Table A1. Simulation study with sample of size 20 and 4000 genes. Two simulation setups are considered. Case 1: No genes are differentially expressed between the two classes. Case 2: Gene expression levels of class 0 patients follow normal distribution with mean 0; for class 1 patients, the 2% differentially expressed genes follow normal mixtures, half with mean $\mu_1 = 0.5$ and half with mean $\mu_2 = 1.5$. The "true" prediction error $\tilde{e}_n$ is the misclassification rate when a prediction rule built on the sample is tested on 1000 independent data with the same structure. Feature selection is performed prior to each application of DLDA or 1NN by choosing the 10 genes having the largest absolute-value t-statistics.

Classifier	Prediction Error Estimation Method	Case 1: No differential genes				Case 2: 2% differential genes			
		Est.	STD	Bias	MSE	Est.	STD	Bias	MSE
DLDA	"True" Error ($\tilde{e}_n$)	0.500	0.016			0.060	0.036		
	Resubstitution	0.002	0.010	**-0.498**	0.249	0.000	0.003	**-0.060**	0.005
	Ordinary Bootstrap	0.196	0.019	**-0.304**	0.093	0.096	0.031	0.035	0.003
	Bootstrap Cross Validation	0.206	0.019	**-0.294**	0.087	0.105	0.032	0.045	0.004
	.632 Bootstrap	0.346	0.033	**-0.154**	0.025	0.168	0.054	**0.108**	0.015
	LOOCV	0.547	**0.219**	0.047	0.050	0.081	**0.096**	0.021	0.009
	Out-Of-Bag Estimation	0.632	**0.160**	**0.132**	0.043	0.093	**0.097**	0.032	0.010
	Leave-One-Out Bootstrap	0.547	0.051	0.046	0.005	0.266	0.086	**0.206**	0.049
	.632+ Bootstrap	0.524	0.044	0.024	0.003	0.216	0.086	**0.155**	0.031
	Adjusted Bootstrap	0.549	0.132	0.049	0.020	0.095	0.094	0.034	0.009

Table A2. Simulation study with sample of size 100 and 4000 genes. Two simulation setups are considered. Case 1: No genes are differentially expressed between the two classes. Case 2: Gene expression levels of class 0 patients follow normal distribution with mean 0; for class 1 patients, the 2% differentially expressed genes follow normal distribution with mean $\mu = 1.5$. The "true" prediction error $\tilde{e}_n$ is the misclassification rate when a prediction rule built on the sample is tested on 1000 independent data with the same structure. Feature selection is performed prior to each application of DLDA or 1NN by choosing the 10 genes having the largest absolute-value t-statistics.

Classifier	Prediction Error Estimation Method	Case 1: No differential genes				Case 2: 2% differential genes			
		Est.	STD	Bias	MSE	Est.	STD	Bias	MSE
DLDA	"True" Error ($\tilde{e}_n$)	0.500	0.015			0.020	0.006		
	Resubstitution	0.140	0.029	**-0.360**	0.131	0.004	0.006	**-0.016**	0.0003
	Ordinary Bootstrap	0.266	0.011	**-0.233**	0.055	0.010	0.004	**-0.010**	0.0001
	Bootstrap Cross Validation	0.268	0.014	**-0.232**	0.054	0.010	0.004	**-0.010**	0.0001
	.632 Bootstrap	0.371	0.020	**-0.129**	0.017	0.015	0.006	**-0.005**	0.0001
	LOOCV	0.506	**0.127**	0.006	0.016	0.020	**0.018**	0.000	0.0003
	Out-Of-Bag Estimation	0.516	**0.074**	0.016	0.006	0.003	0.005	**-0.017**	0.0004
	Leave-One-Out Bootstrap	0.506	0.022	0.006	0.001	0.021	0.007	0.001	0.0001
	.632+ Bootstrap	0.498	0.023	-0.002	0.001	0.015	0.006	**-0.005**	0.0001
	Adjusted Bootstrap	0.506	0.048	0.006	0.003	0.021	0.010	0.001	0.0001

Table A3. Simulation study with sample of size 20 and 800 genes. Two simulation setups are considered. Case 1: No genes are differentially expressed between the two classes. Case 2: Gene expression levels of class 0 patients follow normal distribution with mean 0; for class 1 patients, the 2% differentially expressed genes follow normal mixtures, half with mean $\mu_1 = 0.5$ and half with mean $\mu_2 = 1.5$. The "true" prediction error $\tilde{e}_n$ is the misclassification rate when a prediction rule built on the sample is tested on 1000 independent data with the same structure. Feature selection is performed prior to each application of DLDA or 1NN by choosing the **30** genes having the largest absolute-value t-statistics.

Classifier	Prediction Error Estimation Method	Case 1: No differential genes				Case 2: 2% differential genes			
		Est.	STD	Bias	MSE	Est.	STD	Bias	MSE
DLDA	"True" Error ($\tilde{e}_n$)	0.500	0.015			0.199	0.051		
	Resubstitution	0.000	0.004	**-0.500**	0.250	0.000	0.003	**-0.199**	0.042
	Ordinary Bootstrap	0.200	0.023	**-0.300**	0.091	0.137	0.033	**-0.062**	0.006
	Bootstrap Cross Validation	0.211	0.024	**-0.289**	0.085	0.146	0.034	**-0.052**	0.005
	.632 Bootstrap	0.352	0.040	**-0.148**	0.024	0.241	0.058	0.043	0.005
	LOOCV	0.553	**0.184**	0.053	0.037	0.240	**0.154**	0.041	0.022
	Out-Of-Bag Estimation	0.620	**0.152**	**0.120**	0.038	0.293	**0.156**	0.094	0.029
	Leave-One-Out Bootstrap	0.557	0.064	0.057	0.008	0.382	0.091	**0.183**	0.040
	.632+ Bootstrap	0.530	0.054	0.030	0.004	0.342	0.106	**0.144**	0.029
	Adjusted Bootstrap	0.556	0.124	0.056	0.019	0.273	0.128	0.075	0.018

Table A4. Simulation study with sample of size 100 and 800 genes. Two simulation setups are considered. Case 1: No genes are differentially expressed between the two classes. Case 2: Gene expression levels of class 0 patients follow normal distribution with mean 0; for class 1 patients, the 2% differentially expressed genes follow normal distribution with mean $\mu = 1.5$. The "true" prediction error $\tilde{e}_n$ is the misclassification rate when a prediction rule built on the sample is tested on 1000 independent data with the same structure. Feature selection is performed prior to each application of DLDA or 1NN by choosing the **30** genes having the largest absolute-value t-statistics.

Classifier	Prediction Error Estimation Method	Case 1: No differential genes				Case 2: 2% differential genes			
		Est.	STD	Bias	MSE	Est.	STD	Bias	MSE
DLDA	"True" Error ($\tilde{e}_n$)	0.500	0.016			0.037	0.006		
	Resubstitution	0.091	0.025	**-0.409**	0.168	0.019	0.013	**-0.018**	0.0005
	Ordinary Bootstrap	0.247	0.016	**-0.253**	0.065	0.025	0.011	**-0.012**	0.0003
	Bootstrap Cross Validation	0.248	0.017	**-0.252**	0.064	0.025	0.011	**-0.012**	0.0003
	.632 Bootstrap	0.353	0.023	**-0.147**	0.022	0.034	0.015	**-0.003**	0.0002
	LOOCV	0.508	**0.106**	0.008	0.012	0.037	0.020	-0.001	0.0004
	Out-Of-Bag Estimation	0.512	**0.069**	0.012	0.005	0.035	0.018	**-0.002**	0.0004
	Leave-One-Out Bootstrap	0.506	0.030	0.006	0.001	0.043	0.017	0.006	0.0003
	.632+ Bootstrap	0.495	0.031	-0.004	0.001	0.034	0.015	**-0.003**	0.0002
	Adjusted Bootstrap	0.505	0.050	0.005	0.003	0.039	0.017	0.001	0.0003