## Supplementary Material for "Regularization Methods for High-Dimensional Instrumental Variables Regression With an Application to Genetical Genomics"

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## Proof of Theorem 4

We first present two lemmas that are essential to the proof of Theorem 4, which concern the concentration of the empirical covariance matrix  $\hat{\mathbf{C}}$  around its population version  $\mathbf{C}$  and the score vector

$$\frac{1}{n}\widehat{\mathbf{X}}^{T}(\mathbf{y} - \widehat{\mathbf{X}}\boldsymbol{\beta}_{0}) = \frac{1}{n}\widehat{\mathbf{X}}^{T}\boldsymbol{\eta} - \frac{1}{n}\widehat{\mathbf{X}}^{T}(\widehat{\mathbf{X}} - \mathbf{X})\boldsymbol{\beta}_{0}$$

around zero. These lemmas can be viewed as generalizations of Lemma A.3 and inequality (A.15), respectively. For ease of presentation, we condition on the event of probability  $1 - \pi_0$  that the two error bounds in Condition (C4) hold, and incorporate the probability  $\pi_0$  into the result by the union bound.

**Lemma S.1.** Under Conditions (C4)-(C6), if  $\mu_0 > 0$  and the first-stage error bounds  $e_1$  and  $e_2$  satisfy

$$s(2Le_1 + e_2) \le \frac{\alpha}{(4 - \alpha)\varphi} \wedge \frac{(\mu_0/2)^2}{s},\tag{S.1}$$

then with probability at least  $1 - \pi_0$ , the following inequalities holds:

$$\|(\widehat{\mathbf{C}}_{SS})^{-1}\|_{\infty} \le \frac{4-\alpha}{2(2-\alpha)}\varphi,\tag{S.2}$$

$$\|\widehat{\mathbf{C}}_{S^c S}(\widehat{\mathbf{C}}_{SS})^{-1}\|_{\infty} \le \left\{ \left(1 - \frac{\alpha}{2}\right) \frac{\rho'(0+)}{\rho'_{\mu}(b_0/2)} \right\} \wedge (2cn^{\nu}),$$
 (S.3)

and

$$\Lambda_{\min}(\widehat{\mathbf{C}}_{SS}) > \mu \tau_0. \tag{S.4}$$

*Proof.* It follows from the arguments in the proof of Lemma A.1 and Condition (C4) that

$$\max_{1 \le i,j \le p} \frac{1}{n} |\widehat{\mathbf{x}}_i^T \widehat{\mathbf{x}}_j - (\mathbf{Z} \boldsymbol{\gamma}_{0i})^T \mathbf{Z} \boldsymbol{\gamma}_{0j}| \le 2Le_1 + e_2.$$

Consequently, by the assumption (S.1),

$$\varphi \|\widehat{\mathbf{C}}_{SS} - \mathbf{C}_{SS}\|_{\infty} \le \varphi s(2Le_1 + e_2) \le \frac{\alpha}{4 - \alpha}$$
 (S.5)

and

$$\varphi \|\widehat{\mathbf{C}}_{S^c S} - \mathbf{C}_{S^c S}\|_{\infty} \le \frac{\alpha}{4 - \alpha}.$$
 (S.6)

Then inequality (S.2) follows as in the proof of Lemma A.3.

To show inequality (S.3), by (S.2), (S.5), (S.6), and Condition (C6), we have

$$\begin{split} \|\widehat{\mathbf{C}}_{S^{c}S}(\widehat{\mathbf{C}}_{SS})^{-1} - \mathbf{C}_{S^{c}S}(\mathbf{C}_{SS})^{-1}\|_{\infty} \\ &\leq \|\widehat{\mathbf{C}}_{S^{c}S} - \mathbf{C}_{S^{c}S}\|_{\infty} \|(\widehat{\mathbf{C}}_{SS})^{-1}\|_{\infty} + \|\mathbf{C}_{S^{c}S}(\mathbf{C}_{SS})^{-1}\|_{\infty} \|\widehat{\mathbf{C}}_{SS} - \mathbf{C}_{SS}\|_{\infty} \|(\widehat{\mathbf{C}}_{SS})^{-1}\|_{\infty} \\ &\leq \frac{\alpha}{(4-\alpha)\varphi} \frac{4-\alpha}{2(2-\alpha)}\varphi + \left[\left\{(1-\alpha)\frac{\rho'(0+)}{\rho'_{\mu}(b_{0}/2)}\right\} \wedge (cn^{\nu})\right] \frac{\alpha}{(4-\alpha)\varphi} \frac{4-\alpha}{2(2-\alpha)}\varphi \\ &\leq \frac{\alpha}{2(2-\alpha)} + \left\{\frac{\alpha(1-\alpha)}{2(2-\alpha)}\frac{\rho'(0+)}{\rho'_{\mu}(b_{0}/2)}\right\} \wedge \left(\frac{c}{2}n^{\nu}\right) \\ &\leq \left\{\frac{\alpha}{2}\frac{\rho'(0+)}{\rho'_{\mu}(b_{0}/2)}\right\} \wedge (cn^{\nu}), \end{split}$$

where we have used the inequalities  $\rho'(0+)/\rho'_{\mu}(b_0/2) \ge 1$  and  $\alpha/\{2(2-\alpha)\} \le 1/2 \le cn^{\nu}/2$ . This, along with Condition (C6), implies (S.3).

Finally, it follows from the Hoffman–Wielandt inequality (Horn and Johnson 1985) and the assumption (S.1) that

$$|\Lambda_{\min}(\widehat{\mathbf{C}}_{SS}) - \Lambda_{\min}(\mathbf{C}_{SS})|^2 \le ||\widehat{\mathbf{C}}_{SS} - \mathbf{C}_{SS}||_F^2 \le s^2 (2Le_1 + e_2) \le \left(\frac{\mu_0}{2}\right)^2.$$

In view of the definition of  $\mu_0$ , inequality (S.4) follows. This completes the proof of the lemma.

**Lemma S.2.** Under Conditions (C4)-(C6), if the first-stage error bounds satisfy  $e_1 = O(1)$  and  $e_2 = O(1)$ , then there exist constants  $c_0, c_1, c_2 > 0$  such that, if we choose

$$\mu \ge C_0 n^{\nu} \sqrt{\frac{\log p + \log q}{n} \vee e_2},$$

where  $C_0 = c_0 L \max(\sigma_{p+1}, M\sigma_{\max}, M)$ , then with probability at least  $1 - \pi_0 - c_1(pq)^{-c_2}$ , it holds that

$$\left\| \frac{1}{n} \widehat{\mathbf{X}}^T \boldsymbol{\eta} - \frac{1}{n} \widehat{\mathbf{X}}^T (\widehat{\mathbf{X}} - \mathbf{X}) \boldsymbol{\beta}_0 \right\|_{\infty} < \frac{\alpha}{6cn^{\nu}} \mu \rho'(0+).$$
 (S.7)

*Proof.* As in the proof of Lemma A.2, we write  $n^{-1}\widehat{\mathbf{X}}^T\boldsymbol{\eta} - n^{-1}\widehat{\mathbf{X}}^T(\widehat{\mathbf{X}} - \mathbf{X})\boldsymbol{\beta}_0 = T_1 + \cdots + T_6$ . Letting  $t_0 = \alpha\mu\rho'(0+)/(6cn^{\nu})$ , we bound the six terms similarly as follows:

$$P\left(\|T_1\|_{\infty} \ge \frac{t_0}{6}\right) \le P\left(\left\|\frac{1}{n}\mathbf{Z}^T\boldsymbol{\eta}\right\|_{\infty} \ge \frac{t_0}{6e_1}\right) \le q \exp\left\{-\frac{n}{2\sigma_{p+1}^2}\left(\frac{t_0}{6e_1}\right)^2\right\},\,$$

$$P\left(\|T_2\|_{\infty} \geq \frac{t_0}{6}\right) \leq P\left(\left\|\frac{1}{n}\mathbf{Z}^T\boldsymbol{\eta}\right\|_{\infty} \geq \frac{t_0}{6L}\right) \leq q \exp\left\{-\frac{n}{2\sigma_{p+1}^2} \left(\frac{t_0}{6L}\right)^2\right\},$$

$$P\left(\|T_3\|_{\infty} \geq \frac{t_0}{6}\right) \leq P\left(\max_{1\leq i\leq q,\, 1\leq j\leq p} \left|\frac{1}{n}\mathbf{z}_i^T\boldsymbol{\varepsilon}_j\right|_{\infty} \geq \frac{t_0}{6Me_1}\right) \leq pq \exp\left\{-\frac{n}{2\sigma_{\max}^2} \left(\frac{t_0}{6Me_1}\right)^2\right\},$$

$$P\left(\|T_4\|_{\infty} \geq \frac{t_0}{6}\right) \leq P\left(\max_{1\leq i\leq q,\, 1\leq j\leq p} \left|\frac{1}{n}\mathbf{z}_i^T\boldsymbol{\varepsilon}_j\right|_{\infty} \geq \frac{t_0}{6LM}\right) \leq pq \exp\left\{-\frac{n}{2\sigma_{\max}^2} \left(\frac{t_0}{6LM}\right)^2\right\},$$

$$\|T_5\|_{\infty} \leq M \max_{1\leq i\leq n} \frac{1}{n} \|\mathbf{Z}(\widehat{\boldsymbol{\gamma}}_i - \boldsymbol{\gamma}_{0i})\|_2 \|\mathbf{Z}(\widehat{\boldsymbol{\gamma}}_j - \boldsymbol{\gamma}_{0j})\|_2 \leq Me_2,$$

and

$$||T_6||_{\infty} \leq LM \max_{1 \leq j \leq p} \frac{1}{\sqrt{n}} ||\mathbf{Z}(\widehat{\boldsymbol{\gamma}}_j - \boldsymbol{\gamma}_{0j})||_2 \leq LM\sqrt{e_2}.$$

Combining these bounds and in view of the assumptions  $e_1 = O(1)$  and  $e_2 = O(1)$ , there exist constants  $c_0, c_1, c_2 > 0$  such that, if we choose

$$\mu \ge C_0 n^{\nu} \sqrt{\frac{\log p + \log q}{n} \vee e_2},$$

where  $C_0 = c_0 L \max(\sigma_{p+1}, M\sigma_{\max}, M)$ , then with probability at least  $1 - \pi_0 - c_1(pq)^{-c_2}$ , the desired inequality holds. The completes the proof of the lemma.

Proof of Theorem 4. One can easily show that  $\widehat{\beta} \in \mathbb{R}^p$  is a strict local minimizer of problem (4) if the following conditions hold:

$$\frac{1}{n}\widehat{\mathbf{X}}_{\widehat{S}}^{T}(\mathbf{y} - \widehat{\mathbf{X}}\widehat{\boldsymbol{\beta}}) = \mu \rho'_{\mu}(|\widehat{\boldsymbol{\beta}}_{\widehat{S}}|) \circ \operatorname{sgn}(\widehat{\boldsymbol{\beta}}_{\widehat{S}}), \tag{S.8}$$

$$\left\| \frac{1}{n} \widehat{\mathbf{X}}_{\widehat{S}^c}^T (\mathbf{y} - \widehat{\mathbf{X}} \widehat{\boldsymbol{\beta}}) \right\|_{\infty} < \mu \rho'(0+), \tag{S.9}$$

and

$$\Lambda_{\min}(\widehat{\mathbf{C}}_{\widehat{S}\widehat{S}}) > \mu \tau(\rho_{\mu}; \widehat{\boldsymbol{\beta}}_{\widehat{S}}), \tag{S.10}$$

where  $\circ$  denotes the Hadamard (entrywise) product, and  $|\cdot|$ ,  $\rho'_{\mu}(\cdot)$ , and  $\operatorname{sgn}(\cdot)$  are applied componentwise. It suffices to find a  $\widehat{\boldsymbol{\beta}} \in \mathbb{R}^p$  with the desired properties such that conditions (S.8)–(S.10) hold. Let  $\widehat{\boldsymbol{\beta}}_{S^c} = \mathbf{0}$ . The idea of the proof is to first determine  $\widehat{\boldsymbol{\beta}}_S$  from (S.8), and then show that thus obtained  $\widehat{\boldsymbol{\beta}}$  also satisfies (S.9) and (S.10).

From now on, we condition on the event of probability at least  $1 - \pi_0 - c_1(pq)^{-c_2}$  that the inequalities in Lemmas S.1 and S.2 hold. Using similar arguments to those in the proof of Theorem 3, (S.8) with  $\widehat{S}$  replaced by S can be written in the form

$$\widehat{\boldsymbol{\beta}}_S - \boldsymbol{\beta}_{0S} = (\widehat{\mathbf{C}}_{SS})^{-1} \left\{ \frac{1}{n} \widehat{\mathbf{X}}_S^T \boldsymbol{\eta} - \frac{1}{n} \widehat{\mathbf{X}}_S^T (\widehat{\mathbf{X}}_S - \mathbf{X}_S) \boldsymbol{\beta}_{0S} - \mu \rho'_{\mu} (|\widehat{\boldsymbol{\beta}}_S|) \circ \operatorname{sgn}(\widehat{\boldsymbol{\beta}}_S) \right\}. \tag{S.11}$$

Define the function  $f: \mathbb{R}^s \to \mathbb{R}^s$  by  $f(\boldsymbol{\theta}) = \boldsymbol{\beta}_{0S} + (\widehat{\mathbf{C}}_{SS})^{-1} \{ n^{-1} \widehat{\mathbf{X}}_S^T \boldsymbol{\eta} - n^{-1} \widehat{\mathbf{X}}_S^T (\widehat{\mathbf{X}}_S - \mathbf{X}_S) \boldsymbol{\beta}_{0S} - \mu \rho'_{\mu}(|\boldsymbol{\theta}|) \circ \operatorname{sgn}(\boldsymbol{\theta}) \}$ , and let  $\mathcal{K}$  denote the hypercube  $\{ \boldsymbol{\theta} \in \mathbb{R}^s : \|\boldsymbol{\theta} - \boldsymbol{\beta}_{0S}\|_{\infty} \le 7\varphi \mu \rho'(0+)/4 \}$ .

It follows from (S.2), (S.7), and Condition (C4) that, for  $\theta \in \mathcal{K}$ ,

$$||f(\boldsymbol{\theta}) - \boldsymbol{\beta}_{0S}||_{\infty} \leq ||(\widehat{\mathbf{C}}_{SS})^{-1}||_{\infty} \left\{ \left\| \frac{1}{n} \widehat{\mathbf{X}}_{S}^{T} \boldsymbol{\eta} - \frac{1}{n} \widehat{\mathbf{X}}_{S}^{T} (\widehat{\mathbf{X}}_{S} - \mathbf{X}_{S}) \boldsymbol{\beta}_{0S} \right\|_{\infty} + \mu \rho'(0+) \right\}$$

$$\leq \frac{4 - \alpha}{2(2 - \alpha)} \varphi \left\{ \frac{\alpha}{6cn^{\nu}} \mu \rho'(0+) + \mu \rho'(0+) \right\}$$

$$\leq \frac{3}{2} \varphi \left\{ \frac{1}{6} \mu \rho'(0+) + \mu \rho'(0+) \right\} = \frac{7}{4} \varphi \mu \rho'(0+),$$

that is,  $f(\mathcal{K}) \subset \mathcal{K}$ . Also, the last inequality and the assumption (14) imply that for  $\boldsymbol{\theta} \in \mathcal{K}$ ,  $\|\boldsymbol{\theta} - \boldsymbol{\beta}_{0S}\|_{\infty} \leq b_0/2$ , and hence  $\operatorname{sgn}(\boldsymbol{\theta}) = \operatorname{sgn}(\boldsymbol{\beta}_{0S})$ . Thus, in view of Condition (C4), f is a continuous function on the convex, compact hypercube  $\mathcal{K}$ . An application of Brouwer's fixed point theorem yields that equation (S.11) has a solution  $\widehat{\boldsymbol{\beta}}_S$  in  $\mathcal{K}$ . Moreover,  $\operatorname{sgn}(\widehat{\boldsymbol{\beta}}_S) = \operatorname{sgn}(\boldsymbol{\beta}_{0S})$ , so that  $\widehat{S} = S$ . Therefore, we have found a  $\widehat{\boldsymbol{\beta}}$  that satisfies the desired properties and (S.8).

To verify that  $\widehat{\beta}$  satisfies (S.9), by substituting (S.11), we write

$$\frac{1}{n}\widehat{\mathbf{X}}_{S^c}^T(\mathbf{y} - \widehat{\mathbf{X}}\widehat{\boldsymbol{\beta}}) = \frac{1}{n}\widehat{\mathbf{X}}_{S^c}^T\boldsymbol{\eta} - \frac{1}{n}\widehat{\mathbf{X}}_{S^c}^T(\widehat{\mathbf{X}}_S - \mathbf{X}_S)\boldsymbol{\beta}_{0S} 
- \widehat{\mathbf{C}}_{S^cS}(\widehat{\mathbf{C}}_{SS})^{-1} \left\{ \frac{1}{n}\widehat{\mathbf{X}}_S^T\boldsymbol{\eta} - \frac{1}{n}\widehat{\mathbf{X}}_S^T(\widehat{\mathbf{X}}_S - \mathbf{X}_S)\boldsymbol{\beta}_{0S} - \mu\rho'_{\mu}(|\widehat{\boldsymbol{\beta}}_S|) \circ \operatorname{sgn}(\widehat{\boldsymbol{\beta}}_S) \right\}.$$

Also, we have  $\|\widehat{\boldsymbol{\beta}}_S\|_{\infty} = \|\widehat{\boldsymbol{\beta}}_{0S} + (\widehat{\boldsymbol{\beta}}_S - \boldsymbol{\beta}_{0S})\|_{\infty} \ge \|\widehat{\boldsymbol{\beta}}_{0S}\|_{\infty} - \|\widehat{\boldsymbol{\beta}}_S - \boldsymbol{\beta}_{0S}\|_{\infty} \ge b_0 - b_0/2 = b_0/2$ . This, together with (S.3), (S.7), and Condition (C4), leads to

$$\left\| \frac{1}{n} \widehat{\mathbf{X}}_{S^{c}}^{T}(\mathbf{y} - \widehat{\mathbf{X}}\boldsymbol{\beta}) \right\|_{\infty} \leq \left\| \frac{1}{n} \widehat{\mathbf{X}}_{S^{c}}^{T} \boldsymbol{\eta} - \frac{1}{n} \widehat{\mathbf{X}}_{S^{c}}^{T} (\widehat{\mathbf{X}}_{S} - \mathbf{X}_{S}) \boldsymbol{\beta}_{0S} \right\|_{\infty} + \|\widehat{\mathbf{C}}_{S^{c}S}(\widehat{\mathbf{C}}_{SS})^{-1}\|_{\infty}$$

$$\times \left\{ \left\| \frac{1}{n} \widehat{\mathbf{X}}_{S}^{T} \boldsymbol{\eta} - \frac{1}{n} \widehat{\mathbf{X}}_{S}^{T} (\widehat{\mathbf{X}}_{S} - \mathbf{X}_{S}) \boldsymbol{\beta}_{0S} \right\|_{\infty} + \mu \rho'_{\mu}(b_{0}/2) \right\}$$

$$< \frac{\alpha}{6cn^{\nu}} \mu \rho'(0+) + 2cn^{\nu} \cdot \frac{\alpha}{6cn^{\nu}} \mu \rho'(0+) + \left(1 - \frac{\alpha}{2}\right) \frac{\rho'(0+)}{\rho'_{\mu}(b_{0}/2)} \cdot \mu \rho'_{\mu}(b_{0}/2)$$

$$\leq \frac{\alpha}{6} \mu \rho'(0+) + \frac{\alpha}{3} \mu \rho'(0+) + \left(1 - \frac{\alpha}{2}\right) \mu \rho'(0+) = \mu \rho'(0+).$$

Finally, it follows from (S.4) and the definition of  $\tau_0$  that  $\Lambda_{\min}(\widehat{\mathbf{C}}_{SS}) > \mu \tau_0 \geq \mu \tau(\rho_{\mu}; \widehat{\boldsymbol{\beta}}_S)$ , which verifies (S.10) and completes the proof.