realTox: Real-time imaging of toxicant impact in whole organisms at single cell resolution

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Toxicant exposure changes the transcriptional state of exposed cells but can also influence as a consequence cell behavior such as migration, cell division and regeneration. These processes require investigation in an intact organism in real time to detect these effects as early as possible and with high precision in terms of toxicological outcome.

We used one scenario to investigate the effect of toxicant exposure on complex cell behavior in a developing transgenic zebrafish (Danio rerio) with fluorescently labeled nuclei (H2A.F/Z:GFP) by means of 3D optical microscopy. To achieve the detection of the first fourteen hours of zebrafish development with single cell resolution we have implemented a digital scanned laser light-sheet fluorescence microscopy (DSLM) with very high spatial and temporal resolution. To overcome the problem of inhomogeneous imaging quality due to partially non-transparent embryo regions, two-side illumination and multi-view detection has also been realised. Acquisition of the embryo until the onset of organogenesis has been done under physiological conditions and was only limited by the development of the specimens' tail and limited disk space at the site of acquisition. Following acquisition data has been transferred by Grid-FTP client, stored on the Large Scale Data Facility (LSDF) of the Karlsruhe Institute of Technology and finally processed on a large computing cluster using the HADOOP framework.

Here, we will present our results on quantifying the effect on the gastrulating embryo using DSLM. For the scenario used effects on the formation of head progenitor tissue are demonstrated. Finally, by filtering the image data, identification and tracking of cells of the whole embryo over time and merging a set of experimental data measured at two angles, we are able to reconstruct a digital model of zebrafish embryogenesis with single-cell resolution. First attempts will be shown on the comparison of digital embryos within the control or exposure scenario as well as on the comparison of the digital embryos between the control and chemically treated embryos.
