The cell is the central functional unit of life. Cell behaviors, such as cell division, movements, differentiation, cell death as well as cell shape and size changes, determine how tissues change shape and grow during regeneration and development. However, a generally applicable framework to measure and describe the behavior of the multitude of cells in a developing tissue is still lacking. Furthermore, the specific contribution of individual cell behaviors, and how exactly these cell behaviors collectively lead to the morphogenesis and growth of tissues are not clear for many developmental and regenerative processes. A promising strategy to fill these gaps is the continuing effort of making developmental biology a quantitative science. Recent advances in methods, especially in imaging, enable measurements of cell behaviors and tissue shapes in unprecedented detail and accuracy. Consequently, formalizing hypotheses in terms of mathematical models to obtain testable quantitative predictions is emerging as a powerful tool. Tests of the hypotheses involve the comparison of model predictions to experimentally observed data. The available data is often noisy and based on only few samples. Hence, this comparison of data and model predictions often requires very careful use of statistical inference methods. If one chooses this quantitative approach, the challenges are the choice of observables, i.e. what to measure, and the design of appropriate data-driven models to answer relevant questions. In this thesis, I applied this data-driven modeling approach to vertebrate morphogenesis, growth and regeneration. In particular, I study spinal cord and muscle regeneration in axolotl, muscle development in zebrafish, and neuron development and maintenance in the adult human brain. To do so, I analyzed images to quantify cell behaviors and tissue shapes. Especially for cell behaviors in post-embryonic tissues, measurements of some cell behavior parameters, such as the proliferation rate, could not be made directly.
Hence, I developed mathematical models that are specifically designed to infer these parameters from indirect experimental data. To understand how cell behaviors shape tissues, I developed mechanistic models that causally connect the cell and tissue scales.
Specifically, I first investigated the behaviors of neural stem cells that underlie the regenerative outgrowth of the spinal cord after tail amputation in the axolotl. To do so, I quantified all relevant cell behaviors. A detailed analysis of the proliferation pattern in space and time revealed that the cell cycle is accelerated between 3-4 days after amputation in a high-proliferation zone, initially spanning from 800 µm anterior to the amputation plane. The activation of quiescent stem cells and cell movements into the high-proliferation zone also contribute to spinal cord growth but I did not find contributions by cellular rearrangements or cell shape changes. I developed a mathematical model of spinal cord outgrowth involving all contributing cell behaviors which revealed that the acceleration of the cell cycle is the major driver of spinal cord outgrowth. To compare the behavior of neural stem cells with cell behaviors in the regenerating muscle tissue that surrounds the spinal cord, I also quantified proliferation of mesenchymal progenitor cells and found similar proliferation parameters. I showed that the zone of mesenchymal progenitors that gives rise to the regenerating muscle segments is at least 350 µm long, which is consistent with the length of the high-proliferation zone in the spinal cord.
Second, I investigated shape changes in developing zebrafish muscle segments by quantifying time-lapse movies of developing zebrafish embryos. These data challenged or ruled out a number of previously proposed mechanisms. Motivated by reported cellular behaviors happening simultaneously in the anterior segments, I had previously proposed the existence of a simple tension-and-resistance mechanism that shapes the muscle segments. Here, I could verify the predictions of this mechanism for the final segment shape pattern. My results support the notion that a simple physical mechanism suffices to self-organize the observed spatiotemporal pattern in the muscle segments.
Third, I corroborated and refined previous estimates of neuronal cell turnover rates in the adult human hippocampus. Previous work approached this question by combining quantitative data and mathematical modeling of the incorporation of the carbon isotope 14C. I reanalyzed published data using the published deterministic neuron turnover model but I

extended the model by a better justified measurement error model. Most importantly, I found that human adult neurogenesis might occur at an even higher rate than currently believed. The tools I used throughout were (1) the careful quantification of the involved processes, mainly by image analysis, and (2) the derivation and application of mathematical models designed to integrate the data through (3) statistical inference. Mathematical models were used for different purposes such as estimating unknown parameters from indirect experiments, summarizing datasets with a few meaningful parameters, formalizing mechanistic hypotheses, as well as for model-guided experimental planning. I venture an outlook on how additional open questions regarding cell turnover measurements could be answered using my approach. Finally, I conclude that the mechanistic understanding of development and regeneration can be advanced by comparing quantitative data to the predictions of specifically designed mathematical models by means of statistical inference methods.