Master 2 internship – Modeling of fish oogenesis

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Background and objectives

Model fish species (e.g. zebrafish, medaka, fathead minnow) are largely used to study the impact on the reproductive function of environment perturbations, such as climate change or exposure to pollutants, whether it be on the individual or population scale (ecophysiology/ecotoxicology). The maturation process of gametes (oocytes) in females is indeed particularly sensitive to internal (e.g. metabolic status) and external (temperature, salinity, endocrine disruptors) environment factors. Moreover, this process is a key point to control the reproductive fitness. Yet, to date, the fitness is assessed through rather rough indicators that mostly account for the final output of the gametogenetic process, the spawning performances.

In the framework of a collaboration between the project-team MUSCA and the *Laboratoire de Physiologie et Génétique des Poissons (Centre INRAE Rennes)*, we aim to develop a model of fish oogenesis accouting for the main stages and checkpoints targeted by environment and physiological controls, and enabling one to represent the whole oocyte dynamics from the earliest stages, in addition to the spawning size and frequency.

Work program

The internship work will be dedicated to the formulation, simulation, and parameter estimation of population dynamics models applied to oocytes. Up to now, the models of oocyte growth in different fish species [6, 3] have been limited to a scalar variable (diameter or volume), subject to a constant growth rate, or, at best, a growth rate marginaly impacted by external inputs.

The work wil consist in developping a compartmental model of the oogenesis process in model fishes. Each compartment will represent a given oocyte maturation stage: an oocyte can move forward from one stage to the next (migration) or degenerate within the current stage (death). The dynamics of oocyte populations will be formulated by a system of ordinary differential equations, one the formalisms already implemented to model oogenesis in mammals [1].

A first step will consist in identifying the number and nature of the compartments, using histological [4, 8] and endocrinological [7] classification criteria, as well as the size classes observed experimentally in oocyte numberings. We will rely in particular on data obtained in the course of the DYNAMO ANR projet [5]. A first, linear version of the model will be implemented numerically, and the death and migration rates will be coarsly estimated so that the model outputs meet the order of magnitude of oocyte numbers in the whole population and within each maturation stage.

A second step will consist in identifying the migration and death transitions subject to an hormonal control, which reveal the existence of interactions between oocytes. Such interactions may be either direct (local effect via ovarian hormones such as AMH -anti-Müllerian hormone–) or indirect (remote effect through endocrine loops involving pituitary hormones as FSH–follicle-stimulating hormone– et LH– luteinizing, or the vitellogenin originating from the liver). A second, nonlinear version of the model will be developped to embed these interactions. The interaction terms will be

formulated as functional responses, and will be based on available knowledge in the literature on the effects of the targeted inactivation of AMH [10], FSH or LH [11], FSH and LH receptors [9], and the dose-effects relationships underlying the hormonal feedbacks (e.g. estradiol/vitellogenin [2]).

The master internship will lead to a PhD thesis, whose first objective will be to extend the formulation of the compartimental model and to develop a model for structured populations based on partial differential equations or stochastic individual based models. Such a formalism is more directly suitable for recent experimental data (continuous size distribution of oocytes obtained from 3D microscopy imaging) and will represent more finely the interaction between oocytes and their effect on the model behavior.

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