a tutorial paper. Hence we shall focus here on one major mathematical formalism, namely Ordinary Differential Equations (ODEs). Even here, a thorough survey of all the facets, including recent developments, is too formidable a task. Hence we shall concentrate on a major barrier that ODE-based approaches must overcome, namely, the parameter estimation problem. In addition, from among the many analysis techniques that have been — and are being — developed for ODEs-based models, we shall address the key technique of sensitivity analysis. Following this, we shall describe a novel probabilistic approximation technique that we have developed — in collaboration with David Hsu[11] — using which both the parameter estimation and sensitivity analysis tasks can be considerably eased.

In the next section we introduce the notions of model construction, calibration, validation and analysis. In Sec. 3, we provide a brief overview of the prevalent modeling formalisms. In Sec. 4, we discuss model calibration, also known as parameter estimation. This is followed by a brief discussion of model validation in Sec. 5. In Sec. 6, we turn to important model analysis techniques with the main focus on sensitivity analysis. Finally, we present a recently developed probabilistic approximation method by which a system of ODEs modeling a biochemical network is approximated as a dynamic Bayesian network,[11]. In the concluding section, we summarize the contents of the paper and sketch some future research directions.

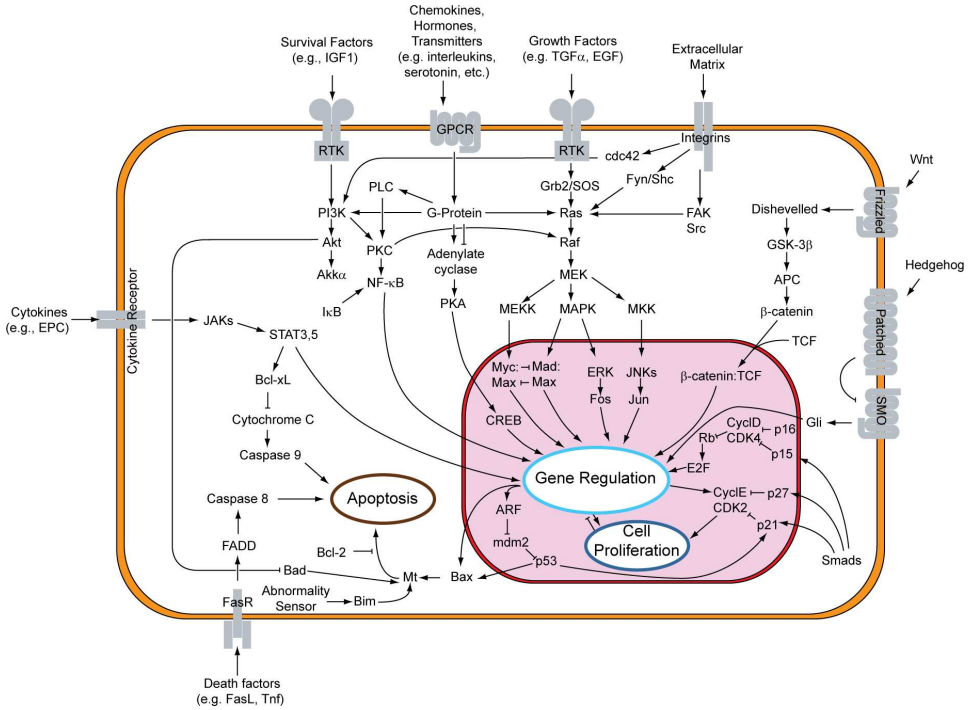

Fig. 2. Overview of some of the important signaling pathways.[8]