Web-based Supplementary Materials for "A Sparse Ising Model with Covariates" by Jie Cheng, Elizaveta Levina, Pei Wang and Ji Zhu

Appendix A

Proof of Theorem 1

For notational convenience, we omit the j indexing each separate regression. Following the literature, we prove the main theorem in two steps: first, we prove the result holds when assumptions **A1** and **A2** hold for I^n and U^n , the sample versions of of I^* and U^* defined in (7) and (8) (Proposition 1). Then we show that if **A1** and **A2** hold for the population versions I^* and U^* , they also hold for I^n and U^n with high probability (Proposition 2). The sample quantities I^n and U^n are defined as

$$\begin{split} \boldsymbol{I}^{n} &= \nabla^{2} \ell(\boldsymbol{\theta}^{*}, \mathcal{D}_{n}) = \frac{1}{n} \sum_{i=1}^{n} \left(p_{j}^{i} (1 - p_{j}^{i}) (\boldsymbol{x}^{i} \otimes \boldsymbol{y}_{\backslash j}^{i}) (\boldsymbol{x}^{i} \otimes \boldsymbol{y}_{\backslash j}^{i})^{T} \right) ,\\ \boldsymbol{U}^{n} &= \frac{1}{n} \sum_{i=1}^{n} (\boldsymbol{x}^{i} \otimes \boldsymbol{y}_{\backslash j}^{i}) (\boldsymbol{x}^{i} \otimes \boldsymbol{y}_{\backslash j}^{i})^{T} . \end{split}$$

PROPOSITION 1: If A1 and A2 are satisfied by I^n and U^n , assume moreover that

$$M_n = \sup \|\boldsymbol{x}\|_{\infty} < \infty \text{ a.s.},$$

$$\lambda_n \geq \frac{8M_n(2-\alpha)}{\alpha} \sqrt{\frac{\log p + \log q}{n}},$$

$$n > Cd^2(\log p + \log q).$$

Then with probability at least $1 - 2 \exp\left(-C\frac{\lambda_n^2 n}{M_n^2}\right)$, the result of Theorem 1 holds.

Proof of Proposition 1. The proof requires several steps. The uniqueness part follows directly from the following lemma:

LEMMA 1: (Shared sparsity and uniqueness of $\hat{\theta}$, Ravikumar et al. (2010)). Define the

sign vector \mathbf{t} for $\boldsymbol{\theta}$ to satisfy the following properties,

$$\begin{cases} \hat{t}_k = sign(\hat{\theta}_k), & \text{if } \hat{\theta}_k \neq 0 \\ |\hat{t}_k| \leqslant 1, & \text{if } \hat{\theta}_k = 0 \end{cases}.$$

Suppose there exists an optimal solution $\hat{\boldsymbol{\theta}}$ with sign $\hat{\boldsymbol{t}}$ defined as above, such that, $\|\hat{\boldsymbol{t}}_{S^C}\|_{\infty} < 1$, then any optimal solution $\tilde{\boldsymbol{\theta}}$ must have $\tilde{\boldsymbol{\theta}}_{S^C} = 0$. Furthermore, if the Hessian matrix $\nabla^2 \ell(\hat{\boldsymbol{\theta}})_{SS}$ is strictly positive definite, then $\hat{\boldsymbol{\theta}}$ is the unique solution.

We now proceed to prove the rest of Proposition 1. For $\hat{\theta}$ to be a solution of (9), the sub-gradient at $\hat{\theta}$ must be 0, i.e.,

$$\nabla \ell(\hat{\boldsymbol{\theta}}, \mathcal{D}_n) + \lambda_n \hat{\boldsymbol{t}} = 0 .$$
(A.1)

Then we can write $\nabla \ell \left(\hat{\boldsymbol{\theta}}, \mathcal{D}_n \right) - \nabla \ell \left(\boldsymbol{\theta}^*, \mathcal{D}_n \right) = -\lambda_n \hat{\boldsymbol{t}} + W^n$, where

$$W^n = -\nabla \ell \left(\boldsymbol{\theta}^*, \mathcal{D}_n\right) = \frac{1}{n} \sum_{i=1}^n (\boldsymbol{x}^i \otimes \boldsymbol{y}^i_{\setminus j}) (y^i_j - p^i_j(\boldsymbol{\theta}^*)) \ .$$

Let $\tilde{\boldsymbol{\theta}}$ denote a point in the line segment connecting $\hat{\boldsymbol{\theta}}$ and $\boldsymbol{\theta}^*$. Applying the mean value theorem gives

$$\boldsymbol{I}^{n}\left(\hat{\boldsymbol{\theta}}-\boldsymbol{\theta}^{*}\right)=W^{n}-\lambda_{n}\hat{\boldsymbol{t}}+R^{n}. \qquad (A.2)$$

where $R^n = \left(\nabla^2 \ell \left(\boldsymbol{\theta}^*, \mathcal{D}_n \right) - \nabla^2 \ell(\tilde{\boldsymbol{\theta}}, \mathcal{D}_n) \right) (\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}^*).$

Now define $\hat{\theta}$ as follows: let S be the index set of true non-zeros in θ^* , let $\hat{\theta}_S$ be the solution of

$$\min_{(\hat{\boldsymbol{\theta}}_{\mathcal{S}},0)} \ell(\hat{\boldsymbol{\theta}},\mathcal{D}_n) + \lambda_n \|\hat{\boldsymbol{\theta}}_{\mathcal{S}}\|_1 , \qquad (A.3)$$

and let $\hat{\boldsymbol{\theta}}_{S^C} = 0$. We will show that this $\hat{\boldsymbol{\theta}}$ is the optimal solution and is sign consistent with high probability.

We set the corresponding sign vector $\hat{\boldsymbol{t}}_{\mathcal{S}}$ for $\hat{\boldsymbol{\theta}}_{\mathcal{S}}$ similarly defined as in Lemma 1, and $\hat{\boldsymbol{t}}_{\mathcal{S}^{C}} = -\frac{1}{\lambda_{n}} \nabla_{\mathcal{S}^{C}} \ell(\hat{\boldsymbol{\theta}}_{\mathcal{S}}, \mathcal{D}_{n})$ as obtained in (A.1). Now we need to show that with high probability,

$$\|\hat{\boldsymbol{t}}_j\|_{\infty} < 1, \qquad \text{for } j \in \mathcal{S}^C$$
 (A.4)

$$\hat{t}_j = sign(\boldsymbol{\theta}_j^*), \text{ for } j \in \mathcal{S} \text{ and } \|\boldsymbol{\theta}_j^*\| \ge \frac{10\lambda_n\sqrt{d}}{\Delta_{\min}}$$
 (A.5)

The following three lemmas form the proof.

LEMMA 2: (Control the remainder term W^n). For $\alpha \in (0, 1]$, assume $\|\boldsymbol{x}\|_{\infty} \leq M_n$ a.s, then,

$$P\left(\frac{2-\alpha}{\lambda_n}\|W^n\|_{\infty} \ge \frac{\alpha}{4}\right) \le 4\exp\left(-\frac{\lambda_n^2 n\alpha^2}{32M_n^2(2-\alpha)^2} + \log p + \log q\right) .$$

This probability goes to 0 as long as $\lambda_n \ge 8M \frac{2-\alpha}{\alpha} \sqrt{\frac{\log p + \log q}{n}}$.

Proof of Lemma 2. We can write $W^n = \frac{1}{n} \sum_{i=1}^n (\boldsymbol{x}^i \otimes \boldsymbol{y}^i_{\backslash j}) (y^i_j - p^i_j(\boldsymbol{\theta}^*)) = \sum_{i=1}^n Z_i$, where Z_{ik} is bounded by M_n/n . Thus by Azuma-Hoeffding Inequality,

$$P\left(\|W^n\|_{\infty} \ge \frac{\lambda_n \alpha}{4(2-\alpha)}\right) \le 2pqP\left(\|W_k^n\|_{\infty} \ge \frac{\lambda_n \alpha}{4(2-\alpha)}\right)$$
$$\le 4\exp\left(-\frac{\lambda_n^2 n\alpha^2}{32M_n^2(2-\alpha)^2} + \log p + \log q\right).$$

LEMMA 3: $(\ell_2$ -consistency of the sub-vector $\hat{\boldsymbol{\theta}}_{\mathcal{S}})$. If $\lambda_n d < \frac{\Delta_{\min}^2}{10\Delta_{\max}M_n}$, and, $\|W^n\|_{\infty} \leq \frac{\lambda_n}{4}$, then

$$\|\hat{\boldsymbol{\theta}}_{\mathcal{S}} - \boldsymbol{\theta}_{\mathcal{S}}^*\|_2 \leqslant \frac{5\lambda_n\sqrt{d}}{\Delta_{\min}}$$

Proof of Lemma 3. Let $G(u_{\mathcal{S}}) = \ell(\boldsymbol{\theta}_{\mathcal{S}}^* + u_{\mathcal{S}}, \mathcal{D}_n) - \ell(\boldsymbol{\theta}_{\mathcal{S}}^*, \mathcal{D}_n) + \lambda_n(\|\boldsymbol{\theta}_{\mathcal{S}}^* + u_{\mathcal{S}}\|_1 - \|\boldsymbol{\theta}_{\mathcal{S}}^*\|_1)$ be a function $G : \mathbb{R}^d \to \mathbb{R}$. It is easy to see that $G(u_{\mathcal{S}})$ is convex and it achieves its minimum at $\hat{u}_{\mathcal{S}} = \hat{\boldsymbol{\theta}}_{\mathcal{S}} - \boldsymbol{\theta}_{\mathcal{S}}^*$. Moreover, G(0) = 0. Thus if we can show that $G(u_{\mathcal{S}})$ is positive on the set $\|u_{\mathcal{S}}\|_2 = B$, then we will have $\hat{u}_{\mathcal{S}} \leqslant B$ due to convexity of $G(u_{\mathcal{S}})$. Note that

$$G(u_{\mathcal{S}}) = -W_{\mathcal{S}}^{nT} u_{\mathcal{S}} + u_{\mathcal{S}}^{T} \nabla^{2} \ell(\boldsymbol{\theta}_{\mathcal{S}}^{*} + \alpha u_{\mathcal{S}}) u_{\mathcal{S}} + \lambda_{n} (\|\boldsymbol{\theta}_{\mathcal{S}}^{*} + u_{\mathcal{S}}\|_{1} - \|\boldsymbol{\theta}_{\mathcal{S}}^{*}\|_{1})$$

Further,

$$|W_{\mathcal{S}}^{nT}u_{\mathcal{S}}| \leq ||W^{n}||_{\infty}||u_{\mathcal{S}}||_{1} \leq \frac{\lambda_{n}}{4}\sqrt{d}||u_{\mathcal{S}}||_{2},$$

$$\Lambda_{\min}(\nabla^{2}\ell(\boldsymbol{\theta}_{\mathcal{S}}^{*}+\alpha u_{\mathcal{S}})) \geq \Delta_{\min}-\Delta_{\max}M_{n}\sqrt{d}||u_{\mathcal{S}}||_{2},$$

$$|\lambda_{n}(||\boldsymbol{\theta}_{\mathcal{S}}^{*}+u_{\mathcal{S}}||_{1}-||\boldsymbol{\theta}_{\mathcal{S}}^{*}||_{1})| \leq \lambda_{n}\sqrt{d}||u_{\mathcal{S}}||_{2}.$$

Combining all of the above, we have

$$G(u_{\mathcal{S}}) \ge \|u_{\mathcal{S}}\|_2 (-\Delta_{\max} M_n \sqrt{d} \|u_{\mathcal{S}}\|_2^2 + \Delta_{\min} \|u_{\mathcal{S}}\|_2 - \frac{5}{4} \lambda_n \sqrt{d}) .$$

Easy algebra shows that if $\lambda_n d \leq \frac{\Delta_{\min}^2}{10\Delta_{\max}M_n}$ and $B = \frac{5\lambda_n\sqrt{d}}{\Delta_{\min}}$, the result follows.

LEMMA 4: (Control the remainder term R^n). If $\lambda_n d \leq \frac{\Delta_{\min}^2}{100M_n \Delta_{\max}} \frac{\alpha}{2-\alpha}$, $||W^n||_{\infty} \leq \frac{\lambda_n}{4}$, then

$$\frac{\|R^n\|_{\infty}}{\lambda_n} \leqslant \frac{25\Delta_{\max}}{\Delta_{\min}^2} M_n \lambda_n d \leqslant \frac{\alpha}{4(2-\alpha)}$$

Proof of Lemma 4. Recall that

$$R^{n} = \left(\nabla^{2}\ell\left(\boldsymbol{\theta}^{*}, \mathcal{D}_{n}\right) - \nabla^{2}\ell\left(\tilde{\boldsymbol{\theta}}, \mathcal{D}_{n}\right)\right)\left(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}^{*}\right)$$

$$= \frac{1}{n}\sum_{i=1}^{n} \left(p_{j}^{i}(\boldsymbol{\theta}^{*})(1 - p_{j}^{i}(\boldsymbol{\theta}^{*})) - p_{j}^{i}(\tilde{\boldsymbol{\theta}})(1 - p_{j}^{i}(\tilde{\boldsymbol{\theta}}))\right)\left(\boldsymbol{x}^{i} \otimes \boldsymbol{y}_{\backslash j}^{i}\right)(\boldsymbol{x}^{i} \otimes \boldsymbol{y}_{\backslash j}^{i})^{T}\left(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}^{*}\right) .$$

Let $\omega_j^i(\boldsymbol{\theta}) = p_j^i(\boldsymbol{\theta})(1 - p_j^i(\boldsymbol{\theta}))$. The k-th element of \mathbb{R}^n has the form

$$\begin{aligned} R_k^n &= \frac{1}{n} \sum_{i=1}^n (\omega_j^i(\boldsymbol{\theta}^*) - \omega_j^i(\tilde{\boldsymbol{\theta}})) Z_k^i(\boldsymbol{x}^i \otimes \boldsymbol{y}_{\backslash j}^i)^T \left(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}^*\right) \\ &= \frac{1}{n} \sum_{i=1}^n \dot{\omega}_j^i(\bar{\boldsymbol{\theta}}) Z_k^i \left(\boldsymbol{\theta}^* - \tilde{\boldsymbol{\theta}}\right)^T (\boldsymbol{x}^i \otimes \boldsymbol{y}_{\backslash j}^i) (\boldsymbol{x}^i \otimes \boldsymbol{y}_{\backslash j}^i)^T \left(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}^*\right) , \end{aligned}$$

where $Z_k^i = x_l^i y_m^i$, for some (l, m). By **A1** and Lemma 3, we have

$$|R_k^n| \leq M_n \Delta_{\max} \|\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}^*\|_2^2 \leq M_n \Delta_{\max} \left(\frac{5\lambda_n \sqrt{d}}{\Delta_{\min}}\right)^2$$
.

Putting all the lemmas together, we are ready to prove Proposition 1.

Proof of Proposition 1. Set $\lambda_n = \frac{8M_n(2-\alpha)}{\alpha} \sqrt{\frac{\log p + \log q}{n}}$. By Lemma 2, we have $\|W^n\|_{\infty} \leq 1$

 $\frac{\lambda_n \alpha}{4(2-\alpha)} \leqslant \frac{\lambda_n}{4} \text{ with probability at least } 1 - 4 \exp(C\lambda_n^2 n/M_n^2). \text{ Choosing } n \geqslant \frac{100^2 \Delta_{\max}^2 (2-\alpha)^2}{\Delta_{\min}^4 \alpha^2} d^2 (\log p + \log q)), \text{ we have } \lambda_n d \leqslant \frac{\Delta_{\min}^2}{100M_n \Delta_{\max}} \frac{\alpha}{2-\alpha}, \text{ thus the conditions of Lemmas 3 and 4 hold.}$ By rewriting (A.2) and utilizing the fact that $\hat{\boldsymbol{\theta}}_{\mathcal{S}^C} = \boldsymbol{\theta}_{\mathcal{S}^C}^* = 0$, we have

$$\boldsymbol{I}_{\mathcal{S}^{C}\mathcal{S}}^{n}(\hat{\boldsymbol{\theta}}_{\mathcal{S}}-\boldsymbol{\theta}_{\mathcal{S}}^{*}) = W_{\mathcal{S}^{C}}^{n}-\lambda_{n}\hat{\boldsymbol{t}}_{\mathcal{S}^{C}}+R_{\mathcal{S}^{C}}^{n}, \qquad (A.6)$$

$$\boldsymbol{I}_{\mathcal{S}\mathcal{S}}^{n}(\hat{\boldsymbol{\theta}}_{\mathcal{S}}-\boldsymbol{\theta}_{\mathcal{S}}^{*}) = W_{\mathcal{S}}^{n}-\lambda_{n}\hat{\boldsymbol{t}}_{\mathcal{S}}+R_{\mathcal{S}}^{n}. \qquad (A.7)$$

Since I_{SS}^n is invertible by assumption, combining (A.6) and (A.7) gives

$$\boldsymbol{I}_{\mathcal{S}^{C}\mathcal{S}}^{n}(\boldsymbol{I}_{\mathcal{S}\mathcal{S}}^{n})^{-1}(W_{\mathcal{S}}^{n}-\lambda_{n}\hat{\boldsymbol{t}}_{\mathcal{S}}+R_{\mathcal{S}}^{n})=W_{\mathcal{S}^{C}}^{n}-\lambda_{n}\hat{\boldsymbol{t}}_{\mathcal{S}^{C}}+R_{\mathcal{S}^{C}}^{n}.$$
(A.8)

To show (A.4), we reorganize (A.8) and use results from Lemmas 2 and 4:

$$\begin{split} \lambda_n \| \hat{\boldsymbol{t}}_{\mathcal{S}^C} \|_{\infty} &= \| \boldsymbol{I}_{\mathcal{S}^C \mathcal{S}}^n (\boldsymbol{I}_{\mathcal{S}\mathcal{S}}^n)^{-1} (W_{\mathcal{S}}^n - \lambda_n \hat{\boldsymbol{t}}_{\mathcal{S}} + R_{\mathcal{S}}^n) - W_{\mathcal{S}^C}^n - R_{\mathcal{S}^C}^n \|_{\infty} \\ &\leqslant \| \boldsymbol{I}_{\mathcal{S}^C \mathcal{S}}^n (\boldsymbol{I}_{\mathcal{S}\mathcal{S}}^n)^{-1} \|_{\infty} (\| W^n \|_{\infty} + \lambda_n + \| R^n \|_{\infty}) + \| W^n \|_{\infty} + \| R^n \|_{\infty} \\ &\leqslant \lambda_n (1 - \frac{\alpha}{2}) \,. \end{split}$$

To show (A.5), it suffices to show that $\|\hat{\boldsymbol{\theta}}_{\mathcal{S}} - \boldsymbol{\theta}_{\mathcal{S}}^*\|_{\infty} \leq \frac{\boldsymbol{\theta}_{\min}^*}{2}$. By Lemma 3,

$$\|\hat{\boldsymbol{\theta}}_{\mathcal{S}} - \boldsymbol{\theta}_{\mathcal{S}}^*\|_{\infty} \leqslant \frac{5\lambda_n\sqrt{d}}{\Delta_{\min}} \leqslant \frac{\boldsymbol{\theta}_{\min}^*}{2}$$

The last inequality follows as long as $\boldsymbol{\theta}_{\min}^* \geq \frac{10\lambda_n\sqrt{d}}{\Delta_{\min}}$. This completes the proof of Proposition 1.

PROPOSITION 2: If I^* and U^* satisfy A1 and A2, and $M_n = \sup ||\boldsymbol{x}||_{\infty} < \infty$ a.s., the following hold for any $\delta > 0$. A and B are some positive constants.

$$P\left\{\Lambda_{\max}\left(\frac{1}{n}\sum_{i=1}^{n}(\boldsymbol{x}^{i}\otimes\boldsymbol{y}_{\backslash j}^{i})(\boldsymbol{x}^{i}\otimes\boldsymbol{y}_{\backslash j}^{i})^{T}\right) \ge D_{\max} + \delta\right\} \leq 2\exp\left(-A\frac{\delta^{2}n}{M_{n}^{2}d^{2}} + B(\log p + \log q)\right)$$
$$P\left(\Lambda_{\min}(\boldsymbol{I}_{\mathcal{SS}}^{n}) \le C_{\min} - \delta\right) \leq 2\exp\left(-A\frac{\delta^{2}n}{M_{n}^{2}d^{2}} + B\log d\right)$$
$$P\left(\||\boldsymbol{I}_{\mathcal{S}^{c}\mathcal{S}}^{n}(\boldsymbol{I}_{\mathcal{SS}}^{n})^{-1}|\|_{\infty} \ge 1 - \frac{\alpha}{2}\right) \leq \exp\left(-A\frac{n}{M_{n}^{2}d^{3}} + B(\log p + \log q)\right)$$

We omit the proof of Proposition 2, which is very similar to Lemmas 5 and 6 in Ravikumar et al. (2010).

Proof of Theorem 1. With Propositions 1 and 2, the proof of Theorem 1 is straightforward. Given that A1 and A2 are satisfied by I^* and U^* and that conditions (13) and (14) hold, on the set $\mathcal{A} = \{ \boldsymbol{x} : M_n = \sup ||\boldsymbol{x}|| < \infty \}$ the assumptions in Proposition 2 are satisfied. Thus with probability at least $1 - \exp(-\frac{C\lambda_n^2 n}{M_n^2})$, the conditions of Proposition 1 hold, and therefore the results in Theorem 1 hold. Finally, let \mathcal{T} stand for the set where the results of Theorem 1 hold. Then by (11) and (12), we have

$$P(\mathcal{T}^c) \leqslant P(\mathcal{T}^c \mid \mathcal{A}) + P(\mathcal{A}^c) \leqslant \exp(-\frac{C\lambda_n^2 n}{M_n^2}) + \exp(-M_n^\delta) \leqslant \exp(-(C'\lambda_n^2 n)^{\delta^*}, \text{ where } 0 < \delta^* < 1.$$

Appendix B

Proof of Result (14). This result follows from that

$$\sqrt{\sum_{k:k\in\mathcal{S}_j} (\hat{\boldsymbol{\theta}}_{jk} - \boldsymbol{\theta}_{jk}^*)^2} = \|\hat{\boldsymbol{\theta}}_j - \boldsymbol{\theta}_j^*\|_2 \leqslant \frac{5\lambda_n\sqrt{d}}{\Delta_{\min}}, \text{ for any } j = 1, \dots, q,$$
$$\implies \|\hat{\boldsymbol{\theta}}_{jk} - \boldsymbol{\theta}_{jk}^*\|_2 \leqslant \frac{5\lambda_n\sqrt{d}}{\Delta_{\min}} \text{ for any } j \neq k,$$
$$\implies \max(\|\hat{\boldsymbol{\theta}}_j^{\max} - \boldsymbol{\theta}_j^*\|_2, \|\hat{\boldsymbol{\theta}}_j^{\min} - \boldsymbol{\theta}_j^*\|_2) \leqslant \sqrt{d\max_{j\neq k} \|\hat{\boldsymbol{\theta}}_{jk} - \boldsymbol{\theta}_{jk}^*\|_2^2} \leqslant \frac{5\lambda_n d}{\Delta_{\min}}$$

Appendix C

Simulation results for section 4.1 and section 4.2 with stability selection

We also investigated our model selection performance when coupled with stability selection for section 4.1 and 4.2. The settings are the same as in those sections and the stability selection results are shown in red curves. As shown from Figures 1 and 2, stability selection does not show much stronger model selection performance under these settings. [Figure 1 about here.]

[Figure 2 about here.]

Appendix D

Simulation results for high-dimensional responses.

We also investigated the model selection performance of our methods when the dimension of the response is large. We set p = 5, n = 100 and $q = \{50, 100, 200\}$. The results are shown in Figure 3. As the dimension q increases, coupling stability selection with the joint approach and the separate-max approach significantly improve model selection performance over the respective original methods. Also the separate-min approach performs the best among the three approaches because it is conservative enough to eliminate many of the false positives.

[Figure 3 about here.]

Appendix E

Simulation results for KNN graphs.

We performed the sparsity effect analysis similar to section 4.1 on k-nearest neighbor graphs. The results are shown in Figure 4. The pattern is similar to section 4.1, where the model selection performance deteriorates as the model sparsity decreases both in terms of edges and effective number of covariates. The red curves represent the results of stability selection. Since the dimension of the variables are relatively low in this case, the improvement of model selection by applying stability selection is not significant.

[Figure 4 about here.]

Appendix F

Numerical results for the tumor suppressor gene study.

We applied stability selection to infer the stable set of important covariates for each pairwise conditional association. Table 1 records the rank list of the edges depending on different covariates. The first two columns of each covariate-related columns are the node names and the third column records the selection frequency. Further, for each node, each covariate, and each stability selection subsample, we computed the "covariate-specific" degree of a node. A ranking of nodes can then be produced for each covariate and each replication. Then we computed the median rank across all stability selection subsamples and ordered nodes by rank for each covariate. The results are listed in Table 2.

[Table 1 about here.]

[Table 2 about here.]



Figure 1. ROC curves for different sparsity settings.



Figure 2. ROC curves for different scale settings.



Figure 3. ROC curves for high-dimensional responses.

Joint Approach, knn=2 Joint Approach, knn=3 Joint Approach, knn=4 True Positive Rate 0.8 0.8 True Positive Rate True Positive Rate 0.6 0.6 0.4 0.4 ρ=0.2 ρ=0.2 =0.2 0.2 0.: 0.2 ρ=0.5 **-** ρ=0.5 **-** ρ=0.5 ρ=0.8 ρ=0.8 ρ=0.8 0 0 0 0 00 0.2 0.3 0.4 0.2 0.3 0.4 0.2 0.3 0.1 0.1 0.1 0.4 False Positive Rate False Positive Rate False Positive Rate Separate-Max Approach, knn=2 Separate-Max Approach, knn=3 Separate-Max Approach, knn=4 0.8 True Positive Rate 0.8 0.8 True Positive Rate True Positive Rate 0.6 0.6 0.4 0.4 ρ=0.2 ρ=0.2 ρ=0.2 0.2 0.2 0.2 **-** ρ=0.5 **-** ρ=0.5 - ρ=0.5 ρ=0.8 ρ=0.8 ρ=0.8 0 **`** 0 0 0 0 0.1 0.2 0.3 False Positive Rate 0.1 0.2 0.3 False Positive Rate 0.4 0.2 0.3 0.4 0.4 0.1 False Positive Rate

Figure 4. ROC curves for varying levels of sparsity, as measured by the parameter β . The red curve corresponds to stability selection over a grid of threshold for selection frequencies.

 Table 1

 Frequency-based ranked list of covariate-dependent inter-chromosomal interactions

Main effect		TP53 mutation status			ER status			Tumor Stage			
Gene1	Gene2	Freq	Gene1	Gene2	Freq	Gene1	Gene2	Freq	Gene1	Gene2	Freq
4q31.3	18q23	0.83	1p13.1	21q21.1	0.5	4q34.3	5q32	0.79	11q23.3	16q24.1	0.58
6p21.32	13q31.2	0.81	2p12	7p21.1	0.5	2p16.1	4q28.3	0.51	3p21.31	5q21.3	0.57
11p15.1	14q22.2	0.71	8p21.3	11q23.3	0.5	4q12	22q11.23	0.49	9q33.1	16q24.1	0.54
$2\alpha^{34}$	Ap11.25 3a13 31	0.68	3p22.1 4a25	0p21.31 8p11.22	0.48 0.48	10q11.21 11a23.3	10q23.2 15q13.1	$0.49 \\ 0.48$	2q24.1 3q23	10q24.1 8p11-22	0.40 0.46
1036.11	2n21	0.61	4q20 4q32.1	17p13.1	0.46	5a22.2	9a21.13	0.46	10a26.3	17p11.22	0.40 0.45
1p31.1	2q32.2	0.6	6p21.32	8p11.22	0.46	9p24.1	10q22.1	0.46	3p12.1	12q23.1	0.44
2q32.1	12q12	0.59	16q23.1	18q21.32	0.46	8p21.3	12q22	0.45	17q21.11	22q11.21	0.44
6p21.32	Xp11.4	0.58	12q23.1	Xq23	0.45	2q22.1	9q33.3	0.44	4q35.1	15q22.1	0.43
9q31.3	14q24.3	0.58	2p21	Xp11.22	0.44	2q23.1	4q28.3	0.44	16q23.3	17p13.1	0.43
6p21.32	9q31.3	0.57	18q21.2	Xq23	0.44	3q24	22q11.23	0.44	3p12.3	7p21.3 7p21.2	0.42
2p25.2 6p21-32	13q20.2 13q21.1	$0.50 \\ 0.54$	2q24.5 6a26	4p14 9p21-3	0.43 0.43	1p51.1 1p13.1	80421.15 8011.22	0.43 0.43	4q22.5 9a34 13	7p21.5 10a11-21	0.41 0.41
10a25.3	12p13.31	$0.54 \\ 0.54$	12a23.1	Xa26.1	0.43	4a21.1	9a33.3	0.43 0.42	2a24.2	9a33.1	0.41 0.4
3p21.1	17p13.2	0.53	15q13.1	Xp22.32	0.43	4q25	10q22.1	0.42	2q24.2	16q24.1	0.4
12p13.31	17q11.2	0.53	4q13.1	5q23.3	0.42	4q32.2	$7\mathrm{p}\dot{2}1.1$	0.41	13q33.1	Xq13.3	0.4
2q32.1	6q14.1	0.52	4q35.1	15q23	0.42	2p25.2	3p22.2	0.38	2q32.1	15q15.1	0.39
5q33.1	11p15.4	0.52	6q14.1	13q22.1	0.42	10q25.1	12q23.3	0.38	3q13.13	7p21.3	0.39
9q34.13	22q11.21	0.52	8p11.22	15q21.2	0.42	4p14	10q22.1	0.37	4q31.22	9q22.33	0.39
$1p_{34.2}$ $2a_{24.1}$	2p24.1 3a13 31	$0.51 \\ 0.51$	2p10.2 3p21-31	13q34 17q21.2	0.41 0.41	4q12 4q12	12p12.3 15q13 1	0.37 0.37	11q23.2 12p12.1	13q21.1 15q14	0.39
2q24.1 3p22.1	6n21.31	$0.51 \\ 0.51$	$5\alpha 12.1$	9n21.2	0.41 0.41	$\frac{4q12}{7a21}$	16q22.1	0.37 0.37	2a32 1	7n21.3	0.33 0.38
3p22.1	15q25.3	0.51	9p24.2	16q24.1	0.41	9q31.2	12q15	0.37	9q22.33	21q21.1	0.38
$9^{-}_{q}21.11$	16q21	0.51	$^{1}8p23.3$	9q22.31	0.39	3p12.1	$9p\dot{2}1.3$	0.36	15q15.1	22q13.1	0.38
6q23.3	14q24.3	0.5	10p12.31	11q14.1	0.39	5q11.2	10q25.1	0.36	4q31.22	9q34.13	0.37
7q21.13	8q21.13	0.5	2q32.3	4p16.1	0.38	14q24.1	18p11.21	0.36	4q31.3	15q22.1	0.37
10q11.21	12p13.32	0.5	4p14	5q12.3	0.38	3p12.3	7p21.1	0.35	5q33.3	16q12.1	0.37
2p16.1 6p21.32	6p12.3 16a12.2	0.49 0.40	3p12.3 5a22.1	12p13.1 18a21 22	0.37	4q31.3 15a25 1	(q21.3 22a11.22	0.35 0.34	6q12 6q15	13q14.12 14q24.2	0.37
6q12	10q12.2 12n11.22	0.49	12a22	15q21.32	0.37 0.37	4n15 33	22q11.23 6a27	$0.34 \\ 0.33$	3n14.3	14q24.3 8n11 22	0.37
9q33.1	12p11.22 14q12	0.49	2p21	Xp22.13	0.36	8p22	11q24.2	0.33	10q26.3	16q12.2	0.36
11q22.2	17q21.31	0.49	3q23	9p21.1	0.36	12q22	22q11.23	0.33	1q31.1	4q28.2	0.35
11q24.3	22q13.2	0.49	4q35.1	17p13.2	0.36	3p12.1	$9p\overline{2}2.2$	0.32	6q14.1	11q23.2	0.35
3p21.1	12q23.3	0.48	5q15	15q23	0.36	9p21.2	10q25.1	0.32	9q21.12	17q12	0.34
4q35.1	8p21.2	0.47	8p11.22	15q14 21-21-1	0.36	9q31.1	12q15	0.32	12q23.1	22q11.23	0.34
(p21.1 11p15.2	14q24.3 18a12.1	0.47 0.47	18q21.33 2q34	21q21.1 8a21 13	0.30	12p12.3 3a26 1	22q11.23 14q32.13	0.32 0.31	0q27 10a23 33	(q31.31 12p13.2	0.33
2a32.2	5a23.2	0.46	2q34 3p13	9n24.2	0.35	4n15.2	12a12	0.31	18q25.55 18q21.1	20p12.2	0.33
4q22.3	15q26.3	0.46	4q28.1	15q15.3	0.35	5q22.1	7p21.1	0.31	5q11.2	9q34.13	0.32
6p21.31	15q25.3	0.46	5q12.3	12q21.2	0.35	5q22.2	10q22.1	0.31	5q33.3	16q12.2	0.32
11q23.1	12q21.31	0.45	7q31.33	16q12.1	0.35	5q33.3	13q14.13	0.31	6q27	11q14.1	0.32
12p13.2	15q21.3	0.44	8p21.3	12p13.1	0.35	3p22.1	17p13.1	0.3	1p13.2	3q25.2	0.31
2p16.2	9q31.3	0.43	3q26.1	11p13 10-121	0.34	4q12	11q23.3	0.3	2p25.2	5q33.3	0.31
$_{4\alpha35}^{31.31}$	9n21.2	$0.43 \\ 0.43$	12a15	$12p_{13,1}$ $13a_{12}$ 12	$0.34 \\ 0.34$	5q14.1 5q21.3	12p11.22 6a26	0.5	3p12.1 4p12	22q11.25 6a24-2	0.31 0.31
12p11.22	16a21	0.43	1a31.1	5a23.3	0.33	8p23.1	10a22.1	0.3	4q12	9p21.3	0.31
14q23.3	22q11.21	0.43	3p11.1	9q34.13	0.33	9p21.2	10q23.2	0.3	6p21.32	10q11.21	0.31
2q23.3	6p12.1	0.42	9p24.1	18q22.3	0.33	$1\bar{3}q33.1$	22q11.23	0.3	6q16.2	7q31.32	0.31
6p21.31	17q11.2	0.42	9q22.32	12p13.31	0.33	15q13.1	Xq24	0.3	7q31.31	8p11.22	0.31
6q24.3	10q11.21	0.42	11q24.3	13q32.1	0.33	18q11.2	22q11.23	0.3	11q24.2	17p11.2	0.31
14q24.3 1p21.1	17p13.1 7a21.12	0.42 0.41	2q34 4a22-3	12q21.2 $Y_{P}11.22$	0.32 0.32				2p25.2 2p24_1	16q23.2 11a14.1	0.3
2p161	4q13.3	0.41 0.41	4q22.3 6p21.32	$12\alpha 21.1$	0.32 0.32				2p24.1 2a24.2	6a26	0.3
3p21.2	8p12	0.41	6q14.1	12q21.1 12q23.1	0.32				4q22.3	11q23.1	0.3
4q21.3	15q26.3	0.41	6q14.3	11q14.1	0.32				6q13	9q21.2	0.3
8p21.3	21q21.1	0.41	6q27	13q12.13	0.32				7p21.3	12p11.23	0.3
8p11.22	15q21.2	0.41	7q21.3	22q12.3	0.32				14q23.1	18q22.1	0.3
1p21.3	4q31.22	0.4	8p22	14q22.1	0.32						
əp20.3 ∕m19	4q28.1 5a22-1	0.4 0.4	∠q21.3 3n21_1	0q22.1 10a21-3	0.31						
-p10 5a32	11p15 4	0.4	3a23	15a25-3	0.31						
6q16.3	13q14.13	0.4	4q34.3	10q21.2	0.31						
11p15.4	17q21.31	0.4	5q21.3	$10\dot{q}26.3$	0.31						
11q22.2	12q21.33	0.4	5q22.2	12q12	0.31						

Table 2Degree-based ranking of nodes

Gene Median rank Gene Median rank Gene Median rank Gene Median rank Gene Median rank Gene Median rank	ian rank
0021.32 21.3 4q13.3 19.73 $10q22.1$ 8.73 22q11.23 15.5	
4q21.1 33.25 $8q21.13$ 24.75 $8q21.13$ 15.5 $9q34.13$ 17	
17q21.31 44.25 $12q23.1$ 32 $9p22.3$ 24.75 $8p11.22$ 18.5	
$2q^{2}4.2$ 48.25 $15q^{2}3$ 40.5 $5q^{3}2$ 25 $10q^{2}5.2$ 24.7	5
$2\hat{q}32.1$ 55 $8\hat{p}11.22$ 41.25 $12\hat{q}23.3$ 26 $16\hat{q}24.1$ 33.2	5
17p13.2 57.25 $2p12$ 47.25 $22q11.23$ 28.25 $11q14.1$ 35.7	5
6q22.31 62 $2q24.3$ 55.5 $12p11.22$ 39 $6p21.32$ 39	
$11q14.1 \ 66 \ 2p21 \ 55.75 \ 12q22 \ 46.25 \ 6q12 \ 46.5$	
11q22.3 66.5 3q26.1 57.25 12p12.3 47.25 2q24.1 47.5	
10q22.1 66.75 21q21.1 57.5 8p21.3 47.5 10p12.31 50	
17q11.2 67.25 $4q24$ 57.75 $3q24$ 51.5 $14q32.12$ 50.5	
9p21.3 69.75 1p21.2 62.5 5q33.3 54.75 6q14.1 51.2	5
$12q21.32 70.75 \qquad 17p13.2 62.75 \qquad 10q25.1 54.75 \qquad 16q23.1 51.25$	5
2q33.1 73 12p13.1 64.5 8p11.22 55.25 10p12.2 51.75	5
$1p36.11 76.25 \qquad 9p24.2 66.5 \qquad 10q23.2 55.5 \qquad 6q13 \qquad 57.25$	5
6q14.3 79.5 $14q32.12$ 69.25 $4q12$ 55.75 $9q33.1$ 59	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	5
11q23.1 83 Xp11.23 71.25 3p12.1 56.5 11q22.2 59.29	5
$12p11.22 85.75 \qquad 4q13.2 71.5 \qquad 3p14.2 58.25 \qquad 16q23.3 59.5$	
14q24.3 87.5 6p21.32 71.75 14q32.12 58.75 9p21.3 63	
$12p11.23 87.75 \qquad 12q21.32 75.25 \qquad 8p22 \qquad 59.5 \qquad 11q24.2 63.25$	5
$7q21.11 88.25 \qquad 4q31.1 76 \qquad 7p21.1 59.75 \qquad 2q36.3 64.5$	
4q13.3 89.25 $8p22$ 76 $Xp11.23$ 65 $12p11.23$ 65.21	5
$11q23.3 89.5 \qquad 12q21.2 77.75 \qquad 17q21.31 65.25 \qquad 10q26.3 65.75$	5
15q25.3 90 9q33.3 79.75 5q14.1 69 15q15.1 66.75	5
6q13 93 17q21.31 81 9p21.2 75 7p21.3 69	
2q32.2	
$10q26.3 98.25 \qquad 2q34 83.25 \qquad 4p13 75.75 \qquad 16q12.2 73$	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	5
Xp11.23 99.5 8p21.1 84.75 21q21.1 78 4q23 75	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
9q31.1 102.25 $1q31.1$ 85.75 $5q13.3$ 80.25 $3p21.31$ 77.5	
13q12.3 103.75 $12p11.22$ 87.5 $5q14.2$ 82.75 $14q24.3$ 80.26	0
8q21.13 106 $21q21.3$ 87.75 $12q12$ 83.25 $6q27$ 82.5	-
9q21.11 106.5 17p13.1 89.25 4p16.1 84.5 11q23.1 84.7(C
7(221.12 - 107.5 - 8p12 - 90 - 5q13.2 - 87.25 - 7p21.1 - 85.5 - 112 - 107.77 - 0.144 - 90 - 57.77 - 0.144 - 90 - 0.12 - 0.144 - 90 -	-
1p12 101.75 $0q14.1$ 92 $3p24.3$ 88 8p12 85.7	D
$2q23.2$ 108 $2q24.2$ 92.25 $10q21$ 88 $12p11.22$ 86 $(q22)^{-1}$	
0q22.32 109.25 $13q22.31$ 92.75 921.3 88.25 $11q14.3$ 87 2-19 21 100.77 $4-97$ 047 14-99 20 97 $9-91.1$ 89	
$3q_{13,31}$ 109.75 $4q_{23}$ 94.5 $14q_{32,13}$ 89.25 $8p_{21,1}$ 88.5	-
0q20 111.25 9p21.2 94.75 $0p14.1$ 90.5 $9q22.51$ 90.27	=
op12 112 4p10.1 90.29 13q13.1 90.79 9p21.2 90.7 19-19 114.95 99-12 0.7 5-92 0.15 4-95 0.15	0
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
11422.2 110 10420.0 101.70 0414.0 91.0 10421.02 91.70 10421.02 10	J
$12p_{10,1}$ 110 0q10 104 $3p_{22,2}$ 91.0 0q24.0 94 11p_19 115.5 $4a_{2}^{2}$ 5.9 104.95 11p_92.2 09 17p_11.9 04	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	5
-12420.1 110.10 -020.0 100.20 $-2p20.2$ 30 $-0p20.0$ 94.20 $-2p20.1$ 116.25 $-17p10$ 106.25 $-1p20.1$ 0.275 $-16a00.1$ 0.4.01	5
16q21 117.5 1p31.3 107.25 3q26.1 94.5 10q21.3 95.76	5