The focus has therefore gradually shifted from break something and \textit{see} what happens to break something and \textit{measure} what happens. The transition is supported by simultaneous advances in the resolution with which we can quantify the abundance of gene products during development. The state of the art has progressed from aggregate measurements of transcript and protein content across entire tissues, to \emph{in vivo} measurements of individual cells, to \emph{in situ} quantification of single-cell expression dynamics. These advances bestow mathematical models with the quantitative insight required to generate testable predictions for further experimental validation.

Unfortunately, quantitative techniques have not been universally adopted by the research community, leading to the sustained prevalence of subjective analysis in the literature. One plausible explanation is that quantification often demands computational proficiency that falls beyond the scope of many experimental labs. Interdisciplinary collaborations are becoming more frequent and should help alleviate this challenge, but they do not provide a permanent solution. These studies could benefit from the introduction of open-source automated analysis software platforms analogous to those that have revolutionized other subdisciplines of biology. For example, without the support of automated sequence alignment software, RNA-seq would be inaccessible to all but a few researchers with extensive programming and statistical modeling experience. Similar tools are therefore needed to support quantitative measurements of gene expression during development, thus lowering the barrier to adoption of data-driven modeling of cell fate decisions.

% \subsection{Deterministic models of developmental patterning}

% \subsection{Cell decisions in stochastic environments}

\section{Quantitative analysis of cell fate decisions}

Quantitative measurements and mathematical models promise to vastly broaden the depth and impact of studies that explore developmental cell fate decisions. They have previously been combined to ask how cell fates are reliably resolved from the spatiotemporal signaling cues encoded in GRN activity. Most such modeling efforts fall into one of two categories; those that directly reproduce measurements, and those that provide a toy representation of the underlying mechanism.

The first class of models strive to parameterize specific biomolecular interactions by fitting a model directly to data. Because development is an inherently dynamic process, these models typically describe the time-evolution of transcripts and proteins using systems of coupled differential equations that are reminiscent of those familiar to chemical engineers and ecologists. Despite the illusion of mechanistic detail, these models still deploy a healthy dose of abstraction. Essentially none of the commonly used rate represent true elementary reactions, instead opting for empirical representations such as linear degradation and cooperative binding kinetics. Nevertheless, many hypothesized cell fate decision mechanisms have been proposed and tested in this manner.

The Drosophila eye imaginal disc is a popular setting for data-driven modeling studies because cells positions relative to the

For instance, Graham

Several of these models attempt to explain photoreceptor specification in the developing eye. Melen et al proposes \cite{Melen}

Of particular relevance to later chapters of this dissertation is a bi-stable switch model proposed by Graham et al, in which two competing transcription factors controls photoreceptor specification the Drosophila eye. They used a cou

Atonal model 🡪 ommatidia

Bistable switch (deterministic)

Zero order ultrasense (deterministic)

Shilo PntP2 model (deterministic)

\cite{Graham2010}

\cite{Raj2010}

Perhaps the most interesting are those that capture dynamic features of gene expression

Development is an inherently dynamic process, as each stage of gene expression is responsible for triggering subsequent events in the developmental program. Unsurprisingly, many genes involved in the coordination of cell fate decisions have been shown to be transiently expressed within a given context.

round of cell fate decisions must trigger subsequent events in the developmental program.

and it becoming increasingly obvious that gene expression dynamics play

Mathematical models have also revealed that

As nuanced changes in expression yield abnormal morphologies in vivo, differences in protein levels manifest as differences in phenotype penetrance(Raj et al., 2010). I aim

Raj et al

Oodenarden

Anderson

Yi et al