1 - Introduction

The video on the left shows an early report on systematical RNA-Seq biases (starting at time index 12:09) presented on the Genome Informatics conference 2009. Observation from these days became the basis of first models that formed the Flux Simulator.
The Flux Simulator aims at modeling RNA-Seq experiments *in silico*: sequencing reads are produced from a reference genome according annotated transcripts. The simulation pipeline models different steps as modules, each with a minimal set of parameters that can be estimated by experimental parameters. The first step is-in fact-a transcriptome simulator. Subsequently, common sources of systematic bias in the abundance and distribution of produced reads are simulated by *in silico* library preparation and sequencing.

Our models do not simulate molecular processes on the level of atoms, but represent a collection of deterministic approaches with a minimal set of parameters that can be estimated from observations of the experiment that is to be reproduced. Model development has to be understood as an iterative process to a maximal convergence of "model world" and "real world". It always requires a careful evaluation of all hypotheses and assumptions by comparison with experimental data.