White paper of the European Network of Zebrafish researchers (EuFishBioMed, COST Action BM0804) on quantitative modeling of developmental and regenerative processes

Small fishes such as the zebrafish have become important and popular models for biomedical research. Zebrafish mutants and transgenic lines provide models for any human diseases. These animals can serve as a means to understand the causes of the diseases and offer economically attractive alternatives to conventional drug screening and toxicity assessment. In addition, due to their small size and transparency, the small fish embryos provide unique access to systems biology of vertebrate organ formation, maintenance and repair.

A unique strength of this animal model is the possibility to combine large-scale phenotypic screens with direct imaging of cells and organs to characterise gene function. In addition, a large tool kit of methods ranging from transgenesis to knock out of genes contributes to investigating gene function in an intact organism. Almost 5000 mutants and transgenic lines are available worldwide. The zebrafish model can thus contribute significantly to the challenge of the post-genome-sequencing era to understand gene function in a global scale. The value of zebrafish models has been significantly further increased by parallel developments in microscopy technologies, which allow to image intact life embryos at subcellular resolution.

It is now important to take the next steps in our scientific exploitation of this model system. Understanding of organ development and regeneration requires quantitative analysis of the interactions of genes and of cells in functional networks. The data therefore need to be integrated in functional and quantitative models of organ development and regeneration. To this end, we need to generate novel genetic sensors and physical methods to derive real time quantitative data of the molecular processes underlying development and regeneration.

We thus urge the EU to consider a call for an interdisciplinary network of zebrafish researchers, physicists, chemists and theoretical biologists to develop the sensor methodology and the mathematical modelling tools for the systems biology of selected model organs of the zebrafish embryo. This network ought to combine the unique imaging capabilities in the zebrafish with the development of biological and chemical sensors and subsequent modelling of the processes based on quantitative measurements. The ultimate goal will be virtual models of developing and regenerating tissues with which the underlying processes can be simulated. This requires the interaction of at least four disciplines. To gather the excellence and the critical mass of research expertise, a measure at the level of an integrated project is necessary.

Modelling and simulation is a fundamental prerequisite to understand the mechanisms of organ formation and regeneration. This knowledge is an essential for the rational design of novel regenerative therapies. Given the increasing demand of these therapeutic measures in our aging societies this work tackles a fundamental problem in Europe.