

The Zebrafish Digital Embryo: Quantitative Reconstruction of Vertebrate Development

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Vertebrate embryonic development is one of the most complex processes encountered in biology. A single cell is transformed into a fully functional organism comprising several tens of thousands cells, which are arranged in intricate organs and tissues able to perform the most impressive tasks. Although capturing and analyzing the morphogenetic dynamics of this process is crucial for basic research as well as for applied medical sciences, comprehensively reconstructing – and even recording – vertebrate embryogenesis has so far been technologically impossible.

The novel light sheet-based microscopy technique DSLM allows recording the development of entire zebrafish embryos *in vivo* and with sub-cellular resolution¹. By imaging at a speed of 1.5 billion volume elements per minute, data in the order of several terabytes were acquired for each embryo over the time course of an entire day, i.e. up to a stage, in which the embryo comprises 20,000 cells and major organs are in a functional state. By using automated image processing algorithms the image data of each embryo were converted into a digital representation of the embryo (the "digital embryo"), i.e. a database with comprehensive information about migratory tracks and divisions of the embryo's cells². The digital embryos permit following single cells as a function of time such that the "fate" as well as the origin of the cells can be reconstructed. By means of these analyses, developmental blueprints of tissues and organs can be determined in a whole-embryo context. Defects in embryonic development or disease models can now be analyzed and understood on a quantitative level.

This approach is also applicable to other model organisms, including mouse and higher invertebrates. Further improvements in the technology, such as the DSLM structured illumination imaging mode, recently enabled *in toto* analyses of *Drosophila* embryogenesis. In the long-term perspective, I envision the "zoo" of digital embryos as a tool to uncover the quantitative rules of development.

¹ *PJ Keller and EHK Stelzer: Quantitative in vivo imaging of entire embryos with Digital Scanned Laser Light Sheet Fluorescence Microscopy. Current Opinion in Neurobiology. 18:624-32 (2008).*

² *PJ Keller, AD Schmidt, J Wittbrodt and EHK Stelzer: Reconstruction of zebrafish early embryonic development by scanned light sheet microscopy. Science. 322:1065-9 (2008).*

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Time: 4pm

Venue: LT20

Host: Prof Paul Matsudaira

**Department of Biological Sciences
Seminar Announcement**