This dissertation focuses on the design of two new algorithmic techniques for the automatic synthesis of parameters in probabilistic models.

The first algorithm finds the model’s parameters by reducing the task to a repeated probabilistic model checking problem, and using sequential hypothesis testing and simulated annealing to efficiently solve it. As a case study, we applied this technique to analyze a model of glucose-insulin metabolism. An important problem was to find model states, if any, where the patient exhibits behaviors that indicate a diabetic or prediabetic condition. We successfully answered this question by synthesizing values of three parameters (viz. pancreatic responsivity to glucose rate of change, pancreatic response to glucose, and the delay between glucose signal and insulin secretion) that ensure that the glucose-insulin subsystem spends at least 20 minutes in a diabetic scenario—conditions that confirm the capability of the model to represent diabetic behavior.

The second algorithm discovers parameters using a combination of a stochastic optimization metaheuristic, hypothesis testing, and Bayesian statistical model checking. We applied this algorithm to discover the amount and schedule of doses (i.e., the parameters) of bacterial lipopolysaccharide (LPS) in an agent-based acute inflammatory response model given expert-provided specifications describing desired clinical outcomes. We synthesized values of twenty-eight unknown parameters such that the model instantiated with the synthesized parameter values satisfies four specifications describing the dynamic behavior of the model in response to administration of LPS.

We have thus demonstrated how our formal methods based algorithmic approaches that exploit probabilistic verification, statistical hypothesis testing, and mathematical optimization metaheuristics, can be used to efficiently and automatically synthesize parameters of complex probabilistic models.