

**STOCHASTIC APPROXIMATION AND ITS
APPLICATIONS (NONCONVEX OPTIMIZATION AND ITS
APPLICATIONS)**

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Because the problem is non-convex, we use a hybrid optimization strategy, consisting of the evolutionary-based CMA-ES algorithm Covariance Matrix Adaptation Evolution Strategy Hansen and Ostermeier, in combination with a subsequent gradient-based optimizer. Thus the exact evaluation of $f(x)$ is impossible to evaluate and it is necessary to use simulation to estimate the objective function value. Multistep signaling cascades are enrolled in many signal-transduction processes. In the parameter space, we derive the normal equivalents of log-normal expectation and covariance to calculate the normal sigma-points, which we then exponentiate see Supplementary Material. In particular, in machine learning, the need to set a learning rate step size has been recognized as problematic. After that, in order to come closer to the solution, the step size is decreased and again the fixed step size is used until the ring around the solution is sufficiently tighten up.

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