Issues in developing multivariable molecular signatures for guiding clinical care decisions: supplemental simulation results

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Additional Simulation Results

In the tables and figures below, N is to the number of samples, and p is the number of variables per sample. All results are from 1000 simulation replicates.

Table 1: Comparison of different approaches to estimating the Area Under the ROC Curve (AUC) and the log odds ratio (OR) in the setting where a dataset is used to both develop the signature and evaluate its performance. The true value of the AUC is 0.5 and the true value of the Log OR is 0.0. Estimates are based on 1000 replicates of the numerical experiment. In each replicate, N = 1000; p = 10 . CV = Cross validation.

Approach	mean AUC	std.dev AUC	Bias AUC	mean OR	std.dev OR	Bias OR
Resubstitution	0.56	0.01	0.06	0.34	0.12	0.34
Partial CV	0.50	0.03	0.00	-0.01	0.18	-0.01
Partial Holdout	0.50	0.03	0.00	0.00	0.20	0.00
Partial Resubstitution	0.54	0.02	0.04	0.24	0.13	0.24
Pre-validation	0.49	0.03	-0.01	-0.02	0.18	-0.02
Leave 10 out CV	0.50	0.03	0.00	0.01	0.18	0.01
Leave 100 out CV	0.50	0.03	0.00	0.00	0.17	0.00
30% Holdout	0.50	0.04	0.00	-0.01	0.24	-0.01
50% Holdout	0.50	0.03	0.00	0.00	0.19	0.00
Bootstrap	0.50	0.02	0.00	0.00	0.11	0.00

Table 2: Comparison of different approaches to estimating the Area Under the ROC Curve (AUC) and the log odds ratio (OR) in the setting where a dataset is used to both develop the signature and evaluate its performance. The true value of the AUC is 0.5 and the true value of the Log OR is 0.0. Estimates are based on 1000 replicates of the numerical experiment. In each replicate, N = 1000; p = 100 . CV = Cross validation.

Approach	mean AUC	std.dev AUC	Bias AUC	mean OR	std.dev OR	Bias OR
Resubstitution	0.66	0.01	0.16	0.95	0.12	0.95
Partial CV	0.61	0.02	0.11	0.59	0.13	0.59
Partial Holdout	0.59	0.03	0.09	0.51	0.19	0.51
Partial Resubstitution	0.61	0.02	0.11	0.66	0.13	0.66
Pre-validation	0.50	0.04	0.00	-0.02	0.26	-0.02
Leave 10 out CV	0.50	0.04	0.00	0.00	0.21	0.00
Leave 100 out CV	0.50	0.03	0.00	0.00	0.19	0.00
30% Holdout	0.50	0.03	0.00	0.00	0.25	0.00
50% Holdout	0.50	0.03	0.00	0.00	0.20	0.00
Bootstrap	0.50	0.02	0.00	0.00	0.10	0.00

Table 3: Comparison of different approaches to estimating the Area Under the ROC Curve (AUC) and the log odds ratio (OR) in the setting where a dataset is used to both develop the signature and evaluate its performance. The true value of the AUC is 0.5 and the true value of the Log OR is 0.0. Estimates are based on 1000 replicates of the numerical experiment. In each replicate, N = 1000; p = 500 . CV = Cross validation.

Approach	mean AUC	std.dev AUC	Bias AUC	mean OR	std.dev OR	Bias OR
Resubstitution	0.72	0.01	0.22	1.33	0.11	1.33
Partial CV	0.68	0.01	0.18	1.03	0.11	1.03
Partial Holdout	0.66	0.02	0.16	0.96	0.18	0.96
Partial Resubstitution	0.65	0.02	0.15	0.89	0.13	0.89
Pre-validation	0.50	0.06	0.00	-0.01	0.33	-0.01
Leave 10 out CV	0.50	0.04	0.00	0.00	0.25	0.00
Leave 100 out CV	0.50	0.03	0.00	0.00	0.21	0.00
30% Holdout	0.50	0.03	0.00	0.00	0.24	0.00
50% Holdout	0.50	0.03	0.00	0.00	0.20	0.00
Bootstrap	0.50	0.01	0.00	0.00	0.08	0.00

Table 4: Comparison of different approaches to estimating the Area Under the ROC Curve (AUC) and the log odds ratio (OR) in the setting where a dataset is used to both develop the signature and evaluate its performance. The true value of the AUC is 0.5 and the true value of the Log OR is 0.0. Estimates are based on 1000 replicates of the numerical experiment. In each replicate, N = 200; p = 10 . CV = Cross validation.

Approach	mean AUC	std.dev AUC	Bias AUC	mean OR	std.dev OR	Bias OR
Resubstitution	0.63	0.03	0.13	0.78	0.27	0.78
Partial CV	0.50	0.08	0.00	-0.01	0.35	-0.01
Partial Holdout	0.50	0.06	0.00	-0.02	0.43	-0.02
Partial Resubstitution	0.60	0.04	0.10	0.56	0.31	0.56
Pre-validation	0.50	0.06	0.00	0.02	0.40	0.02
Leave 10 out CV	0.50	0.08	0.00	0.00	0.34	0.00
Leave 100 out CV	0.50	0.07	0.00	0.00	0.39	0.00
30% Holdout	0.50	0.08	0.00	0.02	0.53	0.02
50% Holdout	0.50	0.06	0.00	0.01	0.43	0.01
Bootstrap	0.50	0.04	0.00	-0.01	0.24	-0.01

Table 5: Comparison of different approaches to estimating the Area Under the ROC Curve (AUC) and the log odds ratio (OR) in the setting where a dataset is used to both develop the signature and evaluate its performance. The true value of the AUC is 0.5 and the true value of the Log OR is 0.0. Estimates are based on 1000 replicates of the numerical experiment. In each replicate, N = 200; p = 100 . CV = Cross validation.

Approach	mean AUC	std.dev AUC	Bias AUC	mean OR	std.dev OR	Bias OR
Resubstitution	0.84	0.03	0.34	2.32	0.37	2.32
Partial CV	0.71	0.04	0.21	1.21	0.34	1.21
Partial Holdout	0.67	0.06	0.17	1.00	0.45	1.00
Partial Resubstitution	0.72	0.04	0.22	1.40	0.33	1.40
Pre-validation	0.50	0.07	0.00	0.01	0.41	0.01
Leave 10 out CV	0.50	0.07	0.00	0.00	0.41	0.00
Leave 100 out CV	0.50	0.07	0.00	0.03	0.43	0.03
30% Holdout	0.49	0.08	-0.01	-0.04	0.52	-0.04
50% Holdout	0.50	0.06	0.00	0.00	0.44	0.00
Bootstrap	0.50	0.04	0.00	-0.01	0.21	-0.01

Table 6: Comparison of different approaches to estimating the Area Under the ROC Curve (AUC) and the log odds ratio (OR) in the setting where a dataset is used to both develop the signature and evaluate its performance. The true value of the AUC is 0.5 and the true value of the Log OR is 0.0. Estimates are based on 1000 replicates of the numerical experiment. In each replicate, N = 200; p = 500 . CV = Cross validation.

Approach	mean AUC	std.dev AUC	Bias AUC	mean OR	std.dev OR	Bias OR
Resubstitution	0.92	0.02	0.42	3.42	0.58	3.42
Partial CV	0.83	0.03	0.33	2.07	0.30	2.07
Partial Holdout	0.76	0.07	0.26	1.77	0.54	1.77
Partial Resubstitution	0.74	0.03	0.24	1.62	0.30	1.62
Pre-validation	0.50	0.08	0.00	0.00	0.48	0.00
Leave 10 out CV	0.50	0.07	0.00	0.02	0.45	0.02
Leave 100 out CV	0.50	0.08	0.00	0.00	0.45	0.00
30% Holdout	0.50	0.08	0.00	0.00	0.54	0.00
50% Holdout	0.50	0.05	0.00	0.03	0.45	0.03
Bootstrap	0.50	0.03	0.00	0.00	0.17	0.00

Table 7: Comparison of different approaches to estimating the Area Under the ROC Curve (AUC) and the log odds ratio (OR) in the setting where a dataset is used to both develop the signature and evaluate its performance. The true value of the AUC is 0.5 and the true value of the Log OR is 0.0. Estimates are based on 1000 replicates of the numerical experiment. In each replicate, N = 200; p = 5000 . CV = Cross validation.

Approach	mean AUC	std.dev AUC	Bias AUC	mean OR	std.dev OR	Bias OR
Resubstitution	0.97	0.01	0.47	4.86	0.77	4.86
Partial CV	0.90	0.02	0.40	2.75	0.27	2.75
Partial Holdout	0.80	0.06	0.30	2.53	0.68	2.53
Partial Resubstitution	0.76	0.03	0.26	1.62	0.33	1.62
Pre-validation	0.50	0.06	0.00	0.00	0.43	0.00
Leave 10 out CV	0.50	0.07	0.00	0.00	0.44	0.00
Leave 100 out CV	0.49	0.09	-0.01	-0.05	0.51	-0.05
30% Holdout	0.50	0.06	0.00	0.03	0.55	0.03
50% Holdout	0.51	0.06	0.01	0.06	0.43	0.06
Bootstrap	0.50	0.02	0.00	-0.01	0.13	-0.01

N = 1000; p = 10

N = 1000; p = 100

N = 1000; p = 500

N = 200; p = 10

N = 200; p = 100

N = 200; p = 500

N = 200; p = 5000

N = 1000; p = 10

N = 1000; p = 100

N = 1000; p = 500

N = 200; p = 10

N = 200; p = 100

N = 200; p = 500

N = 200; p = 5000