A wide range of stochastic systems in the area of manufacturing, transportation, finance, logistics and communication can be modeled as discrete event systems (DES). In general, however, “real world” DESs either do not conform to some assumptions we made in order to obtain a solution, or they are just too complex to yield analytical solutions. In such cases, simulation becomes a very attractive tool for performance evaluation and optimization of DESs. Consequently, the derivatives of the performance measures have to be estimated, which leads to the problem of finding efficient unbiased gradient estimators. From a practical point of view, gradient estimators should, 1) be easy to implement, 2) have low variance and 3) have a low computational effort. This thesis is devoted to developing efficient gradient estimation methods for optimization of DESs and to applying these resulting algorithms to real-life problems.