Biclustering of Binary Data Matrices: The BiBit Workflow

Proof of Concept

July 21, 2018

1 Application of the BiBit Workflow on Generated Scenarios

1.1 Data Generation

In order to demonstrate the effectiveness of the BiBit workflow, four data sets are generated. These data sets contain multiple biclusters with or without noise. Further, due to the column similarity feature of the workflow, overlap between the bicluster columns was also considered in these data sets.

	Data 1	**Data 2**	**Data 3**	**Data 4**
Data Matrix	10000×50	10000×50	10000×50	10000×50
Background Signal	15%	15%	15%	15%
Biclusters	BC1: 200×5	BC1: 200×5	BC1: 200×10	BC1: 200×10
	BC2: 100×5	BC2: 100×5	BC2: 100×10	BC2: 100×10
	BC3: 200×10	BC3: 200×10	BC3: 200×10	BC3: 200×10
	BC4: 100×10	BC4: 100×10	BC4: 100×10	BC4: 100×10
Overlap	None	None	BC1$\cap$BC2: 5 columns	BC1$\cap$BC2: 5 columns
			BC3$\cap$BC4: 2 columns	BC3$\cap$BC4: 2 columns
BC Signal	100%	90%	100%	90%

Table 1: Generated data sets.

	Data 1				**Data 2**				**Data 3**				**Data 4**			
Row Noise	BC1	BC2	BC3	BC4	BC1	BC2	BC3	BC4	BC1	BC2	BC3	BC4	BC1	BC2	BC3	BC4
0	200	100	200	100	121	67	66	32	200	100	200	100	72	24	70	28
1	0	0	0	0	59	23	83	43	0	0	0	0	78	50	79	43
2	0	0	0	0	15	10	34	17	0	0	0	0	33	18	39	25
3	0	0	0	0	5	0	10	6	0	0	0	0	16	6	11	4
4	0	0	0	0	0	0	7	2	0	0	0	0	1	2	1	0

Table 2: Number of rows for 0, 1, 2, 3 and 4 noise levels in the four generated biclusters.

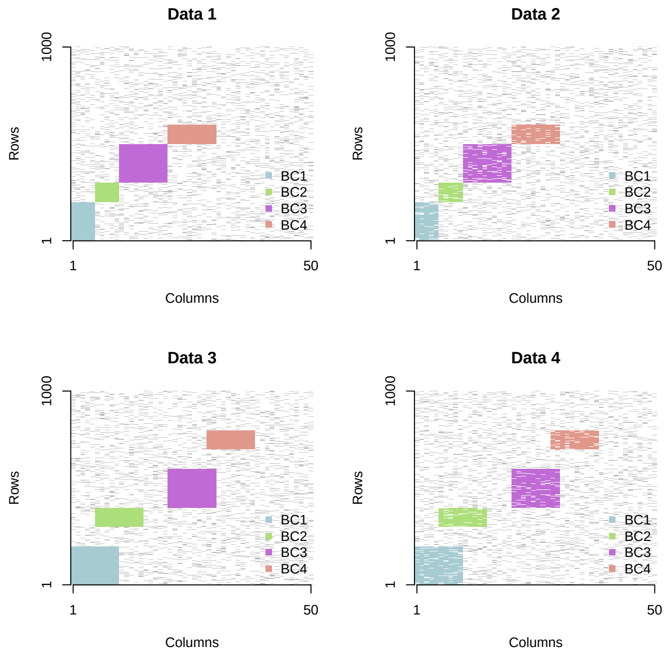


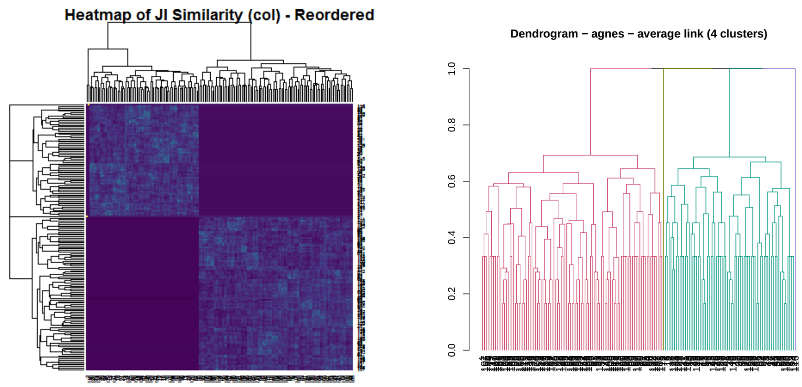
Figure 1: Visualisation of the four generated data sets, unshuffled and subsetted on the first 1000 rows.

1.2 Results

The results of the four generated data sets will now be presented following the BiBit workflow steps described in Chapter 6 in De Troyer (2018).

Data 1: No Overlap & No Noise

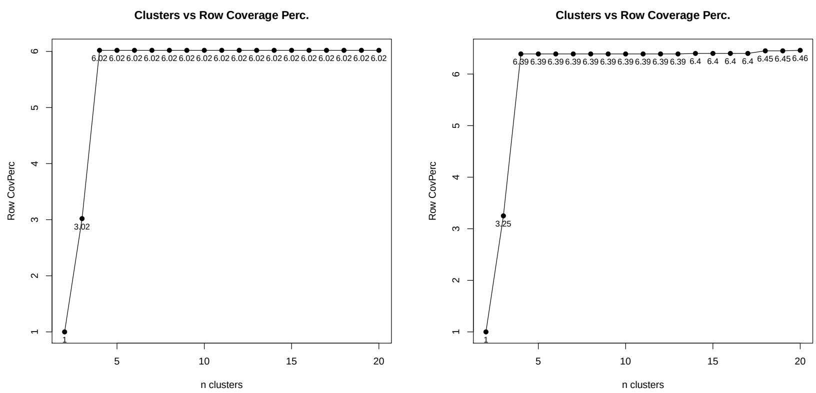
In the first step the original bibit is applied with minimum bicluster dimensions of 50×5 which results in 172 biclusters. Next, the bicluster column similarity is determined and clustered in Figure 2.



(a) (b)

Figure 2: Results of Data 1 for step 2 and 3. Panel a: reordered heatmap of column similarity between the biclusters. Panel b: dendrogram of column similarity using hierarchical clustering with average link.

Due to the two singletons found in Figure 2b, the gap statistic (Tibs2001SEmax) proposes to select two clusters. However, investigating the row coverage plot in Figure 3 suggests that four clusters might be more appropriate.



(a) (b)

Figure 3: Row coverage plot for Data 1 up to 20 clusters. Panel a: zero noise level. Panel b: 10% noise level.

Growing rows on these four merged column patterns results in the biclusters given in Table 3. The biclusters will have a different number of rows depending on the requested noise level. Table 3a reveals that the four simulated perfect biclusters are fully discovered albeit with two addition rows for BC 2.

	BC1	BC2	BC3	BC4
Number of Rows	100	202	200	100
Number of Columns	10	5	10	5

(a)

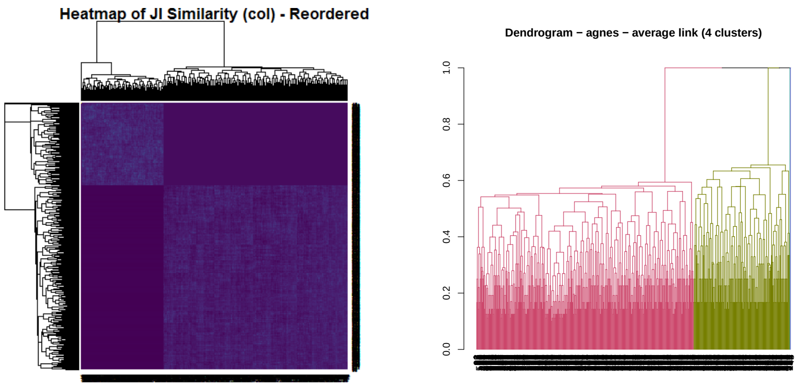
	BC1	BC2	BC3	BC4
Number of Rows	100	219	200	123
Number of Columns	10	5	10	5

(b)

Table 3: Table of final bibit workflow result of Data 2. Panel a: zero noise level. Panel b: noise level of 10% which allows a single zero in each row (due to rounding up).

Data 2: No Overlap & Noise

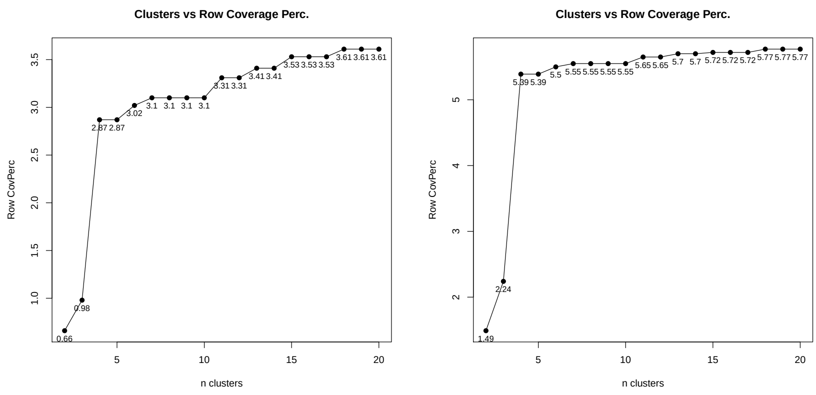
Applying BiBit with minimum bicluster dimensions of 50 × 5 results in 671 biclusters. Next, the clustered column similarity is shown in Figure 4.



(a) (b)

Figure 4: Results of Data 2 for step 2 and 3. Panel a: reordered heatmap of column similarity between the biclusters. Panel b: dendrogram of column similarity using hierarchical clustering with average link.

Again, due to the two singletons (see Figure 4b), the gap statistic (Tibshirani *et al.*, 2001) suggests two clusters. However, similar to the result of Data 1, the row coverage plot seems to indicate 4 clusters (Figure 5).



(a) (b)

Figure 5: Row coverage plot for Data 2 up to 20 clusters. Panel a: zero noise level. Panel b: single noise level.

Growing rows on these four merged column patterns results in the biclusters given in Table 4. The correct column patterns from the simulated biclusters are discovered, but the correct row identification depends on the magnitude of the noise level. The higher the noise level, the more rows that are added to the patterns, and the more noisy rows of the true bicluster (see Table 2) that are detected. However note for BC 1, 3 and 4 that there are a large amount of other rows which also fit this pattern (respecting the pre-selected noise level).

	BC1	BC2	BC3	BC4
Number of Rows	66	32	122	67
Number of Columns	10	10	5	5

(a)

	BC1	BC2	BC3	BC4
Number of Rows	149	75	205	112
Number of Columns	10	10	5	5

(b)

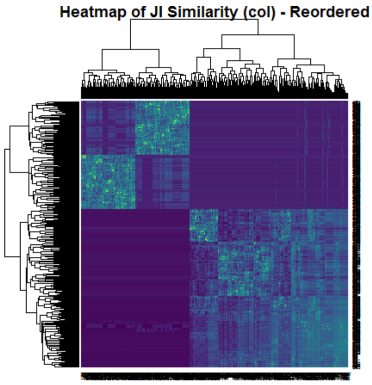
	BC1	BC2	BC3	BC4
Number of Rows	183	92	437	369
Number of Columns	10	10	5	5

(c)

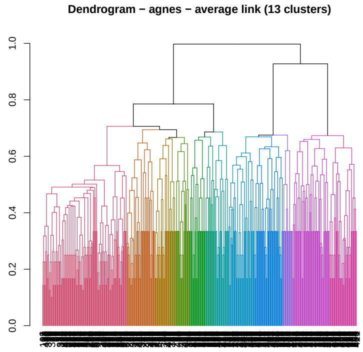
Table 4: Table of final bibit workflow result of Data 2. Panel a: zero noise level. Panel b: noise level of 1. Panel c: noise level of 2.

Data 3: Overlap & No Noise

Applying BiBit with minimum bicluster dimensions of 50×5 results in 481 biclusters. Next, the clustered column similarity is shown in Figure 6.



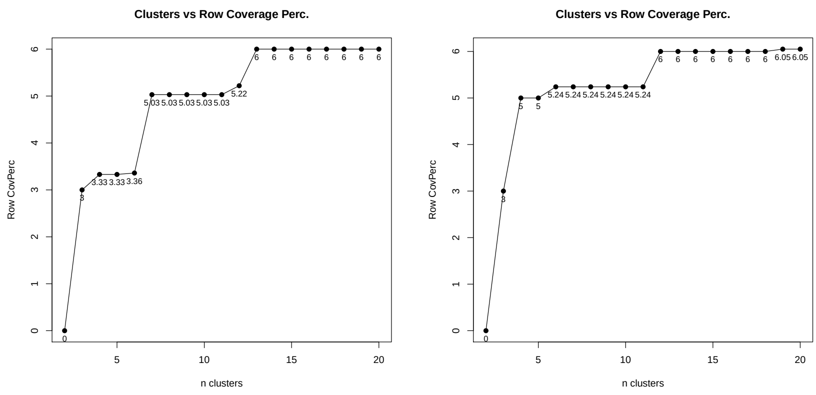
(a)



(b)

Figure 6: Results of Data 3 for step 2 and 3. Panel a: reordered heatmap of column similarity between the biclusters. Panel b: dendrogram of column similarity using hierarchical clustering with average link.

For this data set the gap statistic proposes to select 17 clusters. Depending on the selected noise level this reduces to 8 to 10 biclusters which contain the 4 generated biclusters. Observing the row coverage plots in Figure 7, 4 clusters could be chosen here too. However, depending on the allowed noise, one or two biclusters will be missed, namely BC 1 and BC 2 which had 50% column overlap. More specifically, choosing 4 clusters with a zero noise level overlooks BC 1 and BC 2 for the most part. However, when allowing a single noise level, it is only BC 2 that is not discovered. This is caused by the fact that the discovered biclusters has 11 columns (including the 10 true ones). So in order to match the true generated bicluster rows, some error would need to be allowed.
However, instead, a higher number of clusters is selected based on the row coverage plot in Figure 7. In Figure 7a the row coverage is shown without allowing any noise and 13 clusters seem appropriate. The other plot, Figure 7b, allows a single zero and seems to suggest 12 clusters.



(a) (b)

Figure 7: Row coverage plot for Data 3 up to 20 clusters. Panel a: zero noise level. Panel b: single noise level.

Since Data 3 contains perfect true biclusters, selecting 13 clusters for a noise of 0 seems like a good initial choice. Table 5a shows the resulting 8 biclusters. The generated BC 3 and BC 4 which only had a little overlap are easily identified and correspond with BC8 and BC7 in this table, respectively. The generated BC 1 is also discovered as BC5 in this table. BC6 (with its 11 columns) also includes all the correct columns of this same generated bicluster but not its rows. However, the generated BC 2, which had 50% overlap with the generated BC 1, is not completely discovered in this result in Table 5a. BC2 misidentifies a single column and cannot match the correct rows. BC1 on the other hand discovers the true columns, but due to the extra columns is also unable to match the true rows.

In order to deal with this overlap issue, some noise could be allowed to try and capture all the true biclusters. This result can be found in Table 5b where 12 clusters were chosen with a noise level of 1 which resulted in 6 biclusters. In this result the true generated biclusters are identified in BC4, BC2, BC6 and BC5, respectively. Note that the only reason that the generated BC 2 is discovered in the resulting BC2, is because noise was allowed. Namely, this bicluster contains 11 columns and without error allowance the true rows would not have matched this column pattern.

Finally, it should be noted that if 13 clusters would have been chosen for a noise level of 1, the result would not have been this optimal (see Table 5c). Here the generated biclusters 1, 3 and 4 are discovered correctly in BC5, BC7 and BC6, respectively. However the second generated bicluster once again poses some difficulty. Even though all rows of this bicluster are found in BC2 and BC4, both of them miss a single column. And while BC1 contains all columns (and more), not all rows are identified here. The explanation for this behaviour is that, when going from Table 5c to Table 5b (from 13 to 12 clusters), two patterns seem to have merged together which allowed for a better identification of the second generated bicluster.

	BC1	BC2	BC3	BC4	BC5	BC6	BC7	BC8
Number of Rows	3	17	2	100	200	33	100	200
Number of Columns	12	10	12	9	10	11	10	10

(a)

	BC1	BC2	BC3	BC4	BC5	BC6
Number of Rows	24	101	22	200	100	200
Number of Columns	12	11	12	11	10	10

(b)

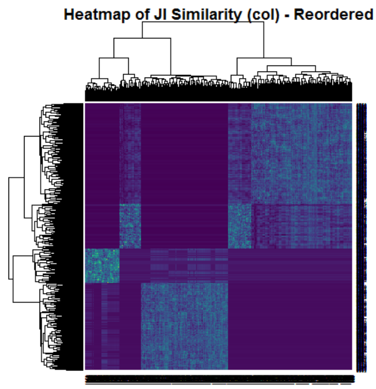
	BC1	BC2	BC3	BC4	BC5	BC6	BC7
Number of Rows	24	101	22	102	200	100	200
Number of Columns	12	10	12	9	11	10	10

(c)

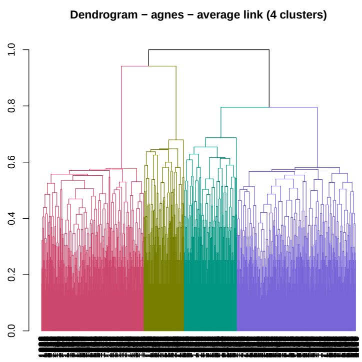
Table 5: Table of final bibit workflow result of Data 3. Panel a: 13 clusters for a zero noise level. Panel b: 12 clusters for a noise level of 1. Panel c: 13 clusters for a noise level of 1.

Data 4: Overlap & Noise

For the fourth data set the original BiBit was applied with minimum bicluster dimensions of 50×25 as well. This results in a large number of biclusters, namely 1381. The column similarity is shown in Figure 8



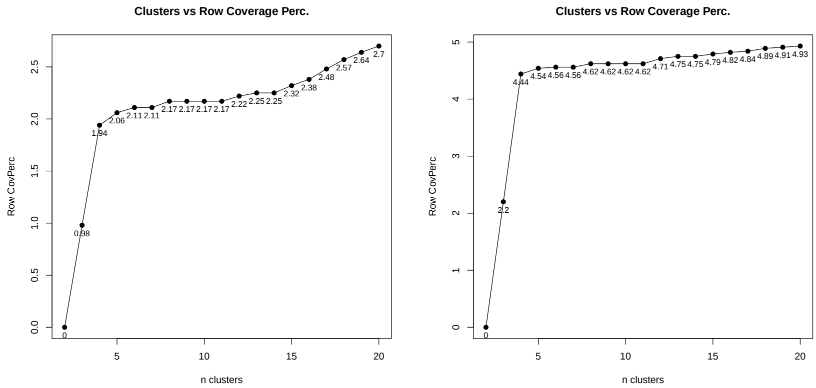
(a)



(b)

Figure 8: Results of Data 4 for step 2 and 3. Panel a: reordered heatmap of column similarity between the biclusters. Panel b: dendrogram of column similarity using hierarchical clustering with average link.

In this example, both the gap statistic (Tibshirani *et al.*, 2001) and the row coverage plots (Figure 9) suggest 4 clusters.



(a) (b)

Figure 9: Row coverage plot for Data 4 up to 20 clusters. Panel a: zero noise level. Panel b: single noise level.

Next, using these four merged column patterns, rows are grown conditioned on multiple noise levels. These results are shown in Table 6 with a noise allowance of 0, 1 and 2. In these results, the column patterns are discovered perfectly (even with the overlap) and identifying the correct rows is simply a matter of sufficiently increasing the noise level.

	BC1	BC2	BC3	BC4
Number of Rows	70	28	24	72
Number of Columns	10	10	10	10

(a)

	BC1	BC2	BC3	BC4
Number of Rows	149	71	74	150
Number of Columns	10	10	10	10

(b)

	BC1	BC2	BC3	BC4
Number of Rows	188	96	98	184
Number of Columns	10	10	10	10

(c)

Table 6: Table of final bibit workflow result of Data 4. Panel a: zero noise level. Panel b: noise level of 1. Panel c: noise level of 2.

1.3 Discussion

It is generally feasible to retrieve the simulated bicluster examples, even with column overlap. Discovering the true biclusters seems to be a matter of playing with the number of cluster choice and the allowed noise level. This is also something that was found during exploration of the case studies where other interesting structures arose when playing with different parameter settings. Further, these examples imply that it is a bit easier to correctly discover the noisy

biclusters in contrast to the perfect ones. For overlapping (column) perfect biclusters, it seems to be advisable to allow a certain degree of noise to be able to capture these structures in the data.
Note that if we would have used automatic noise selection, similar results would have been obtained. Since the automatic noise selection always allows a single zero at least, the process of discovering the bicluster in Data 3 would have been a bit more automated or straight-forward.
Finally, reducing the initial bicluster dimensions too much also has an adverse effect on the workflow analysis. For example, cutting the minimum row size in two to 25 rows results in a lot of initial small biclusters (and column patterns) which do not merge nicely. Therefore, for larger data sets it is advised to not start with too small initial bicluster dimensions, both for this reason and for the reason that otherwise BiBit will identify too many biclusters.

References

De Troyer, E. (2018) *Identifying and Visualising Data Structures in Big and High Dimensional Data using Biclustering*. Ph.D. thesis, Hasselt University.

Tibshirani, R., Walther, G. and Hastie, T. (2001) Estimating the number of data clusters via the gap statistic. *Journal of the Royal Statistical Society B*, **63**, 411–423.