

ODE models for cell-fate differentiation

Jules GUILBERTEAU, Laboratoire Jacques-Louis Lions - Paris

Cell-fate transition can be modelled by ordinary differential equations (ODEs) which describe the behavior of several molecules in interaction, and for which each stable equilibrium corresponds to a possible phenotype (or ‘biological trait’). Such models are widely used in biology in order to describe cell-fate phenomena such as epithelial-mesenchymal transition, hematopoietic stem cells or embryonic stem cells. Nevertheless, these systems have been little studied from a mathematical point of view. In this poster, we focus on simple ODE systems modelling two molecules which each negatively (or positively) regulate the other. It is well-known that such models may lead to monostability or multistability, depending on the selected parameters. However, extensive numerical simulations have led systems biologists to conjecture that in the vast majority of cases, there cannot be more than two stable points.

In this poster, we prove this conjecture, by developing an elegant mathematical framework. More specifically, we provide a criterion ensuring at most bistability, which is indeed satisfied by most commonly used functions. This includes Hill functions, but also a wide family of convex and sigmoid functions. We also characterize the spaces of parameters which lead to either monostability or bistability.

Our main result can be stated as follows :

Théorème 1. *If f and g are two strictly monotonic functions such that $\frac{1}{\sqrt{|f'|}}$ and $\frac{1}{\sqrt{|g'|}}$ are strictly convex, then, for any $\alpha, \beta > 0$, the ODE system*

$$\begin{cases} \dot{x} = \alpha f(y) - x \\ \dot{y} = \beta g(x) - y \end{cases} \quad (1)$$

has at most three equilibria, among which at most two stable equilibria.