Coupling physiologically-based kinetic models of endocrine axes with structured cell population dynamics models: an integrative approach of reproductive toxicity

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The impact of micropollutants on living organisms is a major concern for health and the environment. Endocrine disruptors (ED) interfere with the physiology of organisms and can alter major biological functions, particularly the reproductive function. Fish are species of interest in toxicology, because their aquatic living environment and their physiology make them particularly sensitive to pollutants. Initial work [3, 4] was dedicated to the development of a physiological-based kinetic-toxicodynamic (PBK-TD) model, comprising a system of ODEs, of the HPG axis which regulates the endocrine – and reproductive – function. The model, calibrated with experimental data on adult female zebrafish, was used to assess the influence of ED exposure on hormone secretion and spawning.
More recently, we focused on coupling a PBK-TD model of the type developed in [3] with a quasilinear PDE modelling the dynamics of a size-structured population of female gametes (a.k.a. oocytes), exhibiting nonlinearities accounting for nonlocal interactions between individual cells and hormones in the body. The PDE model of oocyte maturation was introduced and analysed in [1], proving existence and uniqueness of globally bounded weak solutions, and showing via bifurcation analysis that the model can exhibit multistability and stable oscillatory solutions. The coupling of these models enables the integration not only of the data in [3, 4] on hormone and ED levels in different body compartments, but also on oocyte size distribution [2]. Ultimately, this enables one to predict accurately the qualitative and quantitative effects on fish spawning, both in the short and long term.

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