}{\lambda}} \right) e^{\frac{dx}{\lambda} (1-\delta v_s^2)} \right]$$  (C)

where

$$\lambda = \sqrt{\frac{D}{k_{\text{dmiRNA}}}}.$$  (D)

has units of length. Notice that setting $x = L \gg dx$ in eq. (C) leads to $\text{miRNA}(L) = v_{\text{smiRNA}}^0 / k_{\text{dmiRNA}}$, which is the value of the stationary $\text{miRNA}$ concentration of a system in which there is no abnormal cell. Expression (C) can be introduced in the system of equations formed by setting eqs. (2)-(4) equal to 0 to obtain a solution for $\text{Prot}(x)$ under the form

$$\text{Prot}(x) = v_{\text{sRNA}} \left( \frac{T F^4}{K^4 + T F^4} \right) k_{\text{sProt}} k_{\text{dProt}} k_{\text{k1}} k_{\text{k2}} k_{\text{dRNA}} \cdot \text{miRNA}(x) + k_{\text{dRNA}} k_{\text{dC}}.$$  (E)

The ROA is defined as the value of $x$ for which eq. (E) reaches half the value of the “regular” case, for which the rate of $\text{miRNA}$ synthesis is independent of space, which also corresponds to $\lim_{x \to \infty} \text{miRNA}(x)$ as discussed above. The general solution is too long to be of any relevance, but considering that $k_1 \gg 1 \gg k_2$ as in the model hereby studied leads to

$$\text{ROA} \approx \lambda \ln \left[ \left( e^{\frac{dx}{\lambda}} - 1 \right) \frac{\delta v_s}{2} \right] = \frac{dx}{2}$$  (F)

where

$$\delta v_s = \frac{v_{\text{smiRNA}}^0 - v_{\text{smiRNA}}}{v_{\text{smiRNA}}}.$$  (G)

This is the analytical expression given in eq. (6) (in which we re-introduced explicitly the parameters defined by $\lambda$) and compared to the results of the numerical integration of eqs. (1) to (4) in Fig. 3.