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.

<table>
<thead>
<tr>
<th>Downsampling Rate</th>
<th>Independent</th>
<th>Grun</th>
<th>Cell Type</th>
<th>Time Course</th>
<th>Shalek</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.95</td>
<td>Y</td>
<td>30.29</td>
<td>73.13</td>
<td>62.77</td>
<td>50.15</td>
</tr>
<tr>
<td>0.9</td>
<td>Y</td>
<td>30.41</td>
<td>72.58</td>
<td>62.29</td>
<td>49.22</td>
</tr>
<tr>
<td>0.8</td>
<td>Y</td>
<td>28.62</td>
<td>70.32</td>
<td>59.86</td>
<td>46.34</td>
</tr>
<tr>
<td>0.7</td>
<td>Y</td>
<td>24.39</td>
<td>65.23</td>
<td>54.07</td>
<td>40.32</td>
</tr>
<tr>
<td>0.6</td>
<td>Y</td>
<td>16.18</td>
<td>52.29</td>
<td>41.08</td>
<td>28.16</td>
</tr>
<tr>
<td>0.5</td>
<td>Y</td>
<td>9.49</td>
<td>37.13</td>
<td>27.17</td>
<td>17.44</td>
</tr>
<tr>
<td>0.95</td>
<td>N</td>
<td>8.5</td>
<td>45.59</td>
<td>36.73</td>
<td>30.52</td>
</tr>
<tr>
<td>0.9</td>
<td>N</td>
<td>8.52</td>
<td>43.7</td>
<td>35.59</td>
<td>29.38</td>
</tr>
<tr>
<td>0.8</td>
<td>N</td>
<td>8.39</td>
<td>41</td>
<td>33.95</td>
<td>27.84</td>
</tr>
<tr>
<td>0.7</td>
<td>N</td>
<td>8.19</td>
<td>38</td>
<td>31.87</td>
<td>25.97</td>
</tr>
<tr>
<td>0.6</td>
<td>N</td>
<td>7.84</td>
<td>34.37</td>
<td>29.51</td>
<td>23.99</td>
</tr>
<tr>
<td>0.5</td>
<td>N</td>
<td>7.68</td>
<td>32.62</td>
<td>28.43</td>
<td>22.95</td>
</tr>
</tbody>
</table>
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, sclImpute, VIPER with elastic net selection, and VIPER with lasso selection.

<table>
<thead>
<tr>
<th>dataset</th>
<th>dimensionality (n × p)</th>
<th>Proportion of zeros</th>
<th>DrImpute</th>
<th>MAGIC</th>
<th>SAVER</th>
<th>sclImpute</th>
<th>VIPER-Elastic Net</th>
<th>VIPER-Lasso</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grun</td>
<td>251 × 12,184</td>
<td>30%</td>
<td>0.004</td>
<td>0.002</td>
<td>7.26</td>
<td>0.05</td>
<td>0.34</td>
<td>0.33</td>
</tr>
<tr>
<td>Cell Type</td>
<td>1,018 × 13,829</td>
<td>31%</td>
<td>0.04</td>
<td>0.009</td>
<td>30.99</td>
<td>1.67</td>
<td>4.27</td>
<td>3.82</td>
</tr>
<tr>
<td>Time Course</td>
<td>758 × 13,059</td>
<td>34%</td>
<td>0.03</td>
<td>0.007</td>
<td>21.37</td>
<td>0.51</td>
<td>5.42</td>
<td>5.15</td>
</tr>
<tr>
<td>Shalek</td>
<td>1,053 × 16,702</td>
<td>48%</td>
<td>0.05</td>
<td>0.013</td>
<td>46.34</td>
<td>0.20</td>
<td>10.6</td>
<td>10.6</td>
</tr>
</tbody>
</table>