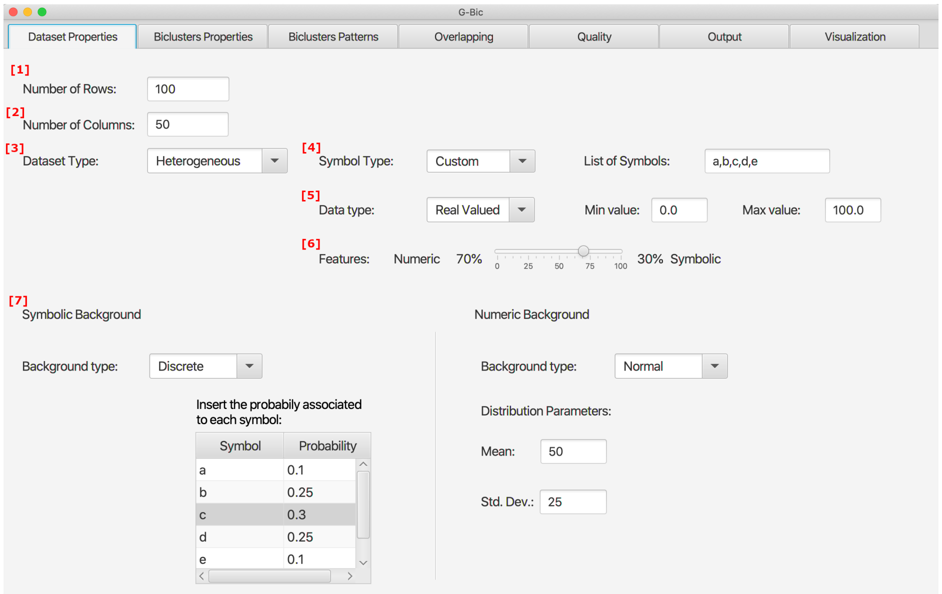
## Additional File 1: Dataset generation using G-Bic

This file introduces the use of G-Bic's *user interface* by presenting a use case for generating a hetereogeneous dataset step by step. Each of the following sections shows the different stages of the generator. In the end, the output produced is analyzed. A video tutorial is available here.

### Dataset Properties

The first step is to define the set of properties that will characterize our dataset $S$. This can be done through the *"Dataset Properties"* tab on the interface, as exemplified in Figure 1.



[1] Number of Rows: 100

[2] Number of Columns: 50

[3] Dataset Type: Heterogeneous

[4] Symbol Type: Custom List of Symbols: a,b,c,d,e

[5] Data type: Real Valued Min value: 0.0 Max value: 100.0

[6] Features: Numeric 70% 30% Symbolic

[7] Symbolic Background

Background type: Discrete

Insert the probabily associated to each symbol:

| Symbol | Probability |
|---|---|
| a | 0.1 |
| b | 0.25 |
| c | 0.3 |
| d | 0.25 |
| e | 0.1 |

Numeric Background

Background type: Normal

Distribution Parameters:

Mean: 50

Std. Dev.: 25

**Figure 1** G-Bic: Dataset properties tab.

Dataset $S$ will be composed by 100 Rows and 50 Columns, thus the parameters *Number of Rows* (1) and *Number of Columns* (2). The *Dataset Type* (3) has a hetegeneous nature, there are three features, two to configure the properties of the symbolic (*Symbol Type* (4)) and numeric data (*Data Type* (5)), and another to configure the proportion between symbolic and and numeric data (*Features* (6)).

Regarding the *Symbolic Type* (4), the user must indicate if the alphabet is composed of default symbols, generated automatically, where the user only indicates the alphabet size (Default Symbol Type). Alternatively, if he/she desires a custom alphabet, the list of symbols will be required (Custom Symbol Type). In our simulation, we decided to generate a custom dataset with five custom symbols, $a, b, c, d, e$.

Considering the *Data Type* (5), the user can choose the numeric properties of the dataset. Currently, both Real Valued and Integer options are available. In both cases, a maximun and minimun range for the number must be selected. In our simulation, we decided to generate real-valued numbers between 0 and 100.

The *Features* slider (6) allows the user to control the proportion between numeric and symbolic features (columns). We generated a dataset consisted of 70% numeric columns.

The last parameter determines how the *background* values (7) of the dataset are distributed: (absence of biclusters): *Uniform*, *Normal*, *Discrete* and *Missing*. If the user chooses *Normal*, or *Discrete*, additional parameters are presented to set the distributions parameters, like the *Mean* and *Standard Deviation* on the *Normal* option, or a table with an editable probability is associated to each symbol, for the *Discrete* one. Since our dataset has a hetegeneous nature, it is needed to define the background for both the symbolic and numeric part. For the discrete, we choose to define the probability for each symbol to be in the symbolic columns. For the numeric background, a normal distribuition was choosen.

### Bicluster Properties

The next step defines the amount and the structure of the planted biclusters on the dataset to be generated. The number of biclusters in dataset $S$ can be defined through parameter *Number of biclusters* (1).

The following two sets of parameters define their structure: Row (1)/Column (2) distribution and respective parameters. The user has available two types of distributions: *Normal* and *Uniform*. The interface dynamically adapts the respective parameters to ask for *Mean* and *Standard Deviation* for the first type, and *Min* and *Max* for the second one. For dataset $S$, its structure follows a uniform distribution, and each bicluster will have a set of rows, columns, and contexts varying between $[6, 8]$ and $[3, 6]$, respectively.

The last parameter, *Contiguity* (4), enables the selection on whether the planted biclusters should be contiguous across the column dimension. In this case, dataset $S$'s biclusters will will not be contiguous.

Figure 2 exemplifies the bicluster's properties tab.

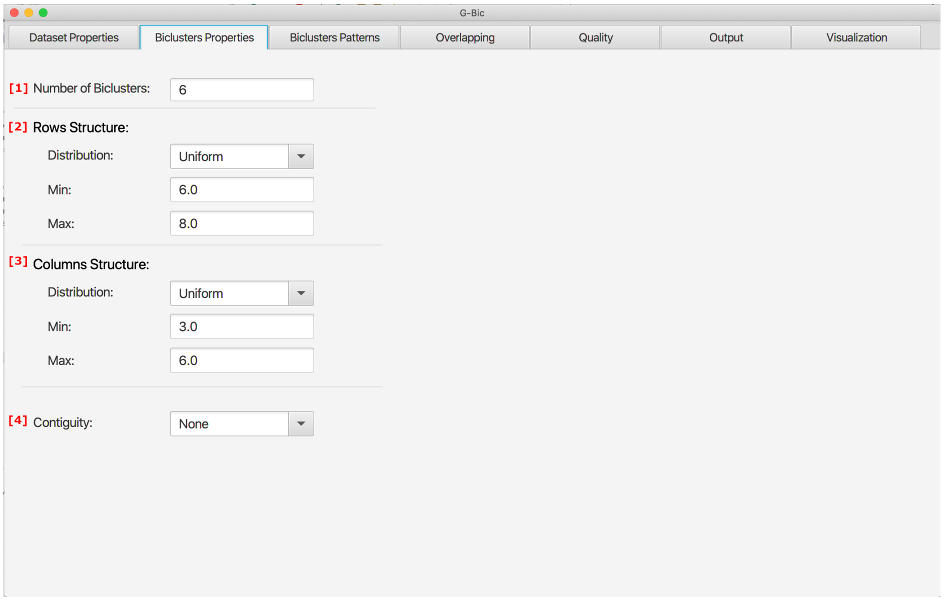
### Bicluster Patterns

We now focus the set of patterns that will be expressed by the set of biclusters planted. The number of patterns chosen will be uniformly distributed across the set of bicluster available. For example, if the user sets four patterns, and the dataset has eight biclusters, two biclusters will be assigned to each type.

Dataset $S$ will have every existing pattern following the *Order Preserving*, *Constant*, *Additive* and *Multiplicative* types. As for the *Order Preserving* pattern on contexts, the user is able to select whether the generated temporal pattern can have an arbitrarily number of increases and decreases along time, or follow a monotonically increasing or decreasing pattern. Figure 3 exemplifies the bicluster's pattern tab.

### Overlapping

The *Overlapping* tab, shown in Figure 4, allows the user to define the number of biclusters that are allowed to overlap and how their interactions are expressed. This interaction is controled by the first parameter *Plaid Coherency* (1), that makes available the two options: *None* and *No Overlapping*. For dataset $S$ the *None* plaid coherency will be chosen.



[1] Number of Biclusters: 6

[2] Rows Structure:

Distribution: Uniform

Min: 6.0

Max: 8.0

[3] Columns Structure:

Distribution: Uniform

Min: 3.0

Max: 6.0

[4] Contiguity: None

**Figure 2** G-Bic: Bicluster properties tab.

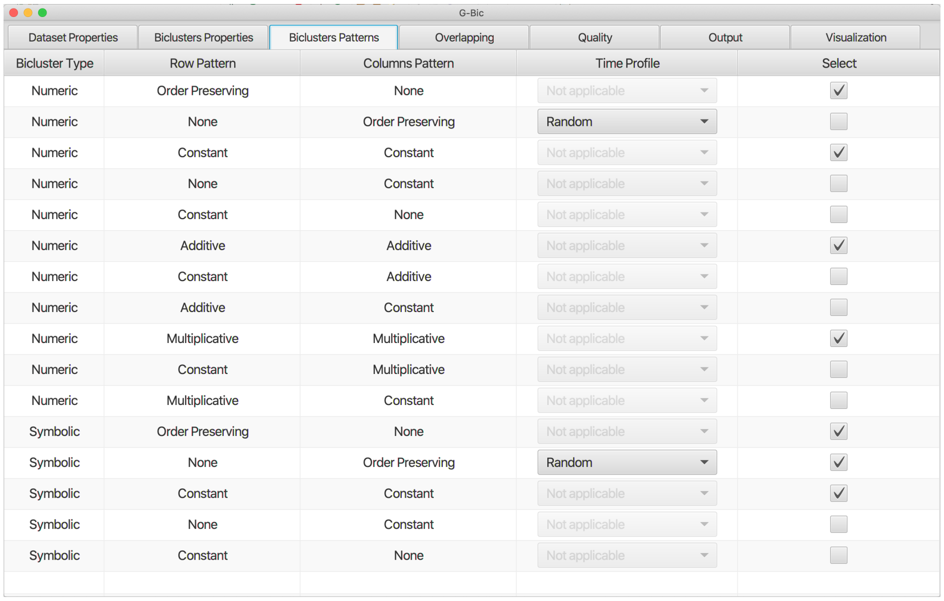
The second step is to set the amount planted biclusters that can overlap. This is done through parameter *% of Overlapping Biclusters* (2). For dataset $S$, this parameter will be set to 50%.

Then the user has to define how the overlapped biclusters will interact with each other. This is done, first, by defining the maximum number of subspaces that can overlap simultaneously, using the parameter *Maximum Number of Biclustering Interactions* (3). Then the user defines how many elements two overlapped biclusters can share, using parameter *% of Overlapping Elements Between Biclusters* (4). Each bicluster on dataset $S$ can overlap with another one, so the number of simultaneous interactions is 2. A set of biclusters can also share 40% of the smallest bicluster's elements. The last three parameters allow the introduction of restrictions on the number of rows (5) and columns (6) that can be shared by a set of overlapping biclusters. We decided to set the % of overlapping rows to 100% and the % of overlapping columns to 80%.

## Quality

The *Quality* tab, illustrated in Figure 5, controls properties from the dataset and the biclusters. Here the user can define the amount of missing values, noise, and errors on both dataset's background and planted biclusters.

For dataset $S$, the *% of Missing Values on Background* (1) is set to 2% percent, while the *% of Missing Values on Planted Biclusters* (2) is 3%. For noise, the *% of Noise on Background* (3) is 10% and the *% of Noise on Planted Biclusters* (4) is 5%. The *Noise Deviation* (5) is set to 1. This means that the noisy value will be, at maximum, at a distance of 1 from the original value. The last setting defines the proportion of errors on the dataset. The *% of Errors on Background* (6) and the *%*



| Bicluster Type | Row Pattern | Columns Pattern | Time Profile | Select |
|---|---|---|---|---|
| Numeric | Order Preserving | None | Not applicable | ☑ |
| Numeric | None | Order Preserving | Random | □ |
| Numeric | Constant | Constant | Not applicable | ☑ |
| Numeric | None | Constant | Not applicable | □ |
| Numeric | Constant | None | Not applicable | □ |
| Numeric | Additive | Additive | Not applicable | ☑ |
| Numeric | Constant | Additive | Not applicable | □ |
| Numeric | Additive | Constant | Not applicable | □ |
| Numeric | Multiplicative | Multiplicative | Not applicable | ☑ |
| Numeric | Constant | Multiplicative | Not applicable | □ |
| Numeric | Multiplicative | Constant | Not applicable | □ |
| Symbolic | Order Preserving | None | Not applicable | ☑ |
| Symbolic | None | Order Preserving | Random | ☑ |
| Symbolic | Constant | Constant | Not applicable | ☑ |
| Symbolic | None | Constant | Not applicable | □ |
| Symbolic | Constant | None | Not applicable | □ |

**Figure 3** G-Bic: Bicluster patterns tab.

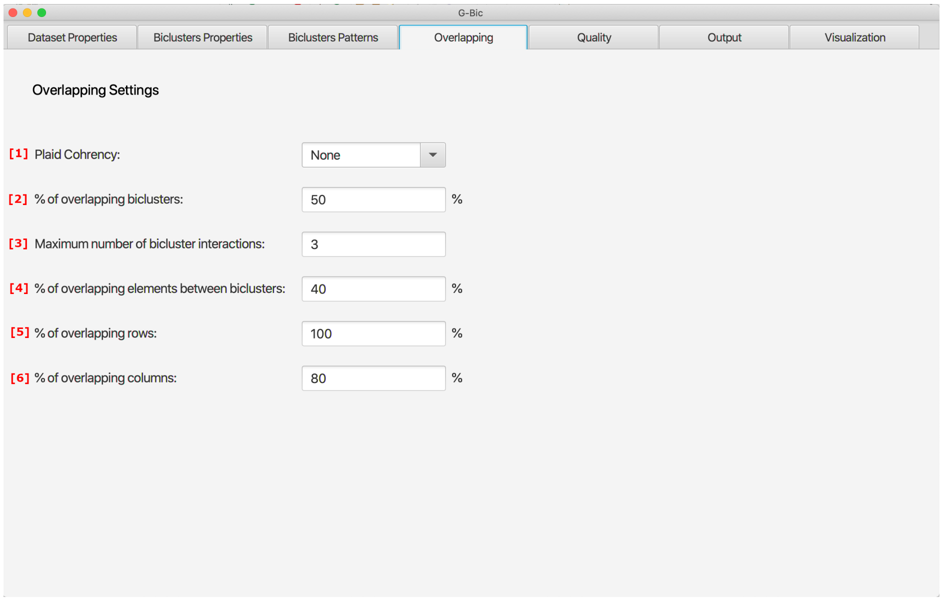
*of Errors on Planted Biclusters* is set to 1%. The error elements will be at a distance from the original values of at least the value of *Noise Deviation* (5). Parameters (1), (3), and (6) control the exact amount of missing values, noise, and errors in the background.

## Output

The last stage before generating the new dataset is defining how and where the output will be stored, as resumed in Figure 6. The first parameter, *Save On* (1) allows the user to decide whether the dataset should be stored on a single or onyo multiple files. Multiple files are worth it when the dataset has large dimensions, since it can be divided in small chunks across several files. The second parameter, *File Name* (2), sets the prefix of the name of all three output files. The first file will contain the dataset in a *tsv* format, with the values separated by a tab delimiter, as shown in Figure 7. The remaining two files will contain the information about the biclusters planted on either *txt* format, illustrated in Figure 8, where some statistics and the summary of the first bicluster, as well as the content for the first context is shown; and also by a *JSON* format, as shown in Figure 9. The last parameter, *Save to Directory* (3), specifies where the output will be stored.

## Visualization

The last tab of the application allows the user to visualize the output, by showing the biiclusters that resulted from the generation process. Figure 10 shows the visualization options. This tab is composed by two sections: 1) One with the information regarding the bicluster's structure, and 2) one with a graphical representation of the bicluster.



Overlapping Settings

[1] Plaid Cohrency: None

[2] % of overlapping biclusters: 50 %

[3] Maximum number of bicluster interactions: 3

[4] % of overlapping elements between biclusters: 40 %

[5] % of overlapping rows: 100 %

[6] % of overlapping columns: 80 %

**Figure 4** G-Bic: Overlapping settings tab.

As the user chooses one of the available biclusters, the left section of the interface shows information that describes the planted subspace, such as, its dimensions, where it is located (on which rows and columns), which are the patterns followed by each dimension, and respective factors, when available (only in additive or multiplicative patterns), the plaid coherency assumed and the degree of missing values, noise and errors.

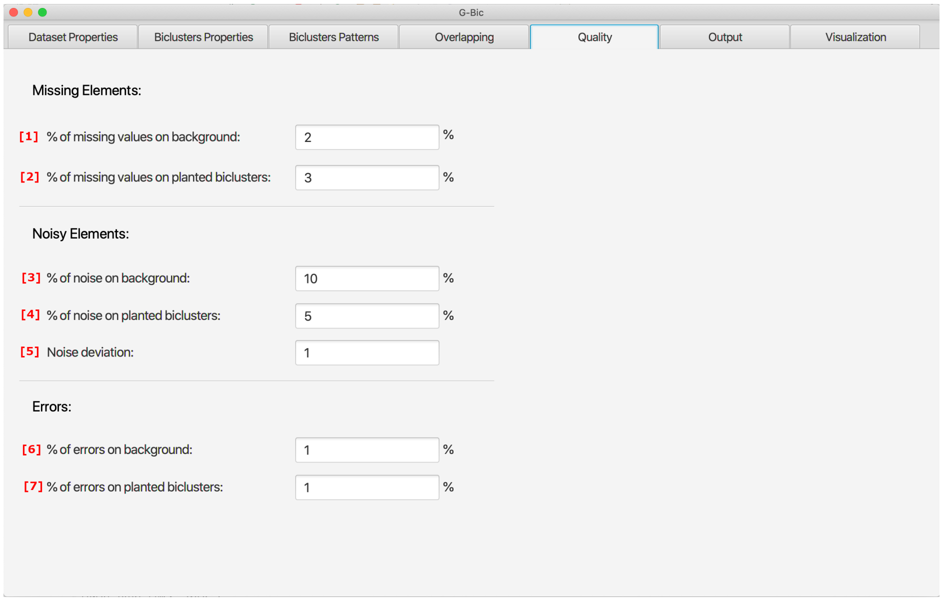
In the right section the user can visualize the values of each context through a new windows that displays a graphical representation of the slice using a heatmap, that easily reflects the pattern expressed, as shown in Figure 11.

## Simulating real data

In this section, we show how G-Bic can be used to produce reference biclusters. We focus on the most popular areas of application of biclustering: gene expression data, text mining, recommendation systems and biomedical data. Example datasets that we reproduced are in 2. To characterize the biclusters, we complement the definitions by Madeira and Oliveira [1] with empirical conclusions by several authors, [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 7, 8, 13, 14, 15], when applying their biclustering algorithms to the chosen datasets, summarized in Table 3.

**Table 2** Example datasets used during the development of some of the existing algorithms

| | Dataset Type | Dataset | Description | Dimensions |
|---|---|---|---|---|
| 1 | Gene Expression | Arabidopsis [6] | Genes × Conditions | 21031 × 351 |
| 2 | Recomendation Systems | MovieLens-20M [7, 8] | Users × Movies | 138000 × 27000 |
| 3 | Text Mining | Reuters-21578 [12] | Terms × Documents | 29930 × 21578 |
| 4 | Clinical Data | PMSI2013[14] | Patients × Clinical Data | 49231 × 7941 |



Missing Elements:

[1] % of missing values on background: 2 %

[2] % of missing values on planted biclusters: 3 %

Noisy Elements:

[3] % of noise on background: 10 %

[4] % of noise on planted biclusters: 5 %

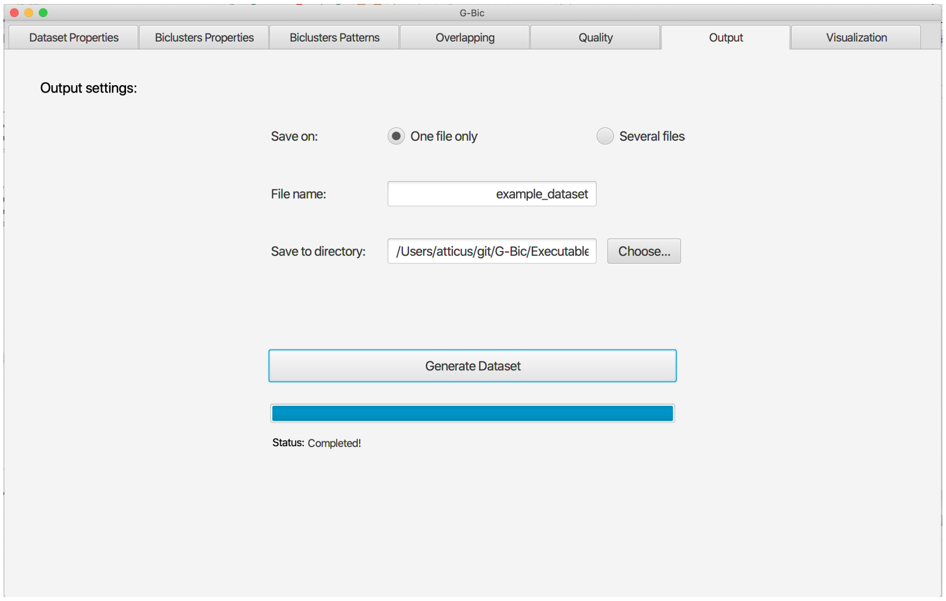
[5] Noise deviation: 1

Errors:

[6] % of errors on background: 1 %

[7] % of errors on planted biclusters: 1 %

**Figure 5** G-Bic: Quality settings tab.



Output settings:

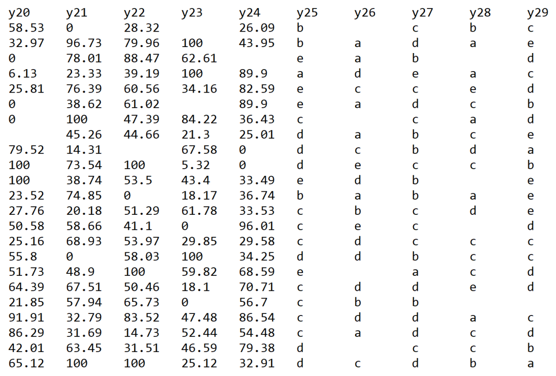
Save on: ● One file only ○ Several files

File name: example_dataset

Save to directory: /Users/atticus/git/G-Bic/Executable

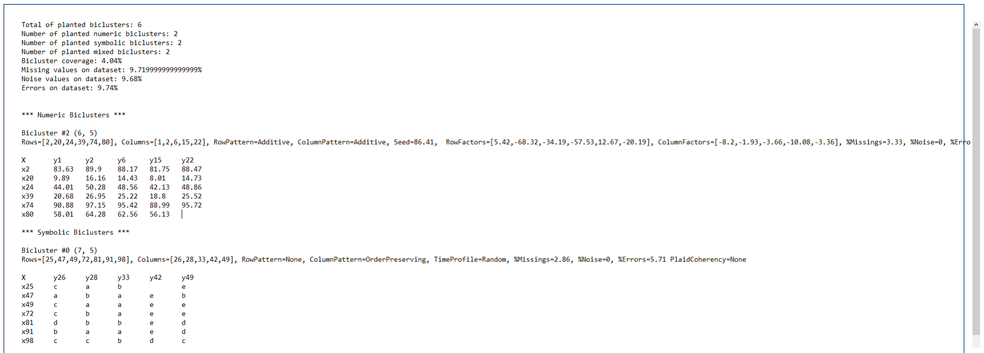
Status: Completed!

**Figure 6** G-Bic: Output tab.



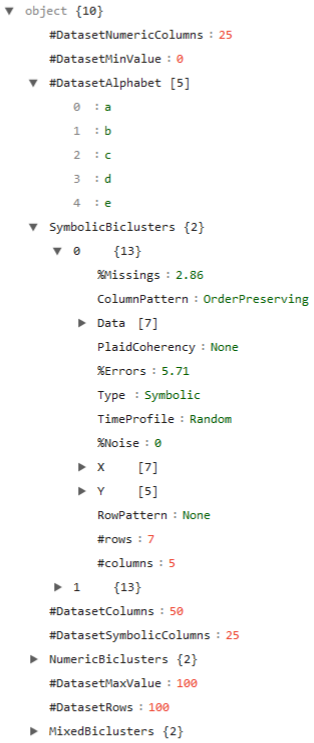
```
y20     y21     y22     y23     y24     y25     y26     y27     y28     y29
58.53   0       28.32           26.09   b               c       b       c
32.97   96.73   79.96   100     43.95   b       a       d       a       e
0       78.01   88.47   62.61           e       a       b               d
6.13    23.33   39.19   100     89.9    a       d       e       a       c
25.81   76.39   60.56   34.16   82.59   e       c       c       e       d
0       38.62   61.02           89.9    e       a       d       c       b
0       100     47.39   84.22   36.43   c               c       a       d
        45.26   44.66   21.3    25.01   d       a       b       c       e
79.52   14.31           67.58   0       d       c       b       d       a
100     73.54   100     5.32    0       d       e       c       c       b
100     38.74   53.5    43.4    33.49   e       d       b               e
23.52   74.85   0       18.17   36.74   b       a       b       a       e
27.76   20.18   51.29   61.78   33.53   c       b       c       d       e
50.58   58.66   41.1    0       96.01   c       e       c               d
25.16   68.93   53.97   29.85   29.58   c       d       c       c       c
55.8    0       58.03   100     34.25   d       d       b       c       c
51.73   48.9    100     59.82   68.59   e               a       c       d
64.39   67.51   50.46   18.1    70.71   c       d       d       e       d
21.85   57.94   65.73   0       56.7    c       b       b
91.91   32.79   83.52   47.48   86.54   c       d       d       a       c
86.29   31.69   14.73   52.44   54.48   c       a       d       c       d
42.01   63.45   31.51   46.59   79.38   d               c       c       b
65.12   100     100     25.12   32.91   d       c       d       b       a
```

**Figure 7** G-Bic: Dataset tsv file.



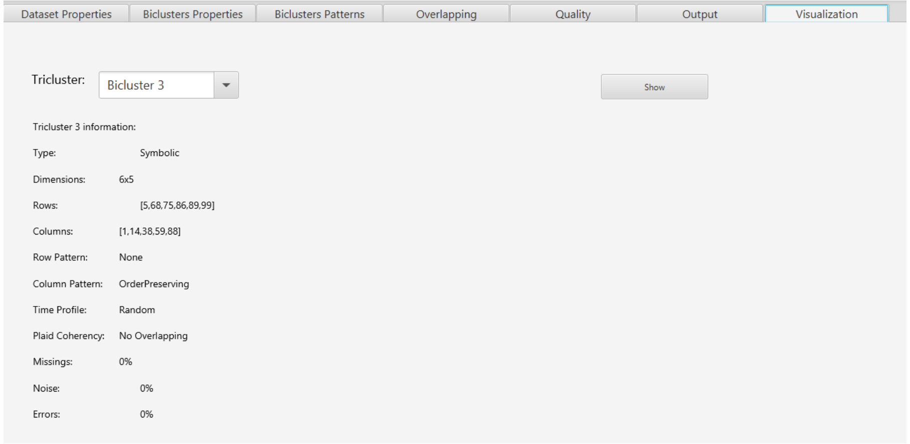
```
Total of planted biclusters: 6
Number of planted numeric biclusters: 2
Number of planted symbolic biclusters: 2
Number of planted mixed biclusters: 2
Bicluster coverage: 4.04%
Missing values on dataset: 9.719999999999999%
Noise values on dataset: 9.68%
Errors on dataset: 9.74%


*** Numeric Biclusters ***

Bicluster #2 (6, 5)
Rows=[2,20,24,39,74,80], Columns=[1,2,6,15,22], RowPattern=Additive, ColumnPattern=Additive, Seed=86.41,  RowFactors=[5.42,-68.32,-34.19,-57.53,12.67,-20.19], ColumnFactors=[-8.2,-1.93,-3.66,-10.08,-3.36], %Missings=3.33, %Noise=0, %Erro

X       y1      y2      y6      y15     y22
x2      83.63   89.9    88.17   81.75   88.47
x20     9.89    16.16   14.43   8.01    14.73
x24     44.01   50.28   48.56   42.13   48.86
x39     20.68   26.95   25.22   18.8    25.52
x74     90.88   97.15   95.42   88.99   95.72
x80     58.01   64.28   62.56   56.13   |

*** Symbolic Biclusters ***

Bicluster #0 (7, 5)
Rows=[25,47,49,72,81,91,98], Columns=[26,28,33,42,49], RowPattern=None, ColumnPattern=OrderPreserving, TimeProfile=Random, %Missings=2.86, %Noise=0, %Errors=5.71 PlaidCoherency=None

X       y26     y28     y33     y42     y49
x25     c       a       b               e
x47     a       b       a       e       b
x49     c       a       a       e       e
x72     c       b       a       e       e
x81     d       b       b       e       d
x91     b       a       a       e       d
x98     c       c       b       d       c
```

**Figure 8** G-Bic: Bicluster's txt file.



```
▼ object {10}
    #DatasetNumericColumns : 25
    #DatasetMinValue : 0
  ▼ #DatasetAlphabet [5]
      0  : a
      1  : b
      2  : c
      3  : d
      4  : e
  ▼ SymbolicBiclusters {2}
    ▼ 0     {13}
          %Missings : 2.86
          ColumnPattern : OrderPreserving
        ▶ Data  [7]
          PlaidCoherency : None
          %Errors : 5.71
          Type  : Symbolic
          TimeProfile : Random
          %Noise : 0
        ▶ X     [7]
        ▶ Y     [5]
          RowPattern : None
          #rows : 7
          #columns : 5
    ▶ 1     {13}
    #DatasetColumns : 50
    #DatasetSymbolicColumns : 25
  ▶ NumericBiclusters {2}
    #DatasetMaxValue : 100
    #DatasetRows : 100
  ▶ MixedBiclusters {2}
```

**Figure 9** G-Bic: Bicluster's JSON file.



Tricluster: Bicluster 3

Tricluster 3 information:

Type: Symbolic

Dimensions: 6x5

Rows: [5,68,75,86,89,99]

Columns: [1,14,38,59,88]

Row Pattern: None

Column Pattern: OrderPreserving

Time Profile: Random

Plaid Coherency: No Overlapping

Missings: 0%

Noise: 0%

Errors: 0%

**Figure 10** G-Bic: Bicluster's summary

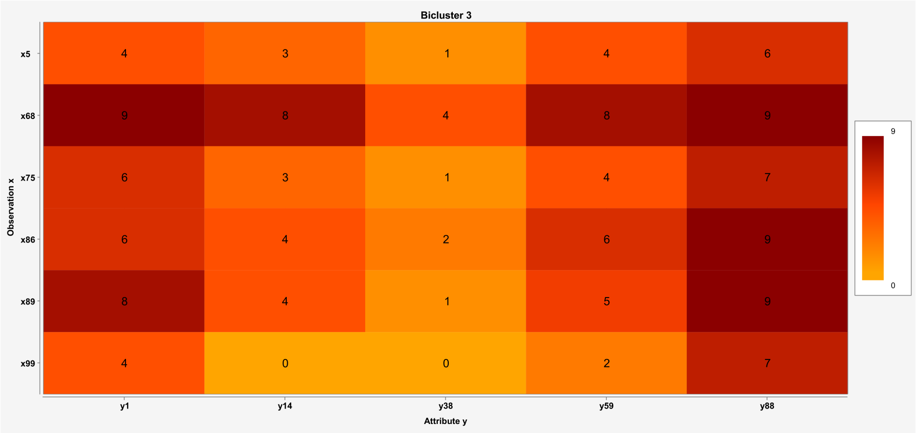


**Figure 11** G-Bic: Heatmap to visualize a bicluster's pattern

**Table 3** Settings to simulate the real datasets

| | Properties | Dataset 1 - Gene Expression | Dataset 2 - Recomendation Systems | Dataset 3 - Text Mining | Dataset 4 - Clinical Data |
|---|---|---|---|---|---|
| Dataset | Data type | Numeric | Numeric | Numeric | Mixed |
| | Dimensions | $21031 \times 351$ | $138000 \times 27000$ | $29930 \times 21578$ | $49231 \times 7941$ |
| | Background | Uniform | Missing | Missing | Missing |
| | Missings | 0% | 95,5% | 98% | 99,81% |
| | Noise | 10% | 0% | 0% | 0% |
| | Errors | 0% | 0% | 0% | 3% |
| Biclusters | Number | 417 | 3000 | 30 | 70 |
| | Patterns | Additive, Order Preserving | Order Preserving | Constant and Order-Preserving | Mixed |
| Overlapping | Plaid Coherency | Additive | No Overlapping | No Overlapping | No Overlapping |
| | % Overlapping Bics | 10% | 0% | 0% | 0% |

## References

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