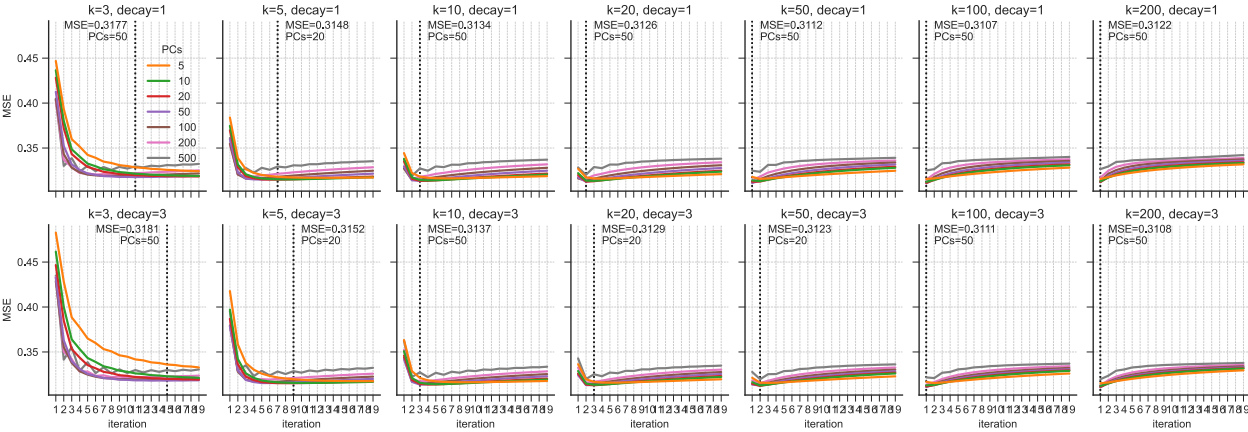


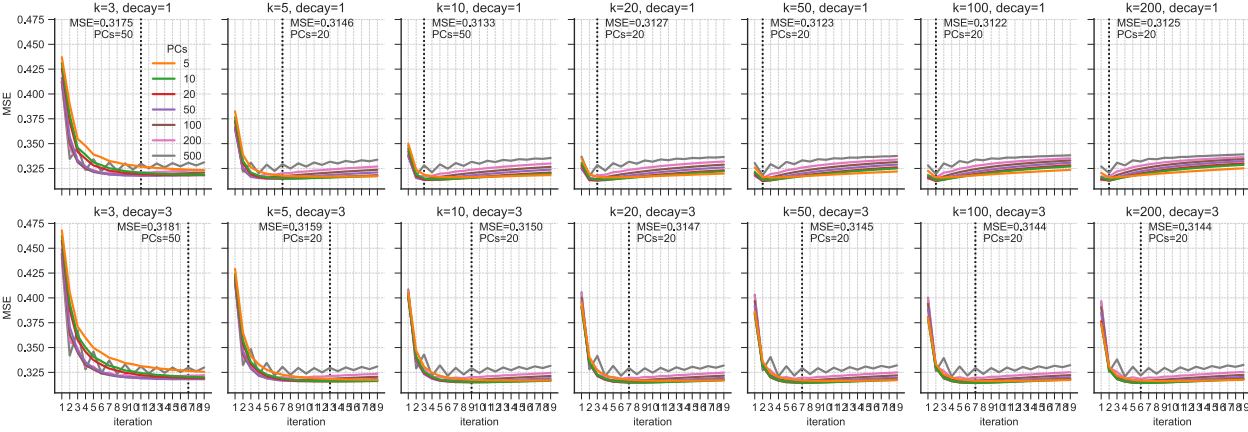
Denoise type=mean, distances

Optimal: MSE=0.3107, it=1, PCs=50, k=100



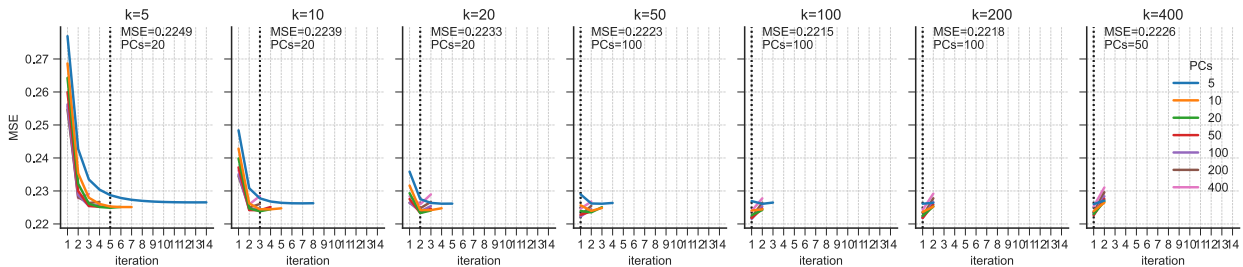
Denoise type=mean, connectivities

Optimal: MSE=0.3122, it=2, PCs=20, k=100

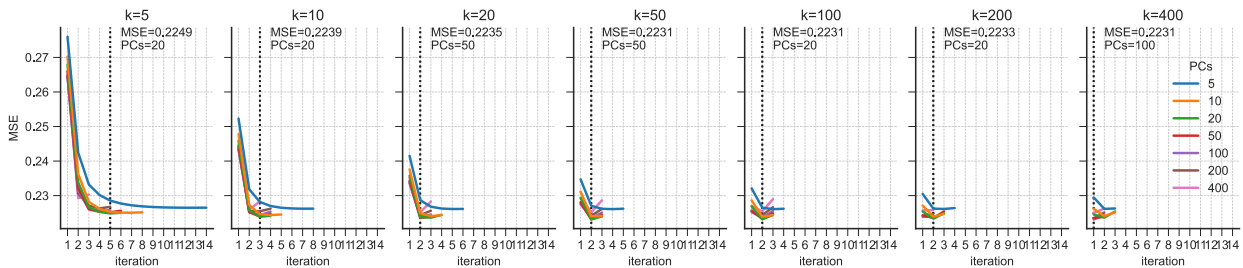


(A) BM data. DEWAKSS objective function values, mean square error, MSE during optimization of a range of hyperparameters, number of principal components (PCs) = {5, 10, 20, 50, 100, 200, 500}, number of initial neighbors (k) = {3, 5, 10, 20, 50, 100, 200} and decay = {1, 3}. Optimal settings are found to be 50 PCs, decay = 1, and k = 100 with MSE = 0.3107

Denoise type=mean, distances
Optimal: MSE=0.2215, it=1, PCs=100, k=100

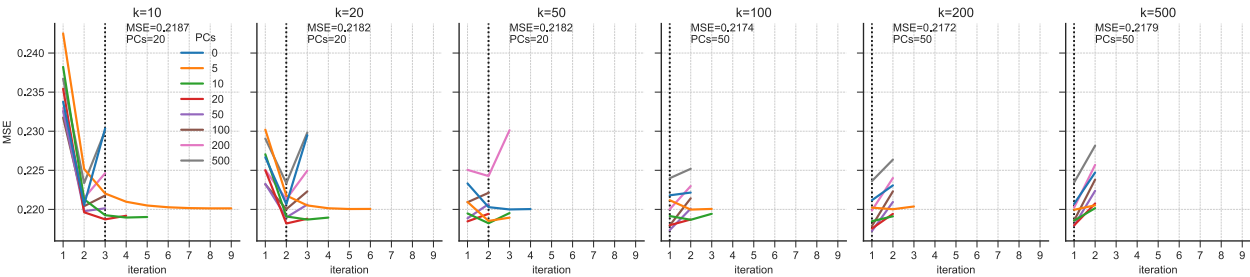


Denoise type=mean, connectivities
Optimal: MSE=0.2231, it=1, PCs=100, k=400

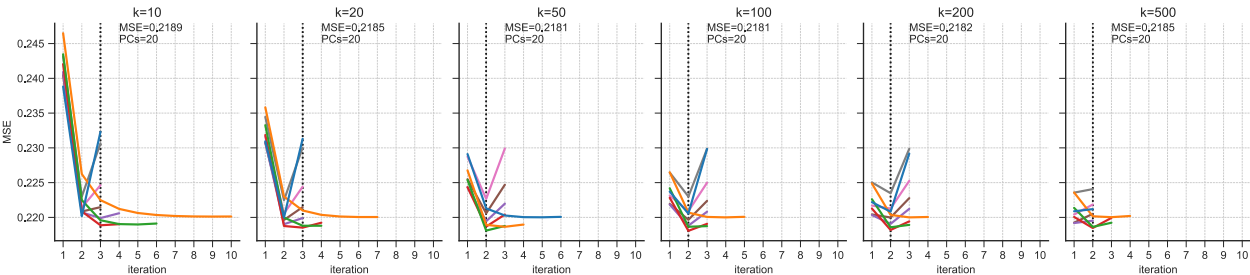


(B) EMT data. DEWÄKSS objective function values, mean square error, MSE during optimization of a range of hyperparameters, number of principal components (PCs) = {5, 10, 20, 50, 100, 200, 400}, number of initial neighbors (k) = {5, 10, 20, 50, 100, 200, 400}. The top row uses distances on the kNN-G and the bottom row uses connectivities of the kNN-G. Optimal settings are found to be 100PCs, $k = 100$ using distances with MSE = 0.2215. The algorithm's option to stop after the minimum is found is used here to stop the algorithm once the optimum (min MSE) is found.

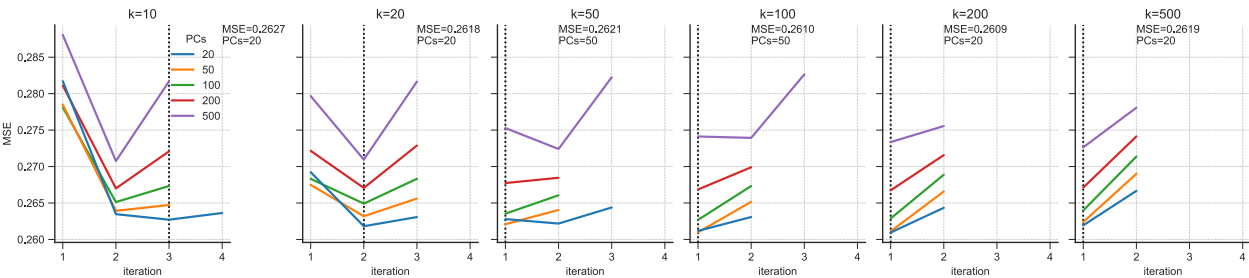
Denoise type=mean, distances
Optimal: MSE=0.2172, it=1, PCs=50, k=200



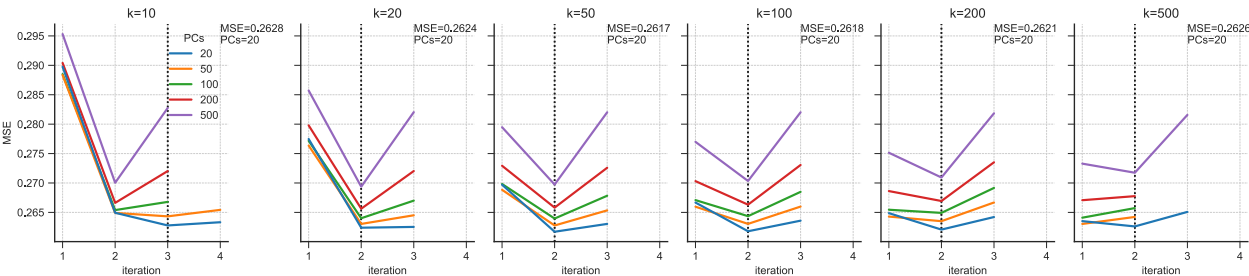
Denoise type=mean, connectivities
Optimal: MSE=0.2181, it=2, PCs=20, k=100



Denoise type=mean, distances
Optimal: MSE=0.2609, it=1, PCs=20, k=200

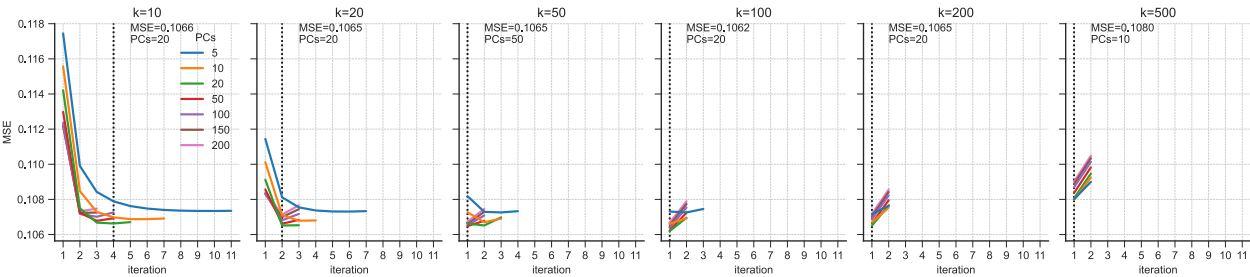


Denoise type=mean, connectivities
Optimal: MSE=0.2617, it=2, PCs=20, k=50

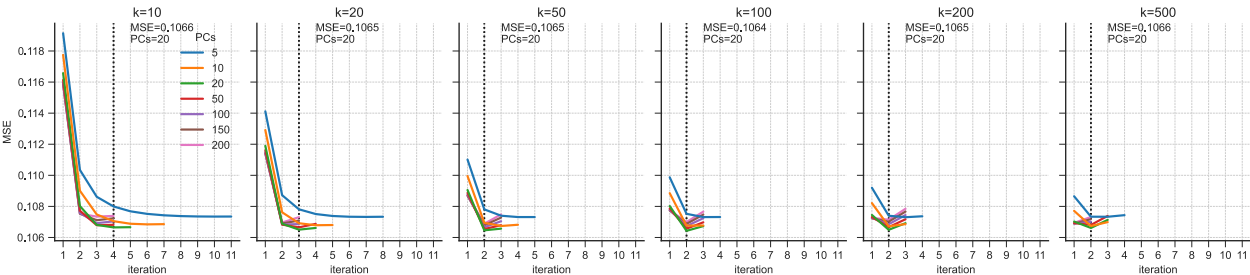


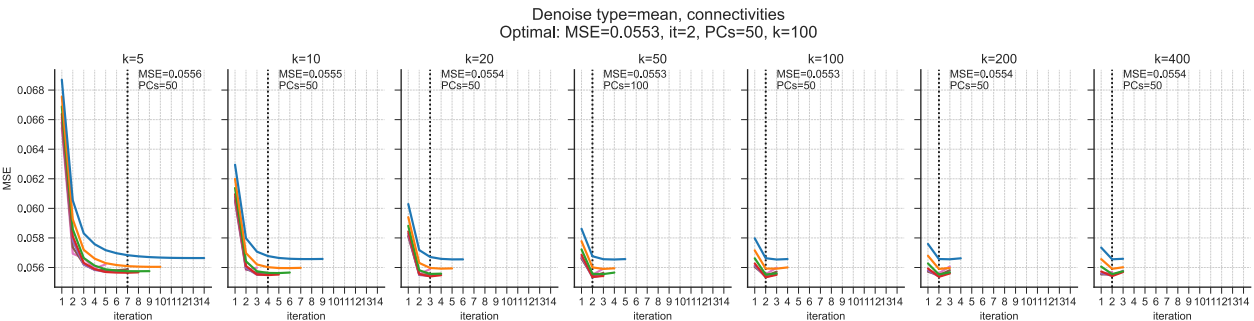
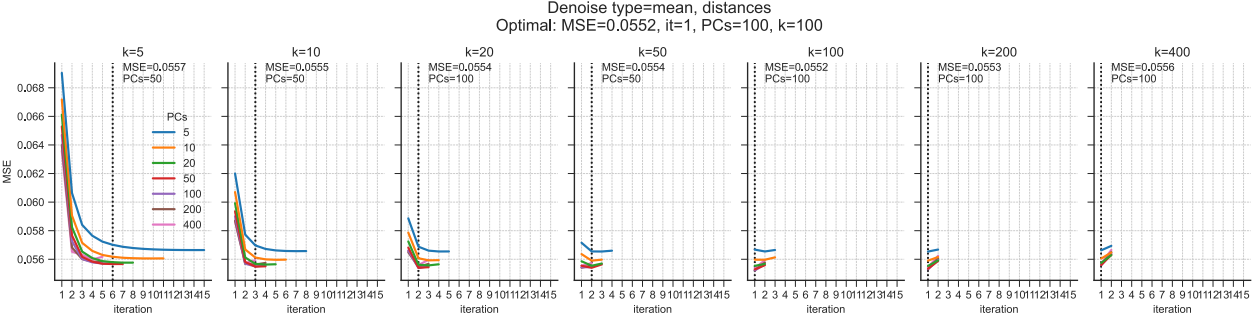
(D) Jackson et al. [21] YPDRapa growth condition

Denoise type=mean, distances
Optimal: MSE=0.1062, it=1, PCs=20, k=100



Denoise type=mean, connectivities
Optimal: MSE=0.1064, it=2, PCs=20, k=100





(F) La Manno et al. [25] DentateGyrus

S6 Fig: Optimal hyperparameter search for single-cell datasets. Each figure shows the algorithm, using distances (top row) and connectivities (bottom row). Each panel is scaled to the maximum number of observed iterations (x-axis) for any configuration run, with the objective function value MSE on the y-axis. The colored lines indicate the number of PCs used as input in the kNN-G distance computation. Each column corresponds to the initial number of neighbors k used for constructing the kNN-G.