

Supplementary Material for: Comparison of Statistical Methods for Finding Network Motifs

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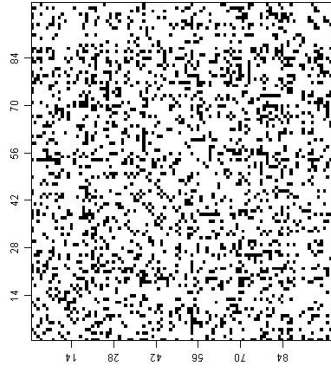
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University of Bristol

This is an extension to the appendix of the above paper. Here we provide the full set of adjacency matrices for all methods and all choices of tuning parameters.

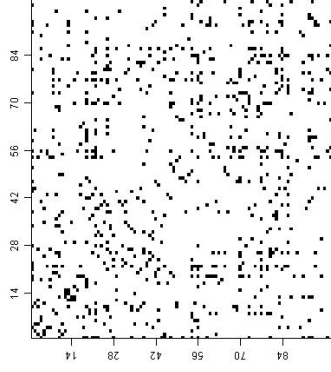
A *E. coli* data: additional adjacency matrices



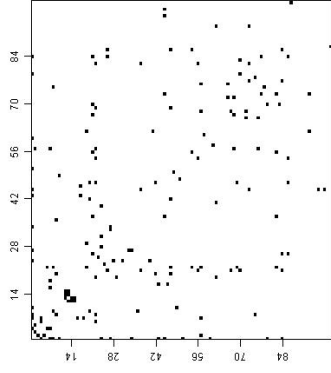
(a) $\lambda = 0.00005$



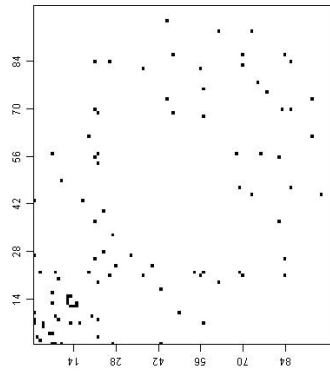
(b) $\lambda = 0.0005$



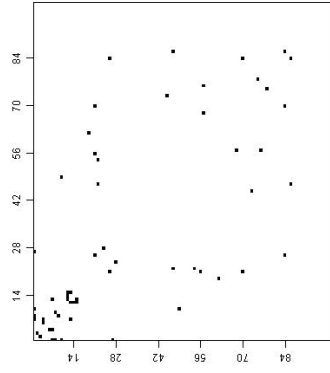
(c) $\lambda = 0.005$



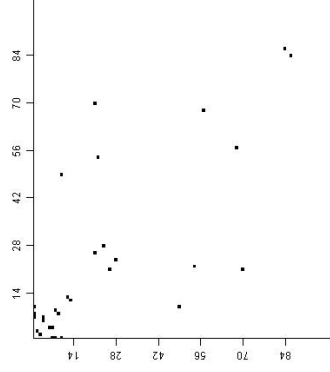
(d) $\lambda = 0.05$



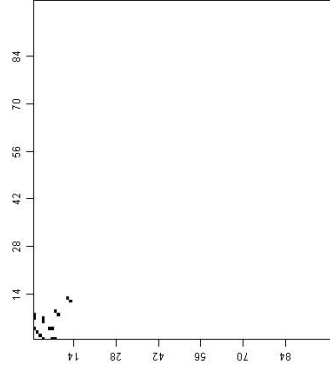
(e) $\lambda = 0.1$



(f) $\lambda = 0.2$

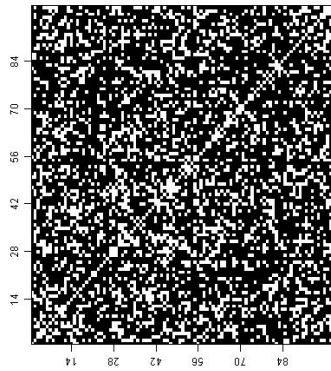


(g) $\lambda = 0.5$

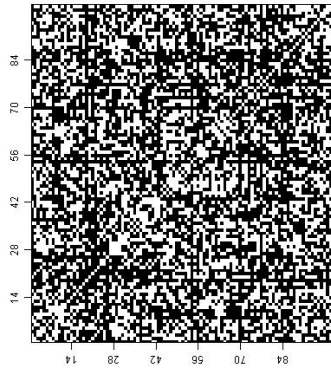


(h) $\lambda = 1$

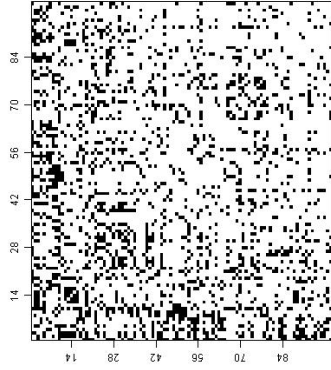
Figure 1: Plots of the estimated adjacent matrices for *E. coli* data with Neighbourhood selection.



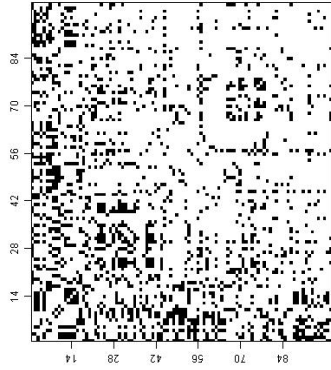
(a) $\lambda = 0.00005$



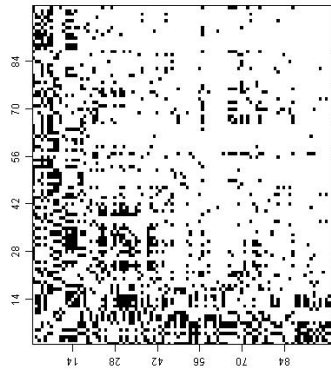
(b) $\lambda = 0.0005$



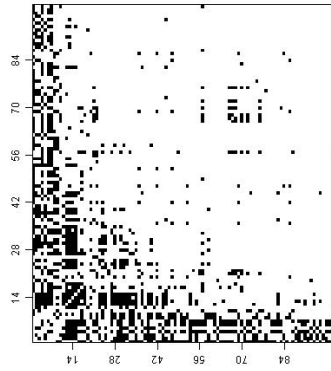
(c) $\lambda = 0.05$



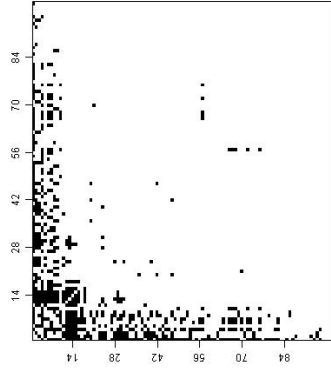
(d) $\lambda = 0.1$



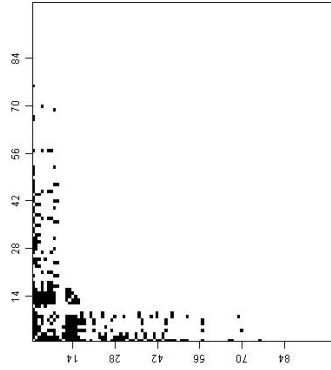
(e) $\lambda = 0.2$



(f) $\lambda = 0.5$

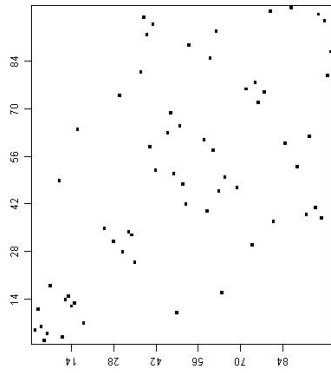


(g) $\lambda = 1$

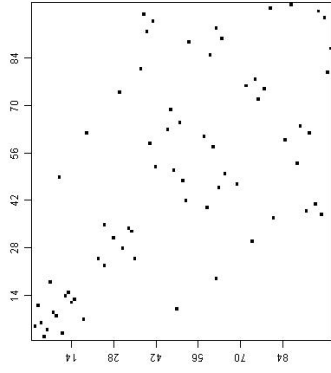


(h) $\lambda = 1.4$

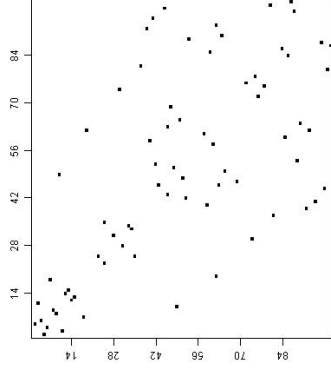
Figure 2: Plots of the estimated adjacent matrices for *E. coli* data with G-Lasso.



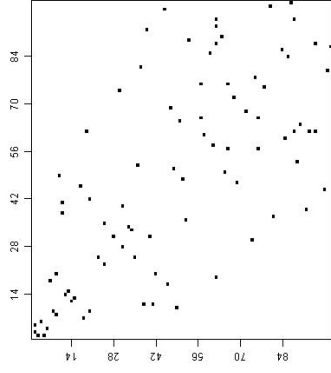
(a) $\alpha = 0.00000001$



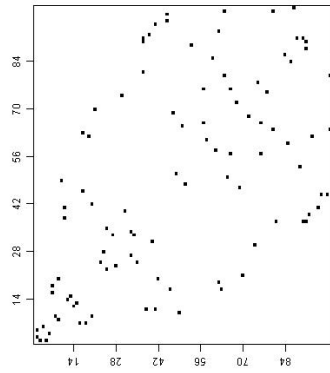
(b) $\alpha = 0.000001$



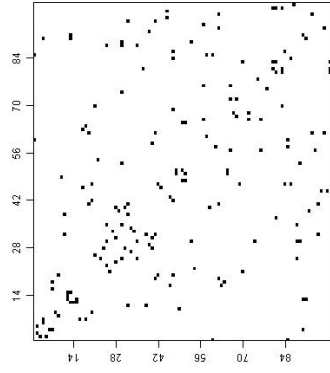
(c) $\alpha = 0.00001$



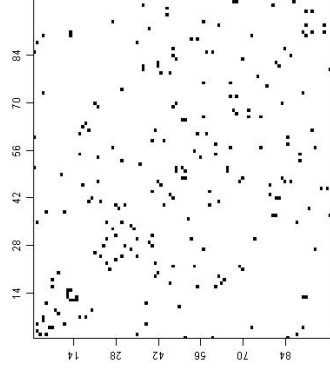
(d) $\alpha = 0.0001$



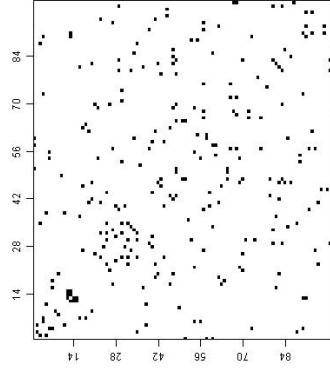
(e) $\alpha = 0.01$



(f) $\alpha = 0.05$



(g) $\alpha = 0.1$



(h) $\alpha = 0.2$

Figure 3: Plots of the estimated adjacent matrices for *E. coli* data with PC-algorithm.

B ROC-Curves for *E. coli* data

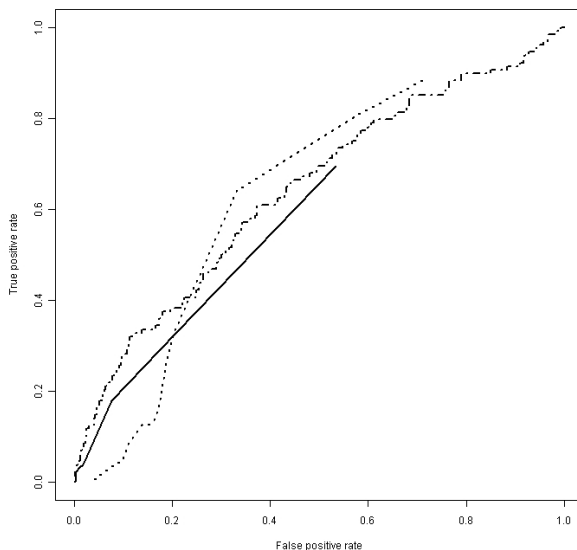


Figure 4: ROC curves for G-Lasso estimator (dotted), Neighbourhood selection (solid), and Shrinkage estimator (dotdash).

C Simulation design

First, we give some more details on the simulation design. The synthetic data is simulated from multivariate normal distributions with concentration matrices corresponding to the three types of motifs as described in the main text. Each network is based on a single network motif which is replicated a certain number of times (i.e. matches) and with a specific size (i.e. motif size). The network has also a fixed, but sparse, number of interactions (i.e. edges) out of all possible interactions. A Gaussian sample of size $n = 150$, with mean zero and covariance matrix according to the given network is then simulated several times (i.e. replications). The variances (i.e. the diagonal) are equal to one. Characteristic aspects of each network are summarized in Table 1. In the smallest networks, 9 variables are not part of the motif and they are marginally and conditionally independent.

| | Matches | Edges | Total edges | Motif size | Replications | Partial correlation |
|------------------------------|---------|-------|-------------|------------|--------------|---------------------|
| GROUP 1 ($p = 20$) | | | | | | |
| HUB (Fig. ??a) | 1 | 10 | 190 | 11 | 2000 | 0.316 |
| CASCADE (Fig. ??b) | 1 | 10 | 190 | 11 | 2000 | 0.5 (last edge 0.7) |
| PAIRWISE (Fig. ??c) | 10 | 10 | 190 | 2 | 2000 | 0.581 |
| GROUP 2 ($p = 100$) | | | | | | |
| HUB | 9 | 91 | 4950 | 11 (12) | 100 | 0.316 |
| CASCADE | 9 | 91 | 4950 | 11 (12) | 100 | 0.5 (last edge 0.7) |
| PAIRWISE | 50 | 50 | 4950 | 2 | 100 | 0.581 |
| GROUP 3 ($p = 200$) | | | | | | |
| HUB | 18 | 182 | 19900 | 11 (12) | 100 | 0.316 |
| CASCADE | 18 | 182 | 19900 | 11 (12) | 100 | 0.5 (last edge 0.7) |
| PAIRWISE | 100 | 100 | 19900 | 2 | 100 | 0.581 |

Table 1: Settings for synthetic data

For $p = 100$, one network motif has size 12, and for $p = 200$ two motifs have size 12.

For the comparative study with both real data and synthetic data, we consider the following methods:

- Neighbourhood selection with the following penalty terms,
 - real data:
 $\lambda \in \{5e-05, 5e-04, 5e-03, 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4\}$;
 - synthetic data:
 $\lambda \in \{5e-04, 5e-03, 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5\}$.
- G-Lasso with a list of different penalty terms,
 - real data:
 $\lambda \in \{5e-05, 5e-04, 5e-03, 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4\}$;
 - synthetic data:
 $\lambda \in \{0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5\}$.
- Shrinkage estimator with two types of statistical test (at FDR 5%):
 - empirical Bayes approach;
 - t-test approach (if $n > p$).
- MLE (if $n > p$) with two types of statistical test (at FDR 5%):
 - empirical Bayes approach;

- t-test approach.
- PC-algorithm (moralizing the estimated DAG) with a list of different significance level,
 - real data:
 $\alpha \in \{1e-08, 1e-07, 1e-06, 1e-05, 1e-04, 1e-03, 0.01, 0.05, 0.1\}$;
 - synthetic data:
 $\alpha \in \{1e-08, 1e-07, 1e-06, 1e-05, 1e-04, 1e-03, 0.01, 0.05, 0.1\}$.

D *Synthetic data* data: additional plot of adjacent matrices for Neighbourhood selection

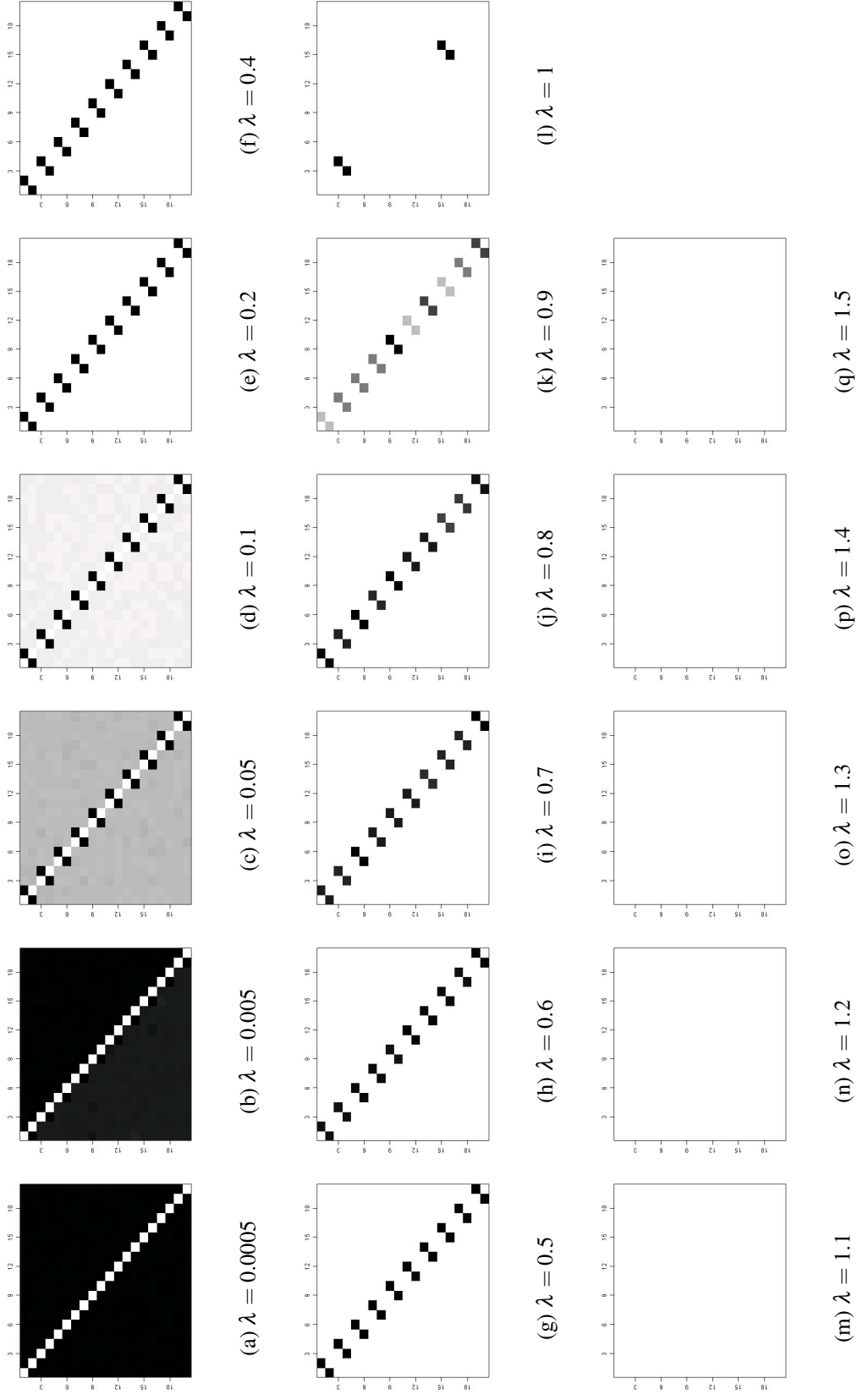


Figure 5: Plot of the estimated adjacent matrices with Neighbourhood selection for pairwise structure with $p = 20$.

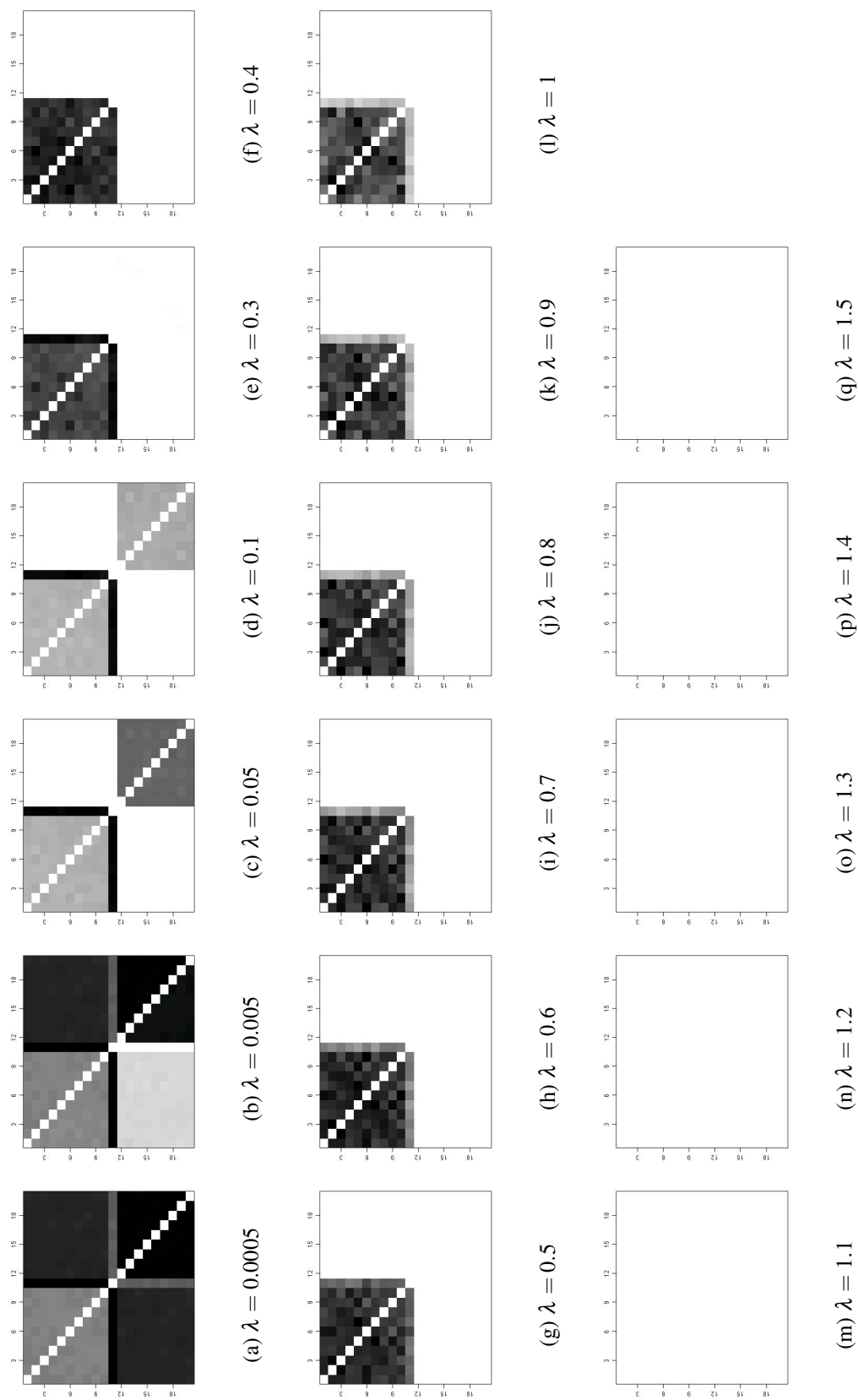


Figure 6: Plot of the estimated adjacent matrices with Neighbourhood selection for hub structure with $p = 20$.

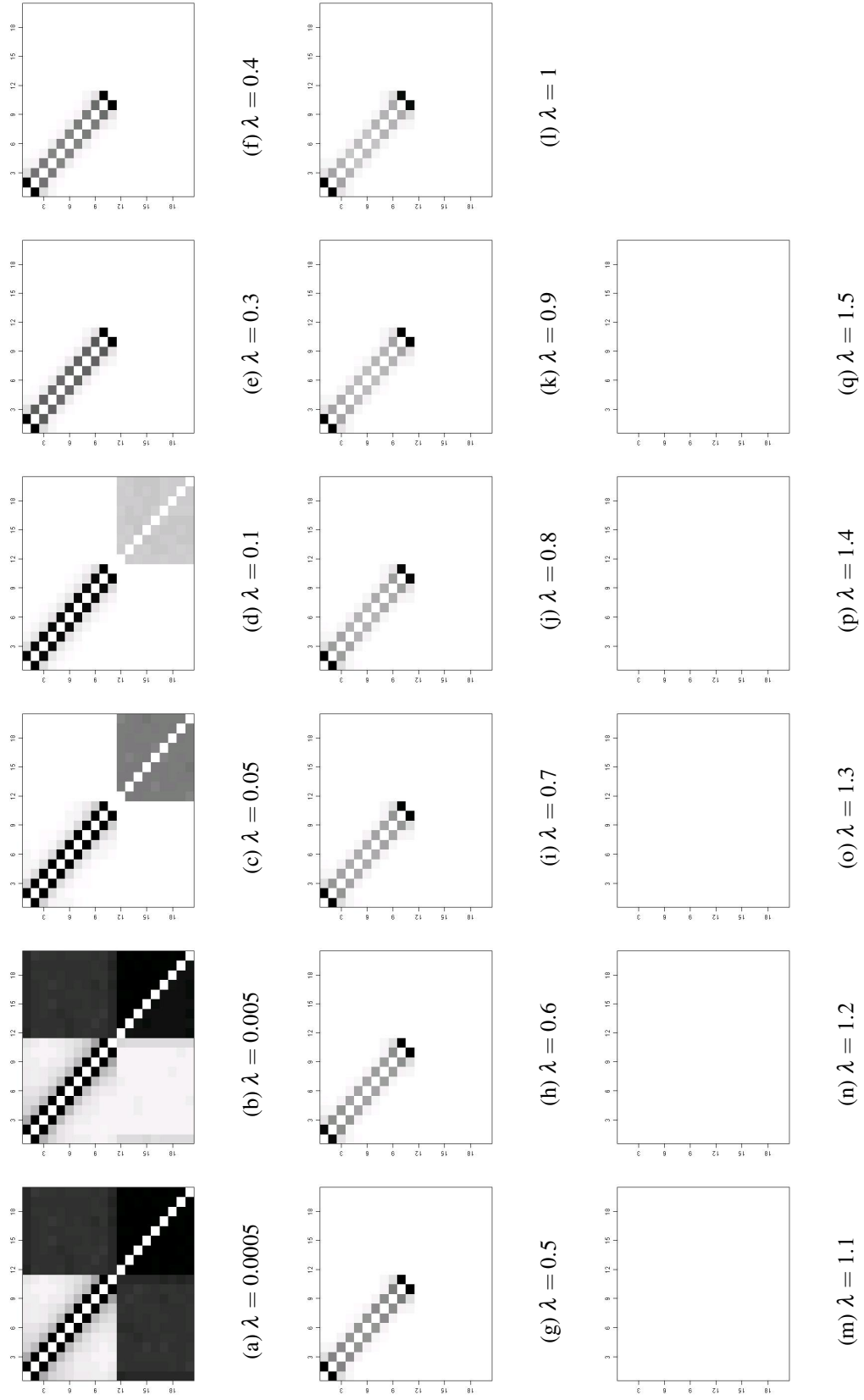


Figure 7: Plot of the estimated adjacent matrices with Neighbourhood selection for cascade structure with $p = 20$.

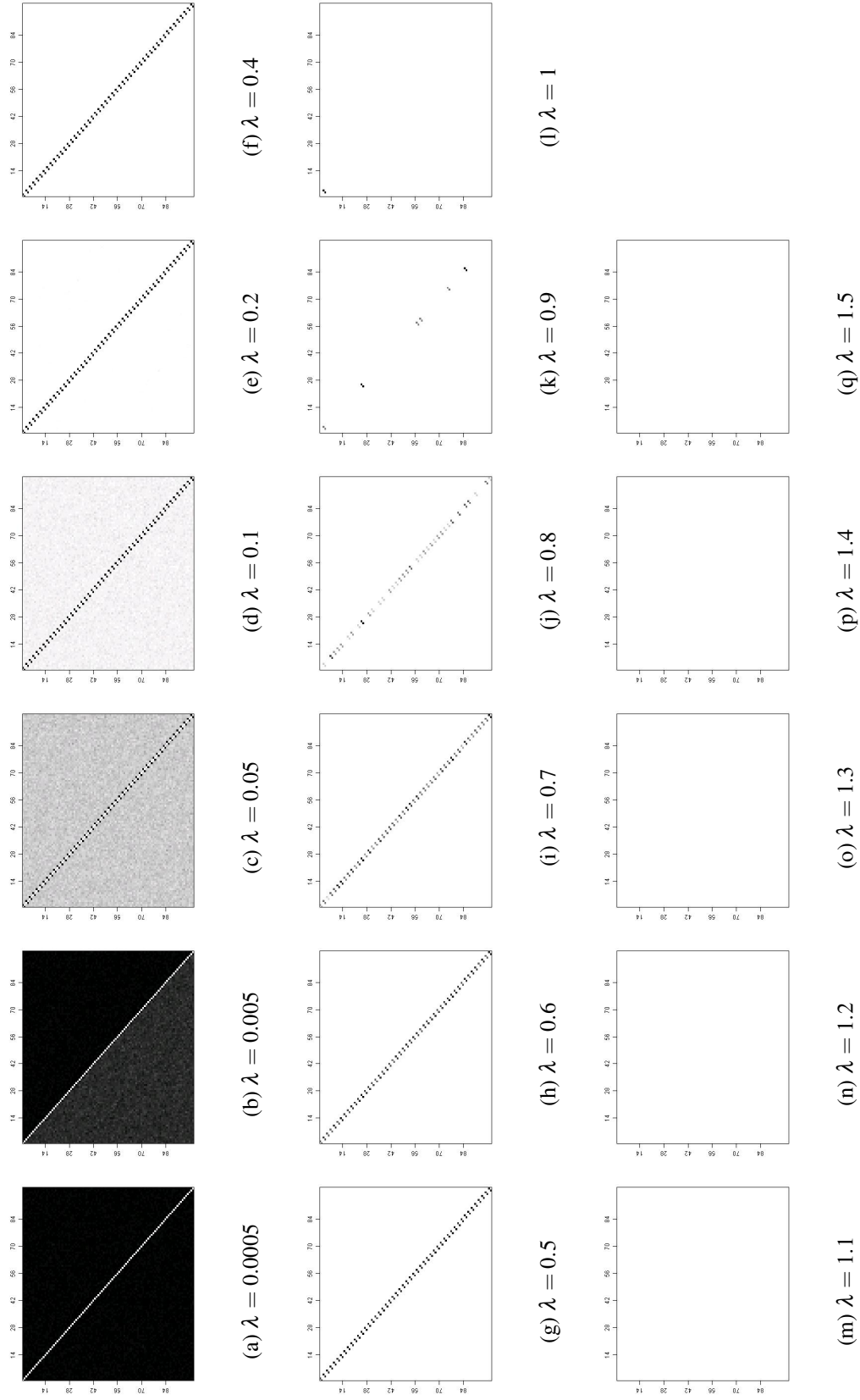


Figure 8: Plot of the estimated adjacent matrices with Neighbourhood selection for pairwise structure with $p = 100$.

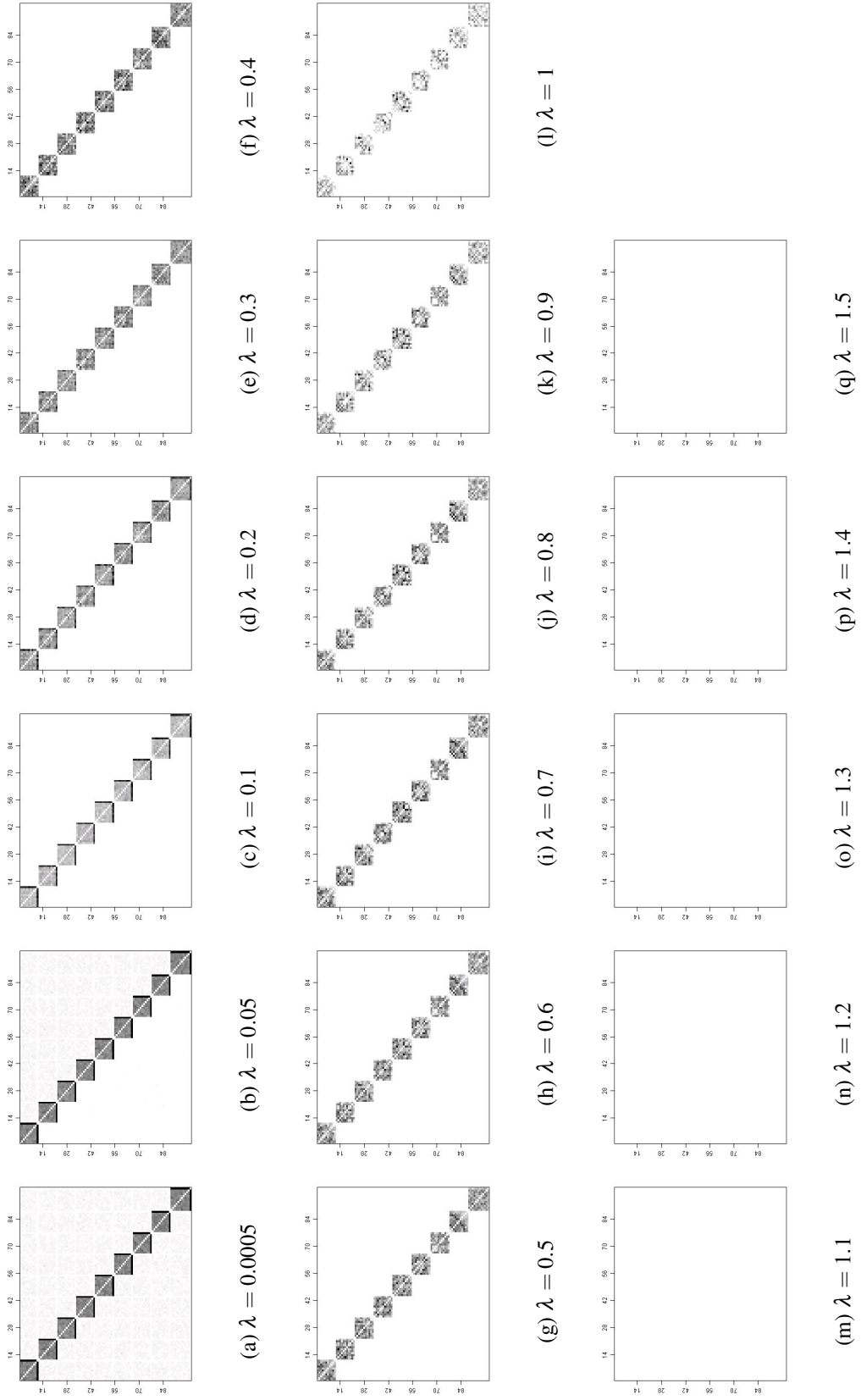


Figure 9: Plot of the estimated adjacent matrices with Neighbourhood selection for hub structure with $p = 100$.

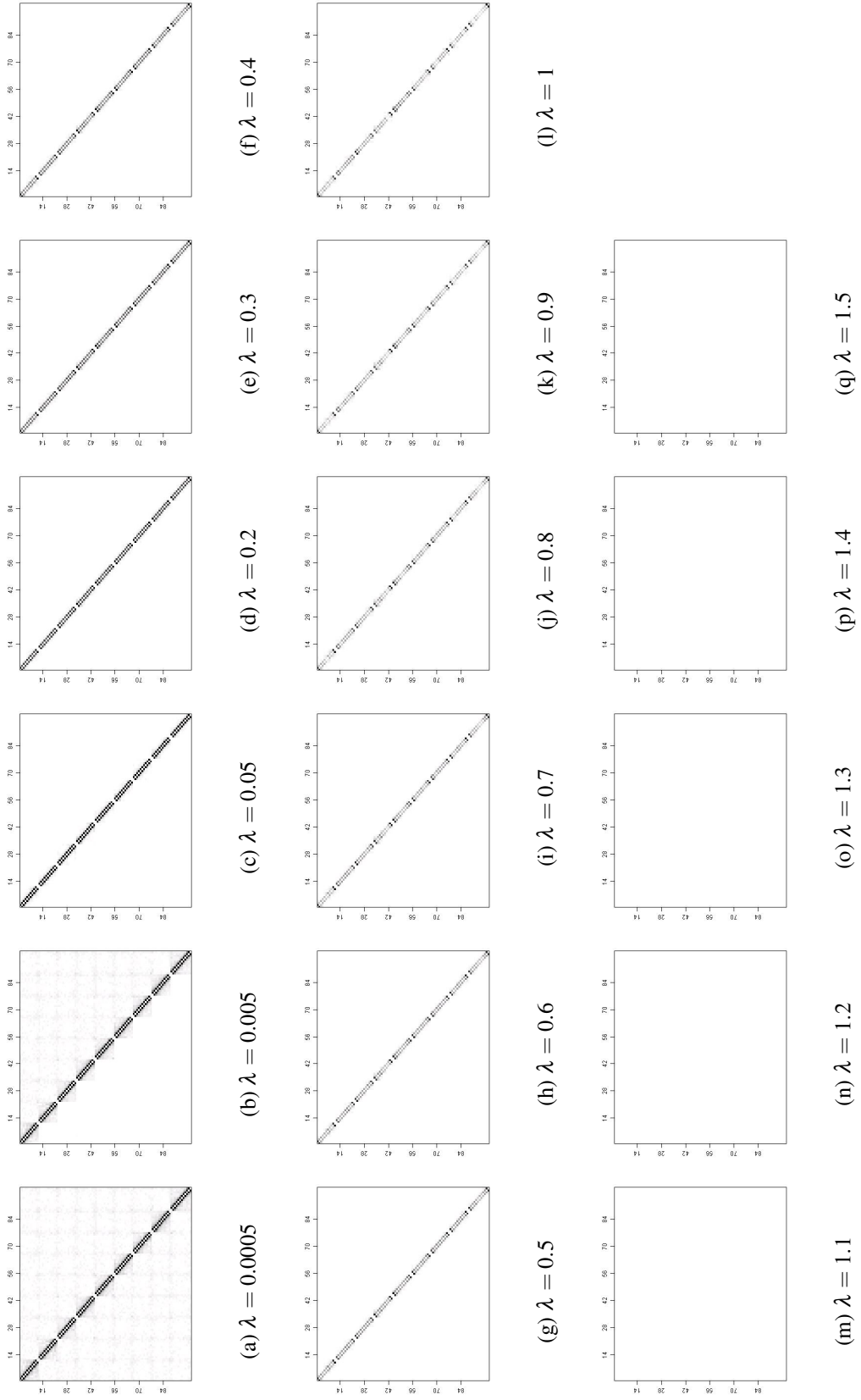


Figure 10: Plot of the estimated adjacent matrices with Neighbourhood selection for cascade structure with $p = 100$.

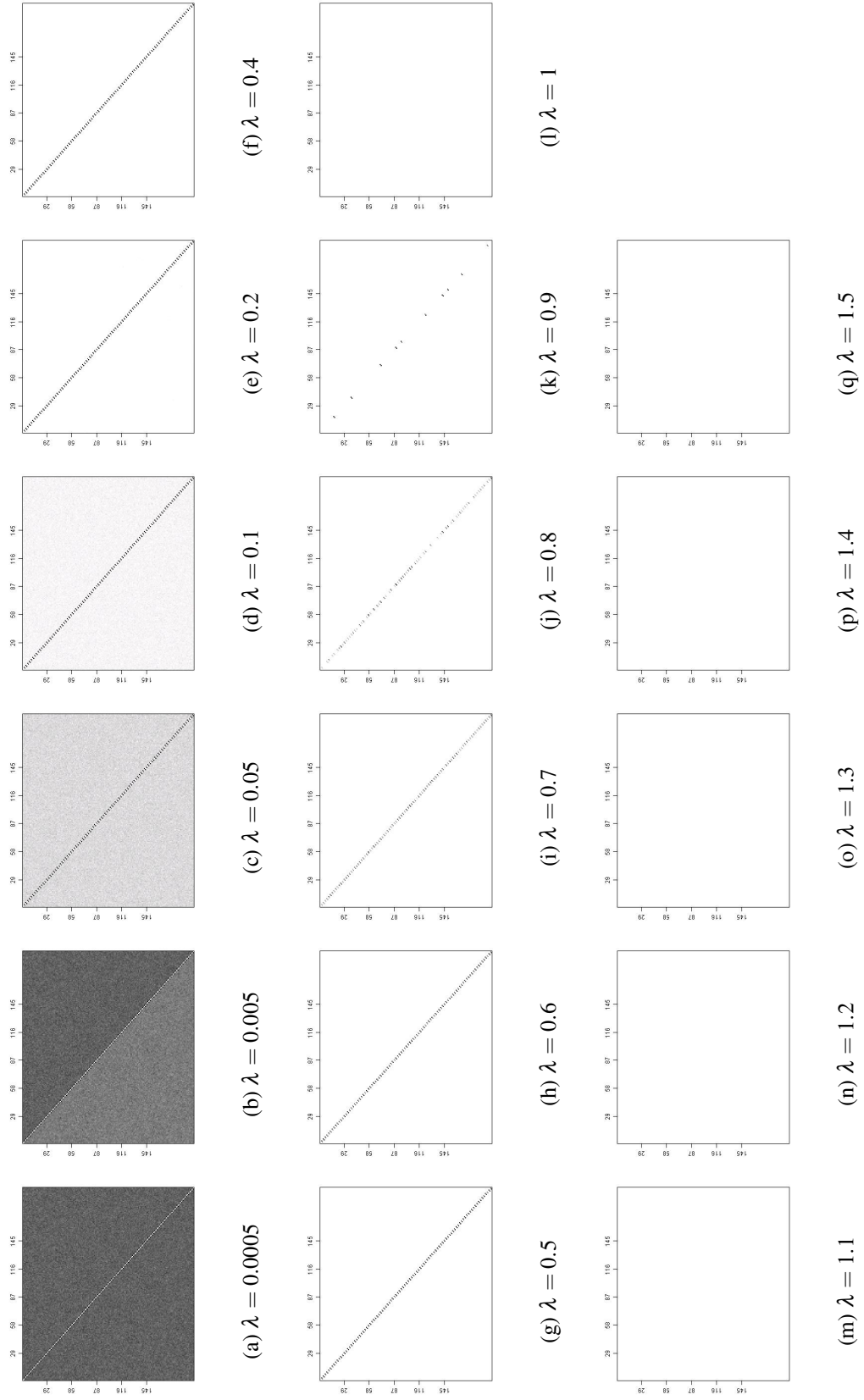
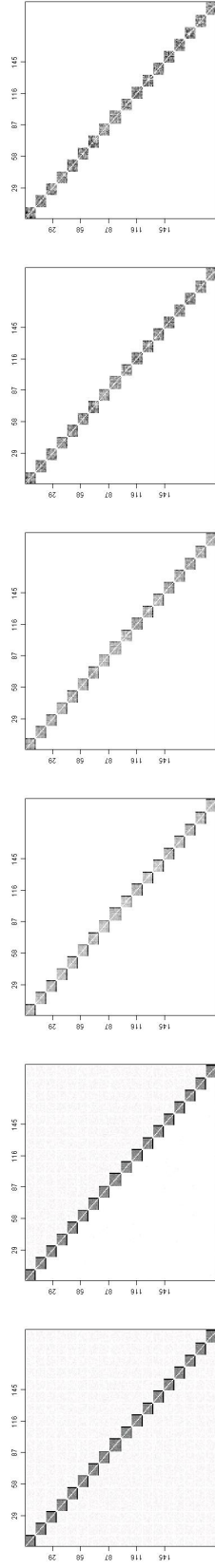
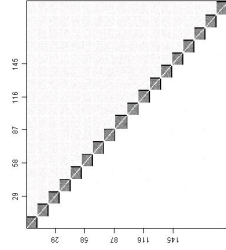


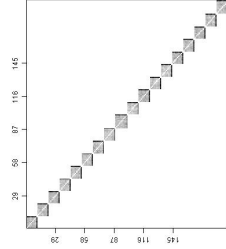
Figure 11: Plot of the estimated adjacent matrices with Neighbourhood selection for pairwise structure with $p = 200$.



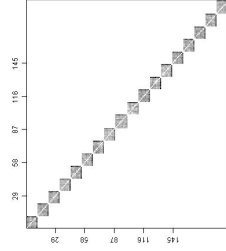
(a) $\lambda = 0.0005$



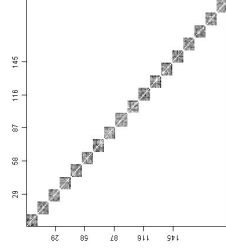
(b) $\lambda = 0.005$



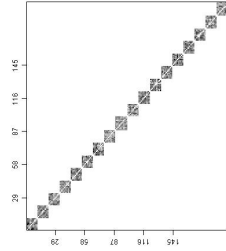
(c) $\lambda = 0.1$



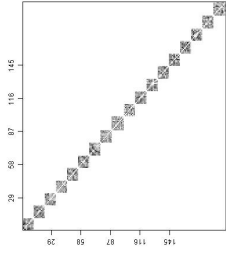
(d) $\lambda = 0.2$



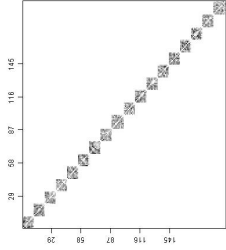
(e) $\lambda = 0.3$



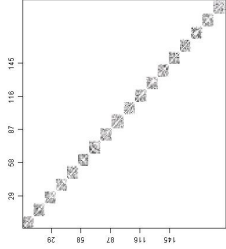
(f) $\lambda = 0.4$



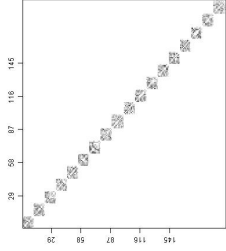
(g) $\lambda = 0.5$



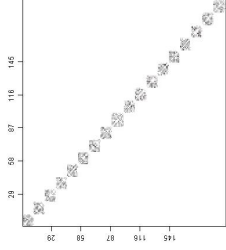
(h) $\lambda = 0.6$



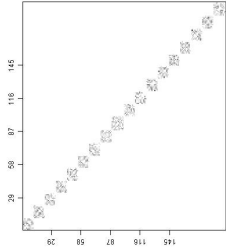
(i) $\lambda = 0.7$



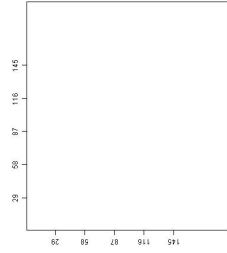
(j) $\lambda = 0.8$



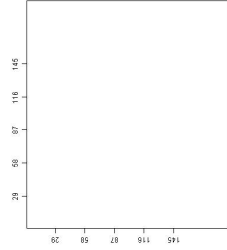
(k) $\lambda = 0.9$



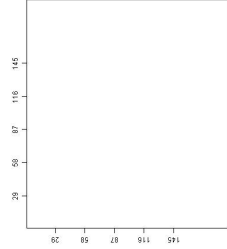
(l) $\lambda = 1$



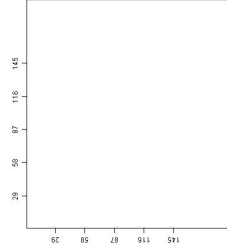
(m) $\lambda = 1.1$



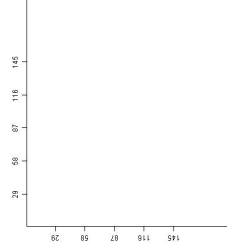
(n) $\lambda = 1.2$



(o) $\lambda = 1.3$



(p) $\lambda = 1.4$



(q) $\lambda = 1.5$

Figure 12: Plot of the estimated adjacent matrices with Neighbourhood selection for hub structure with $p = 200$.

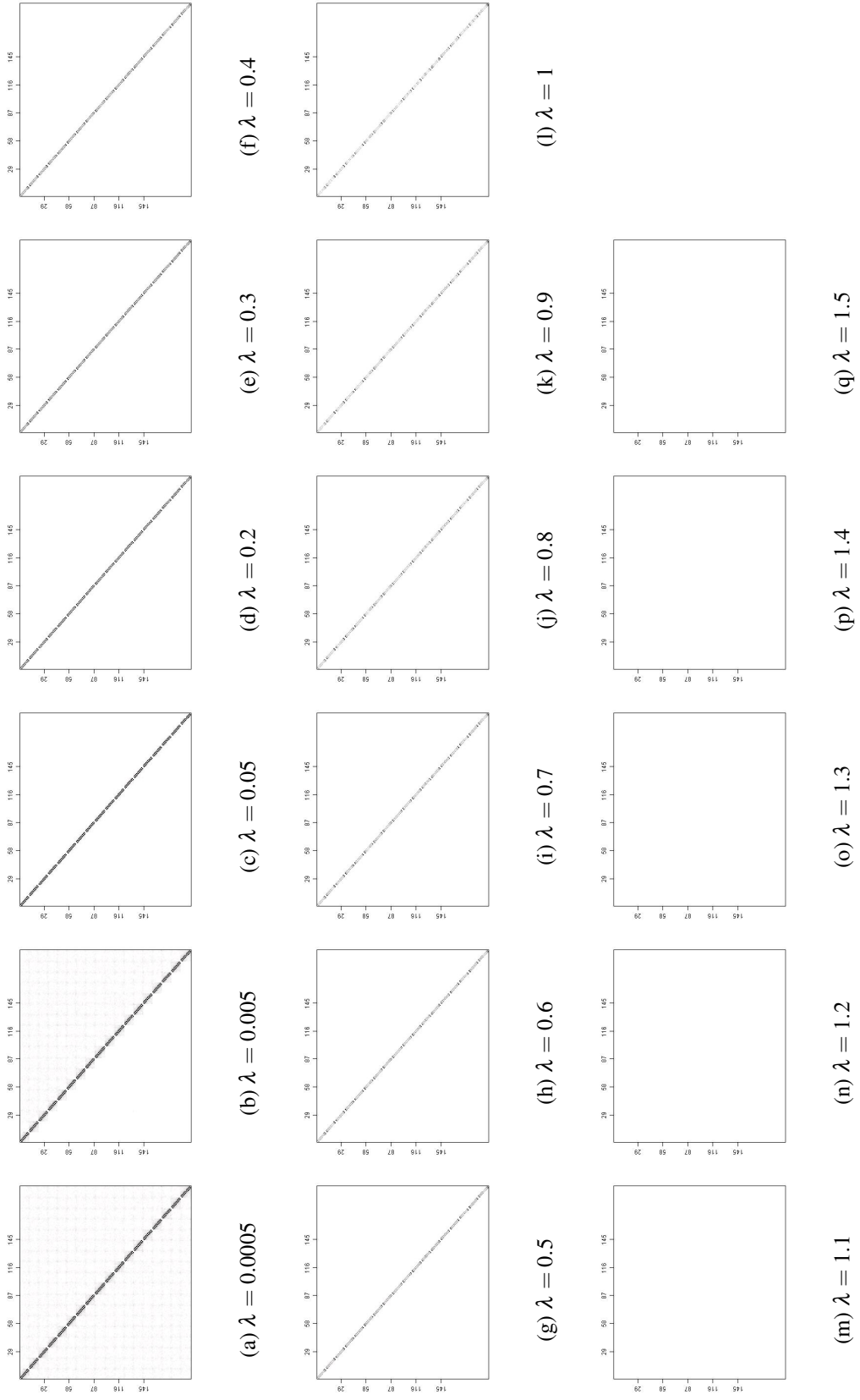


Figure 13: Plot of the estimated adjacent matrices with Neighbourhood selection for cascade structure with $p = 200$.

E *Synthetic data* data: additional plot of adjacent matrices for G-Lasso

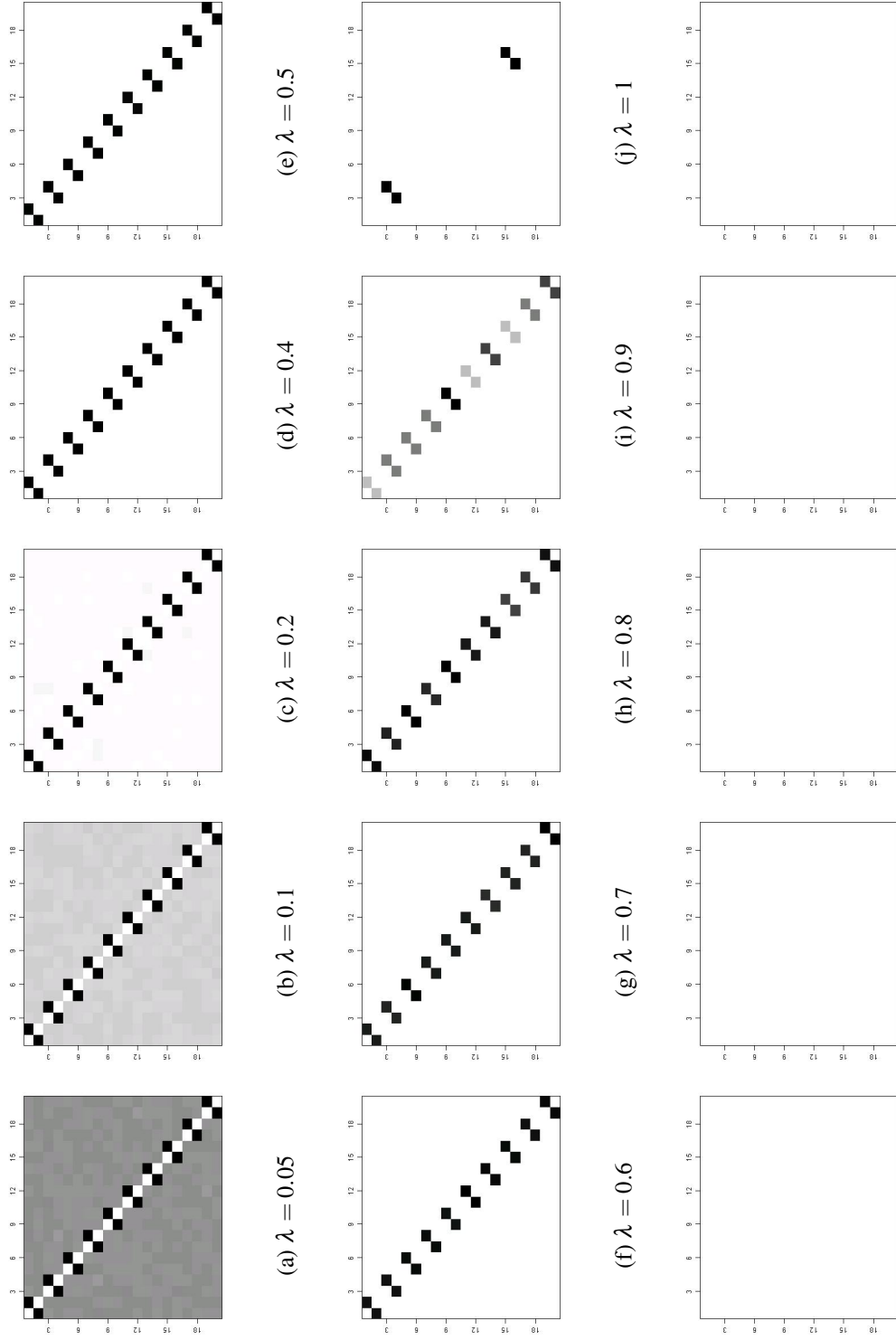


Figure 14: Plot of the estimated adjacent matrices with G-Lasso for pairwise structure with $p = 20$.

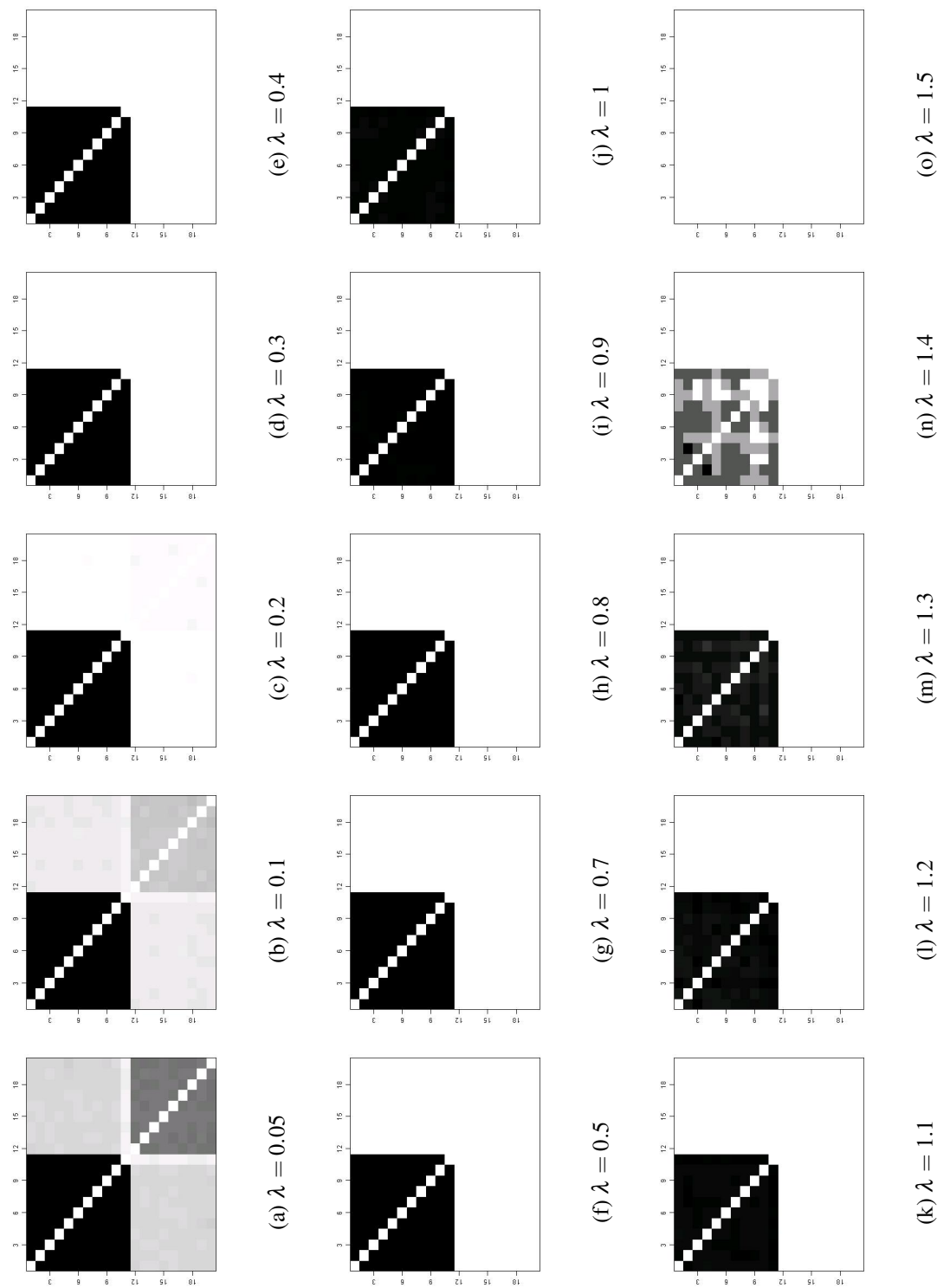


Figure 15: Plot of the estimated adjacent matrices with G-Lasso for hub structure with $p = 20$.

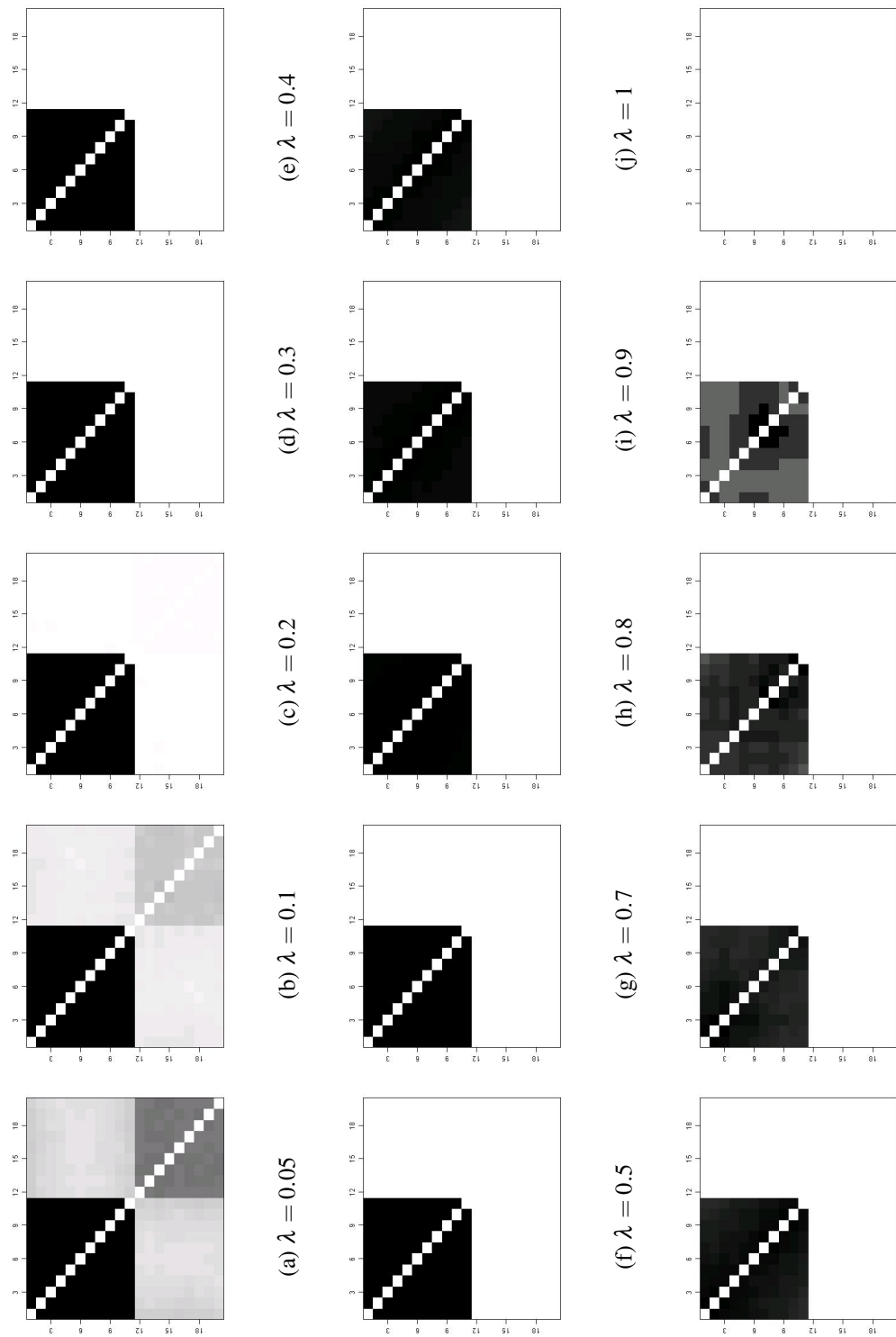


Figure 16: Plot of the estimated adjacent matrices with G-Lasso for cascade structure with $p = 20$.

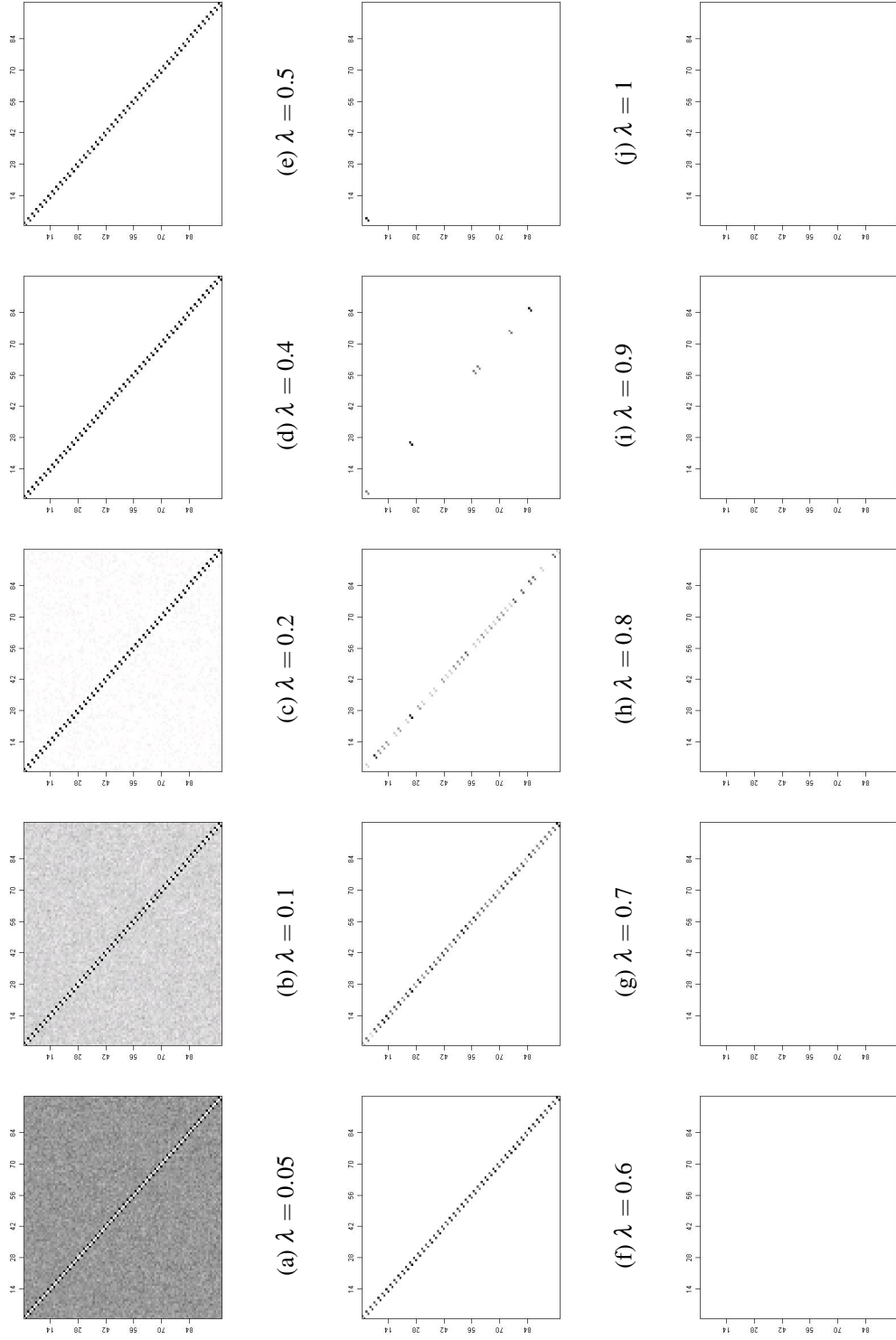


Figure 17: Plot of the estimated adjacent matrices with G-Lasso for pairwise structure with $p = 100$.

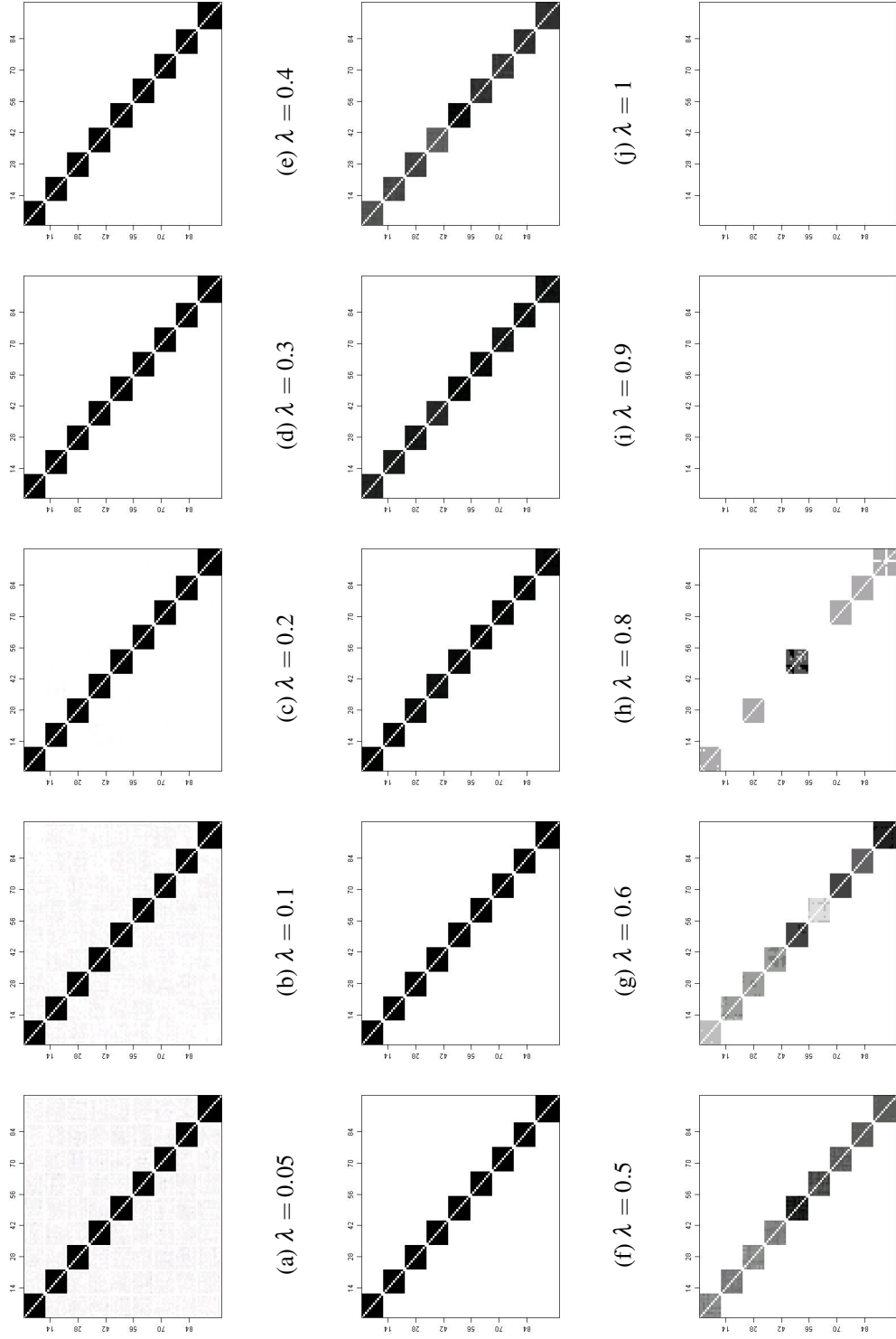


Figure 18: Plot of the estimated adjacent matrices with G-Lasso for hub structure with $p = 100$.

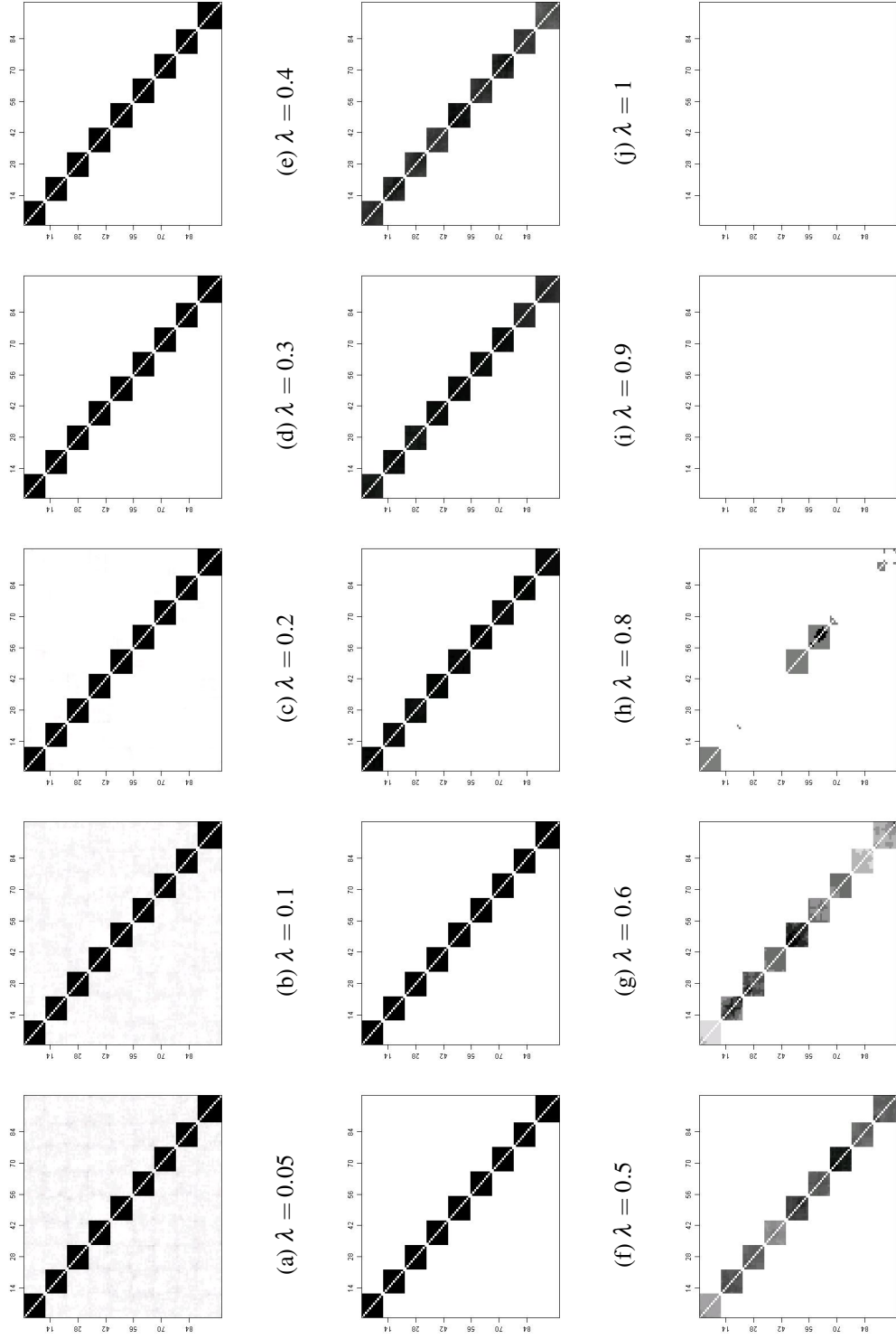


Figure 19: Plot of the estimated adjacent matrices with G-Lasso for cascade structure with $p = 100$.

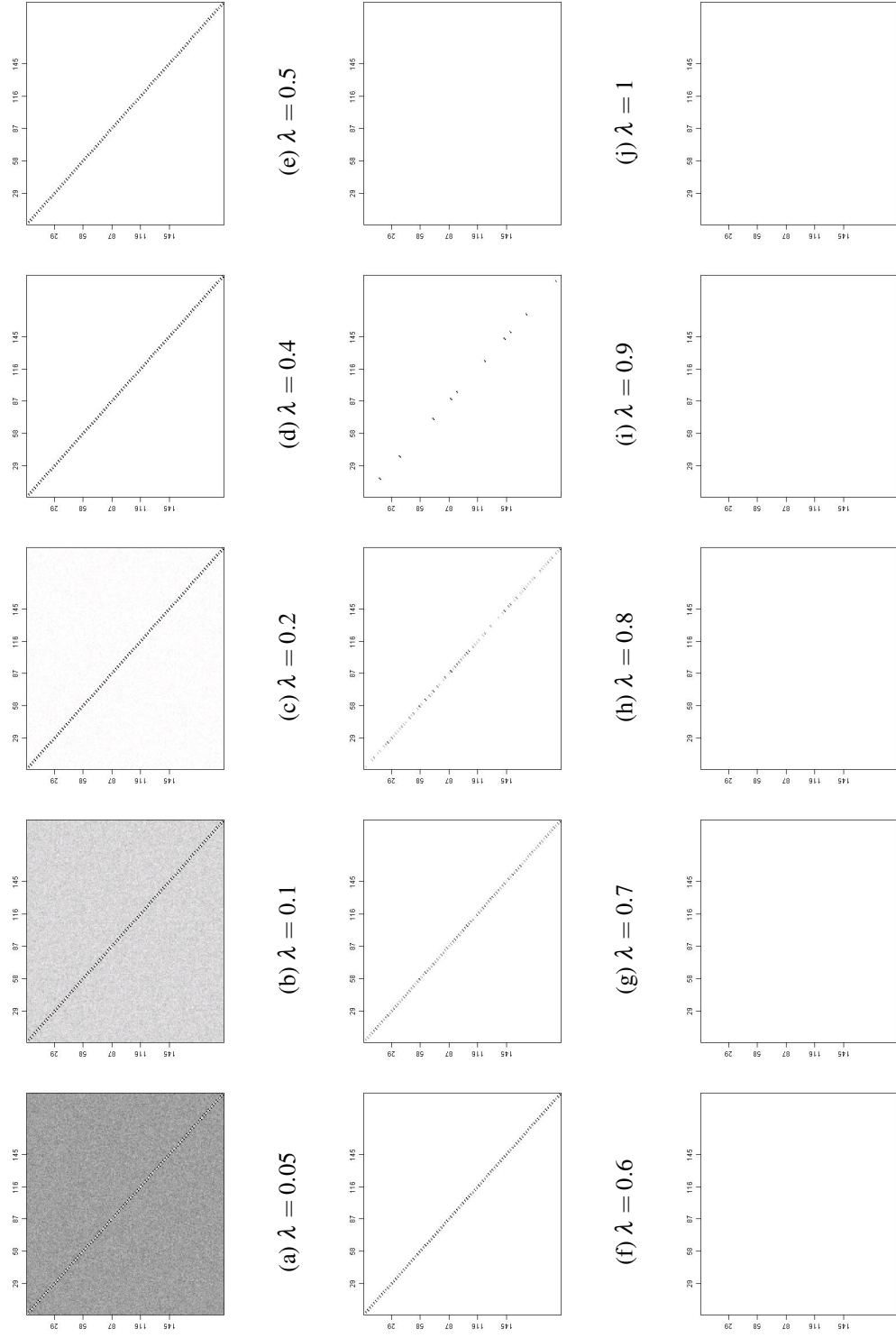


Figure 20: Plot of the estimated adjacent matrices with G-Lasso for pairwise structure with $p = 200$.

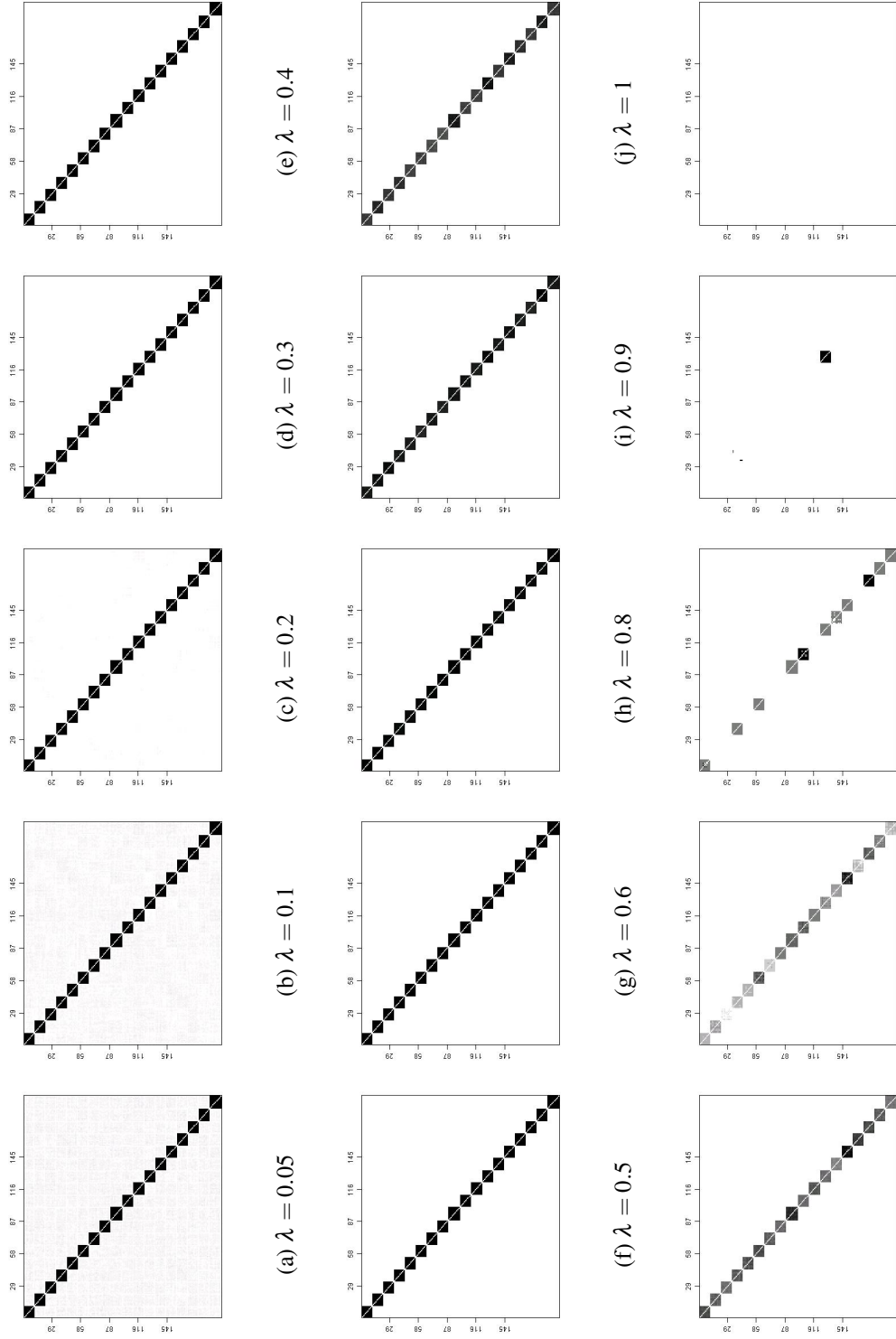


Figure 21: Plot of the estimated adjacent matrices with G-Lasso for hub structure with $p = 200$.

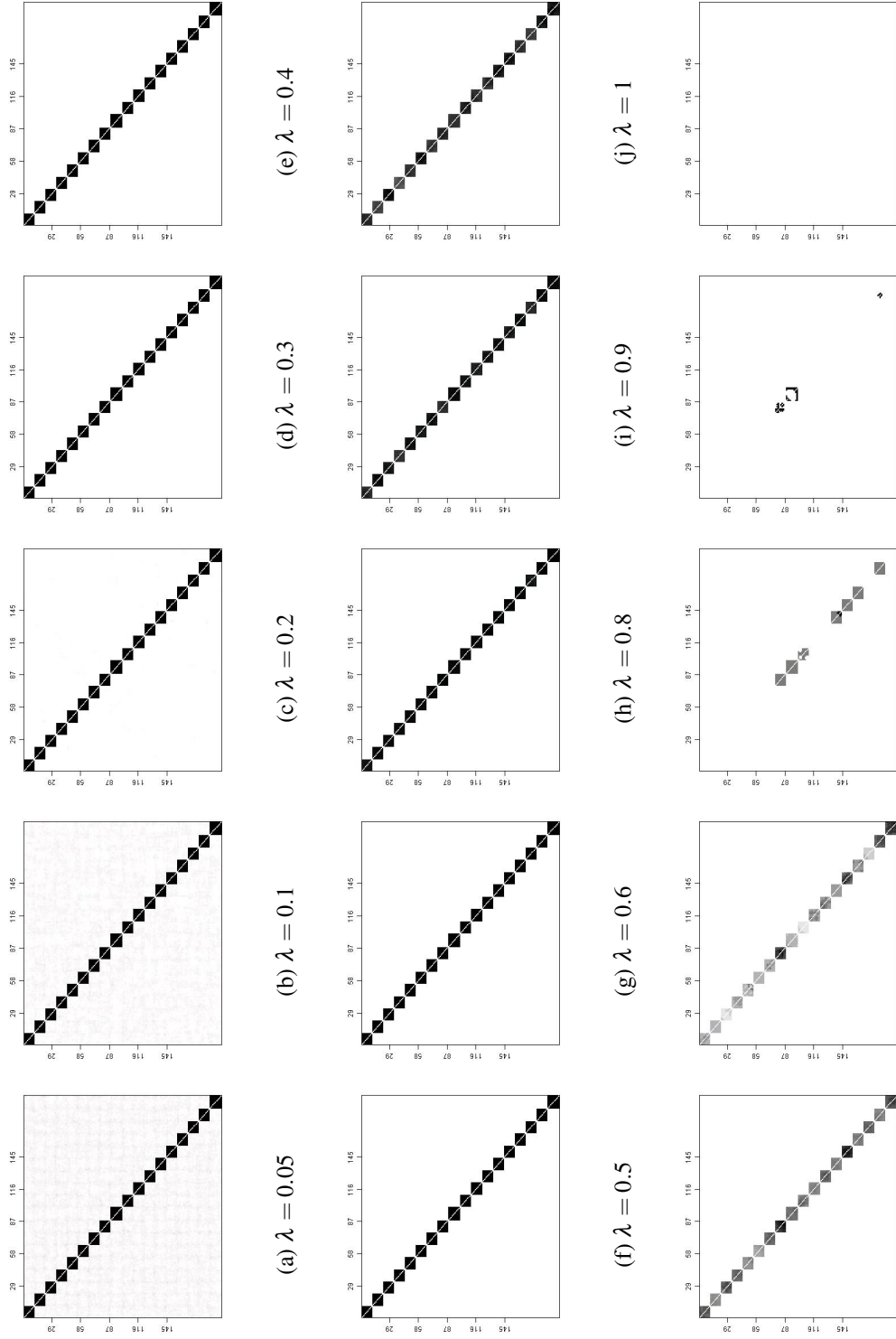
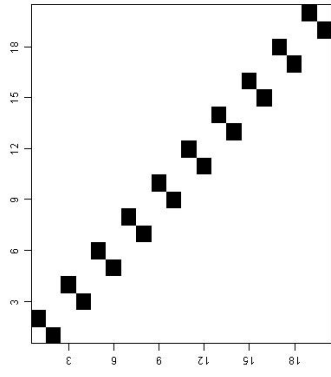
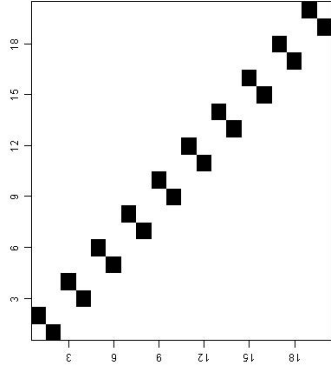


Figure 22: Plot of the estimated adjacent matrices with G-Lasso for cascade structure with $p = 200$.

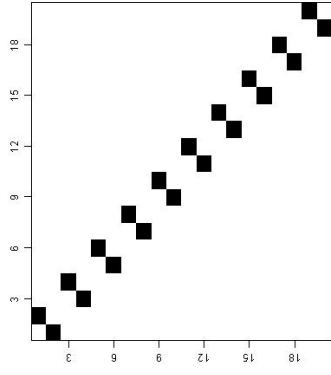
F *Synthetic data* data: additional plot of adjacent matrices for PC-algorithm



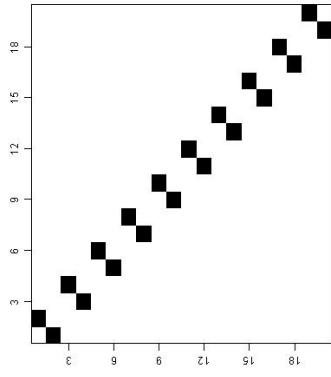
(a) $\alpha = 0.00000001$



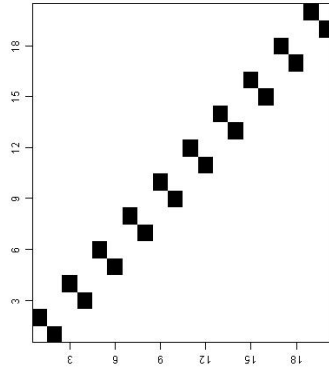
(b) $\alpha = 0.0000001$



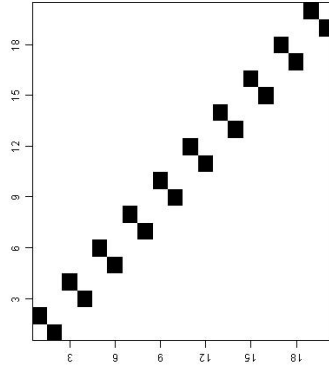
(c) $\alpha = 0.00001$



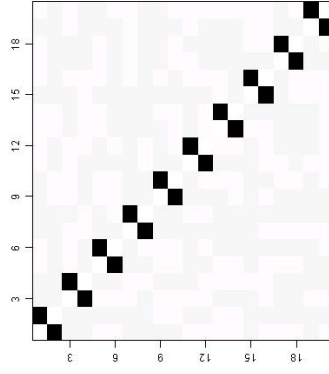
(d) $\alpha = 0.0001$



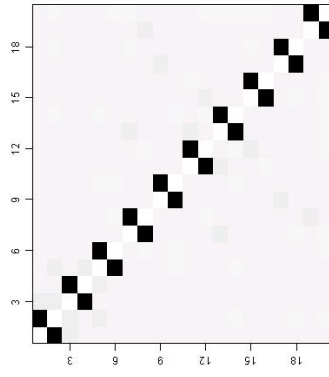
(e) $\alpha = 0.001$



(f) $\alpha = 0.01$

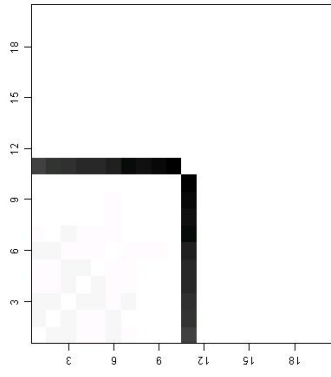


(g) $\alpha = 0.05$

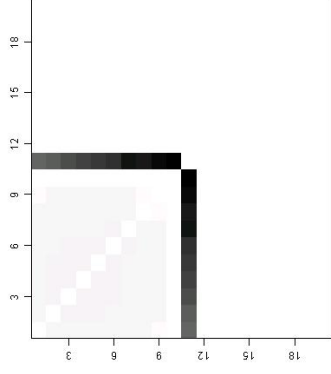


(h) $\alpha = 0.1$

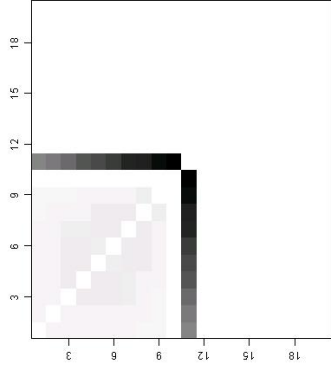
Figure 23: Plot of the estimated adjacent matrices with PC-algorithm for pairwise structure with $p = 20$.



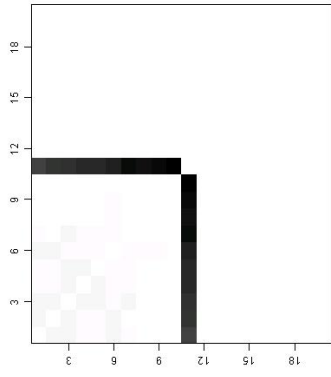
(a) $\alpha = 0.00000001$



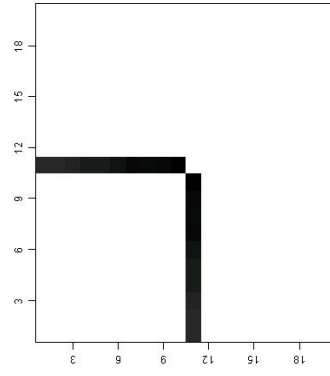
(b) $\alpha = 0.0000001$



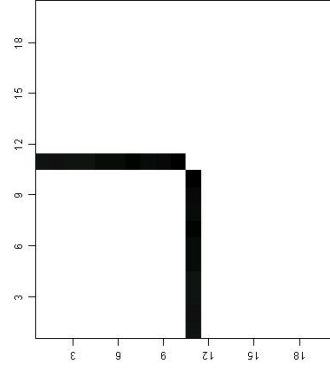
(c) $\alpha = 0.000001$



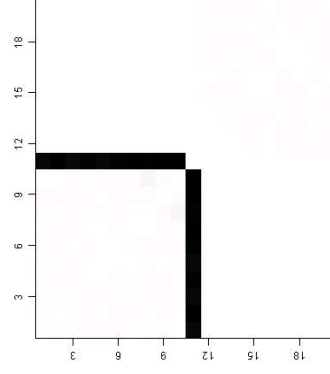
(d) $\alpha = 0.00001$



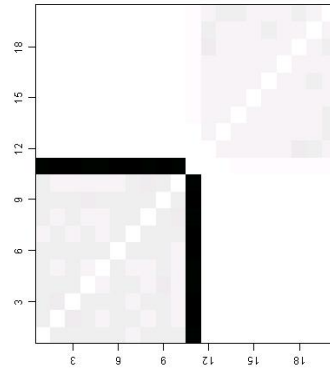
(e) $\alpha = 0.0001$



(f) $\alpha = 0.001$

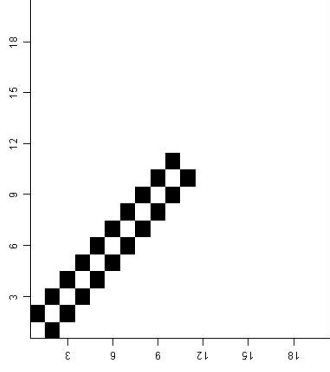
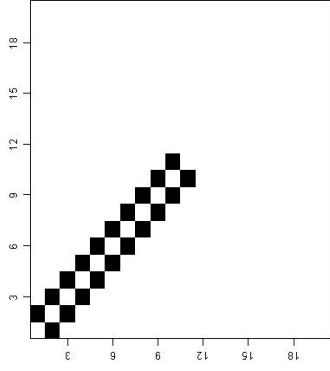
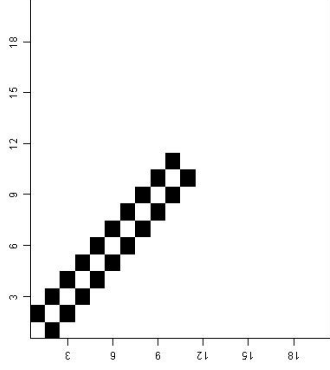
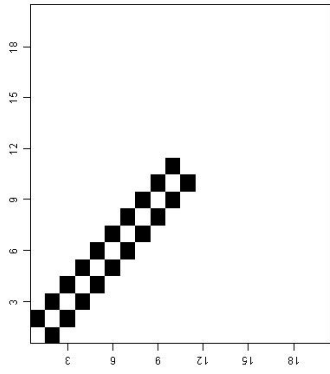


(g) $\alpha = 0.01$



(h) $\alpha = 0.05$

Figure 24: Plot of the estimated adjacent matrices with PC-algorithm for hub structure with $p = 20$.

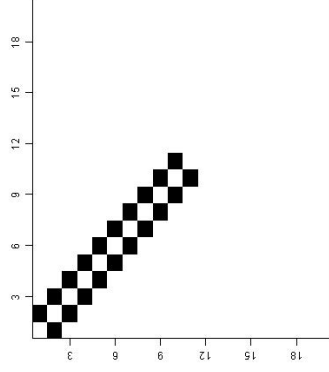


(a) $\alpha = 0.0000001$

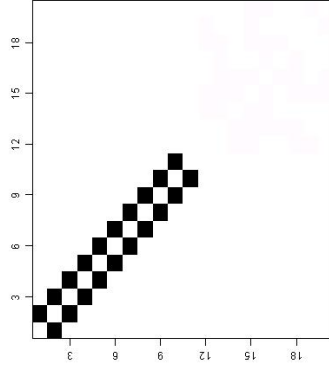
(b) $\alpha = 0.000001$

(c) $\alpha = 0.00001$

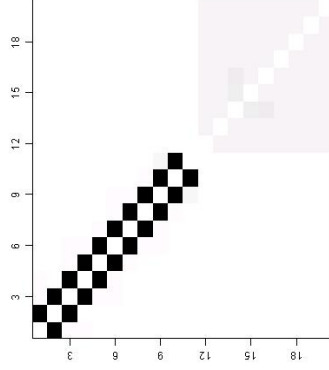
(d) $\alpha = 0.0001$



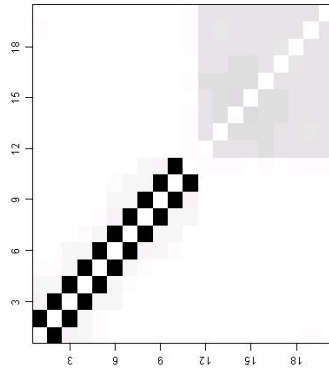
(e) $\alpha = 0.001$



(f) $\alpha = 0.01$

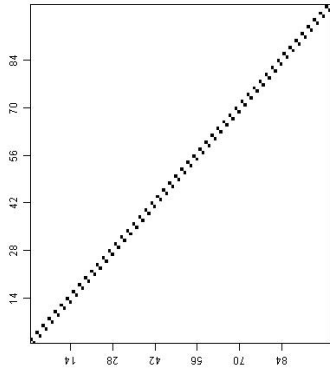


(g) $\alpha = 0.05$

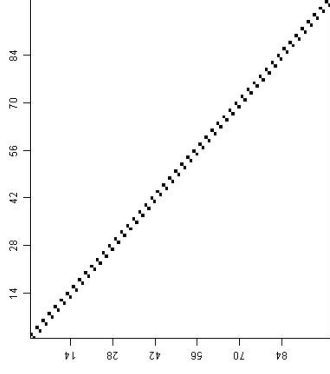


(h) $\alpha = 0.1$

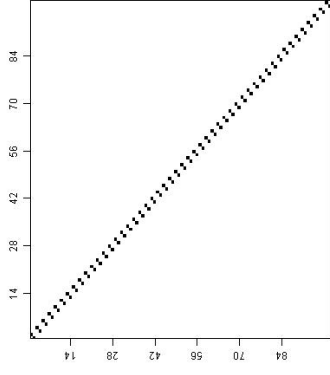
Figure 25: Plot of the estimated adjacent matrices with PC-algorithm for cascade structure with $p = 20$.



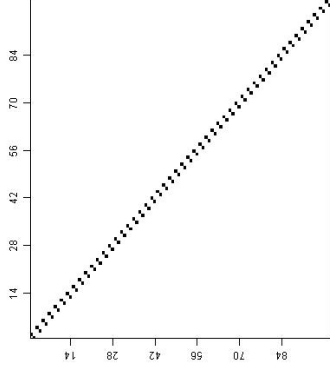
(a) $\alpha = 0.00000001$



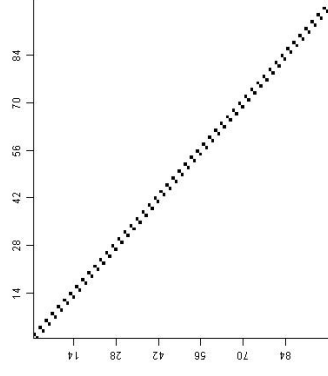
(b) $\alpha = 0.0000001$



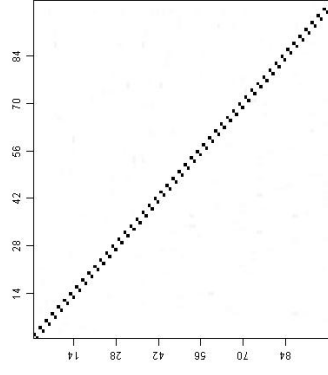
(c) $\alpha = 0.000001$



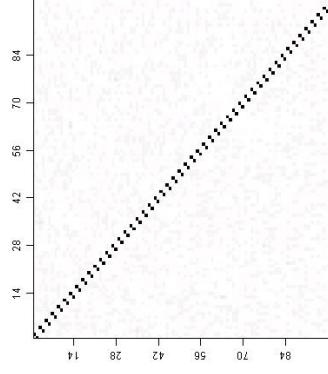
(d) $\alpha = 0.00001$



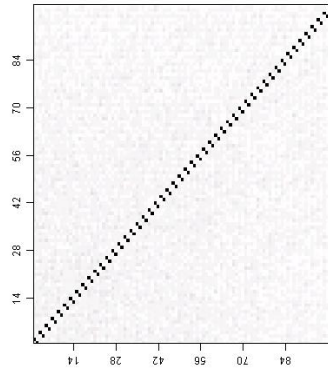
(e) $\alpha = 0.001$



(f) $\alpha = 0.01$

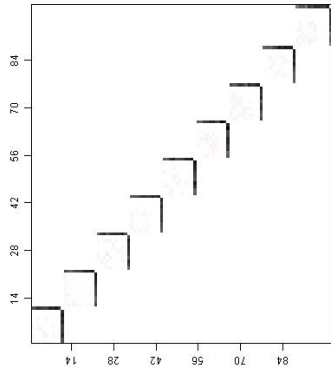


(g) $\alpha = 0.05$

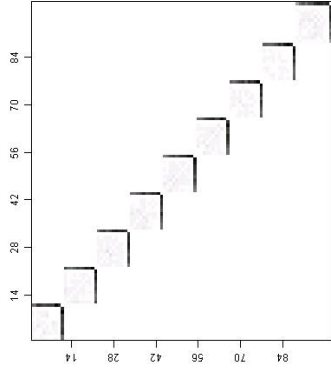


(h) $\alpha = 0.1$

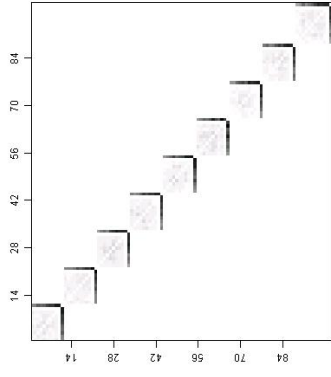
Figure 26: Plot of the estimated adjacent matrices with PC-algorithm for pairwise structure with $p = 100$.



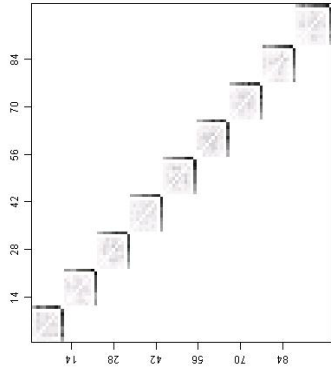
(a) $\alpha = 0.00000001$



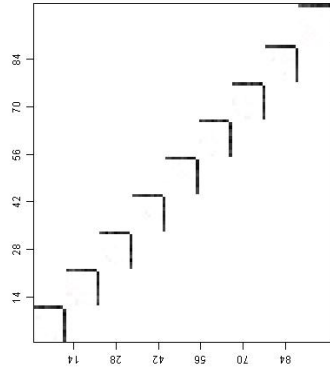
(b) $\alpha = 0.0000001$



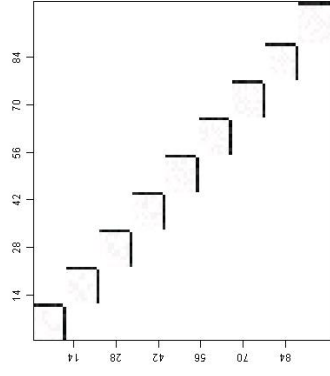
(c) $\alpha = 0.000001$



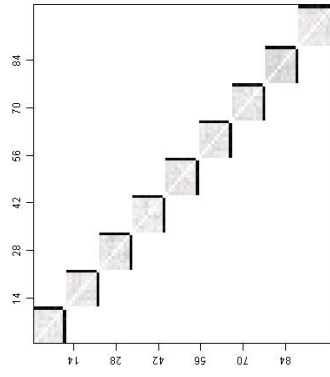
(d) $\alpha = 0.00001$



(e) $\alpha = 0.0001$



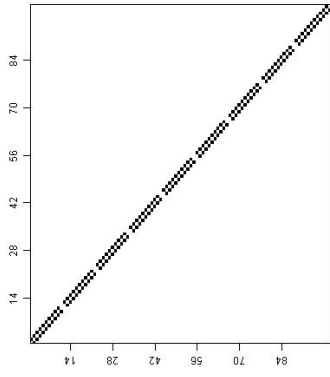
(f) $\alpha = 0.001$



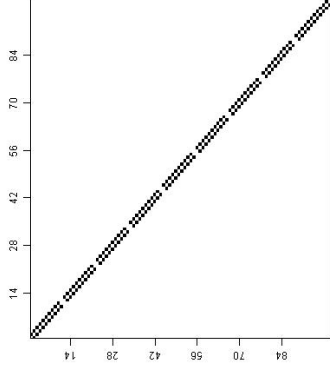
(g) $\alpha = 0.01$

(h) $\alpha = 0.05$

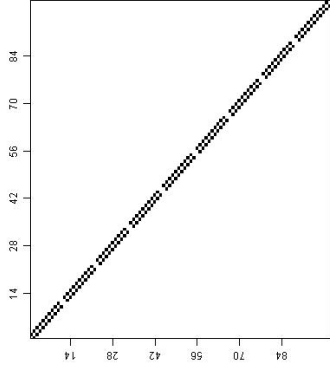
Figure 27: Plot of the estimated adjacent matrices with PC-algorithm for hub structure with $p = 100$.



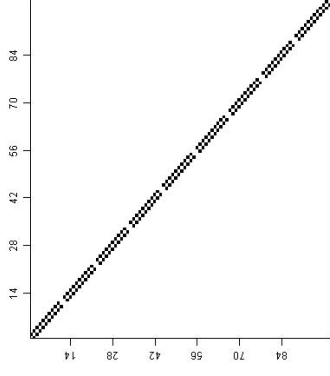
(a) $\alpha = 0.0000001$



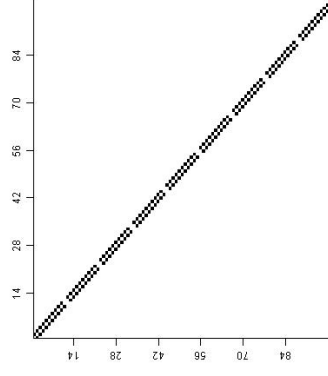
(b) $\alpha = 0.000001$



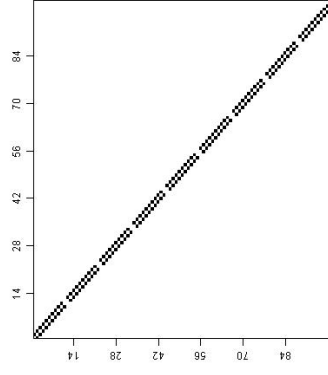
(c) $\alpha = 0.00001$



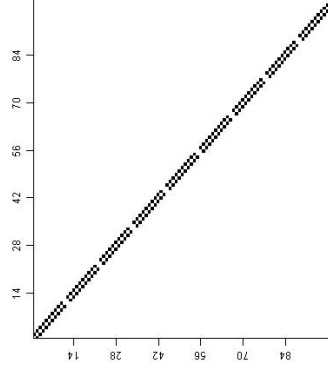
(d) $\alpha = 0.0001$



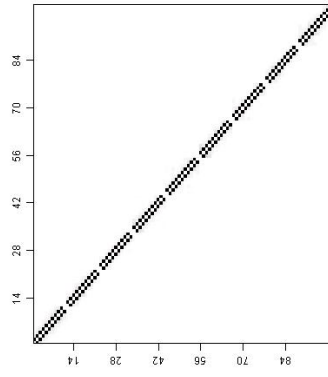
(e) $\alpha = 0.001$



(f) $\alpha = 0.01$

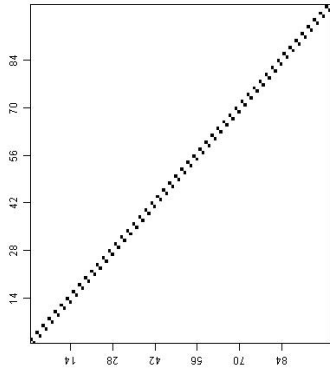


(g) $\alpha = 0.05$

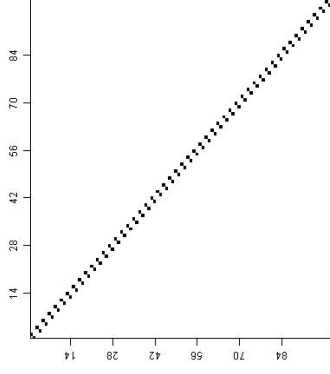


(h) $\alpha = 0.1$

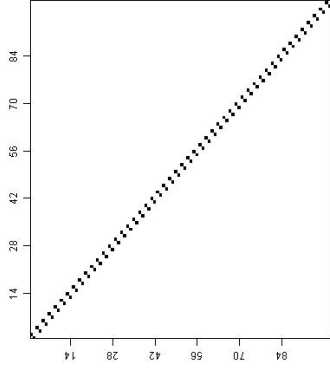
Figure 28: Plot of the estimated adjacent matrices with PC-algorithm for cascade structure with $p = 100$.



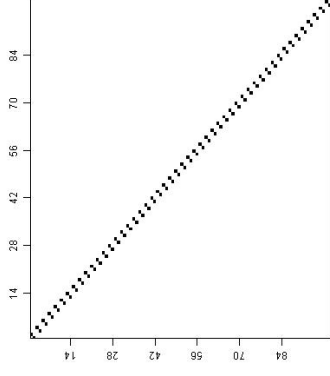
(a) $\alpha = 0.00000001$



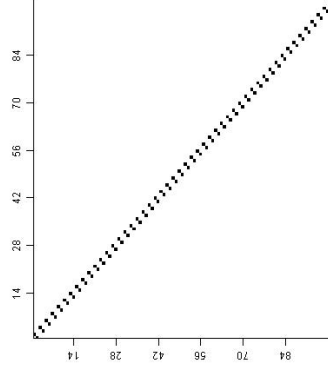
(b) $\alpha = 0.0000001$



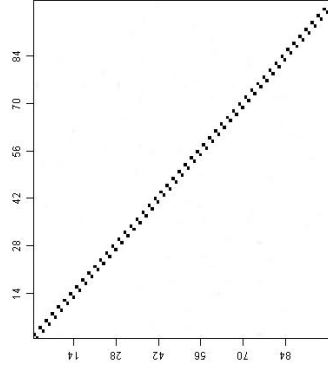
(c) $\alpha = 0.000001$



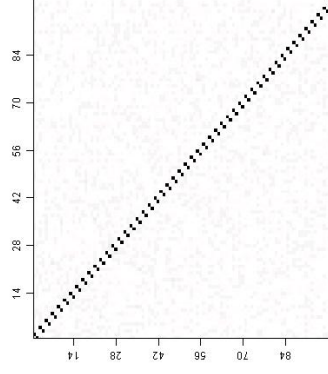
(d) $\alpha = 0.0001$



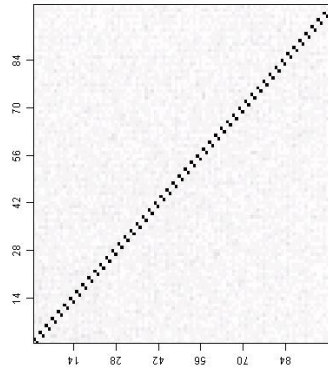
(e) $\alpha = 0.001$



(f) $\alpha = 0.01$



(g) $\alpha = 0.05$



(h) $\alpha = 0.1$

Figure 29: Plot of the estimated adjacent matrices with PC-algorithm for pairwise structure with $p = 200$.

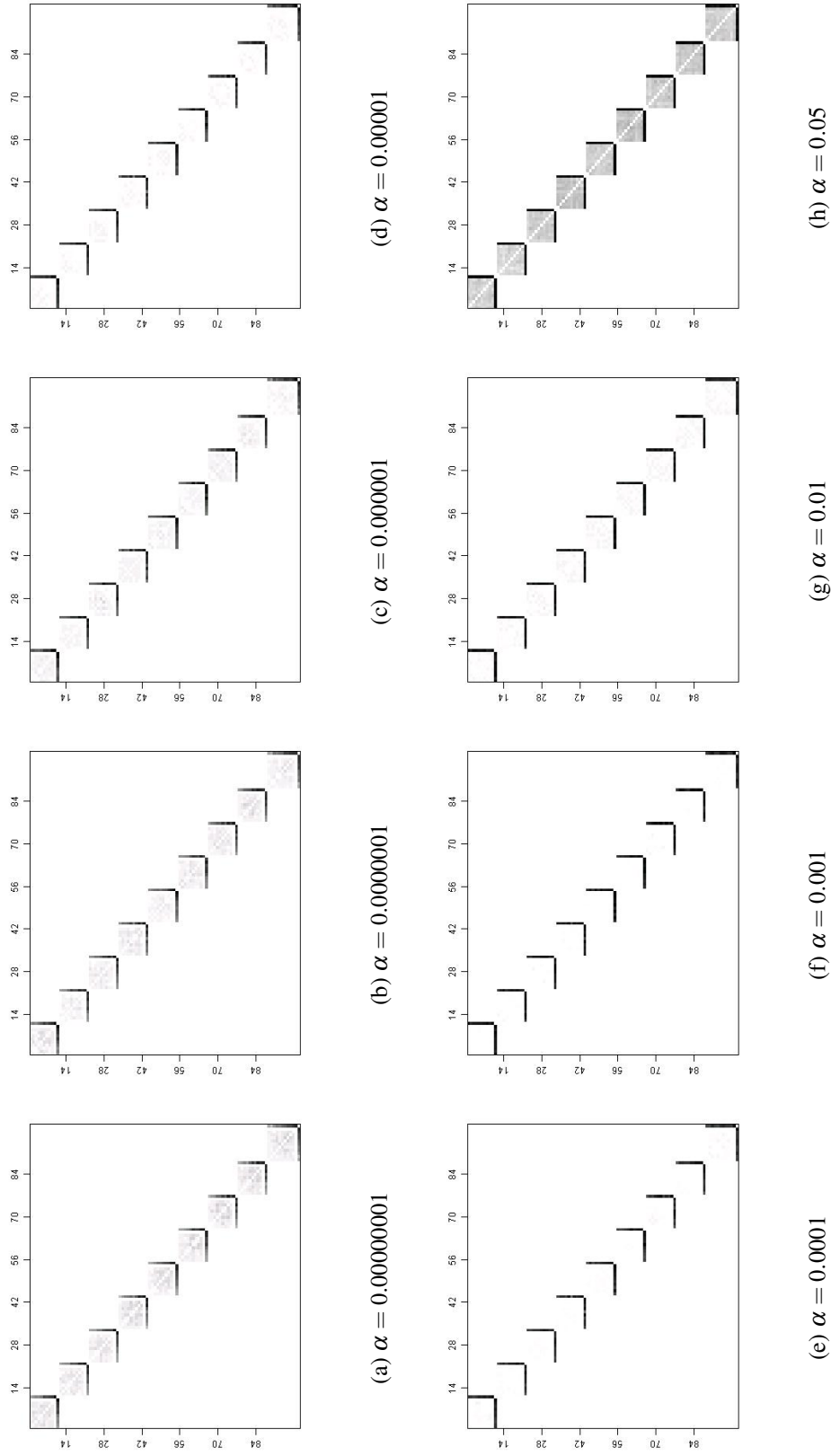
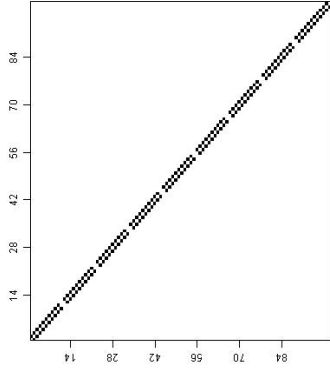
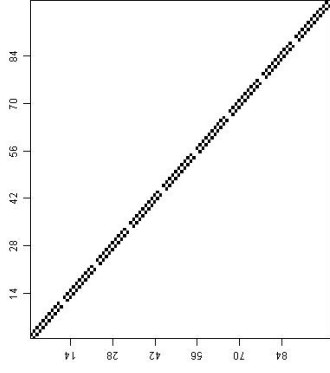
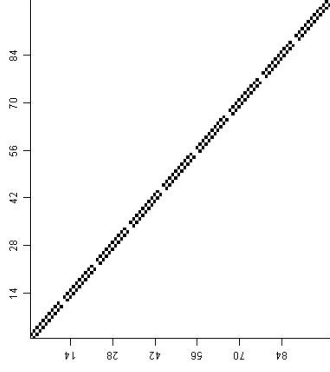
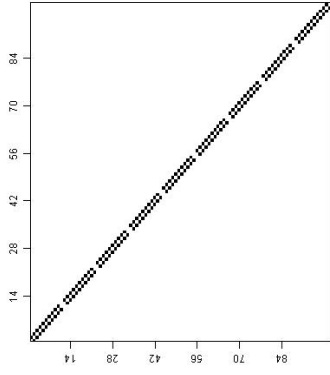


Figure 30: Plot of the estimated adjacent matrices with PC-algorithm for hub structure with $p = 200$.

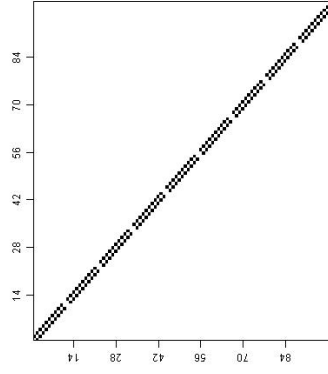
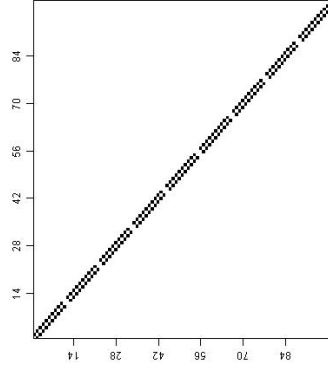
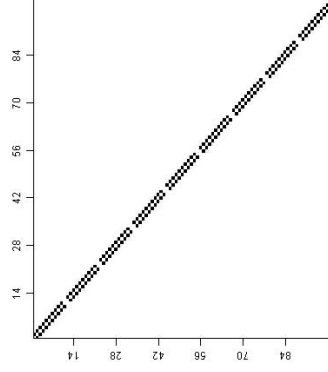
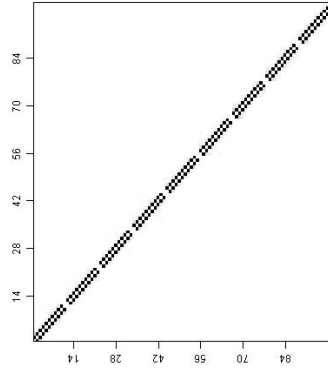


(a) $\alpha = 0.0000001$

(b) $\alpha = 0.000001$

(c) $\alpha = 0.00001$

(d) $\alpha = 0.0001$



(e) $\alpha = 0.001$

(f) $\alpha = 0.01$

(g) $\alpha = 0.05$

(h) $\alpha = 0.1$

Figure 31: Plot of the estimated adjacent matrices with PC-algorithm for cascade structure with $p = 200$.

G *Synthetic data data: ROC curves for all methods*

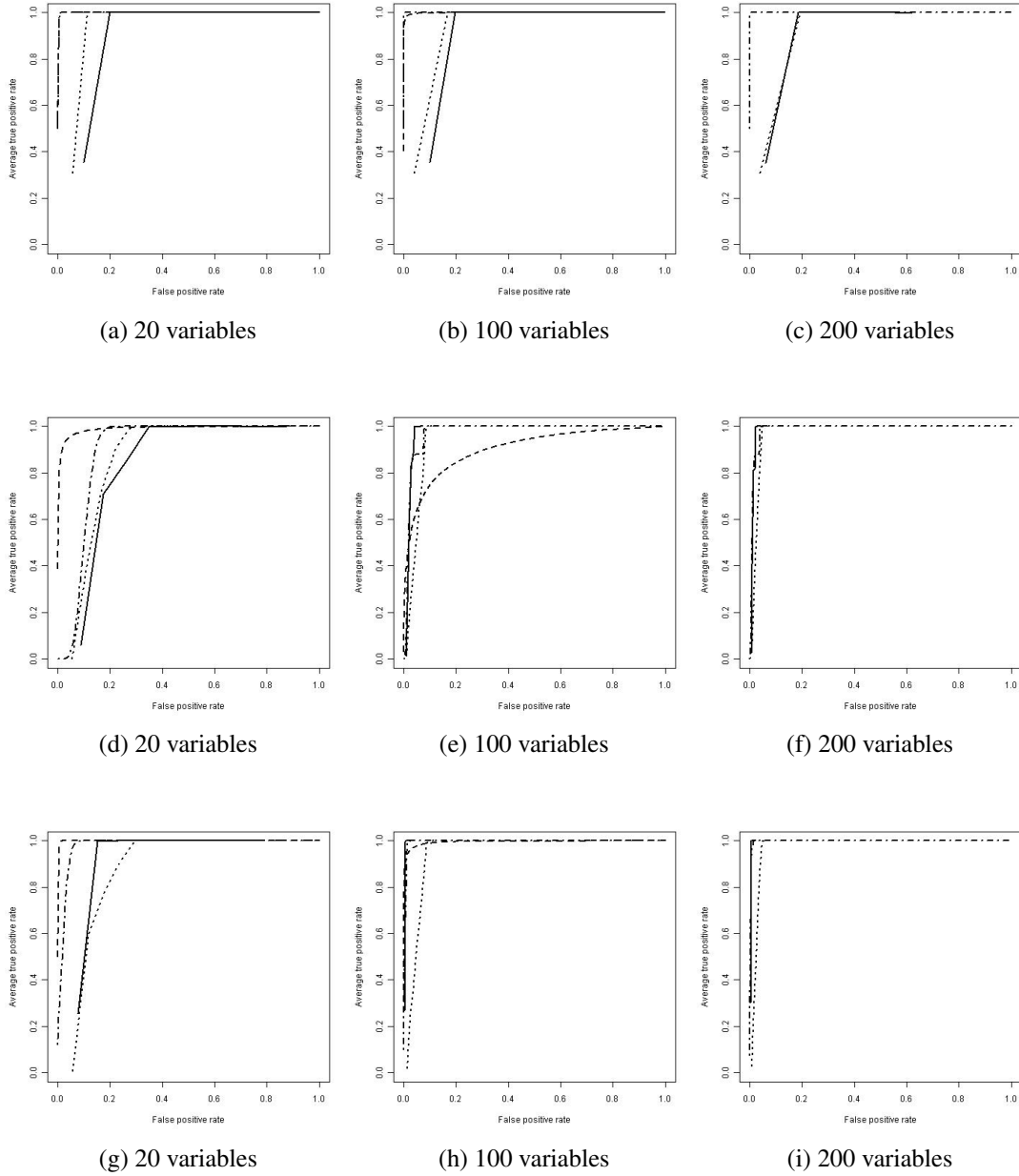


Figure 32: ROC curves for ML estimator (dashed), G-Lasso estimator (dotted), Neighbourhood selection (solid), and Shrinkage estimator (dotdash). The first row refers to the pairwise structures, the second row refers to the hub structures, and the third row refers to the cascade structures