Asymptotic behaviour of an integro-differential selection-advection equation

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PhD under the supervision of Nastassia Pouradier Duteil and Camille Pouchol

Motivation

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Cell differentiation: Process in which a cell changes its type.

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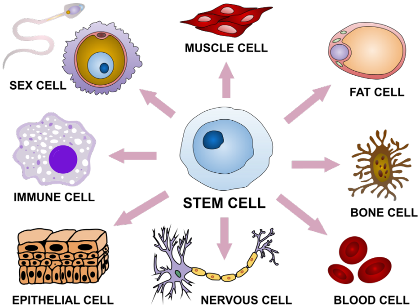

Figure: Stem cell differentiation

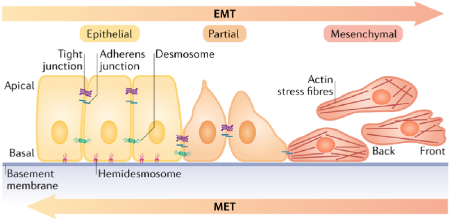

Figure: Epithelial-Mesenchymal Transition

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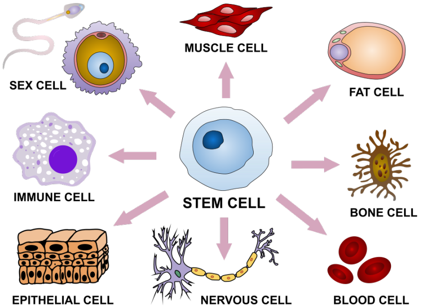

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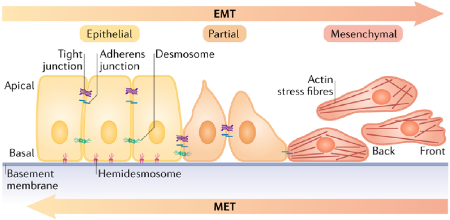

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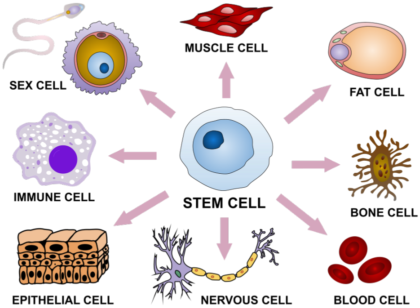

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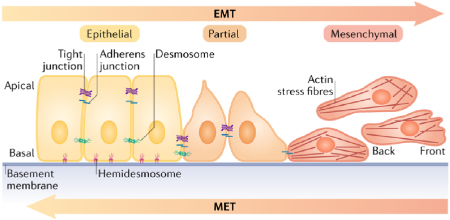

Figure: Epithelial-Mesenchymal Transition

- Cell types are characterised by **phenotypic traits**: size, shape, concentrations of molecules...
- **Purpose:** Developing a model for a population of cells undergoing differentiation, focusing on a phenotypic trait $x \in \mathbb{R}$.

Advection equation

- Single cell undergoing differentiation: modelled by an ODE

$$\begin{cases} \dot{x}(t) = a(x(t)) \\ x(0) = x_0 \end{cases}$$

  - $x(t)$: phenotypic trait of the cell at time t.
  - x_0: initial phenotypic trait.

  For EMT: [Lu, Jolly et al., 2013] (Among many others)

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- **Advection equation**: A population of cells undergoing differentiation:

$$\begin{cases} \partial_t n(t,x) + \partial_x \left(a(x) n(t,x)\right) = 0 \\ n(0,x) = n^0(x) \end{cases} \qquad \text{(ADV)}$$

  - $n(t,x)$: size of the population with phenotypic trait x at time t.
  - n^0: initial population distribution.

Integro-Differential Selection Equation

- **Logistic model:** Evolution of a uniform population of cells

$$\begin{cases} \dot{N}(t) = (R - N(t))N(t) \\ N(0) = N^0 \end{cases}$$

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- **Selection Equation:** Evolution of a phenotype-structured population. [*Transport equations in Biology*, Perthame, 2006]

$$\begin{cases} \partial_t n(t,x) = (r(x) - \rho(t))\, n(t,x) \\ \rho(t) = \int_{\mathbb{R}} n(t,x) dx \\ n(0,x) = n^0(x) \end{cases} \tag{SEL}$$

  - $x \in \mathbb{R}$: a phenotypic trait.
  - $n(t,x)$: size of the population with phenotypic trait x at time t.
  - $\rho(t)$: total population size at time t.
  - r: 'fitness' function.
  - n^0: initial population distribution.

Selection-Advection Equation

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- Concentration ? (only a finite number of trait is preserved), *i.e* n converges to a sum of dirac masses.
- Preservation of a continuous set of traits ? *i.e* n converges to a continuous/L^1 function.

Asymptotic behaviour of the advection equation

$$\begin{cases} \partial_t n(t,x) + \partial_x \left(a(x) n(t,x)\right) = 0 & \forall x \in \mathbb{R} \\ n(0,x) = n^0(x) & \forall x \in \mathbb{R} \end{cases} \tag{ADV}$$

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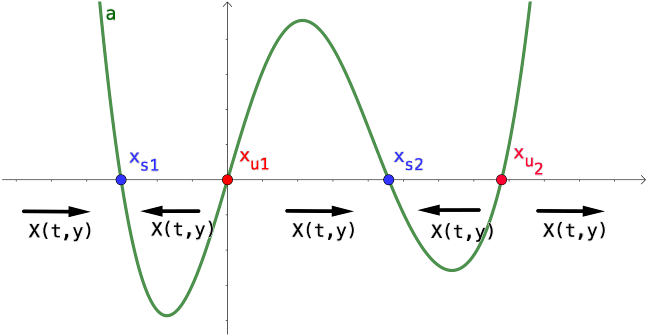
- Let us denote $x_1, ..., x_p$ the roots of a which are asymptotically stable for the ODE $\dot{x} = a(x)$.

$n(t,\cdot)$ concentrates around $x_1, ...x_p$ when t goes to $+\infty$.

Example



- $X(t, y)$: **Characteristic curves**:

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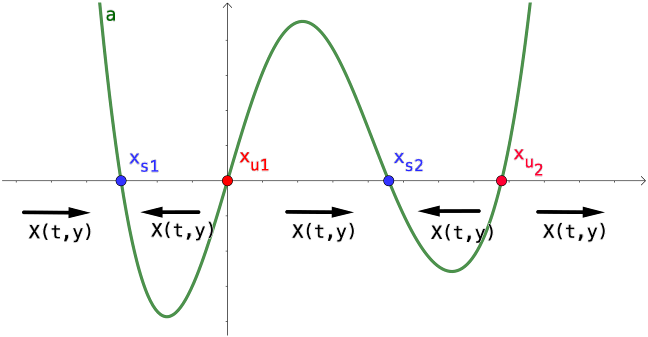

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$$n(t,\cdot) \underset{t \to +\infty}{\rightharpoonup} A_1 \delta_{x_{s1}} + A_2 \delta_{x_{s2}},$$

$$A_1 = \int_{-\infty}^{x_{u1}} n^0(x)dx, \quad A_2 = \int_{x_{u_1}}^{x_{u2}} n^0(x)dx.$$

Asymptotic behaviour of the Selection Equation

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- $n^0 \in \mathcal{C}_c(\mathbb{R}),\ n^0 \geq 0,\ n^0 \not\equiv 0.$
- $r \in \mathcal{C}^2(\mathbb{R}),\ r^M := \max\limits_{\text{supp}(n^0)} r > 0,\ \operatorname{argmax}\limits_{\text{supp}(n^0)} r = \{x_1, ..., x_p\}.$

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[Lorenzi, Pouchol 2019]

ρ converges to r^M, and $n(t,\cdot)$ concentrates around $x_1, ..., x_p$ when t goes to $+\infty$.

Moreover, if $\forall i \in \{1,...,p\}$, $f''(x_i) < 0$, then $n(t,x) \underset{t\to+\infty}{\rightharpoonup} r^M \sum\limits_{i=1}^{p} \alpha_i \delta_{x_i}$, with

$\alpha_i = A\frac{n^0(x_i)}{|f''(x_i)|}$, A such that $\sum\limits_{i=1}^{p} \alpha_i = 1$.

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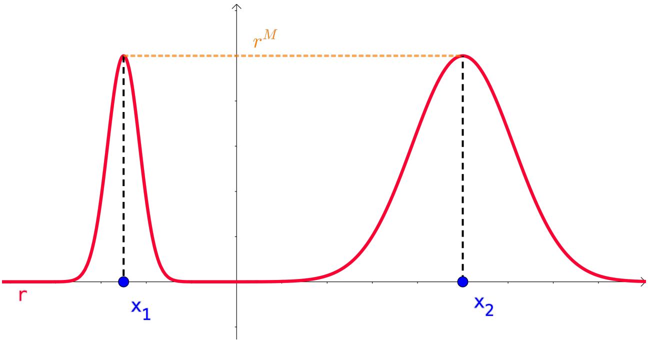

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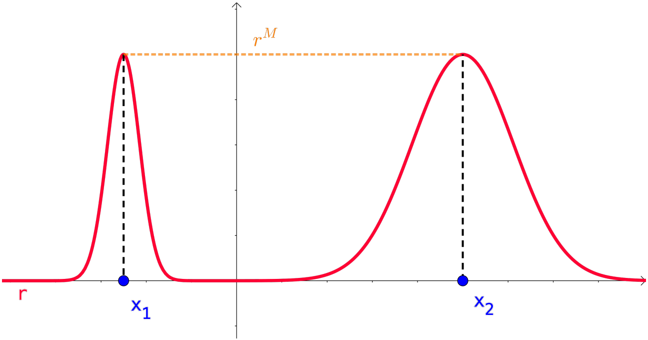

$$n(t,\cdot) \underset{t\to+\infty}{\rightharpoonup} A_1\delta_{x_1} + A_2\delta_{x_2},$$

$$A_1 + A_2 = r^M.$$

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Key idea:

Computing the limit of $R(t) := \frac{S'(t)}{S(t)}$, where

$$S(t) := \int_{\mathbb{R}} n^0(Y(t,x)) e^{\int_0^t r(Y(s,x)) - a'(Y(s,x))ds} dx,$$

$$\begin{cases} \dot{Y}(t,x) = -a(Y(t,x)) \\ Y(0,x) = x \end{cases}$$

Summary of the method

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ODE satisfied by ρ

$$\dot{\rho}(t) = (R(t) - \rho(t))\,\rho(t)$$

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- If there exist $C, \delta > 0$ s.t $|R(t) - \bar{R}| \leq Ce^{-\delta t}$, then there exist $C', \delta' > 0$ such that $|\rho(t) - \bar{R}| \leq C'e^{-\delta' t}$

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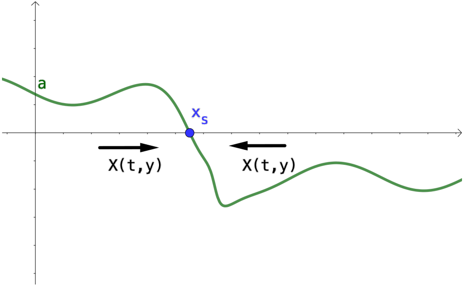
3. **Third step:** Determine the asymptotic behaviour of n.

Semi-explicit expression of n

$$n(t,x) = n^0\left(Y(t,x)\right) e^{\int_0^t r(Y(s,x)) - a'(Y(s,x)) - \rho(s) ds}$$

Unique asymptotically stable point



- a has a unique root, denoted x_s.
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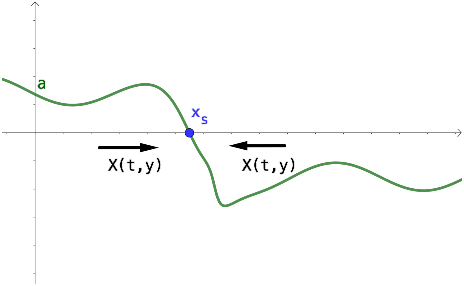

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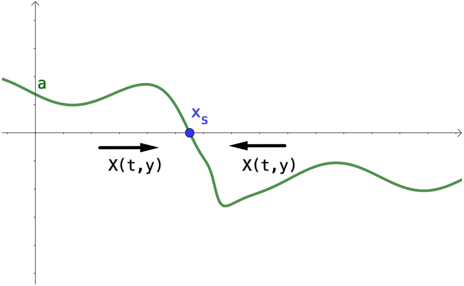

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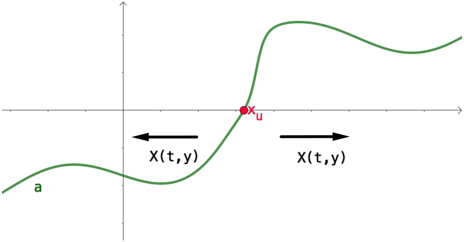

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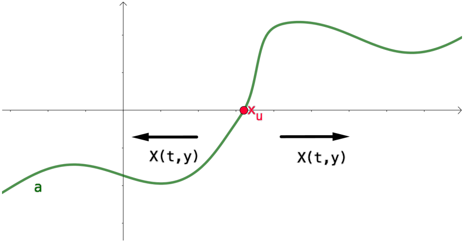

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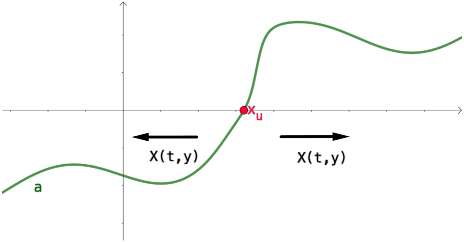

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If $r(x_u) < a'(x_u)$:

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- $n(t,\cdot) \xrightarrow{L^1} 0$

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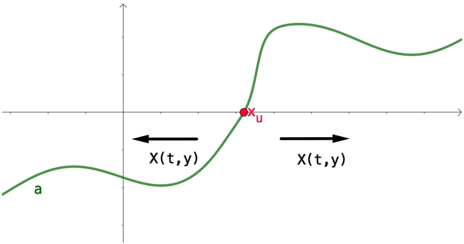

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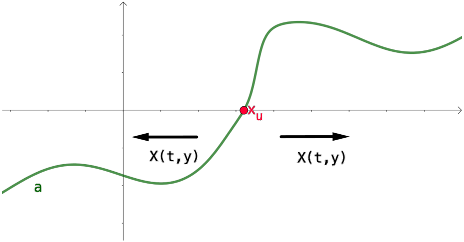

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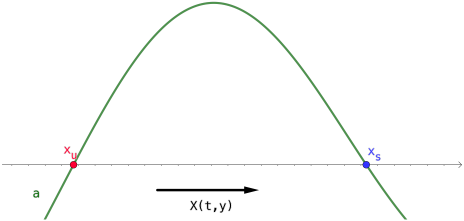
If $r(x_u) > a'(x_u)$:

- $\rho(t) \underset{t\to+\infty}{\longrightarrow} r(x_u) - a'(x_u)$ (with an exponential speed)
- $n(t,\cdot) \xrightarrow{L^1} \bar{n}, \quad \bar{n}(x) = Ae^{\int_{x_u}^{x} \frac{r(s)-a'(s)-\left(r(x_u)-a'(x_u)\right)}{a(s)}ds} \qquad \int_{\mathbb{R}} \bar{n}(x)dx = r(x_u) - a'(x_u)$

A segment between two roots



- a has exactly two roots $x_u < x_s$.
- $a'(x_u) > 0, \quad a'(x_s) < 0$.
- supp $\left(n^0\right) \subset [x_u, x_s]$.
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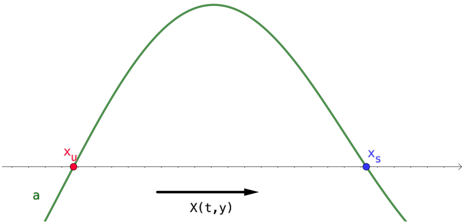

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Lemma

$$R(t) \underset{t\to+\infty}{\longrightarrow} \begin{cases} r(x_s) & \text{if } r(x_s) > r(x_u) - a'(x_u) \\ r(x_u) - a'(x_u) & \text{if } r(x_s) < r(x_u) - a'(x_u) \end{cases} \qquad \text{(with an exponential speed)}$$

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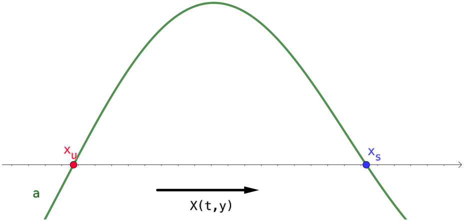

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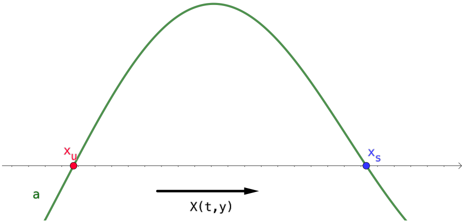
A segment between two roots



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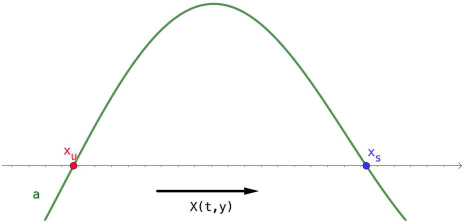

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If $r(x_s) < r(x_u) - a'(x_u)$:

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A more general example

Problem: The limit of R is difficult to determine in general.

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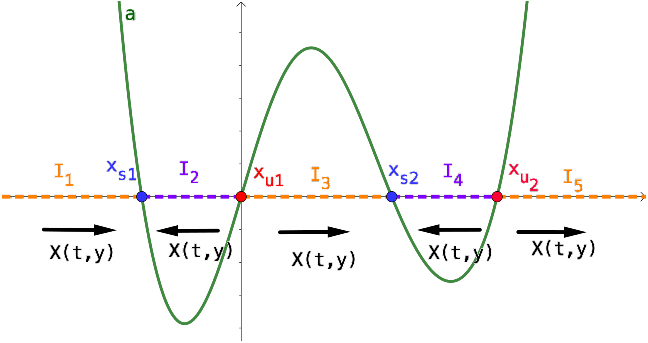

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- One can apply the previous method on each interval.

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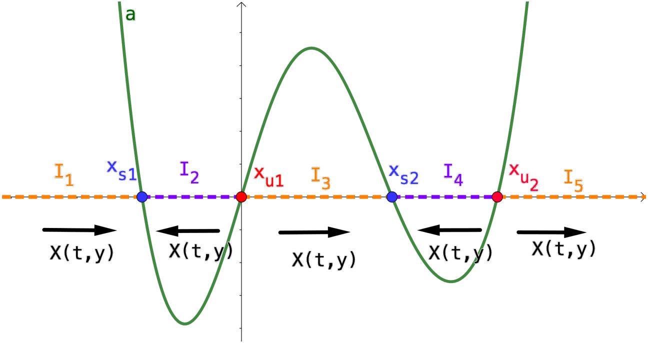

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Four possible behaviours (depending on the values of r, n^0 and a' at the equilibria):

- $n(t,\cdot) \underset{t\to+\infty}{\rightharpoonup} r(x_{s1})\delta_{x_{s1}}$
- $n(t,\cdot) \underset{t\to+\infty}{\rightharpoonup} r(x_{s2})\delta_{x_{s2}}$
- $n(t,\cdot) \xrightarrow{L^1} \bar{n}_1$, $\mathrm{supp}(\bar{n}_1) \subset [x_{s1}, x_{s2}]$
- $n(t,\cdot) \xrightarrow{L^1} \bar{n}_2$, $\mathrm{supp}(\bar{n}_2) \subset [x_{s2}, +\infty)$

Thank you for your attention