

Downsampling Rate	Independent	Grun	Cell Type	Time Course	Shalek
0.95	Y	30.29	73.13	62.77	50.15
0.9	Y	30.41	72.58	62.29	49.22
0.8	Y	28.62	70.32	59.86	46.34
0.7	Y	24.39	65.23	54.07	40.32
0.6	Y	16.18	52.29	41.08	28.16
0.5	Y	9.49	37.13	27.17	17.44
0.95	N	8.5	45.59	36.73	30.52
0.9	N	8.52	43.7	35.59	29.38
0.8	N	8.39	41	33.95	27.84
0.7	N	8.19	38	31.87	25.97
0.6	N	7.84	34.37	29.51	23.99
0.5	N	7.68	32.62	28.43	22.95

Table S1: Percentage of zero values that are due to down-sampling in the down-sampling experiment based on four real data sets. In the experiment, down-sampling rate ranges from 0.5 to 0.95 and the dropout rate is either dependent (N) or independent (Y) of the expression level. The remaining percentage of zero values that are not due to down-sampling are due to dropout events.

dataset	dimensionality ( $n \times p$ )	Proportion of zeros	DrImpute	MAGIC	SAVER	scImpute	VIPER-Elastic Net	VIPER-Lasso
Grun	251 $\times$ 12,184	39%	0.004	0.002	7.25	0.05	0.34	0.33
Cell Type	1,018 $\times$ 13,829	31%	0.04	0.009	30.09	1.67	4.27	3.82
Time Course	758 $\times$ 13,059	34%	0.03	0.007	21.37	0.51	5.42	5.15
Shalek	1,053 $\times$ 16,702	48%	0.05	0.013	46.34	0.20	10.6	10.6

Table S2: Computing time in hours for different imputation methods in the four real datasets. Number of cells ( $n$ ), number of genes ( $p$ ) as well as the proportion of zero entries in each data are listed. Computing time is evaluated on an Intel E5-2680v4 2.4GHz CPU. Methods for comparison include DrImpute, MAGIC, SAVER, scImpute, VIPER with elastic net selection, and VIPER with lasso selection.