

Supplemental file for the manuscript:

Comparative Analysis of Six Correlation Metrics on Identifying DNA Co-Methylation Patterns

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Supplemental 8x8 tables

Table S1 includes a few 8x8 matrices comparing correlation scores computed for pairs using different sample sizes (10, 30, and 53). Pink cells have counts comprising 20%-40% of the row total. Blue cells have counts comprising 40%-70% of the row total. Green cells have counts comprising 70%-100% of the row totals.

The 8x8 matrices in Table S1 show a much stronger agreement (indicated by stronger diagonals) between the 30N and 53N sample correlations as opposed to the comparisons with the 10 sample correlations. This stronger diagonal is evident when comparing sample sizes for every metric and data type. Specifically, for all 30N x 53N 8x8 tables, at least 80% of the correlations generated with 30 samples fell within the corresponding diagonal cell of the 53N 8x8 table or one cell to the right or left. This indicated that most CG pairs consistently received similar correlation scores using 30 samples as compared to 53 samples. This strong agreement was not present when comparing 10N and 30N correlation scores, or when comparing 10N and 53N correlation scores. In general, there appeared to be a strong tendency for higher sample sizes (30N and 53N) to assign lower scores to many of the pairs that have high correlations scores when only 10 samples are provided. As a result, the 8x8 tables for 30N and 53N samples show a higher concentration of scores in the most crowded intervals for each metric ($[-0.25, 0]$ and $[0, 0.25]$ for Pearson, Spearman, and Kendall correlations; $[0, 0.25]$ for Hoeffding; $[0.25, 0.5]$ for Distance and MIC correlations).

Table S1: 8x8 matrices comparing correlation scores with different sample sizes

A. B.Pearson

B.Pearson.10kx10k.30N [-1,-0.75]*10k.30N [-0.75,-0.5]*10k.30N [-0.5,-0.25]*kx10k.30N [-0.25,0]*kx10k.30N [0.0,0.25]*x10k.30N [0.25,0.5]*x10k.30N [0.5,0.75]*kx10k.30N [0.75,1]																	Total Count
B.pearson.10kx10k.10N [-1,-0.75]	6.4%	4761	21.075%	157261	24.157%	180255	21.569%	160947	15.746%	117496	7.891%	58885	2.525%	18844	0.632%	4718	746167
B.pearson.10kx10k.10N [-0.75,-0.5]	0.946%	36985	8.814%	344396	19.913%	778103	25.635%	1001662	23.407%	914601	14.287%	558259	5.441%	212602	1.554%	60741	3907349
B.pearson.10kx10k.10N [-0.5,-0.25]	0.444%	36585	4.619%	380619	15.011%	1236852	24.679%	2033482	26.21%	2159653	18.511%	1525292	8.034%	662055	2.489%	205148	8239686
B.pearson.10kx10k.10N [-0.25,0]	0.359%	40831	3.107%	353173	11.342%	1289317	22.184%	2521711	17.349%	3108847	21.914%	2490997	10.397%	1181892	3.344%	380212	11369800
B.pearson.10kx10k.10N [0.0,0.25]	0.315%	36543	2.317%	268808	8.702%	1009525	18.964%	2200044	27.36%	3173966	25.23%	2926931	13.011%	1509456	4.097%	475331	11606064
B.pearson.10kx10k.10N [0.25,0.5]	0.255%	22373	1.673%	146713	6.427%	563349	15.367%	1346943	25.63%	2246516	28.448%	2493488	17.195%	1507169	5.003%	438518	8765069
B.pearson.10kx10k.10N [0.5,0.75]	0.172%	7638	1.059%	46853	4.124%	182480	10.928%	483504	21.184%	937214	29.761%	1316691	25.365%	1122170	7.403%	327529	4420479
B.pearson.10kx10k.10N [0.75,1]	0.064%	611	0.441%	4169	1.784%	16683	5.374%	50788	12.512%	118252	23.334%	220523	35.579%	336248	20.909%	197612	945066
B.Pearson.10kx10k.53N [-1,-0.75]*10k.53N [-0.75,-0.5]*10k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]																	Total Count
B.pearson.10kx10k.10N [-1,-0.75]	6.08%	45367	22.39%	167074	24.202%	180589	23.544%	175684	16.236%	121155	5.981%	44633	1.308%	9767	0.254%	1898	746167
B.pearson.10kx10k.10N [-0.75,-0.5]	0.511%	19985	7.169%	280119	19.644%	767590	30.614%	1196220	26.675%	1042320	11.71%	457556	2.998%	117148	0.675%	26411	3907349
B.pearson.10kx10k.10N [-0.5,-0.25]	0.152%	12564	2.874%	236884	13.821%	1138849	29.751%	2451421	31.505%	2595928	16.126%	1328789	4.657%	383748	1.11%	91503	8239686
B.pearson.10kx10k.10N [-0.25,0]	0.119%	13626	1.745%	198376	10.248%	1164898	26.532%	3015911	33.671%	3827427	19.937%	2266324	6.214%	706444	1.53%	173974	11369800
B.pearson.10kx10k.10N [0.0,0.25]	0.104%	12078	1.294%	150124	7.925%	919409	22.877%	2653982	34.059%	3951140	23.806%	2741660	8.037%	932426	1.894%	219785	11606064
B.pearson.10kx10k.10N [0.25,0.5]	0.083%	7309	0.937%	82197	5.92%	518957	18.624%	1632432	32.385%	2838634	28.236%	2474960	11.478%	1006138	2.332%	204442	8765069
B.pearson.10kx10k.10N [0.5,0.75]	0.054%	2419	0.582%	25757	3.747%	165801	13.199%	583959	26.834%	1187161	31.6%	1398011	20.072%	888002	3.909%	172969	4420479
B.pearson.10kx10k.10N [0.75,1]	0.023%	219	0.219%	2070	1.578%	14920	6.56%	60077	15.519%	146669	25.598%	241918	33.845%	319859	16.859%	159334	945066
B.Pearson.10kx10k.53N [-1,-0.75]*10k.53N [-0.75,-0.5]*10k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]																	Total Count
B.pearson.10kx10k.30N [-1,-0.75]	39.459%	90492	51.964%	119169	7.757%	17791	0.78%	1790	0.035%	81	0.001%	4	0%	0	0%	0	229327
B.pearson.10kx10k.30N [-0.75,-0.5]	1.174%	19991	45.186%	769078	46.491%	791279	6.575%	111920	0.516%	8792	0.05%	863	0.003%	68	0%	1	1701992
B.pearson.10kx10k.30N [-0.5,-0.25]	0.033%	1746	4.175%	219488	55.23%	2903346	37.047%	1947515	3.263%	171542	0.223%	11724	0.024%	1296	0.001%	87	5256744
B.pearson.10kx10k.30N [-0.25,0]	0.009%	920	0.257%	25197	10.634%	1042123	65.116%	6380824	22.986%	2252473	0.908%	89008	0.082%	8083	0.004%	453	9799081
B.pearson.10kx10k.30N [0.0,0.25]	0.002%	358	0.063%	8097	0.787%	100562	23.752%	3034696	65.214%	8332154	9.93%	1268824	0.239%	30613	0.009%	1241	12776545
B.pearson.10kx10k.30N [0.25,0.5]	0%	57	0.012%	1479	0.129%	10502	2.385%	276521	39.865%	4620876	54.235%	6286522	3.342%	387455	0.027%	3154	11591066
B.pearson.10kx10k.30N [0.5,0.75]	0%	3	0.001%	92	0.013%	906	0.243%	15963	4.803%	314629	49.295%	3229909	44.795%	2934329	0.846%	55424	6550436
B.pearson.10kx10k.30N [0.75,1]	0%	0	0%	1	0%	4	0.021%	457	0.473%	9887	4.202%	87816	47.932%	1001688	47.37%	989956	2089809

B. Spearman

Spearman.10kx10k.30N [-1,-0.75]*k.30k.30N [-0.75,-0.5]*k.30k.30N [-0.5,-0.25]*kx10k.30N [-0.25,0]*kx10k.30N [0.0,0.25]*x10k.30N [0.25,0.5]*x10k.30N [0.5,0.75]*kx10k.30N [0.75,1]																	Total Count
Spearman.10kx10k.10N [-1,-0.75]	7.452%	56832	22.348%	170424	26.049%	198647	24.052%	183418	14.734%	112359	4.839%	36902	0.519%	3958	0.003%	28	762568
Spearman.10kx10k.10N [-0.75,-0.5]	0.965%	36392	9.806%	369436	22.114%	833128	29.718%	1119605	25.345%	954865	10.661%	401059	1.374%	51801	0.012%	474	3767360
Spearman.10kx10k.10N [-0.5,-0.25]	0.192%	14973	4.668%	363417	16.823%	1309536	28.458%	2251242	30.6%	2381932	16.545%	1287886	2.676%	208364	0.034%	2690	7784040
Spearman.10kx10k.10N [-0.25,0]	0.064%	7712	2.44%	291257	12.308%	1468930	25.081%	2993235	32.481%	3876390	22.723%	2711901	4.81%	574036	0.089%	10710	11934171
Spearman.10kx10k.10N [0.0,0.25]	0.025%	3077	1.306%	159475	8.563%	1045101	20.821%	2541016	31.774%	3877691	28.764%	3510313	8.507%	1038293	0.235%	28771	12203737
Spearman.10kx10k.10N [0.25,0.5]	0.009%	812	0.699%	58488	5.584%	466619	16.12%	1349698	28.82%	2408133	33.422%	2792632	14.617%	1221336	0.725%	60951	8355579
Spearman.10kx10k.10N [0.5,0.75]	0.003%	150	0.35%	14965	3.246%	138801	10.976%	469282	23.267%	994761	34.456%	1473107	24.497%	1047351	3.201%	136666	4275283
Spearman.10kx10k.10N [0.75,1]	0%	9	0.13%	1186	1.351%	12333	5.317%	48505	13.805%	125941	27.044%	246719	35.113%	320328	17.236%	15724	912262
Spearman.10kx10k.53N [-1,-0.75]*k.53N [-0.75,-0.5]*k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]																	Total Count
Spearman.10kx10k.10N [-1,-0.75]	4.464%	34044	23.409%	178510	26.411%	201404	25.107%	191461	15.294%	116634	4.75%	36222	0.552%	4214	0.01%	79	762568
Spearman.10kx10k.10N [-0.75,-0.5]	0.389%	14673	7.761%	292421	21.63%	814901	33.083%	1246390	26.707%	1006165	9.287%	349883	1.117%	42089	0.022%	838	3767360
Spearman.10kx10k.10N [-0.5,-0.25]	0.071%	5577	3.162%	246164	15.745%	1225634	32.557%	2354263	33.175%	2582390	13.533%	1053484	1.713%	133375	0.04%	3153	7784040
Spearman.10kx10k.10N [-0.25,0]	0.03%	3677	1.693%	202084	11.624%	1387276	29.215%	3486610	36.522%	4358615	18.249%	2177923	2.6%	310299	0.063%	7634	11934171
Spearman.10kx10k.10N [0.0,0.25]	0.018%	2239	1.051%	128308	8.501%	1037561	24.801%	3026688	37.417%	4566378	23.802%	2904789	4.287%	523248	0.119%	14526	12203737
Spearman.10kx10k.10N [0.25,0.5]	0.011%	978	0.703%	58795	6.044%	505071	19.788%	1653421	35.693%	2982387	29.62%	274967	7.801%	651823	0.336%	28137	8355579
Spearman.10kx10k.10N [0.5,0.75]	0.007%	333	0.44%	18837	3.922%	167701	14.11%	603245	30.029%	1283827	33.827%	1446224	15.914%	680381	1.748%	74735	4275283
Spearman.10kx10k.10N [0.75,1]	0.003%	30	0.21%	1923	1.869%	17055	7.243%	66083	18.416%	168009	29.424%	268430	30.329%	276680	12.502%	114052	912262
Spearman.10kx10k.53N [-1,-0.75]*k.53N [-0.75,-0.5]*k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]																	Total Count
Spearman.10kx10k.30N [-1,-0.75]	36.237%	43470	61.099%	73293	2.632%	3158	0.029%	35	0%	1	0%	0	0%	0	0%	0	119957
Spearman.10kx10k.30N [-0.75,-0.5]	1.243%	17761	48.85%	697897	46.187%	659858	3.695%	52800	0.023%	330	0%	2	0%	0	0%	1	1428648
Spearman.10kx10k.30N [-0.5,-0.25]	0.005%	320	6.287%	344110	56.017%	3065906	36.039%	1972449	1.647%	90155	0.002%	155	0%	0	0%	0	5473095
Spearman.10kx10k.30N [-0.25,0]	0%	0	0.107%	11706	14.164%	1546378	62.063%	3776634	23.127%	2524938	0.536%	58598	0%	17	0%	0	10912721
Spearman.10kx10k.30N [0.0,0.25]	0%	0	0.36%	0	0.548%	80764	25.778%	375711	61.665%	908458	12.709%	178397	4.097%	14293	0%	0	14732072
Spearman.10kx10k.30N [0.25,0.5]	0%	0	0%	0	0.004%	541	1.907%	237711	41.232%	513947	52.102%	6492547	4.738%	590487	0.003%	397	44611159
Spearman.10kx10k.30N [0.5,0.75]	0%	0	0%	0	0%	0	0.026%	1171	5.033%	224776	52.823%	2358823	40.612%	1813355	1.504%	67162	4465467
Spearman.10kx10k.30N [0.75,1]	0%	0	0%	0	0%	0	0%	0	0.046%	185	4.485%	17823	51.279%	203768	44.189%	175595	397371

C. Kendall

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E. B.Distance

B.Distance.10kx10k.30N [-1,-0.75]*10k.30N [-0.75,-0.5]*10k.30N [-0.5,-0.25]*kx10k.30N [-0.25,0]*kx10k.30N [0.0,0.25]*x10k.30N [0.25,0.5]*x10k.30N [0.5,0.75]*kx10k.30N [0.75,1]	Total Count
B.distance.10kx10k.10N [-1,-0.75]	0
B.distance.10kx10k.10N [-0.75,-0.5]	0
B.distance.10kx10k.10N [-0.5,-0.25]	0
B.distance.10kx10k.10N [-0.25,0]	0
B.distance.10kx10k.10N [0.0,0.25]	7789
B.distance.10kx10k.10N [0.25,0.5]	25302940
B.distance.10kx10k.10N [0.5,0.75]	22099132
B.distance.10kx10k.10N [0.75,1]	2585139
B.Distance.10kx10k.53N [-1,-0.75]*10k.53N [-0.75,-0.5]*10k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]	
B.distance.10kx10k.10N [-1,-0.75]	0
B.distance.10kx10k.10N [-0.75,-0.5]	0
B.distance.10kx10k.10N [-0.5,-0.25]	0
B.distance.10kx10k.10N [-0.25,0]	0
B.distance.10kx10k.10N [0.0,0.25]	7789
B.distance.10kx10k.10N [0.25,0.5]	25302940
B.distance.10kx10k.10N [0.5,0.75]	22099132
B.distance.10kx10k.10N [0.75,1]	2585139
B.Distance.10kx10k.53N [-1,-0.75]*10k.53N [-0.75,-0.5]*10k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]	
B.distance.10kx10k.10N [-1,-0.75]	0
B.distance.10kx10k.10N [-0.75,-0.5]	0
B.distance.10kx10k.10N [-0.5,-0.25]	0
B.distance.10kx10k.10N [-0.25,0]	0
B.distance.10kx10k.10N [0.0,0.25]	7789
B.distance.10kx10k.10N [0.25,0.5]	25302940
B.distance.10kx10k.10N [0.5,0.75]	22099132
B.distance.10kx10k.10N [0.75,1]	2585139

F. M.Distance

M.Distance.10kx10k.30N [-1,-0.75]*10k.30N [-0.75,-0.5]*10k.30N [-0.5,-0.25]*kx10k.30N [-0.25,0]*kx10k.30N [0.0,0.25]*x10k.30N [0.25,0.5]*x10k.30N [0.5,0.75]*kx10k.30N [0.75,1]	Total Count
M.distance.10kx10k.10N [-1,-0.75]	0
M.distance.10kx10k.10N [-0.75,-0.5]	0
M.distance.10kx10k.10N [-0.5,-0.25]	0
M.distance.10kx10k.10N [-0.25,0]	0
M.distance.10kx10k.10N [0.0,0.25]	4173
M.distance.10kx10k.10N [0.25,0.5]	24608498
M.distance.10kx10k.10N [0.5,0.75]	22825204
M.distance.10kx10k.10N [0.75,1]	2557125
M.Distance.10kx10k.53N [-1,-0.75]*10k.53N [-0.75,-0.5]*10k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]	
M.distance.10kx10k.10N [-1,-0.75]	0
M.distance.10kx10k.10N [-0.75,-0.5]	0
M.distance.10kx10k.10N [-0.5,-0.25]	0
M.distance.10kx10k.10N [-0.25,0]	0
M.distance.10kx10k.10N [0.0,0.25]	4173
M.distance.10kx10k.10N [0.25,0.5]	24608498
M.distance.10kx10k.10N [0.5,0.75]	22825204
M.distance.10kx10k.10N [0.75,1]	2557125
M.Distance.10kx10k.53N [-1,-0.75]*10k.53N [-0.75,-0.5]*10k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]	
M.distance.10kx10k.10N [-1,-0.75]	0
M.distance.10kx10k.10N [-0.75,-0.5]	0
M.distance.10kx10k.10N [-0.5,-0.25]	0
M.distance.10kx10k.10N [-0.25,0]	0
M.distance.10kx10k.10N [0.0,0.25]	4173
M.distance.10kx10k.10N [0.25,0.5]	24608498
M.distance.10kx10k.10N [0.5,0.75]	22825204
M.distance.10kx10k.10N [0.75,1]	2557125

G. MIC

MIC.10kx10k.30N [-1,-0.75]*10k.30N [-0.75,-0.5]*10k.30N [-0.5,-0.25]*kx10k.30N [-0.25,0]*kx10k.30N [0.0,0.25]*x10k.30N [0.25,0.5]*x10k.30N [0.5,0.75]*kx10k.30N [0.75,1]	Total Count
M.MIC.10kx10k.10N [-1,-0.75]	0
M.MIC.10kx10k.10N [-0.75,-0.5]	0
M.MIC.10kx10k.10N [-0.5,-0.25]	0
M.MIC.10kx10k.10N [-0.25,0]	0
M.MIC.10kx10k.10N [0.0,0.25]	24239589
M.MIC.10kx10k.10N [0.25,0.5]	17934298
M.MIC.10kx10k.10N [0.5,0.75]	7117834
M.MIC.10kx10k.10N [0.75,1]	703279
MIC.10kx10k.53N [-1,-0.75]*10k.53N [-0.75,-0.5]*10k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]	
M.MIC.10kx10k.10N [-1,-0.75]	0
M.MIC.10kx10k.10N [-0.75,-0.5]	0
M.MIC.10kx10k.10N [-0.5,-0.25]	0
M.MIC.10kx10k.10N [-0.25,0]	0
M.MIC.10kx10k.10N [0.0,0.25]	24239589
M.MIC.10kx10k.10N [0.25,0.5]	17934298
M.MIC.10kx10k.10N [0.5,0.75]	7117834
M.MIC.10kx10k.10N [0.75,1]	703279
MIC.10kx10k.53N [-1,-0.75]*10k.53N [-0.75,-0.5]*10k.53N [-0.5,-0.25]*kx10k.53N [-0.25,0]*kx10k.53N [0.0,0.25]*x10k.53N [0.25,0.5]*x10k.53N [0.5,0.75]*kx10k.53N [0.75,1]	
M.MIC.10kx10k.10N [-1,-0.75]	0
M.MIC.10kx10k.10N [-0.75,-0.5]	0
M.MIC.10kx10k.10N [-0.5,-0.25]	0
M.MIC.10kx10k.10N [-0.25,0]	0
M.MIC.10kx10k.10N [0.0,0.25]	24239589
M.MIC.10kx10k.10N [0.25,0.5]	17934298
M.MIC.10kx10k.10N [0.5,0.75]	7117834
M.MIC.10kx10k.10N [0.75,1]	703279

Supplemental bin plots

Figure S1 provides additional comparisons between Hoeffding's D statistic and other correlation methods. Along with Figure 3 C and D, Figure S1 A displays a noisy relationship with wide tails. This indicates a large range of Hoeffding scores corresponding to high correlations with the opposing metric. In contrast, Figure S1 B, like Figure 2 D, shows narrower tails indicating a more robust relationship between the two metrics.

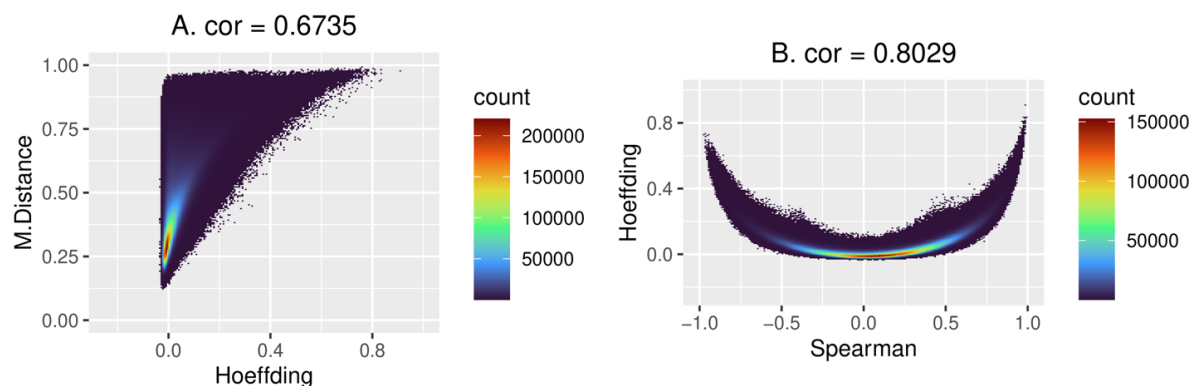


Figure S1. Additional scatterplot comparisons with Hoeffding's D Statistic

(A) *Hoeffding vs. M.Distance*, (B) *Spearman vs. Hoeffding*

Figure S2, together with Figure 2 F, shows all four comparisons of M.Pearson and B.Pearson plotted against Spearman and Kendall coefficients. The shape exhibited by the following graphs matches that of Figure 2 F. All four of these bin plots have a clear diagonal, with the slope of the diagonal being smaller when comparing to Kendall rather than Spearman. When comparing M.Pearson and B.Pearson to both Kendall and Spearman, strong Pearson correlations are assigned a wide range of scores by the opposing metric. In all four graphs, the size of the range of Kendall or Spearman values assigned to a fixed Pearson value remains relatively constant. In contrast, different values of Kendall or Spearman coefficients on the y-axis may obtain drastically different ranges of corresponding Pearson scores. Strong Kendall and Spearman scores correspond to a limited range of Pearson scores, while Kendall and Spearman scores near 0 are matched by Pearson scores ranging from strongly negative to strongly positive in all three bin plots in Figure S2, as well as in Figure 2 F.

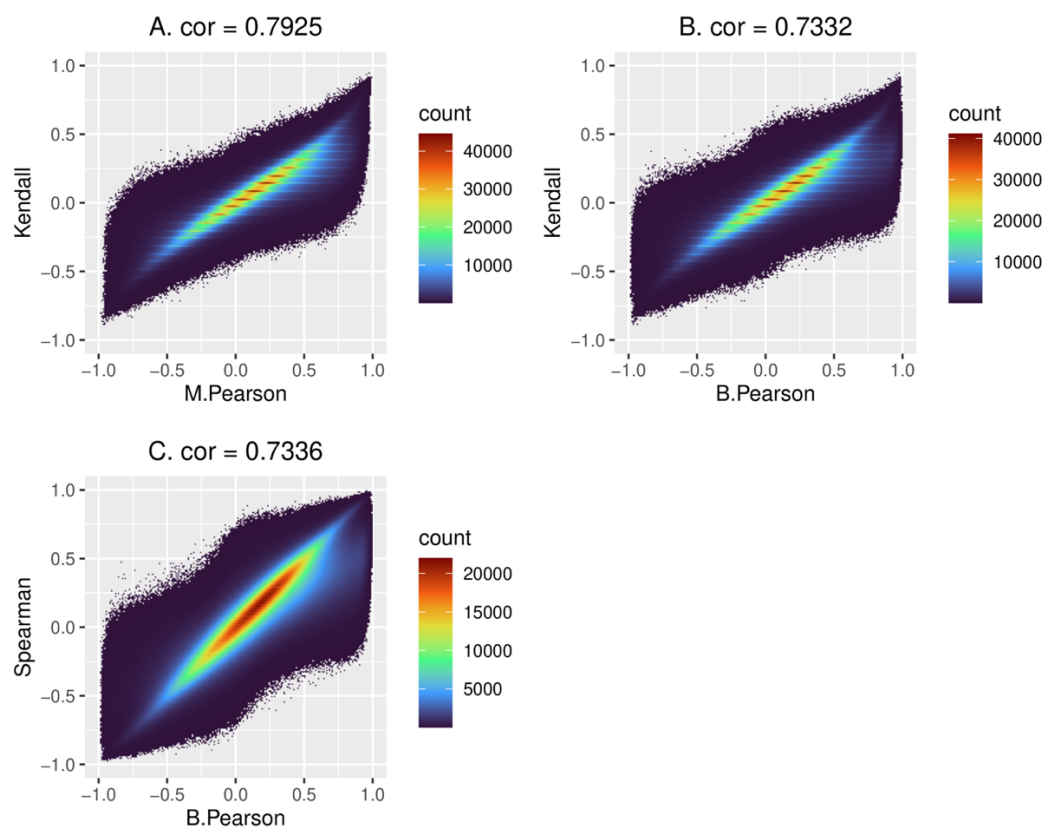


Figure S2. Scatterplots comparing Pearson correlations to Kendall/Spearman correlations

(A) *M.Pearson vs. Kendall*, (B) *B.Pearson vs. Kendall*, (C) *B.Pearson vs. Spearman*

Figure S3 provides additional comparisons between MIC and other correlation methods. As in Figure 3 B, Figure S3 A and B exhibit a loose chevron shape with significant noise, which indicated a large amount of disagreement between MIC and the opposing metrics as to whether the data were highly correlated or not. In Figure S3 C, the chevron is not apparent because Distance correlation only produces positive scores; however, the lower boundary of the plot is similar to that of Figure 3 B, with a large concentration of points having strong Distance coefficients and low MIC coefficients. Out of all the bin plot comparisons made with MIC, Figure S3 A and B most closely match the plot produced by Reshef et al. comparing Pearson and MIC.

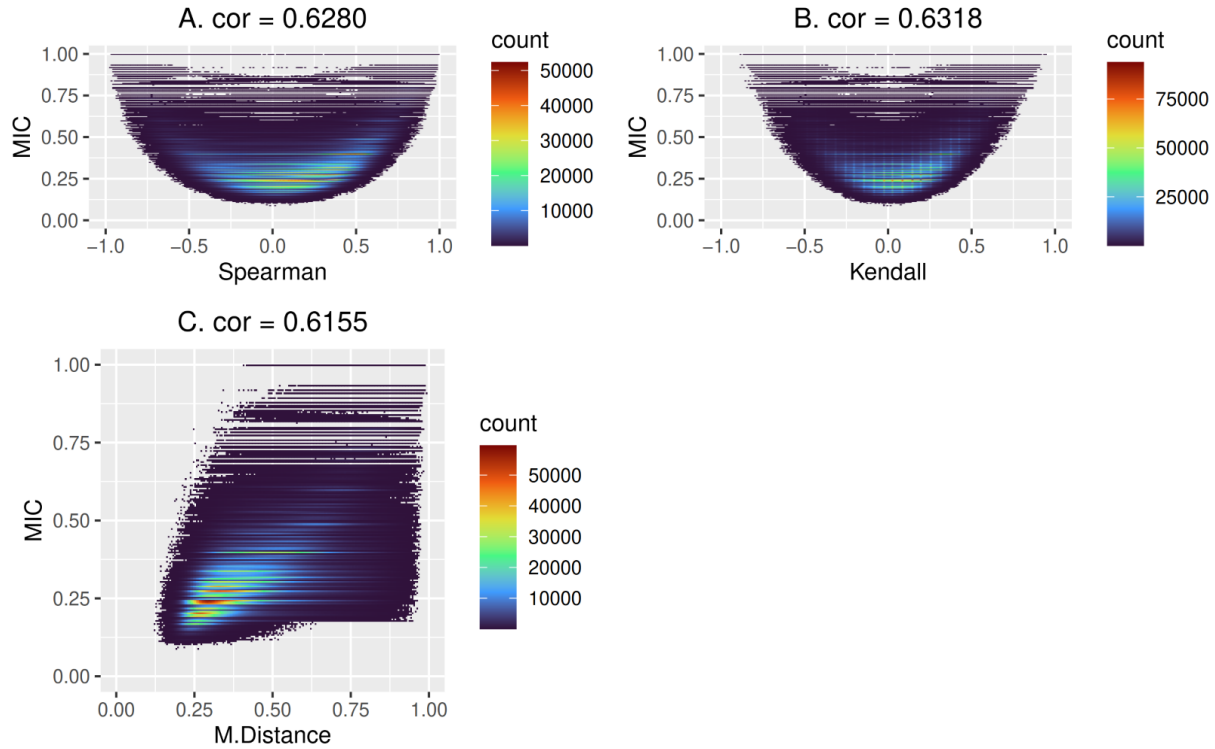


Figure S3. Additional scatterplot comparisons with MIC
 (A) *M.Distance* vs. *MIC*, (B) *Kendall* vs. *MIC*, (C) *Spearman* vs. *MIC*