Mathematical modelling of stem cell dynamics during post-embryonic organ growth

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The current work is devoted to the mathematical modelling of the development of fish respiratory organs, called gills or branchiae. The gills are analysed in the attempt to answer three main developmental questions *via* mathematical modelling. Firstly, how many stem cells are needed to build the organ? What kind of heterogeneities exist among these stem cells? And, finally, what properties and relations with each-other do these stem cells have, that give the organ its shape?

Relying on experimental data from our collaborators, a variety of methods is used to study the aforementioned aspects. These methods were selected, adapted and developed based on the goal of each project and on the available data. Thus, a combination of stochastic and deterministic techniques is employed throughout the thesis, including Gillespie-type simulations, Markov chains theory and compartmental models.

The study of stem cell numbers and heterogeneities is approached *via* stochastic simulations extended from the algorithm of Gillespie, and further improved by Markov chains methods. Results suggest that not only very few stem cells are sufficient to build and maintain the organ but, more importantly, these stem cells are heterogeneous in their division behaviour.

For the study of growth and shape of gills, multiple deterministic models based on different assumptions and investigating various hypotheses have been developed. All these models have a compartmental structure, with increasing number of compartments governed by indicator functions which, in turn, depend on explicit or implicit algebraic equations. Results suggest that the main stem cell types, responsible for growing the organ, slow down their proliferation in time, either due to ageing or to the lack of sufficient nutrients.

Investigating such avenues could extend our understanding of the activity of mammalian cancer stem cells which possess similar properties to adult stem cells in fish, as they have the ability to both drive growth and maintain homeostasis. Such an overall understanding of fish stem cells could also have possible applications in wound healing and organ regeneration in higher vertebrates, processes which are driven by stem cells directed back into active and rapid proliferation due to injury and stress conditions.