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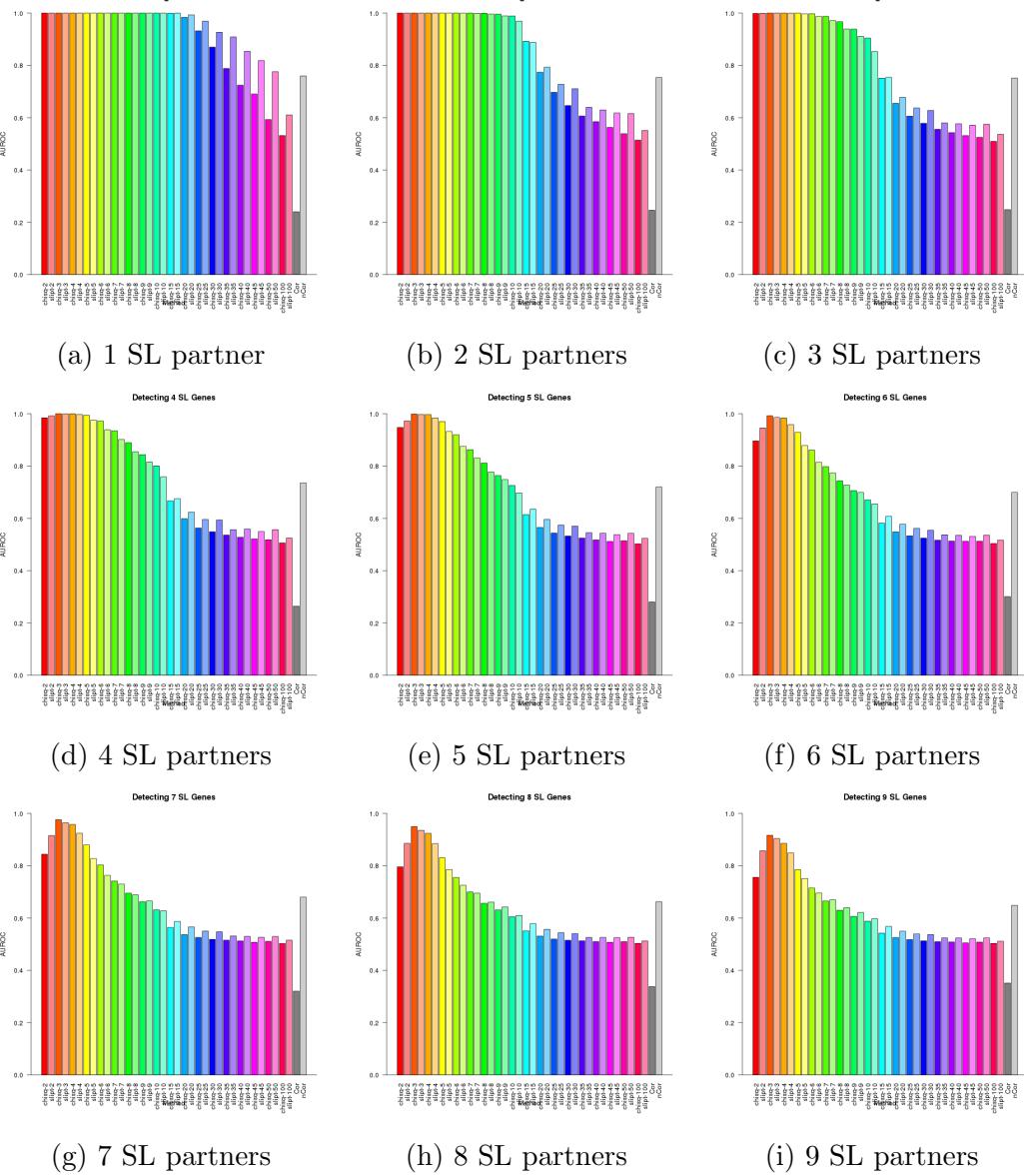
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## **Appendix N**

### **Performance of SLIPT and $\chi^2$**



**Figure N.1: Performance is affected by inhibition in graphs. Synthetic Lethal Detection Compared with  $\chi$**

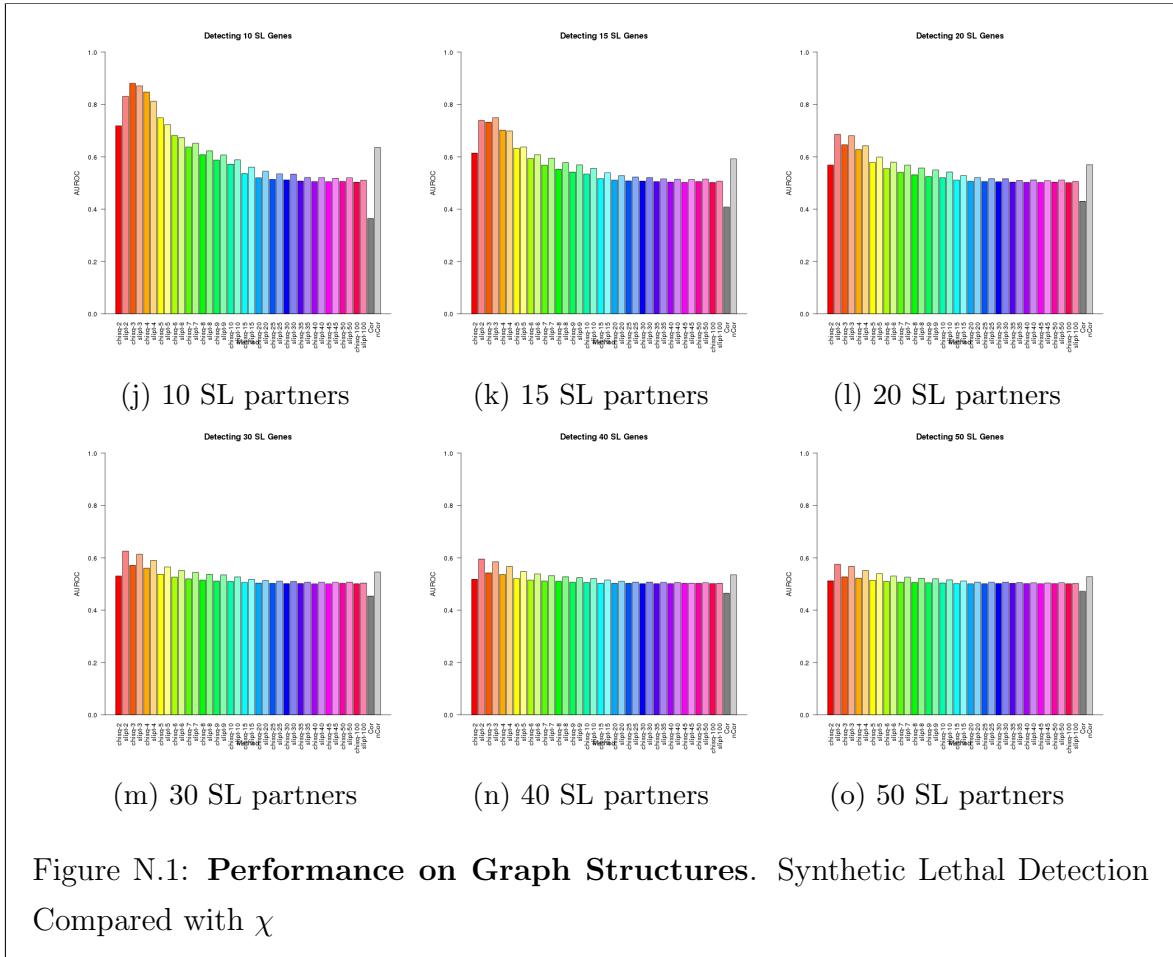


Figure N.1: **Performance on Graph Structures.** Synthetic Lethal Detection Compared with  $\chi$

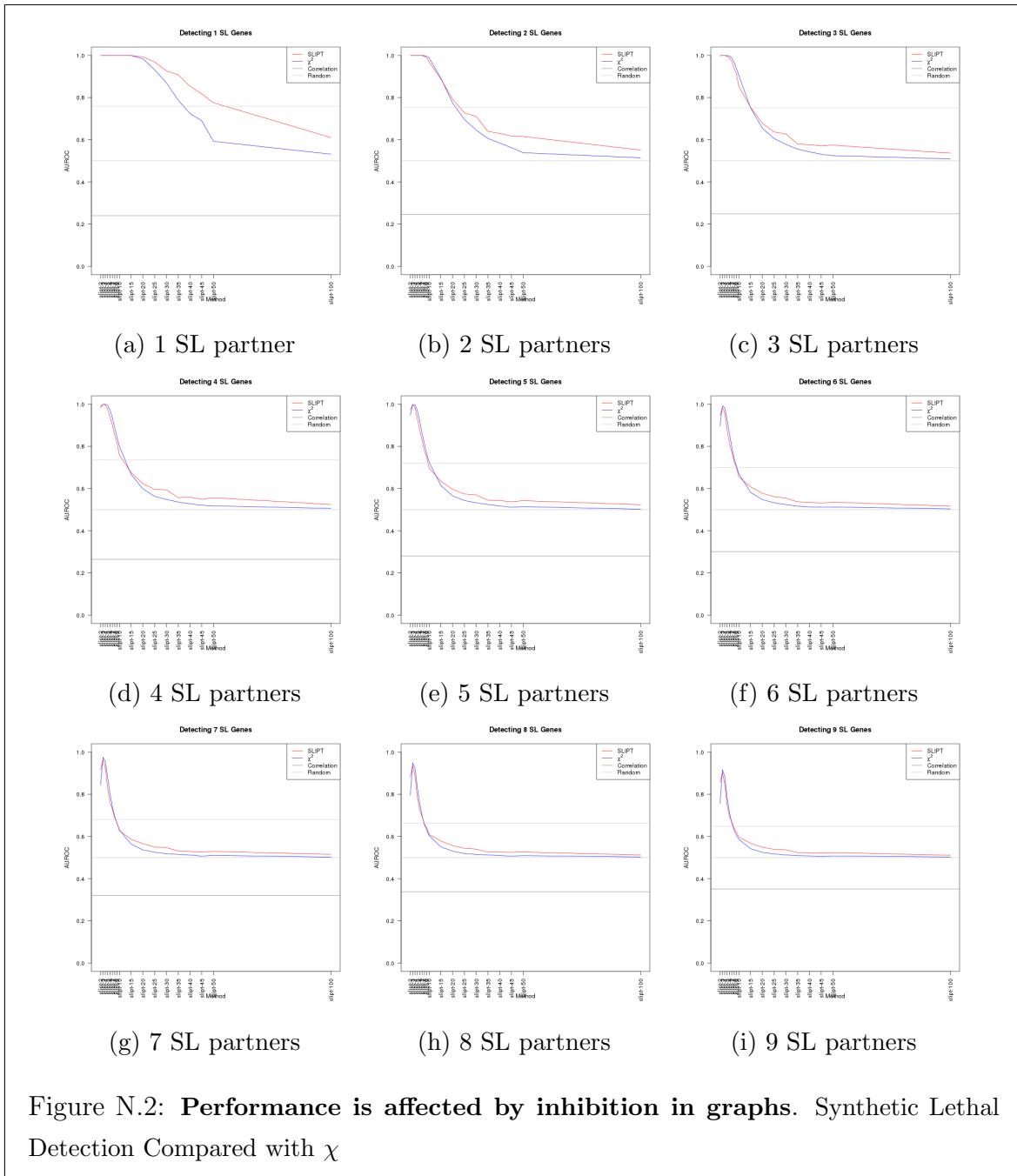


Figure N.2: **Performance is affected by inhibition in graphs.** Synthetic Lethal Detection Compared with  $\chi$

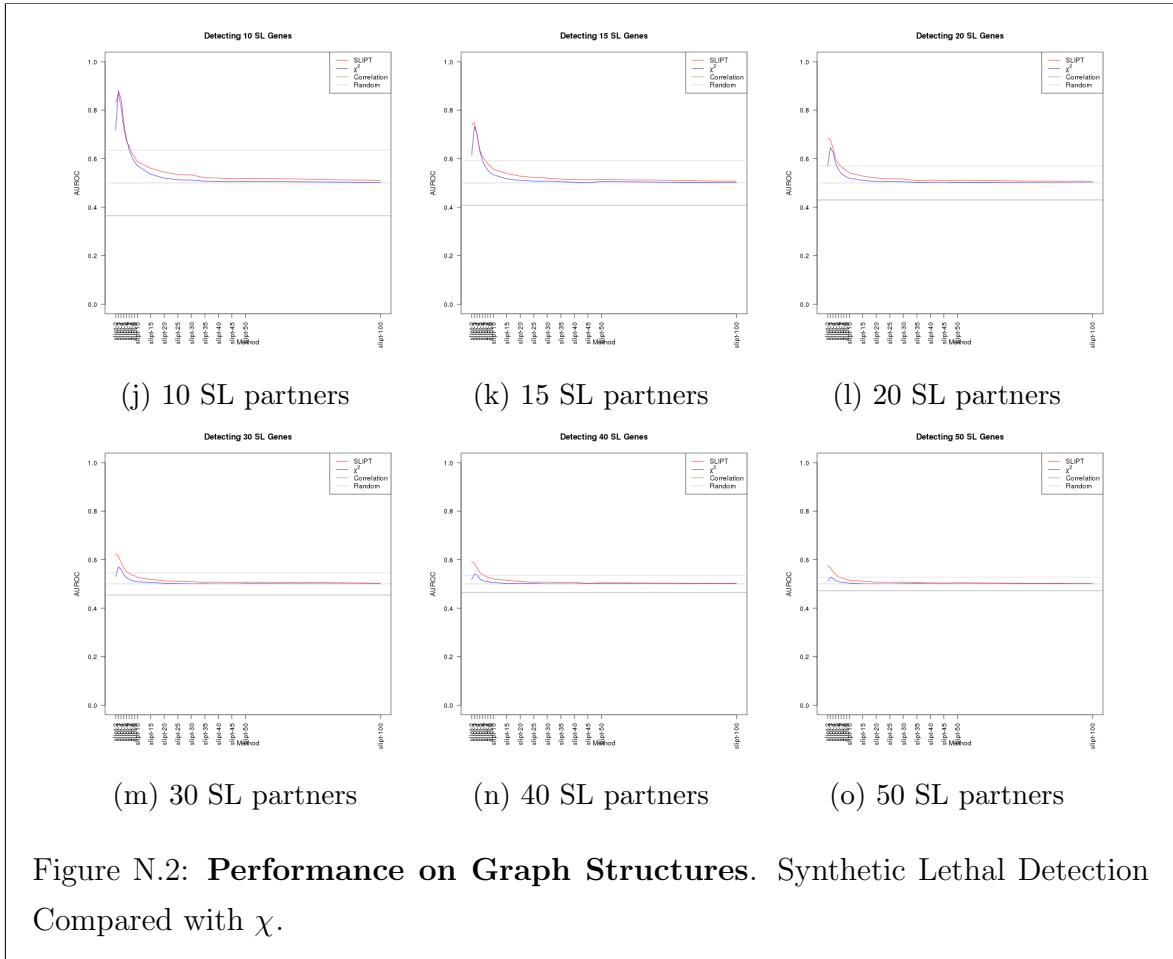


Figure N.2: **Performance on Graph Structures.** Synthetic Lethal Detection Compared with  $\chi^2$ .

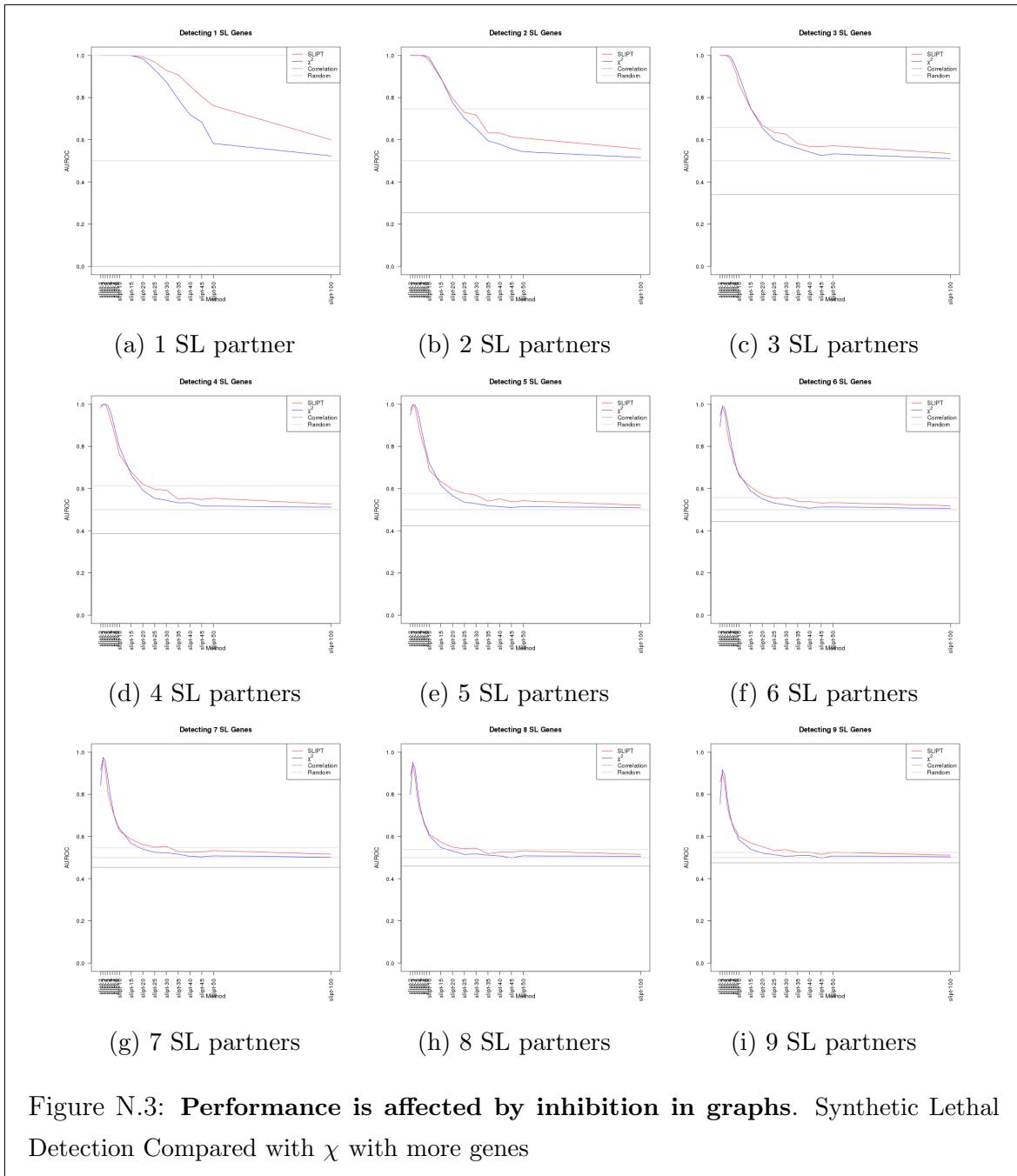


Figure N.3: **Performance is affected by inhibition in graphs.** Synthetic Lethal Detection Compared with  $\chi$  with more genes

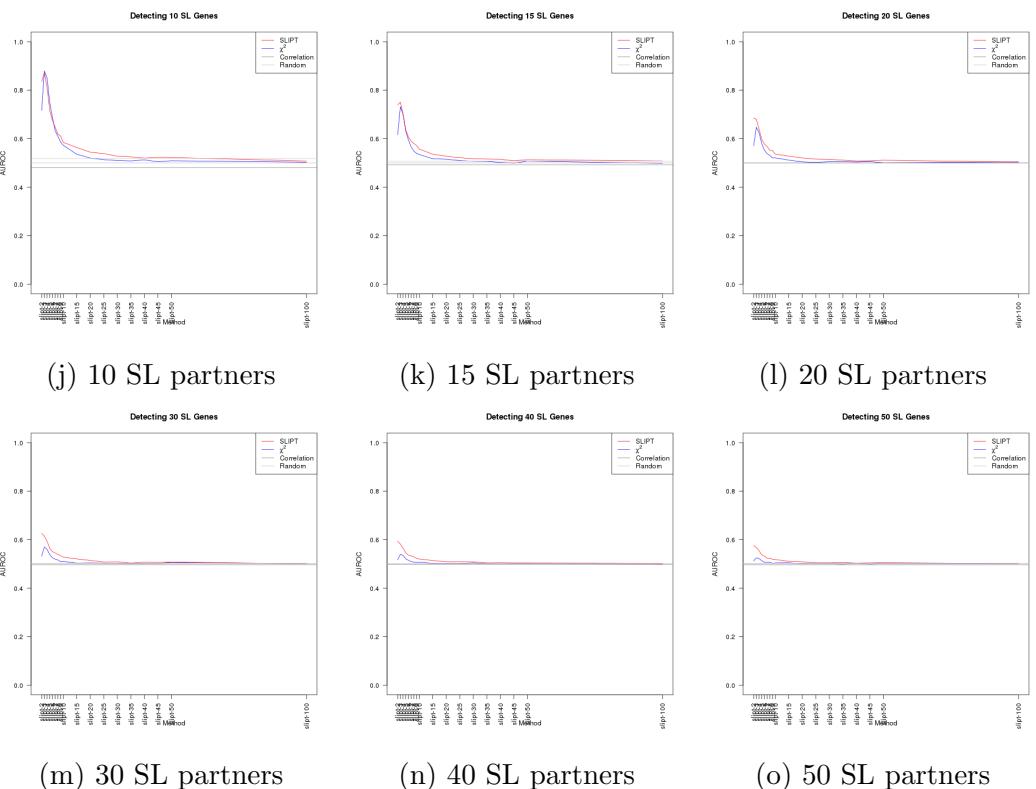


Figure N.3: **Performance on Graph Structures.** Synthetic Lethal Detection Compared with  $\chi^2$  with more genes.

## N.0.1 Correlated Query Genes affects Specificity

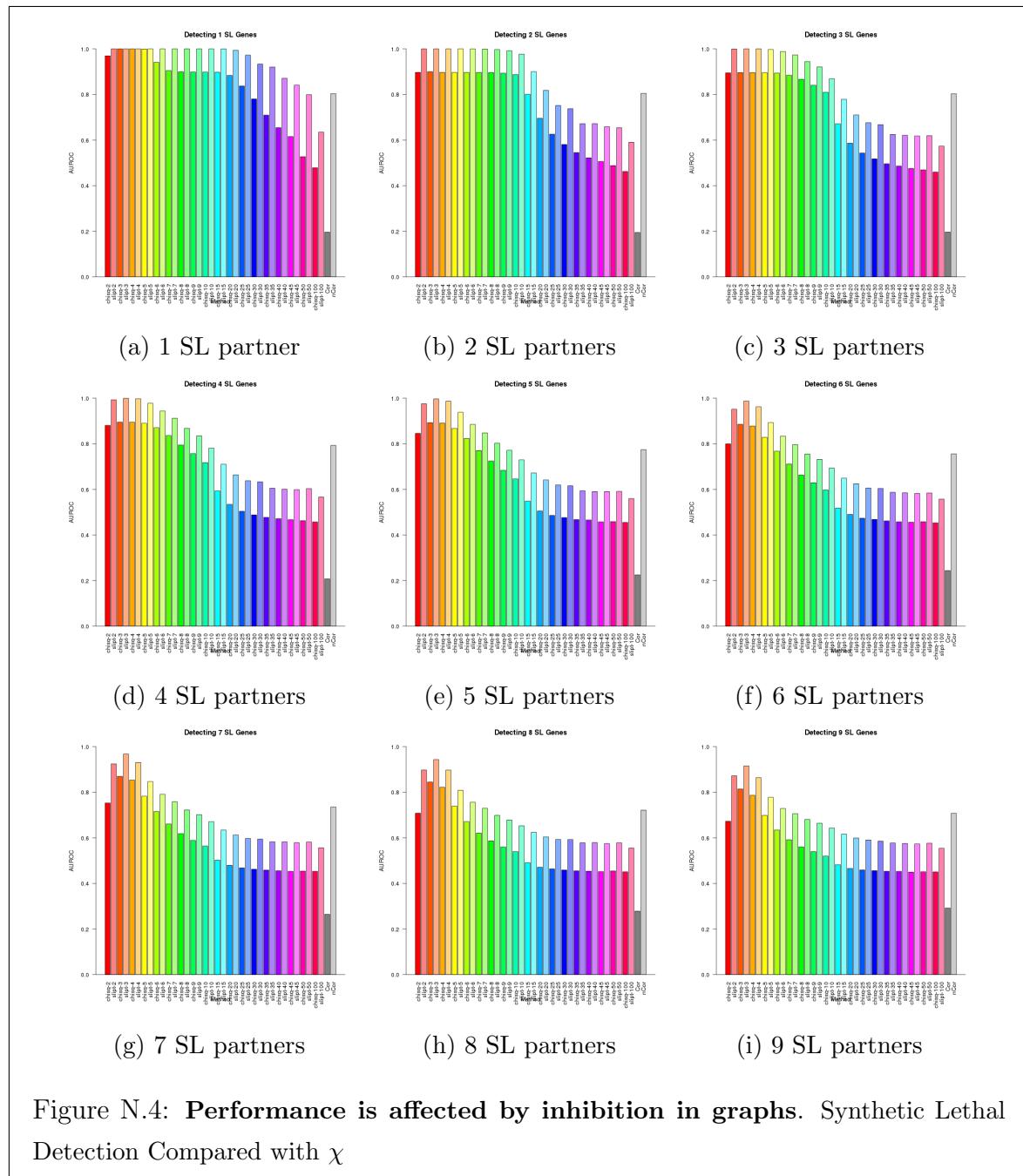


Figure N.4: **Performance is affected by inhibition in graphs.** Synthetic Lethal Detection Compared with  $\chi$

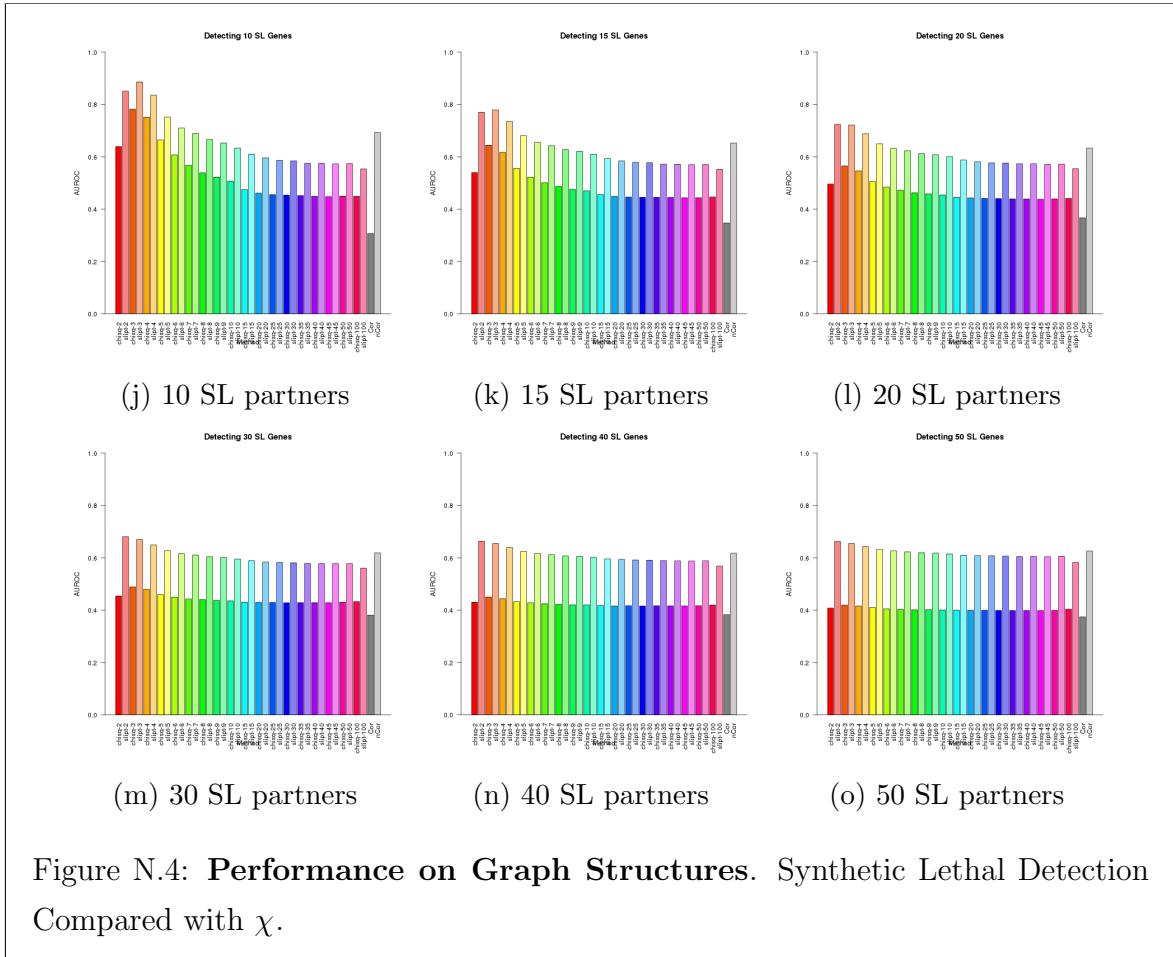


Figure N.4: **Performance on Graph Structures.** Synthetic Lethal Detection Compared with  $\chi$ .

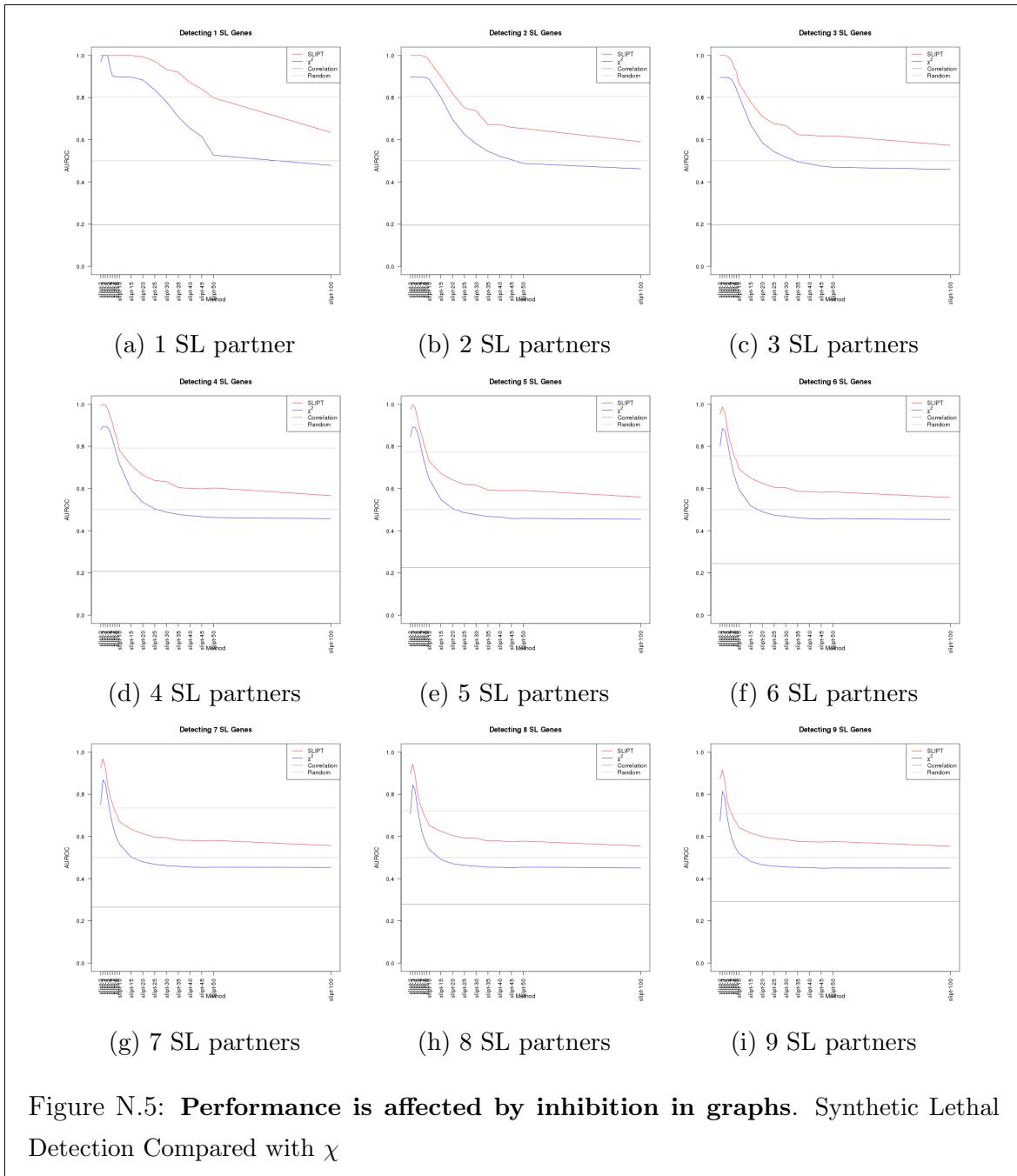


Figure N.5: **Performance is affected by inhibition in graphs.** Synthetic Lethal Detection Compared with  $\chi^2$

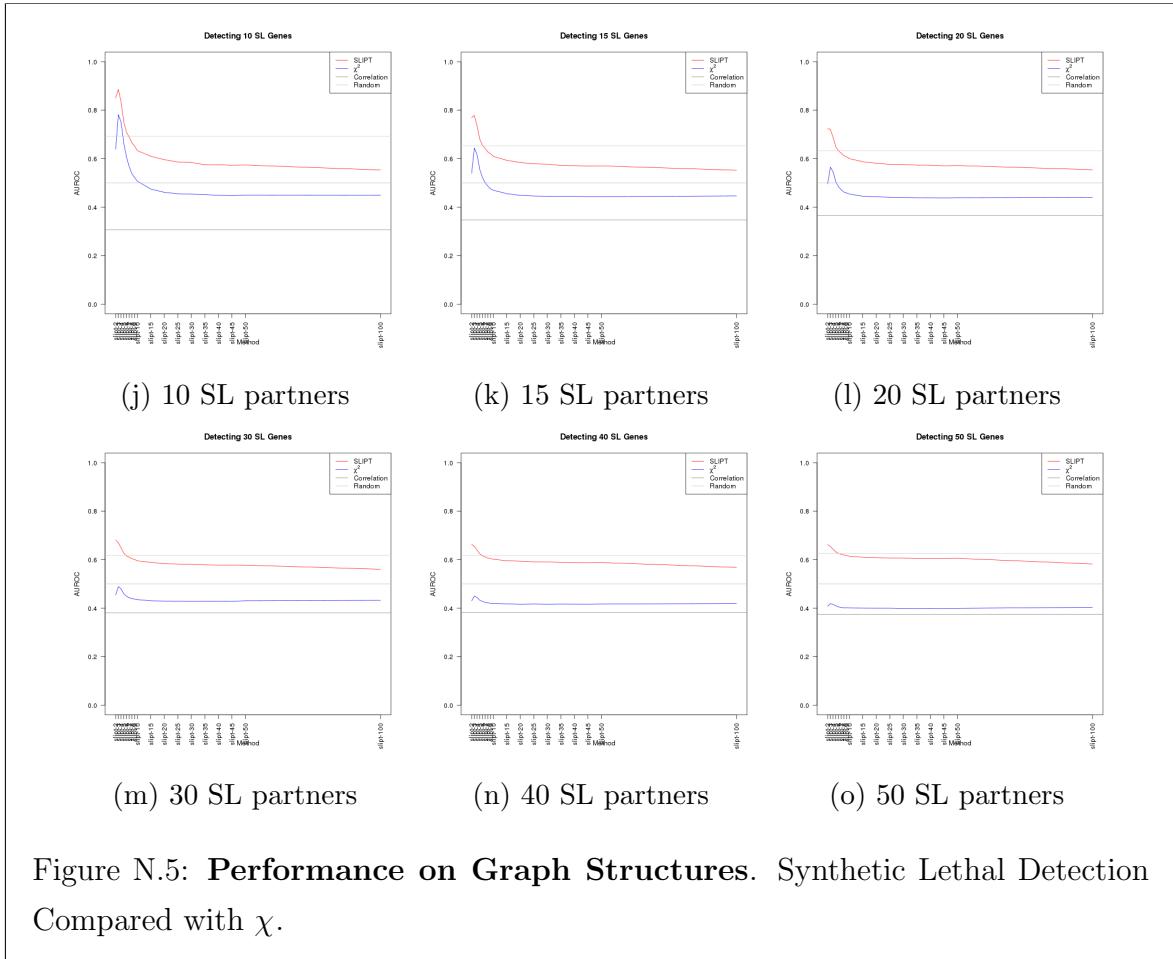
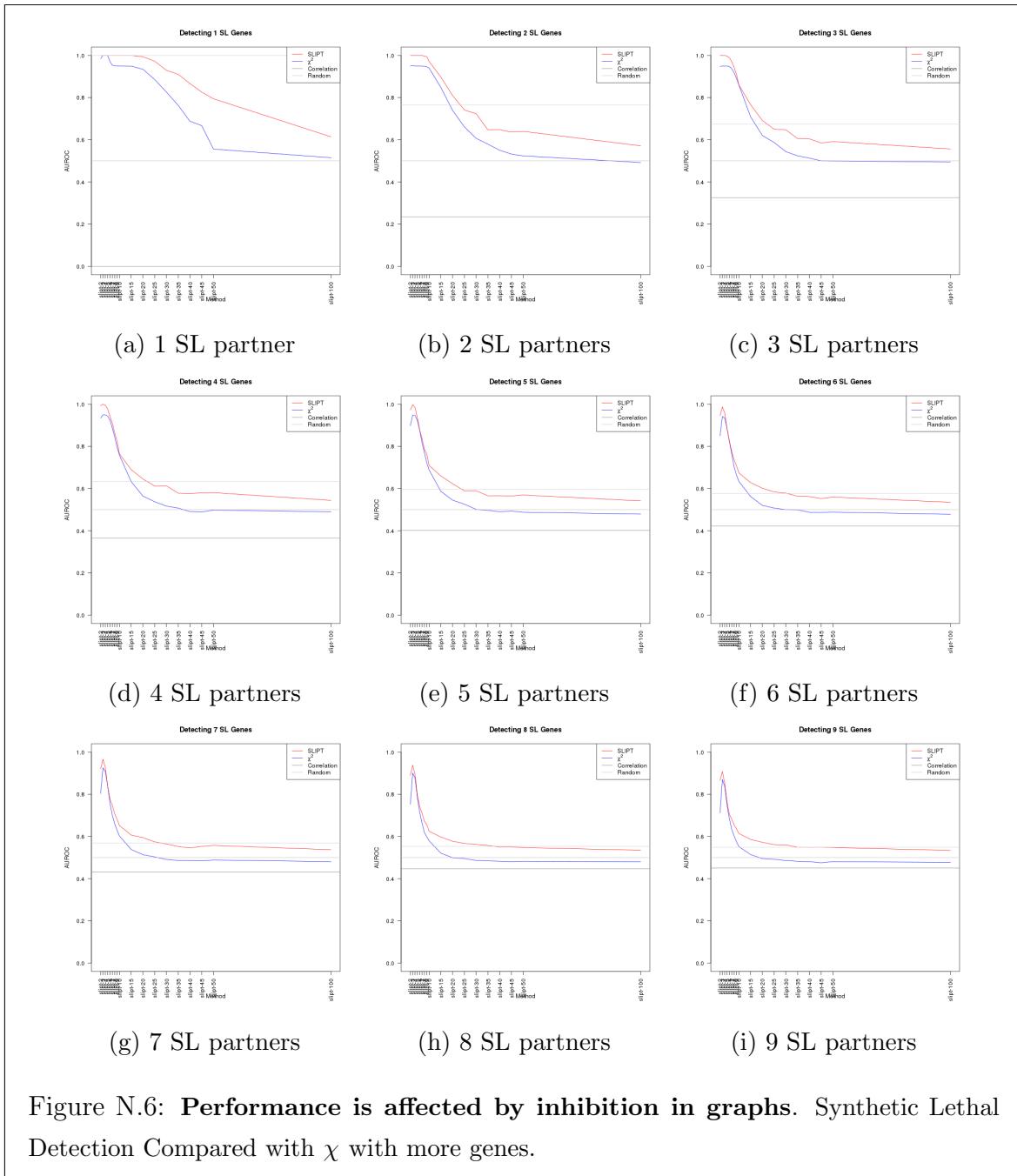
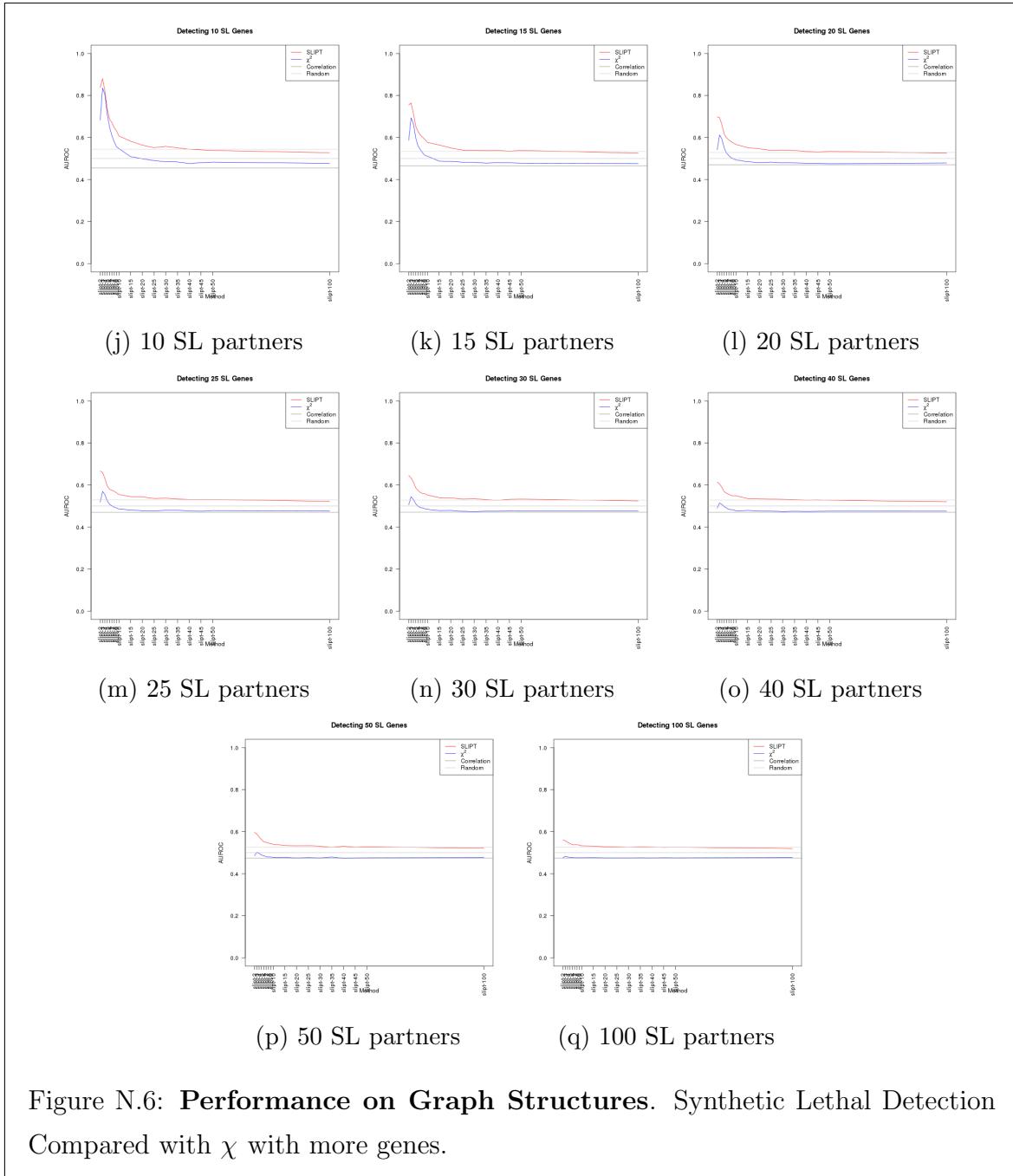


Figure N.5: **Performance on Graph Structures.** Synthetic Lethal Detection Compared with  $\chi^2$ .





**Figure N.6: Performance on Graph Structures.** Synthetic Lethal Detection Compared with  $\chi$  with more genes.

# Appendix O

## Graph Structures

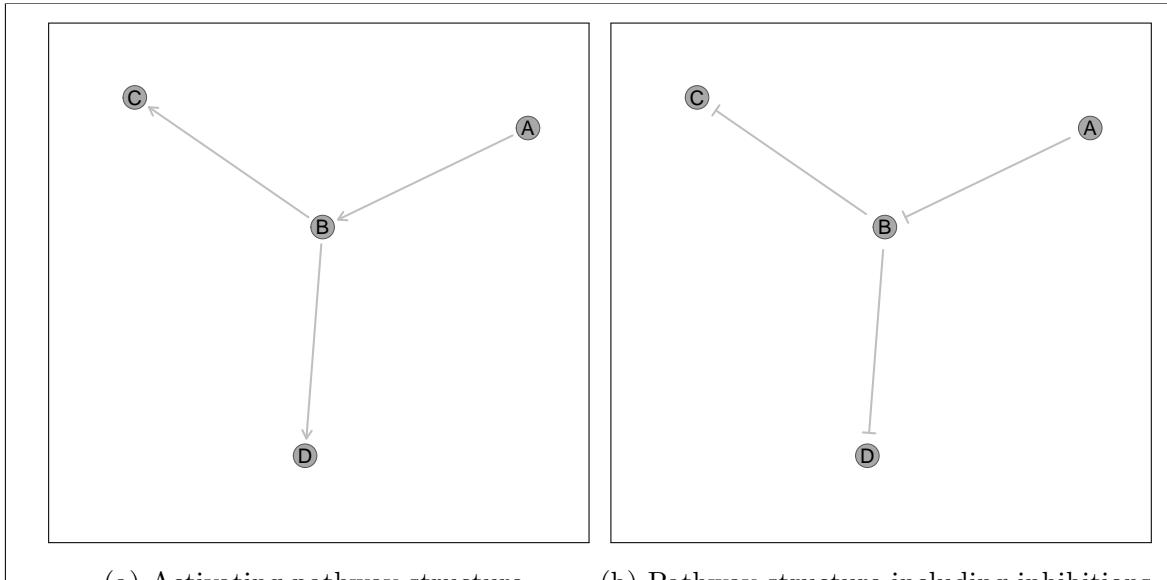
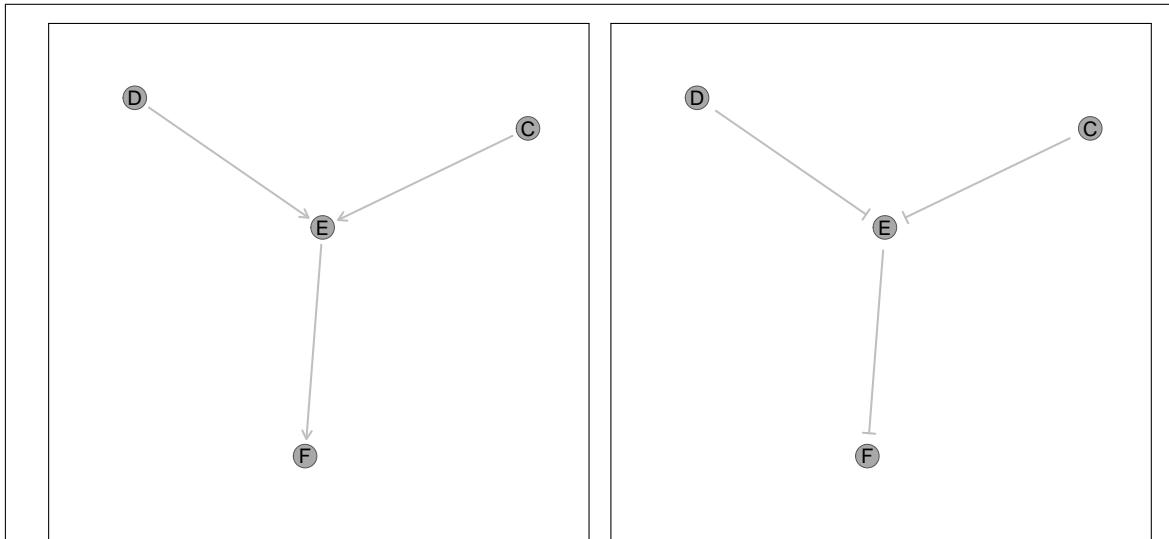
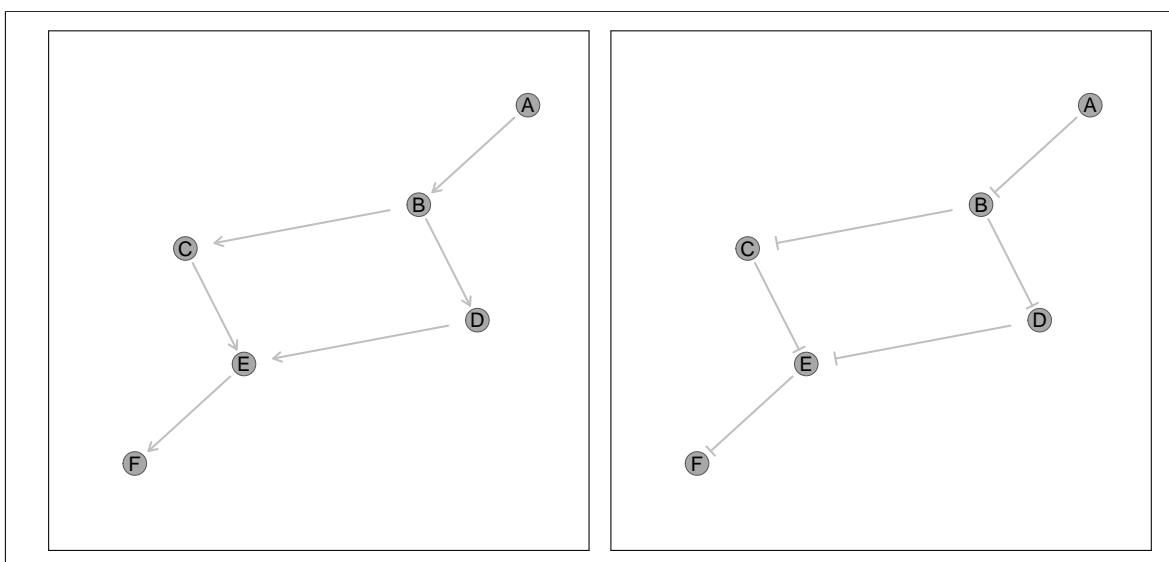


Figure O.1: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.



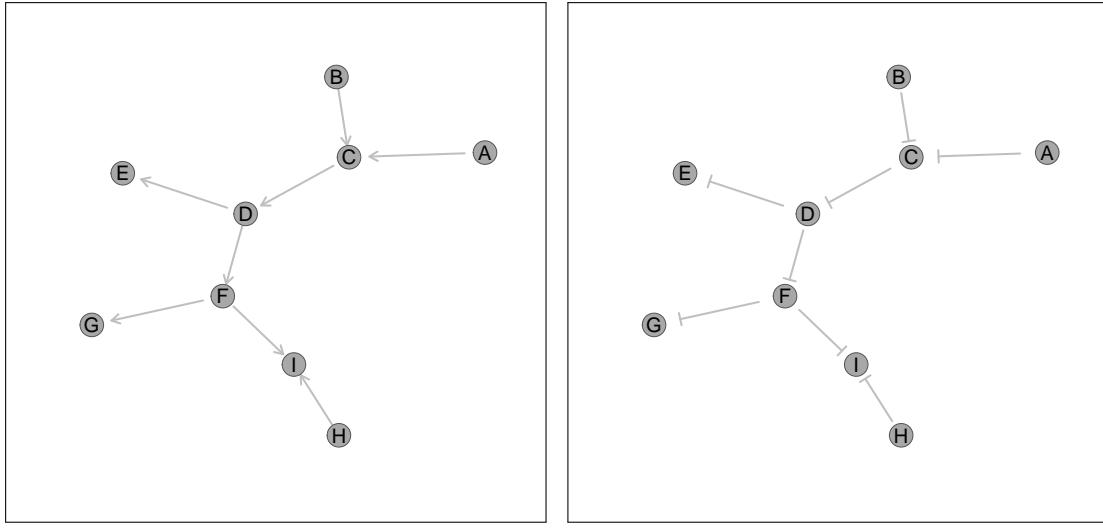
(a) Activating pathway structure      (b) Pathway structure including inhibitions

Figure O.2: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

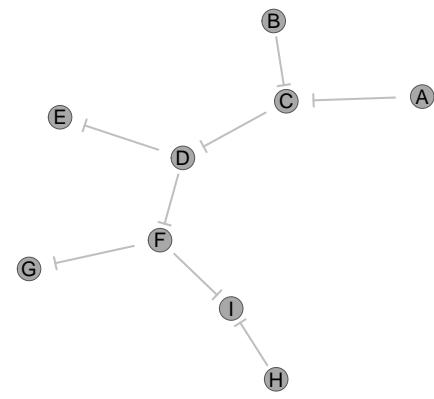


(a) Activating pathway structure      (b) Pathway structure including inhibitions

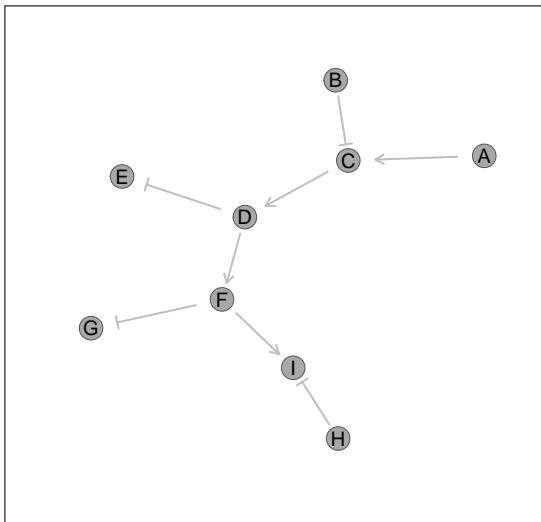
Figure O.3: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.



(a) Activating pathway structure



(b) Pathway structure including inhibitions



(c) Pathway structure including inhibitions

**Figure O.4: Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

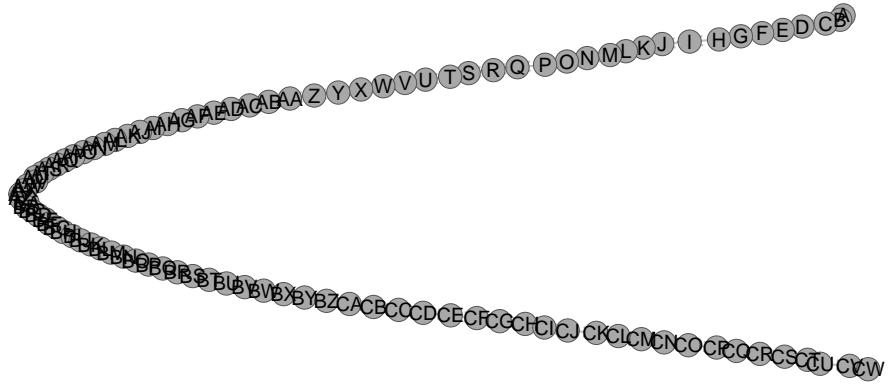


Figure O.5: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

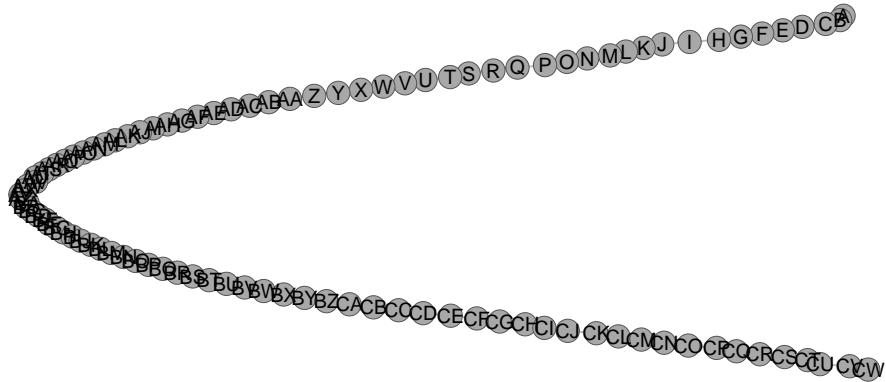
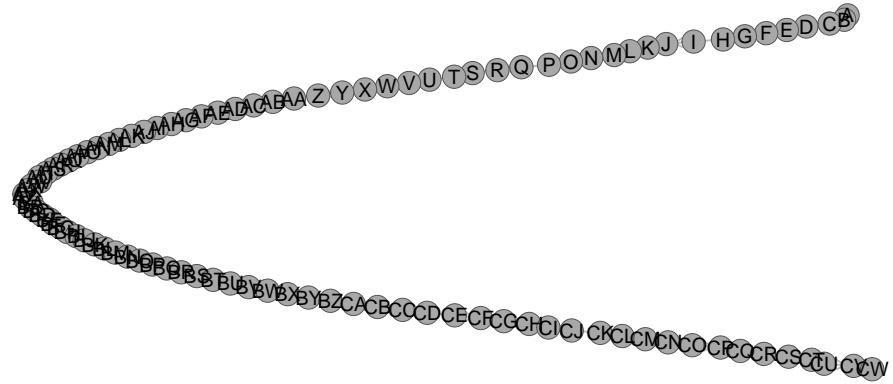
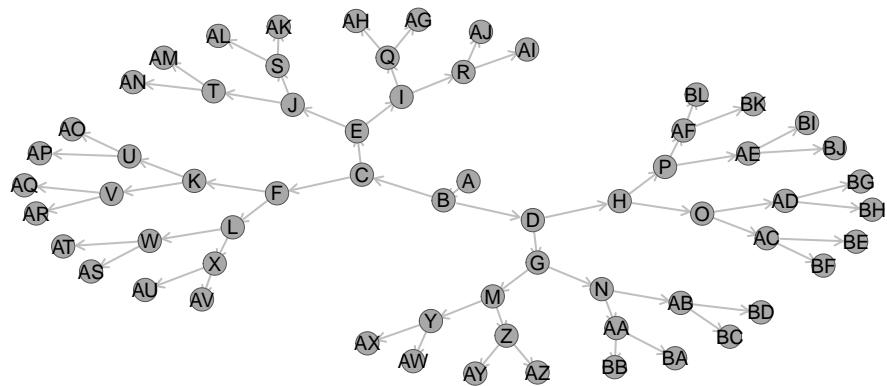


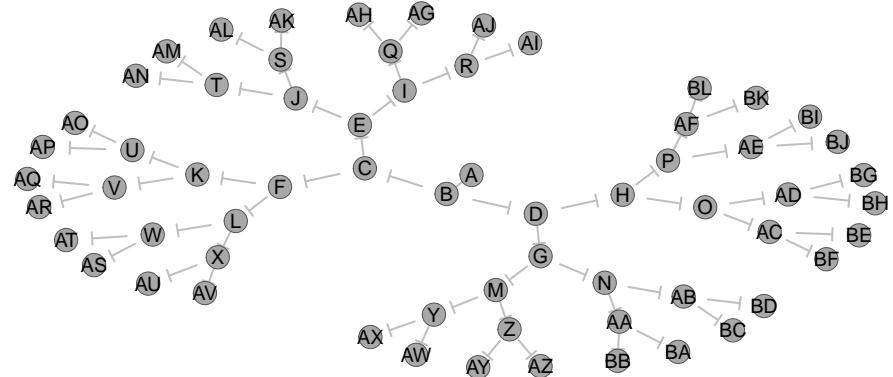
Figure O.6: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.



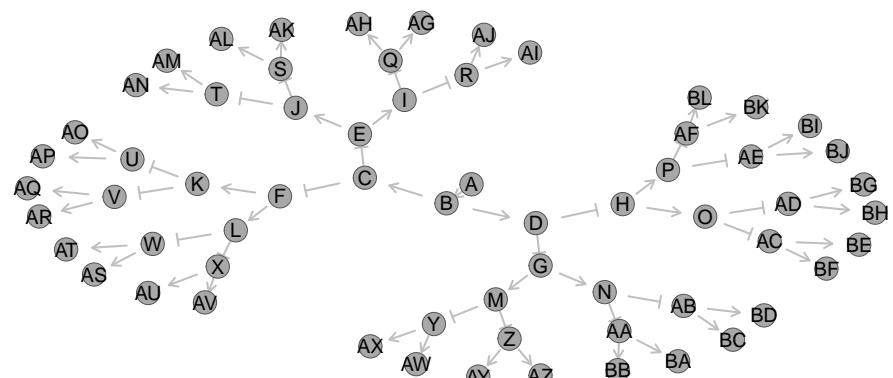
**Figure O.7: Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.



**Figure O.8: Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.



**Figure O.9: Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.



**Figure O.10: Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

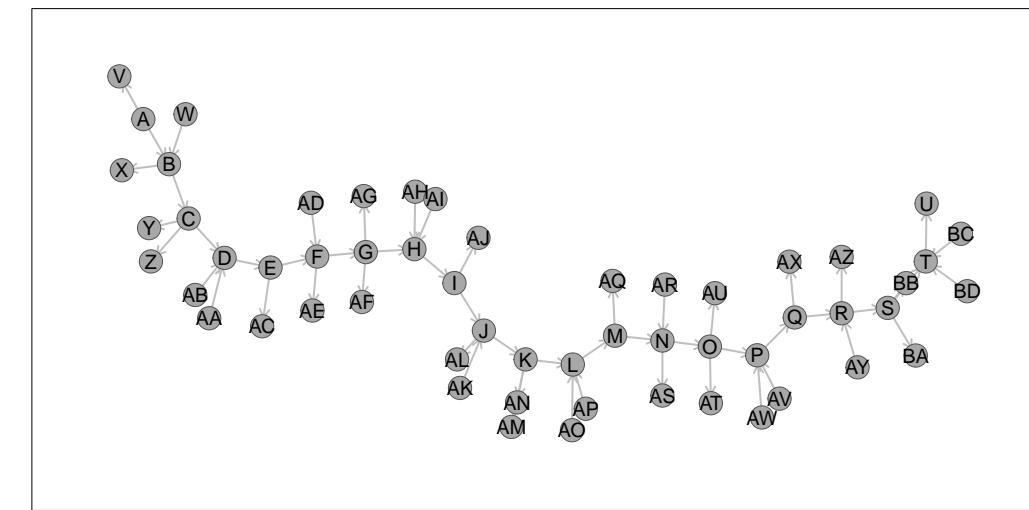


Figure O.11: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

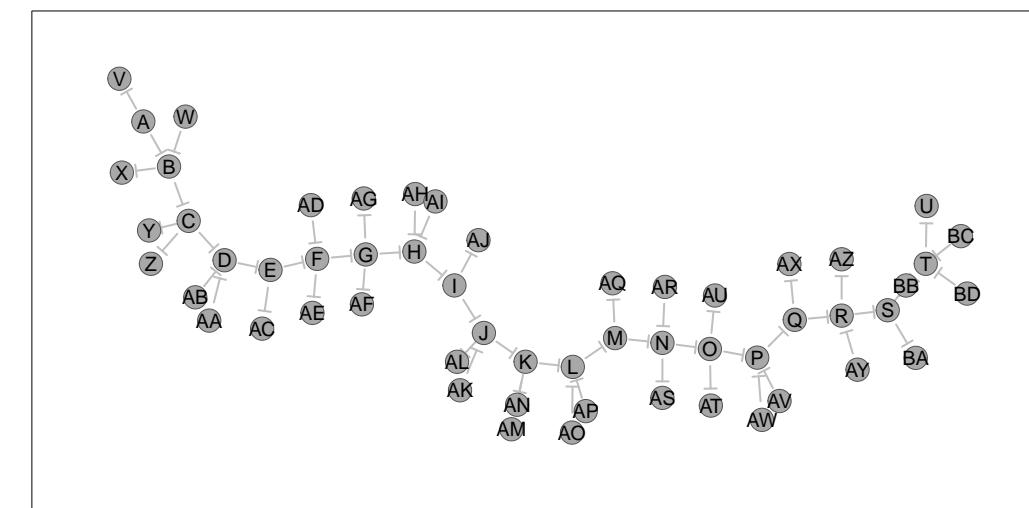


Figure O.12: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

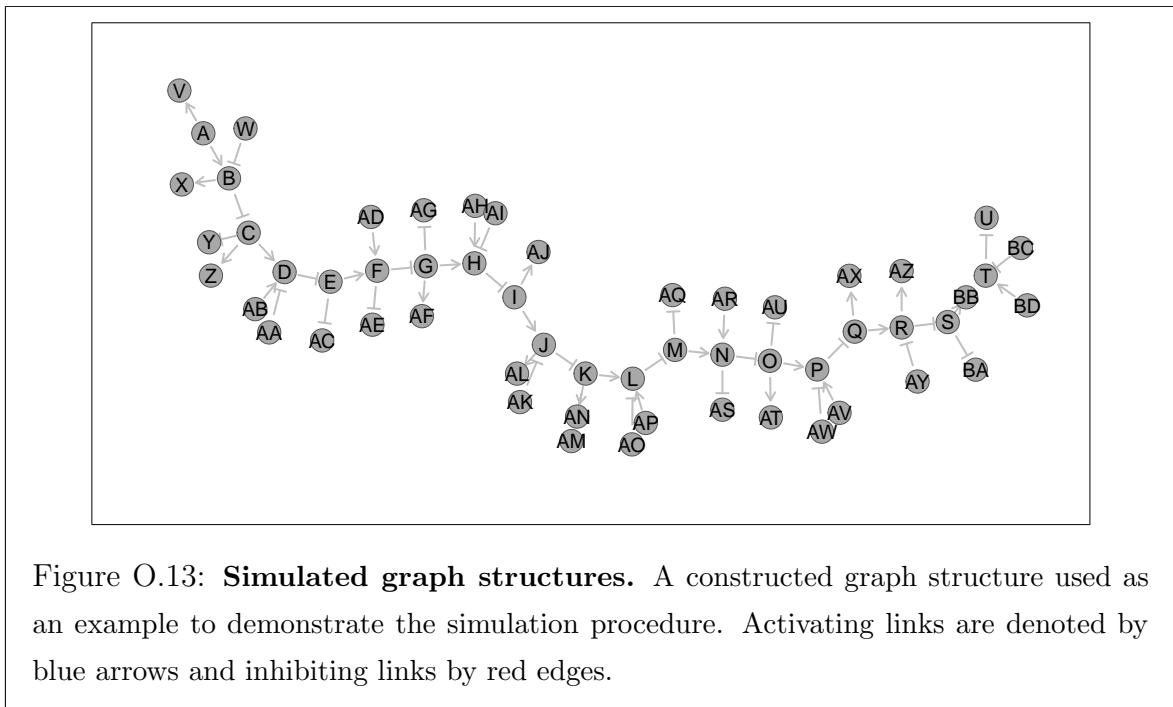


Figure O.13: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

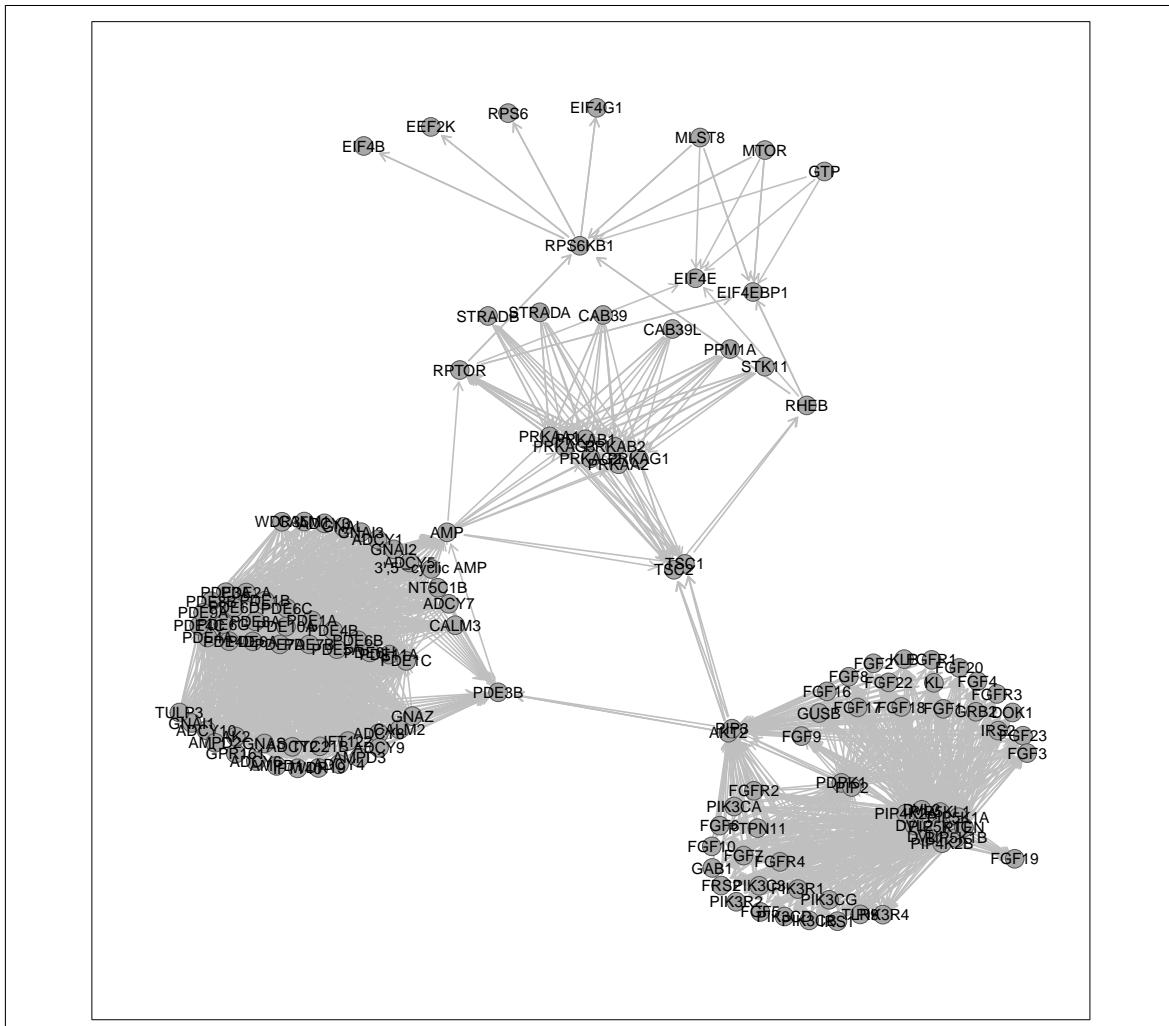
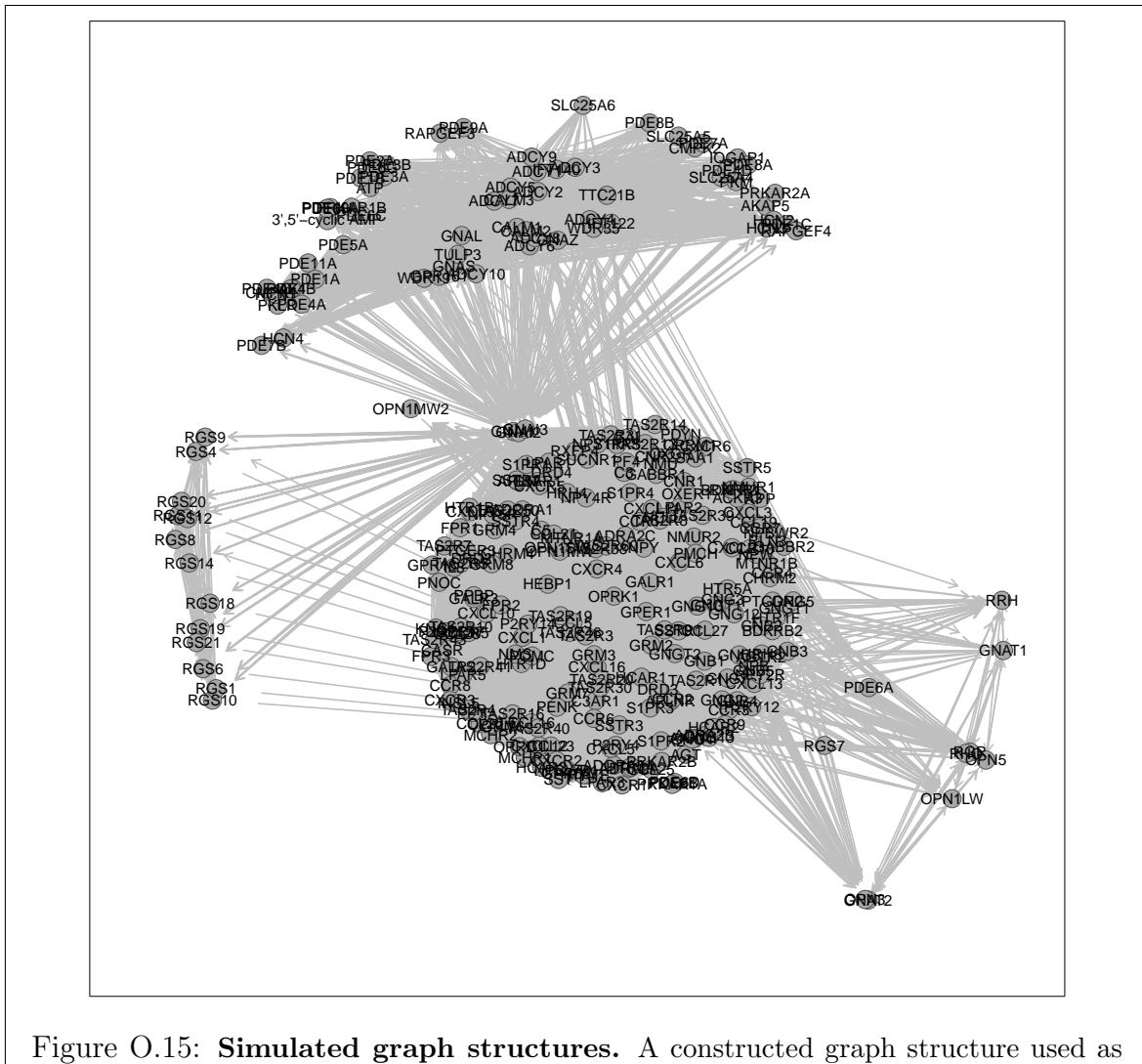
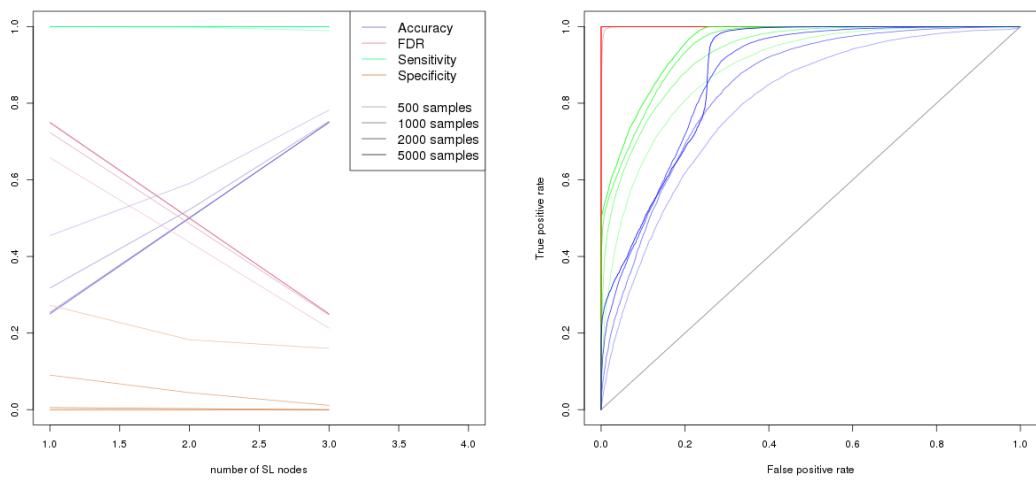


Figure O.14: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.



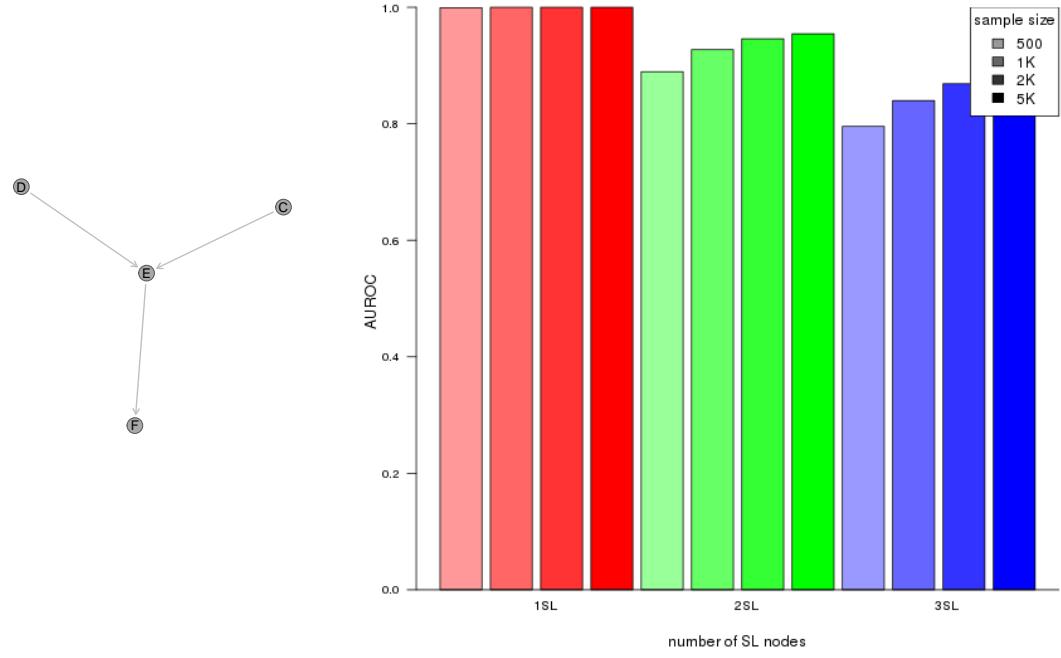
## Appendix P

### Graph Simulations



(a) Statistical evaluation

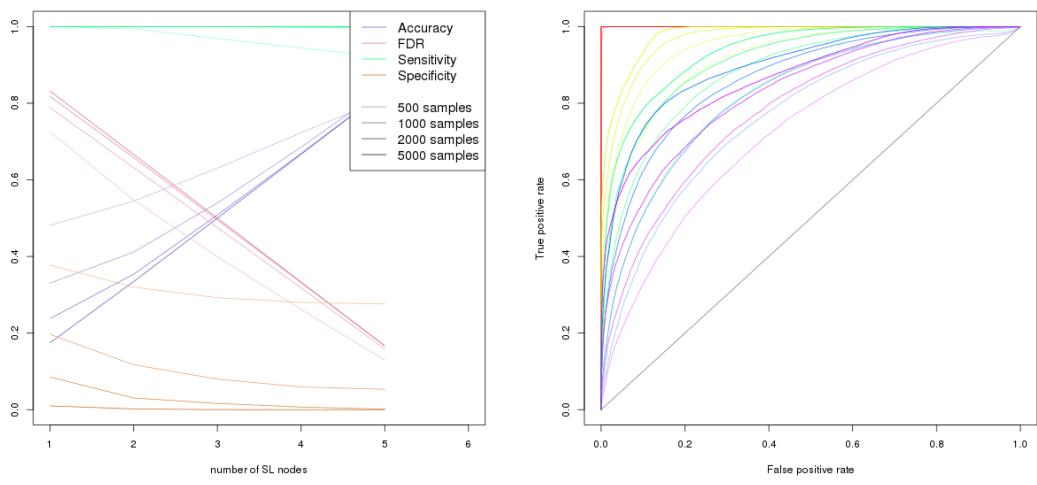
(b) Receiver operating characteristic



(c) Graph Structure

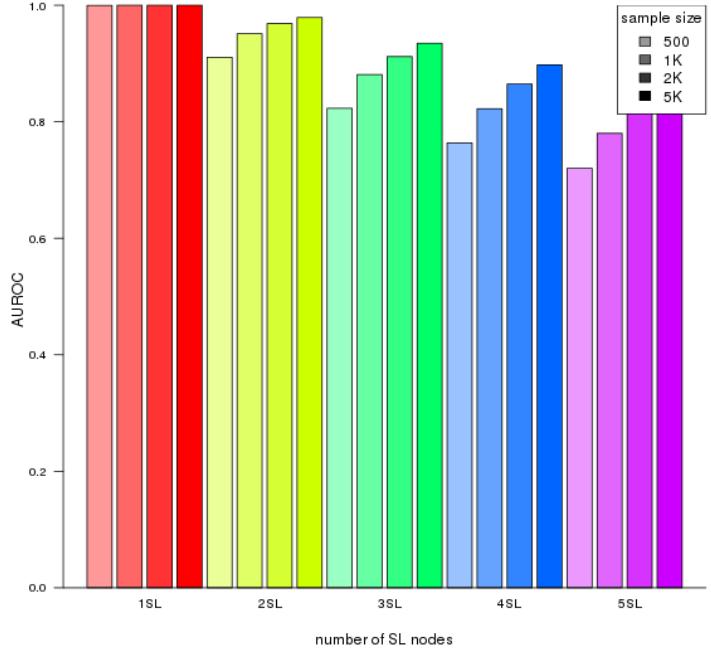
(d) Statistical performance

Figure P.1: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation

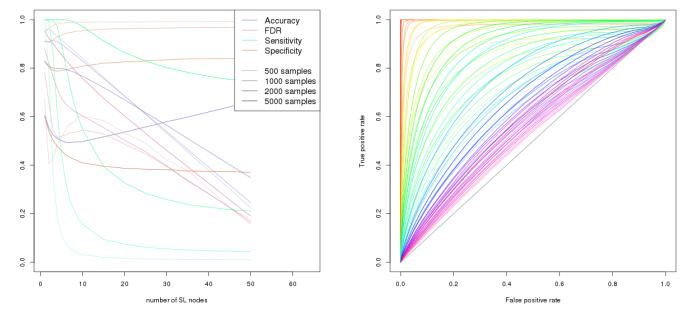
(b) Receiver operating characteristic



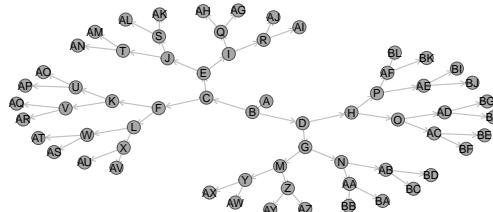
(c) Graph Structure

(d) Statistical performance

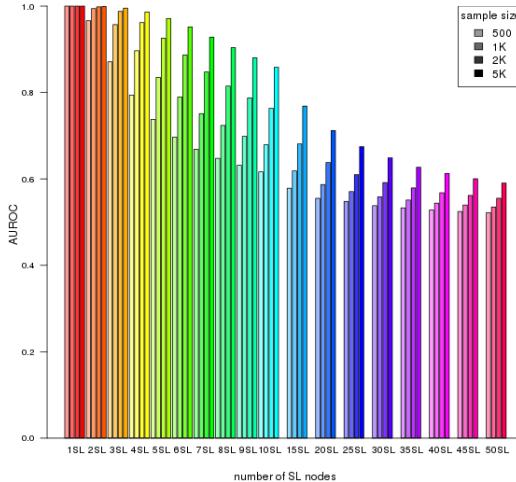
**Figure P.2: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation (b) Receiver operating characteristic

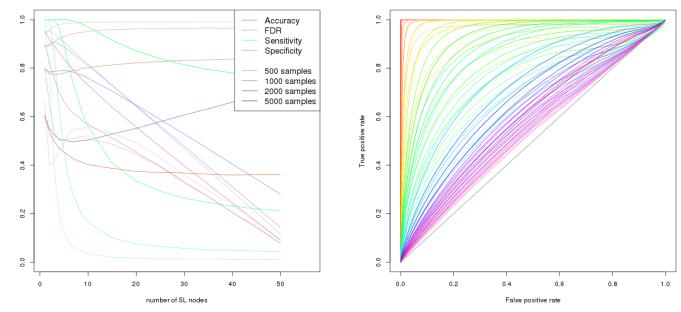


(c) Graph Structure

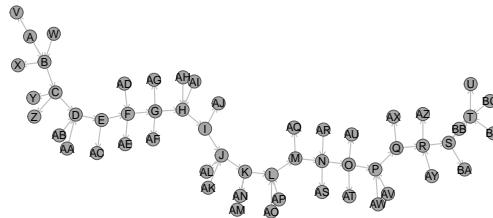


(d) Statistical performance

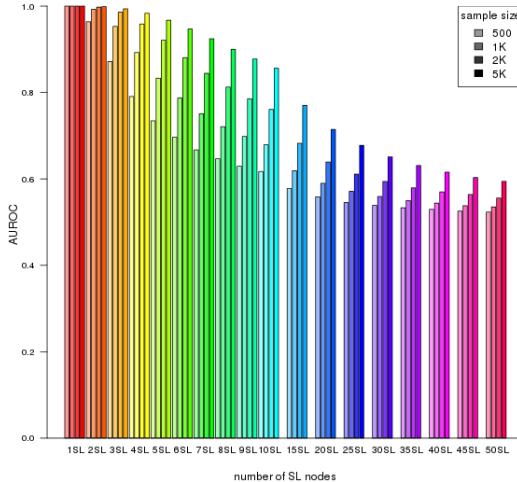
Figure P.3: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation    (b) Receiver operating characteristic



(c) Graph Structure

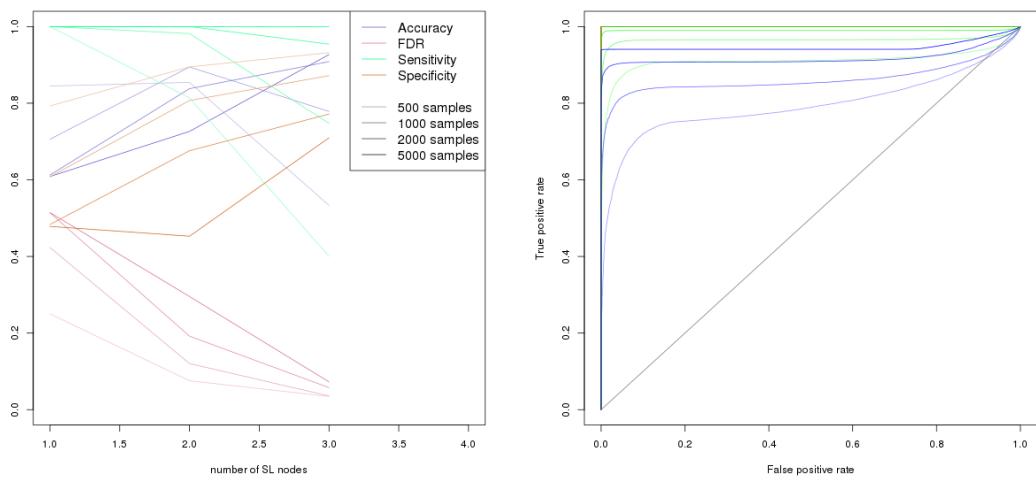


(d) Statistical performance

**Figure P.4: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.

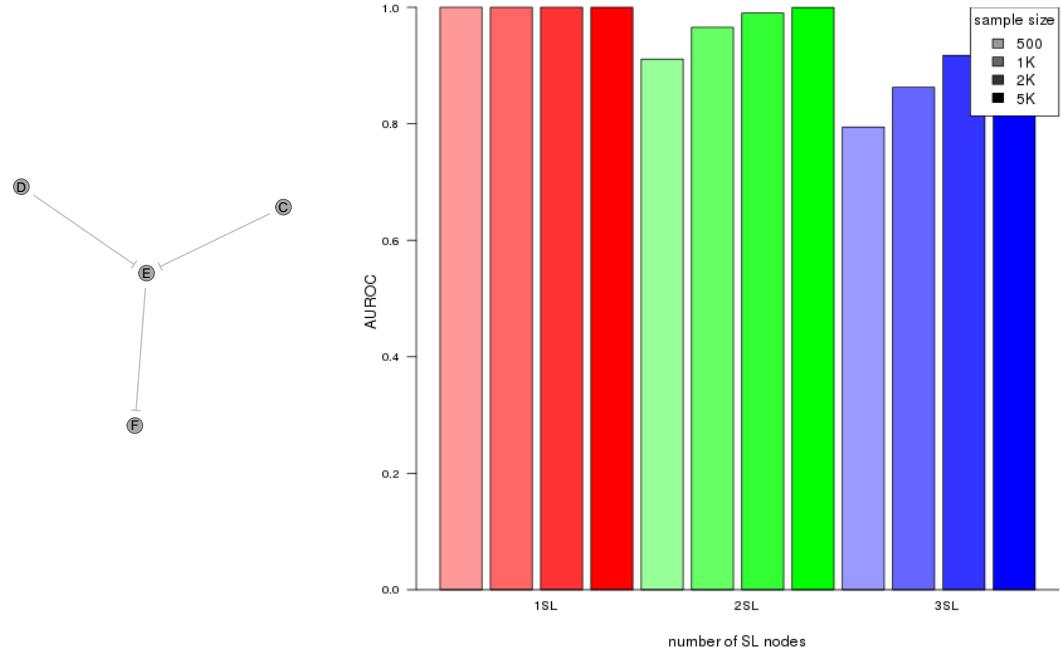
## **Appendix Q**

### **Graph Simulations with Inhibition**



(a) Statistical evaluation

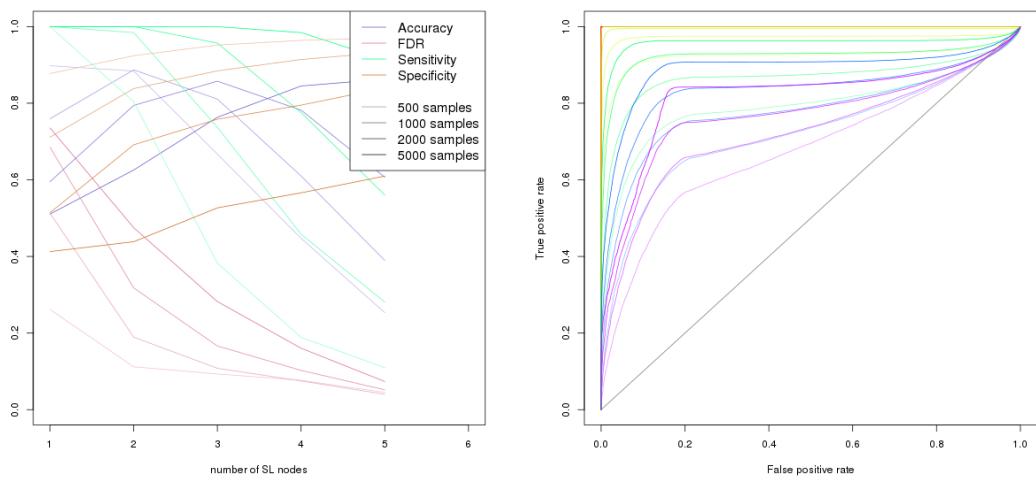
(b) Receiver operating characteristic



(c) Graph Structure

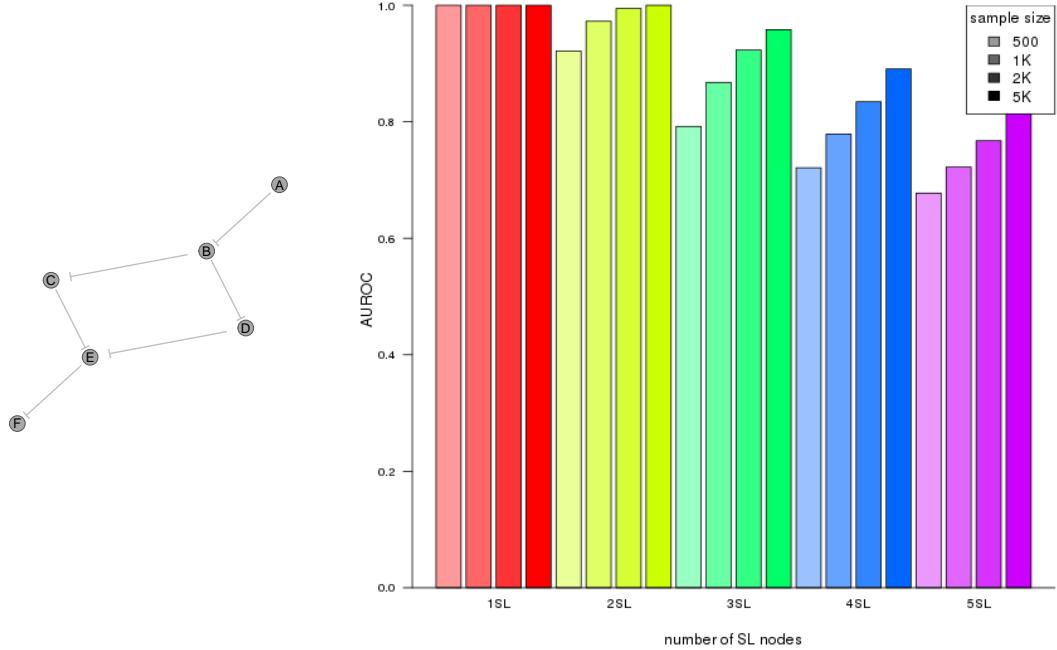
(d) Statistical performance

**Figure Q.1: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation

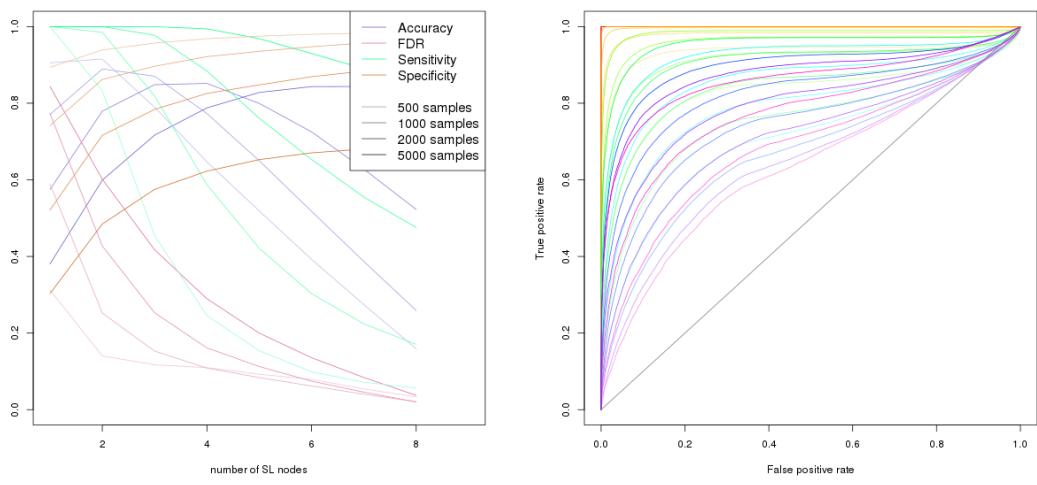
(b) Receiver operating characteristic



(c) Graph Structure

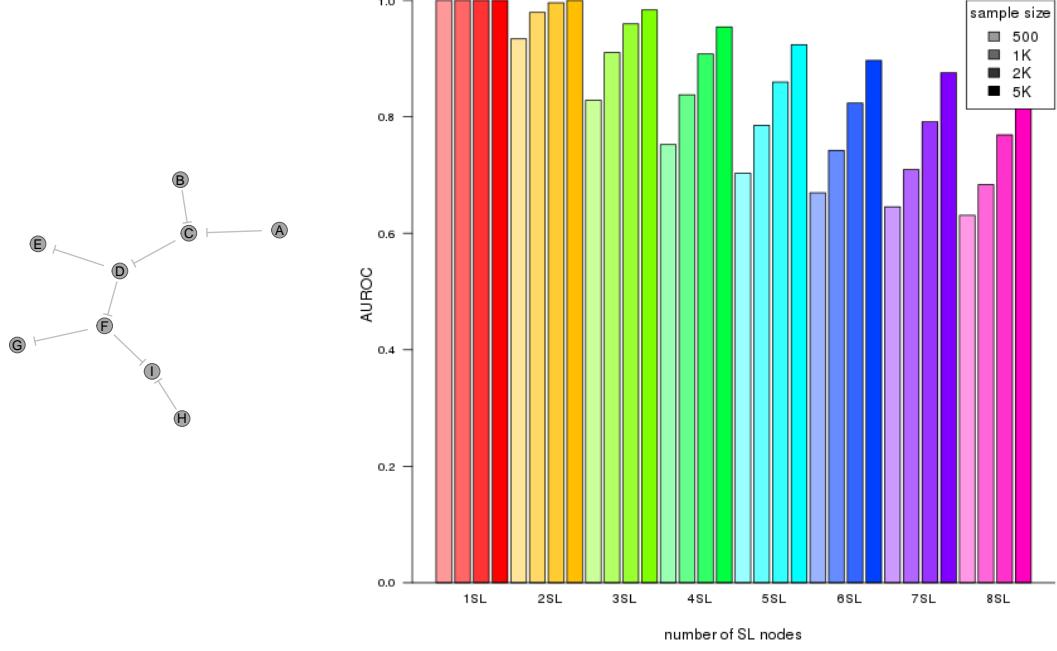
(d) Statistical performance

**Figure Q.2: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation

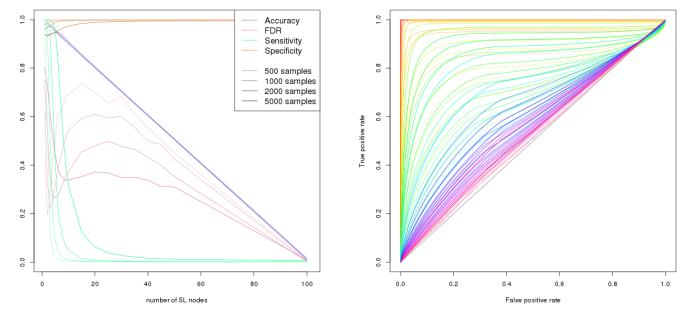
(b) Receiver operating characteristic



(c) Graph Structure

(d) Statistical performance

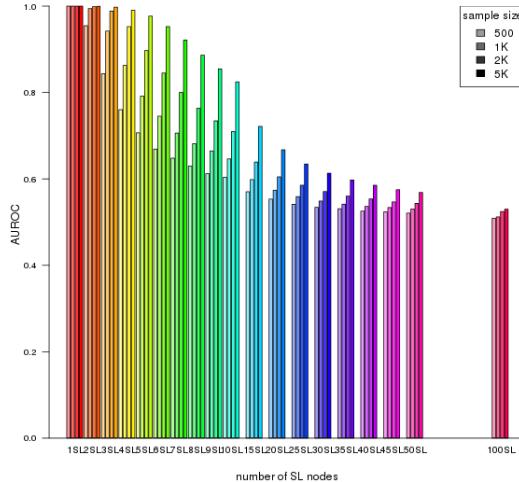
**Figure Q.3: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation    (b) Receiver operating characteristic

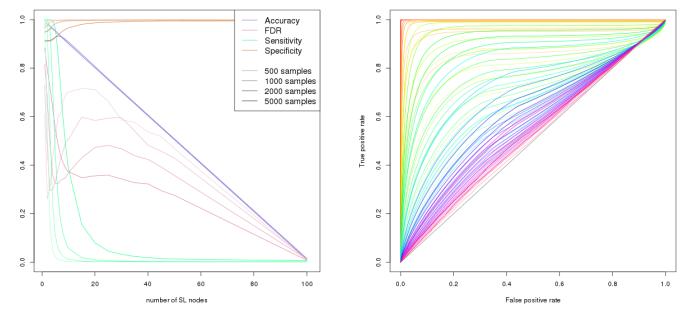


(c) Graph Structure



(d) Statistical performance

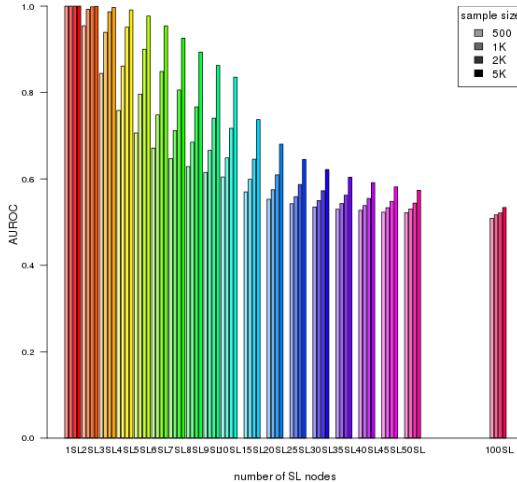
**Figure Q.4: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation    (b) Receiver operating characteristic

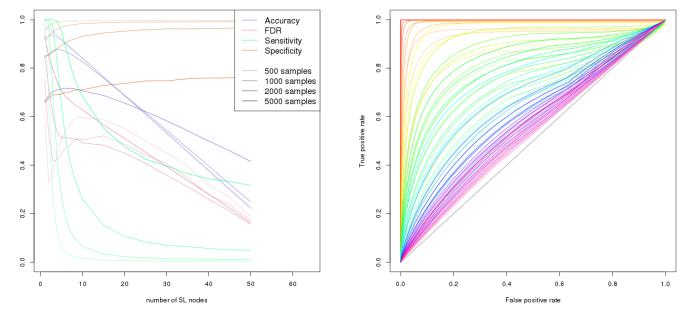


(c) Graph Structure

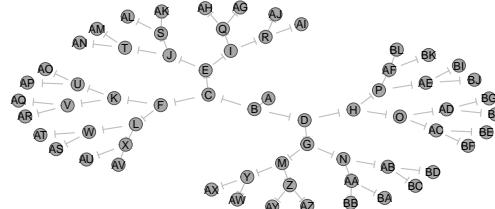


(d) Statistical performance

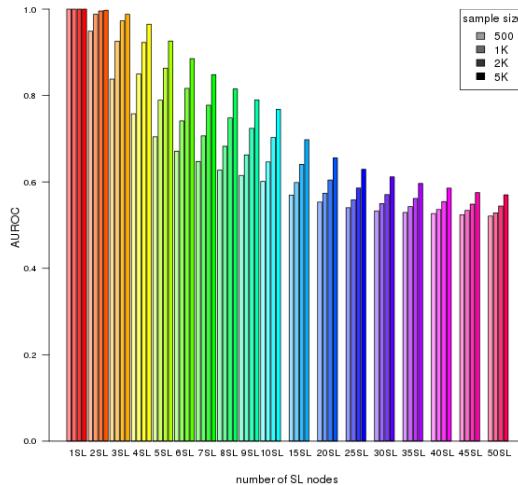
**Figure Q.5: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation (b) Receiver operating characteristic

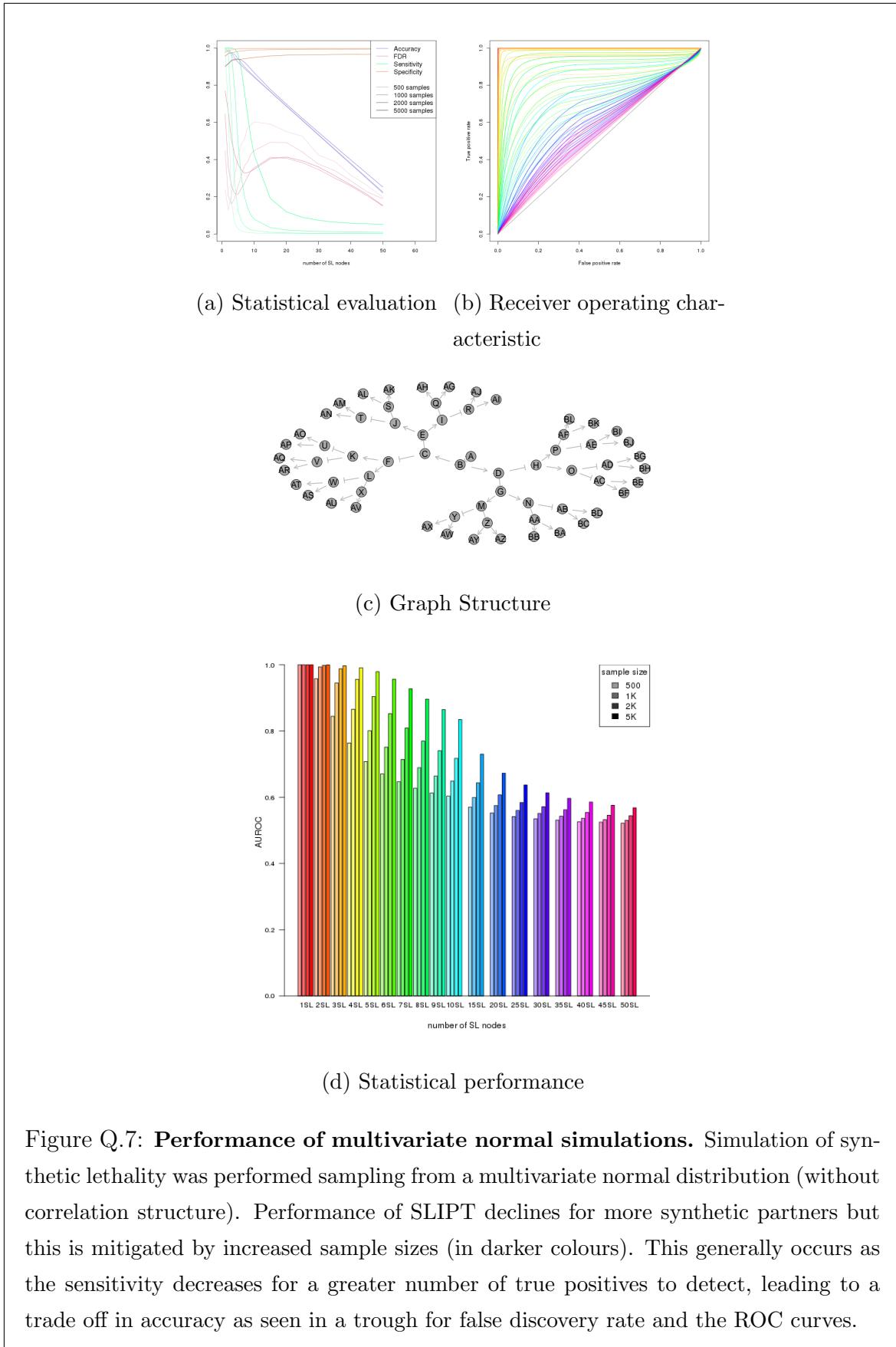


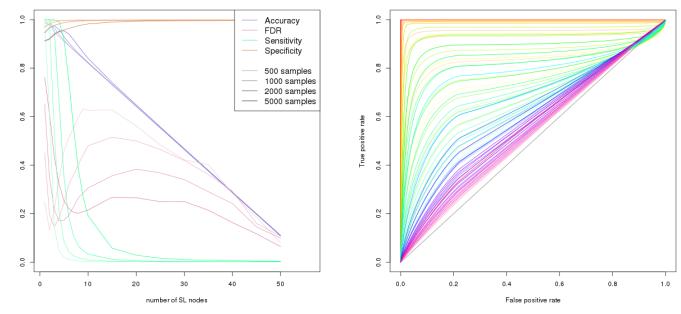
(c) Graph Structure



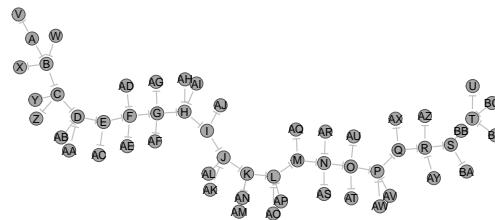
(d) Statistical performance

**Figure Q.6: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.

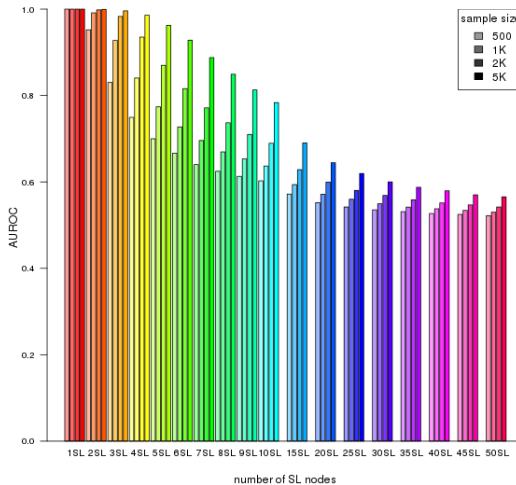




(a) Statistical evaluation    (b) Receiver operating characteristic

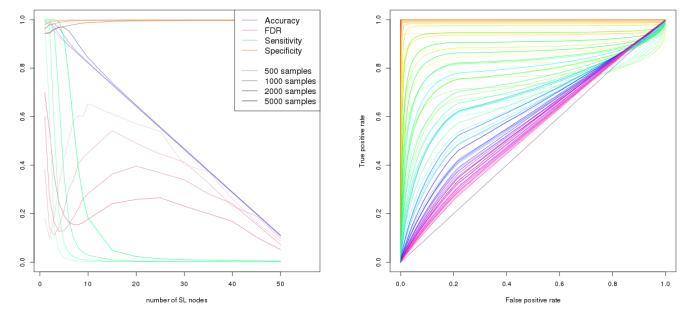


(c) Graph Structure

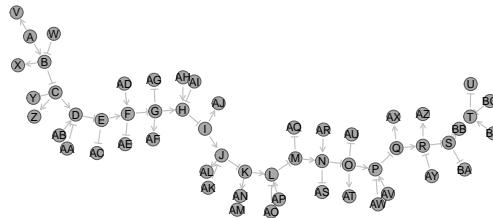


(d) Statistical performance

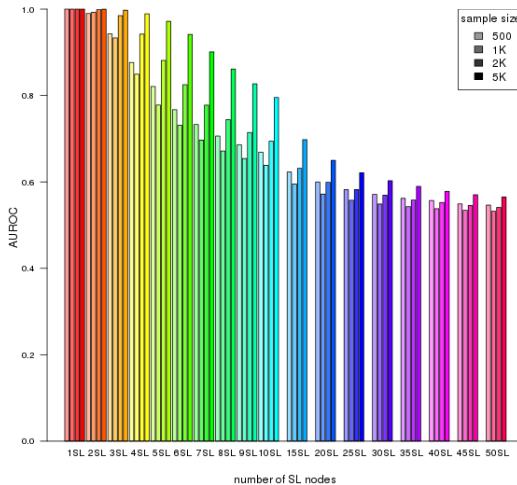
**Figure Q.8: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation    (b) Receiver operating characteristic



(c) Graph Structure

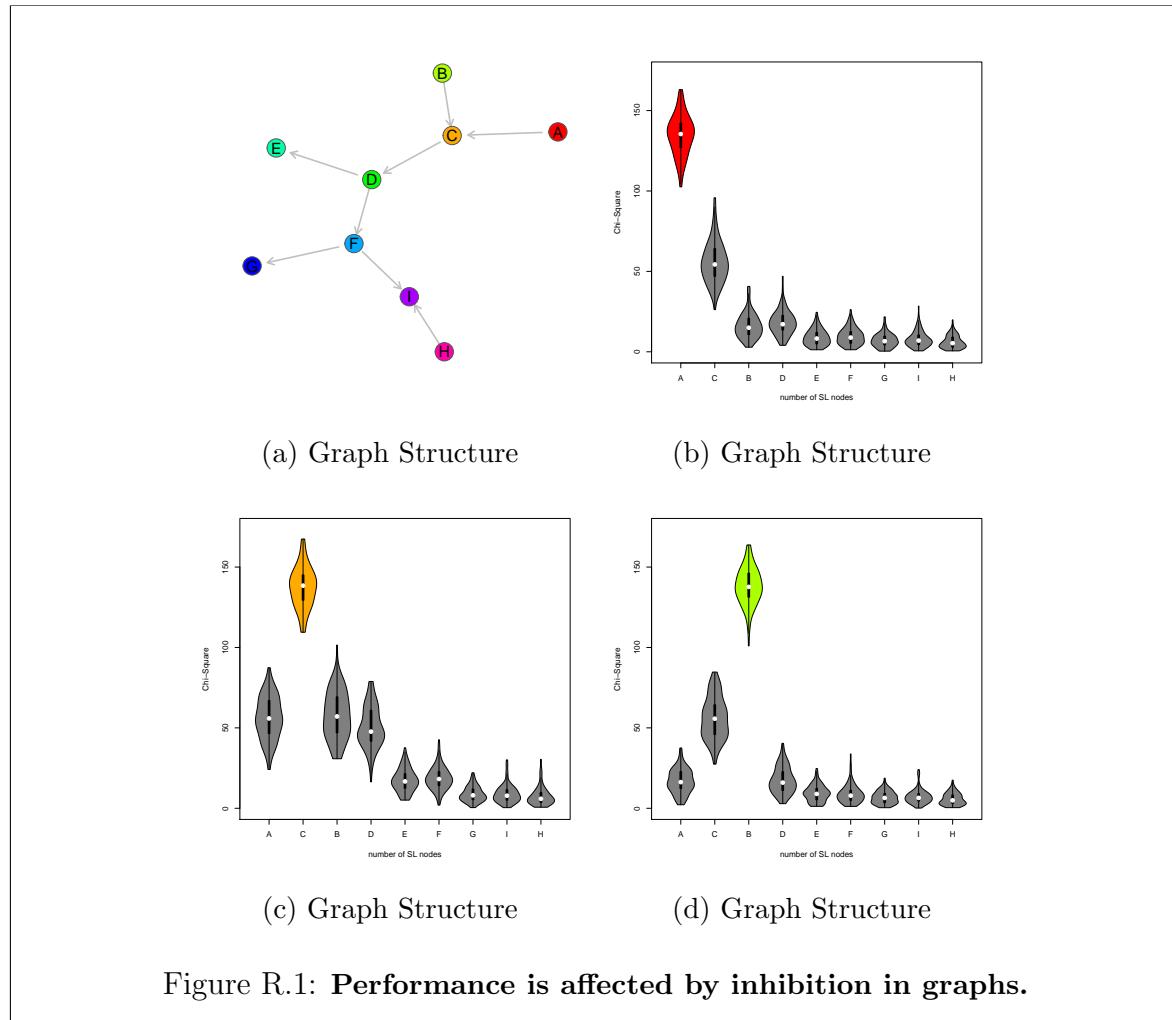


(d) Statistical performance

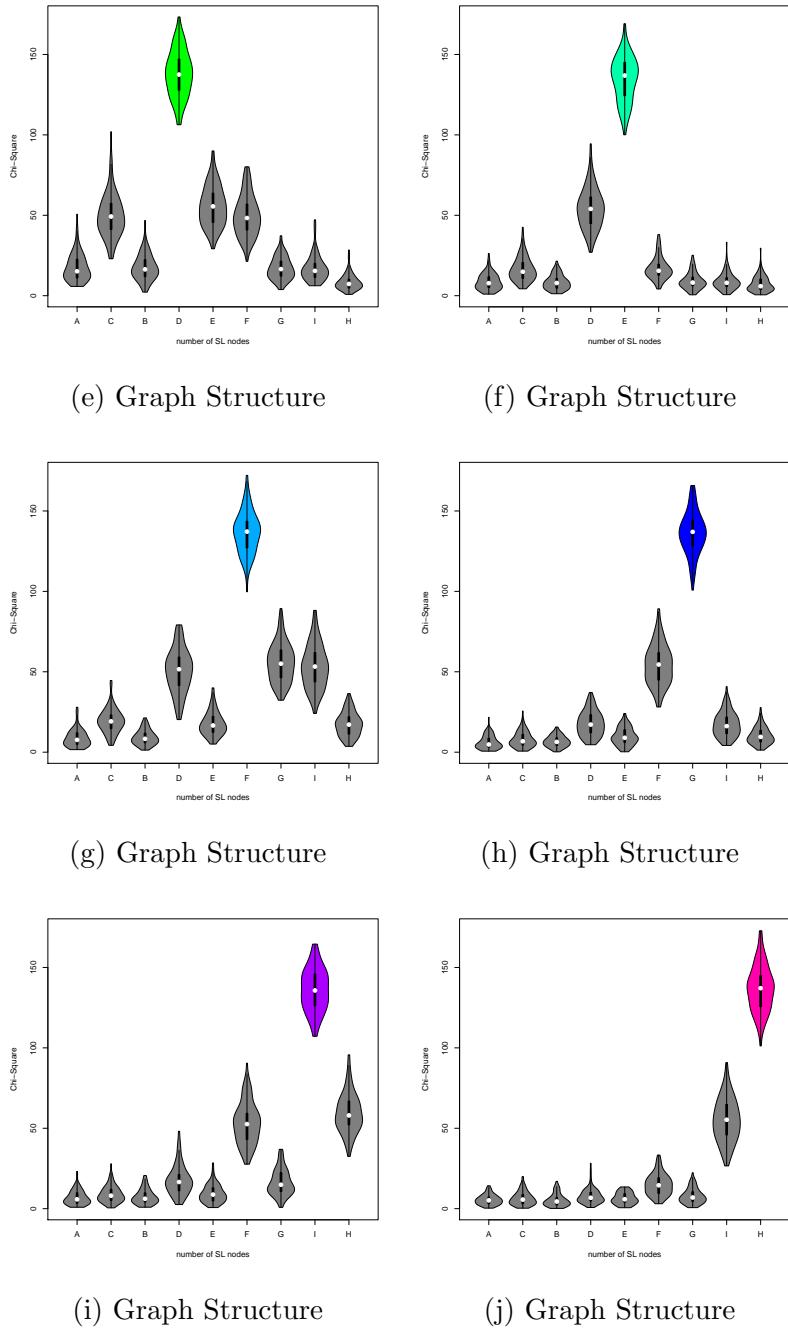
**Figure Q.9: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.

## Appendix R

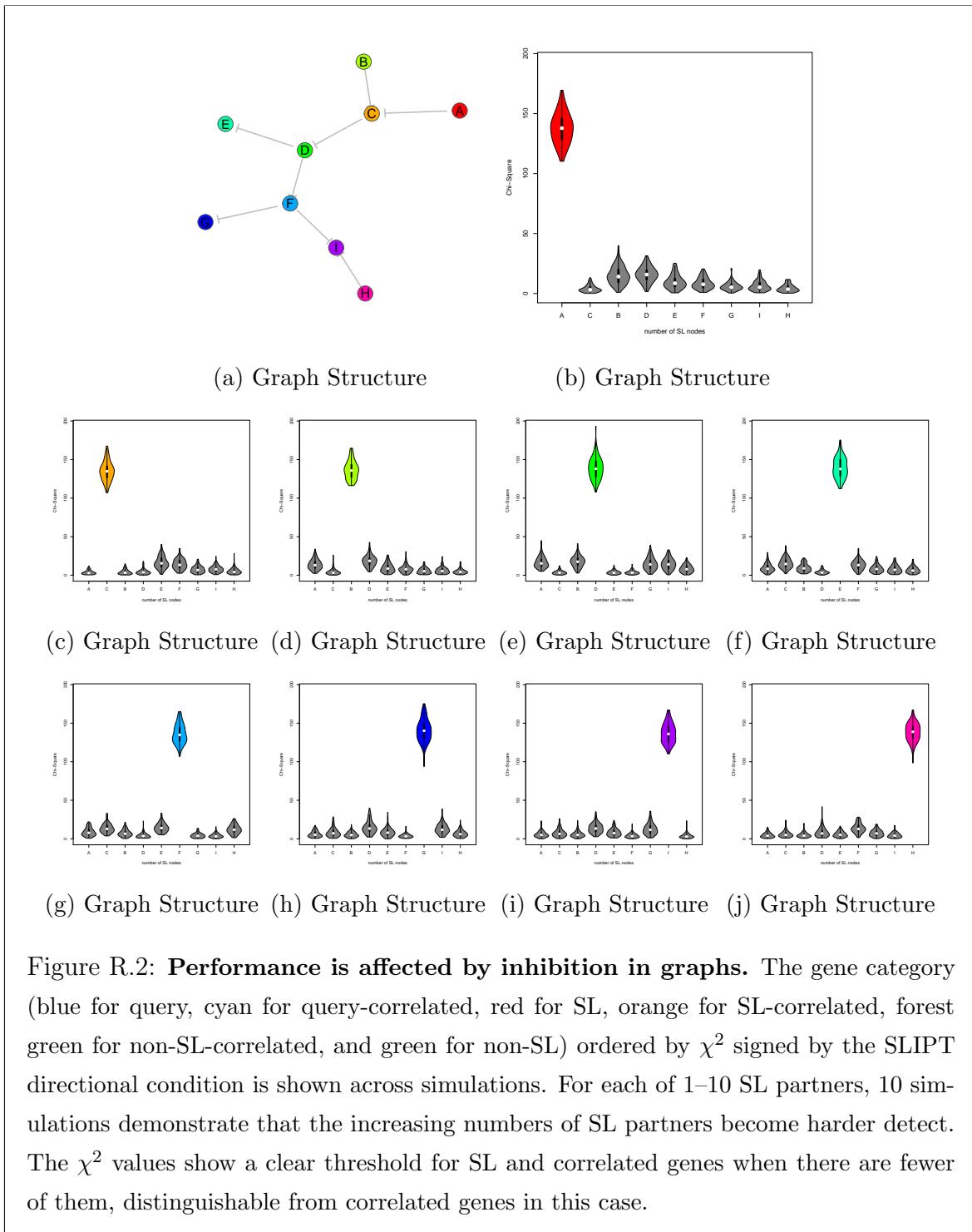
# Simulation across Graph Structures

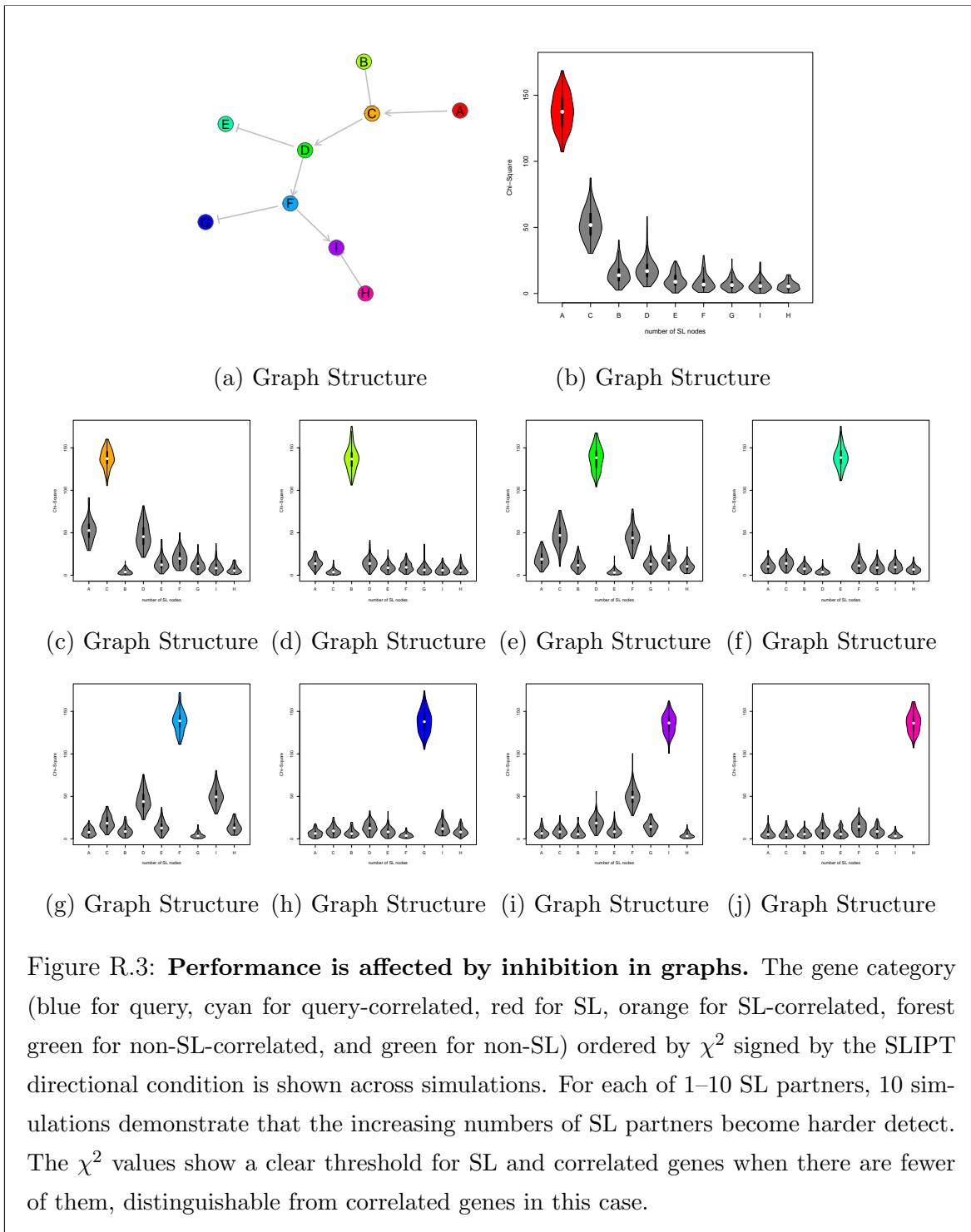


subfigure subcaption



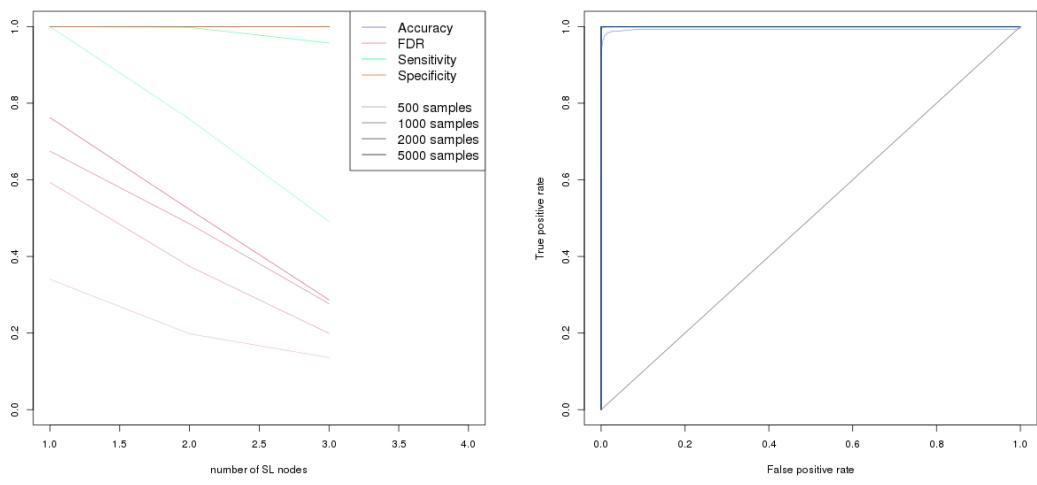
**Figure R.1: Performance is affected by inhibition in graphs.** The gene category (blue for query, cyan for query-correlated, red for SL, orange for SL-correlated, forest green for non-SL-correlated, and green for non-SL).





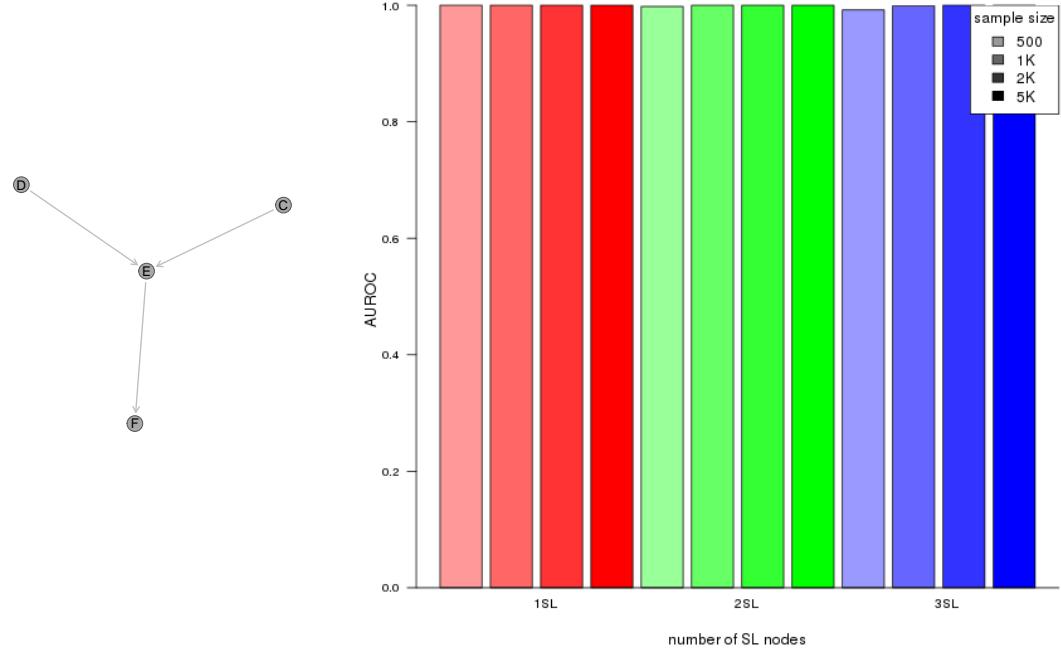
## Appendix S

### Graph Simulations 20K genes



(a) Statistical evaluation

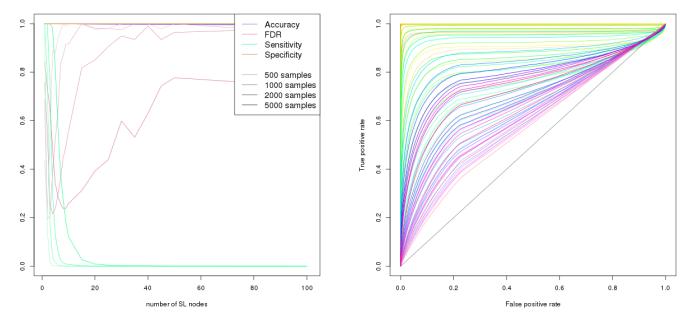
(b) Receiver operating characteristic



(c) Graph Structure

(d) Statistical performance

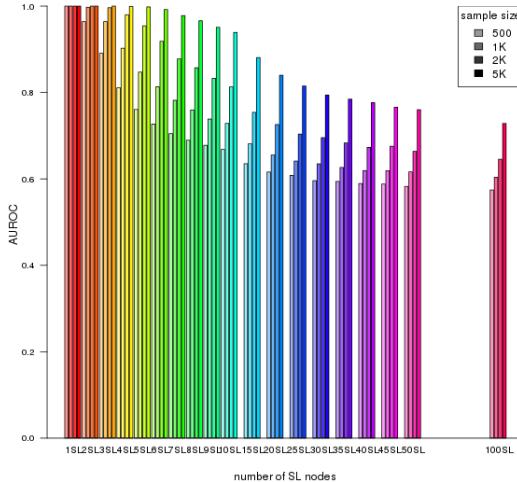
Figure S.1: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation (b) Receiver operating characteristic

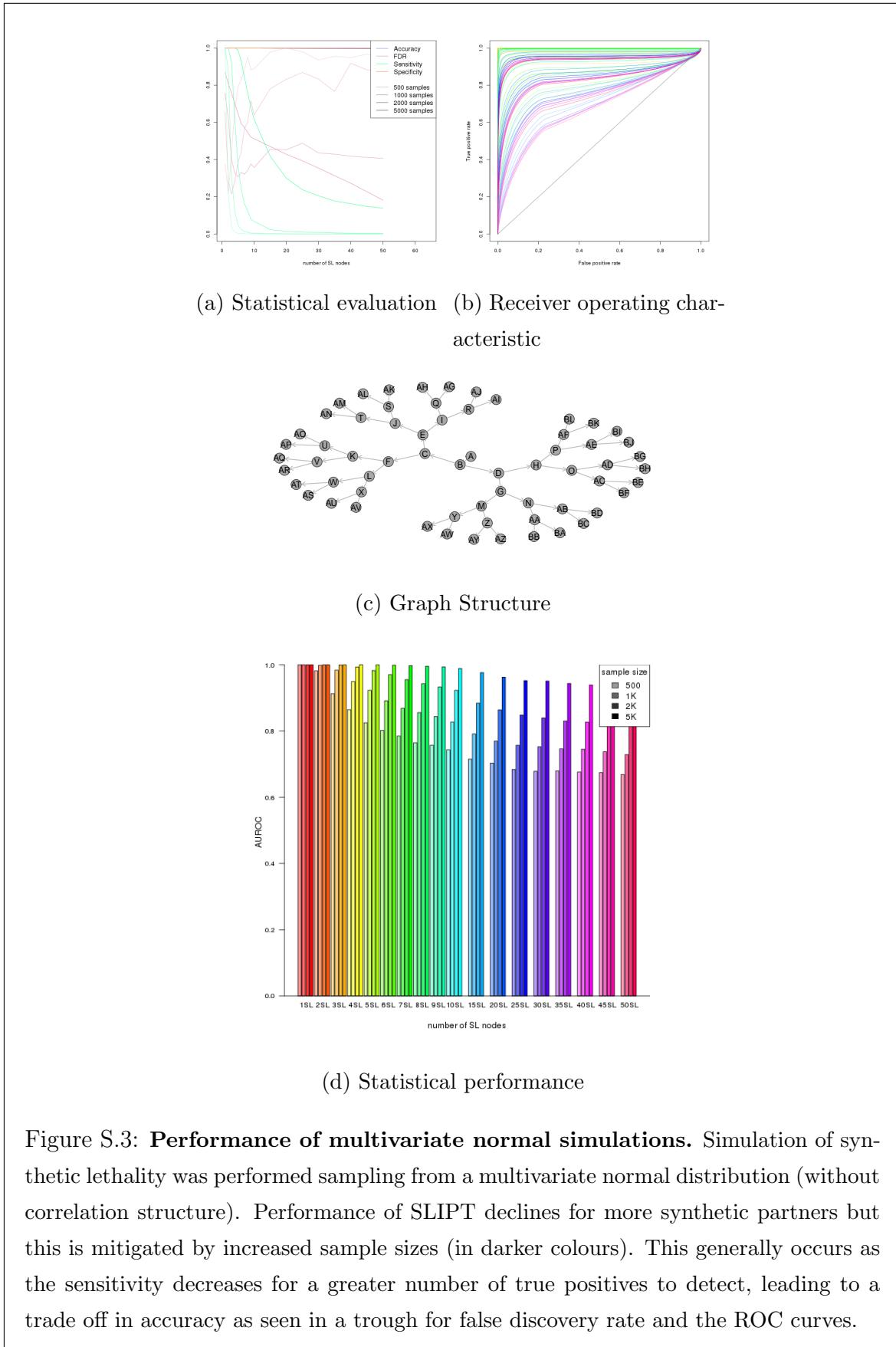


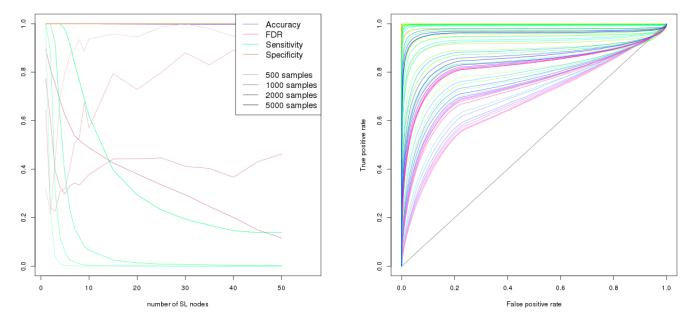
(c) Graph Structure



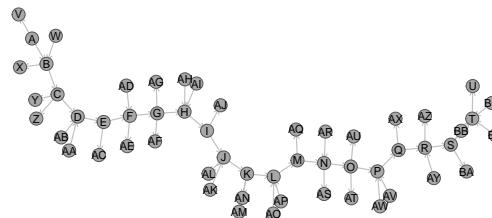
(d) Statistical performance

**Figure S.2: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.

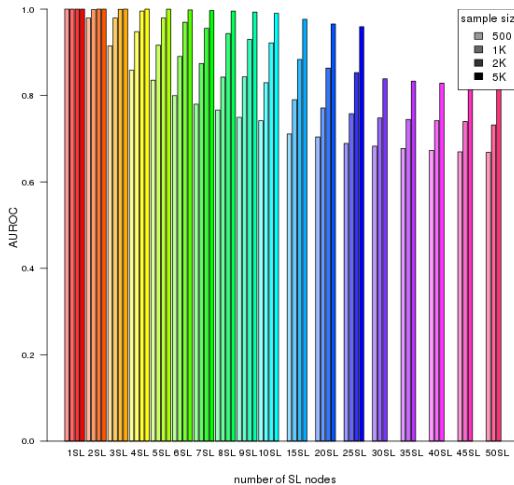




(a) Statistical evaluation    (b) Receiver operating characteristic



(c) Graph Structure

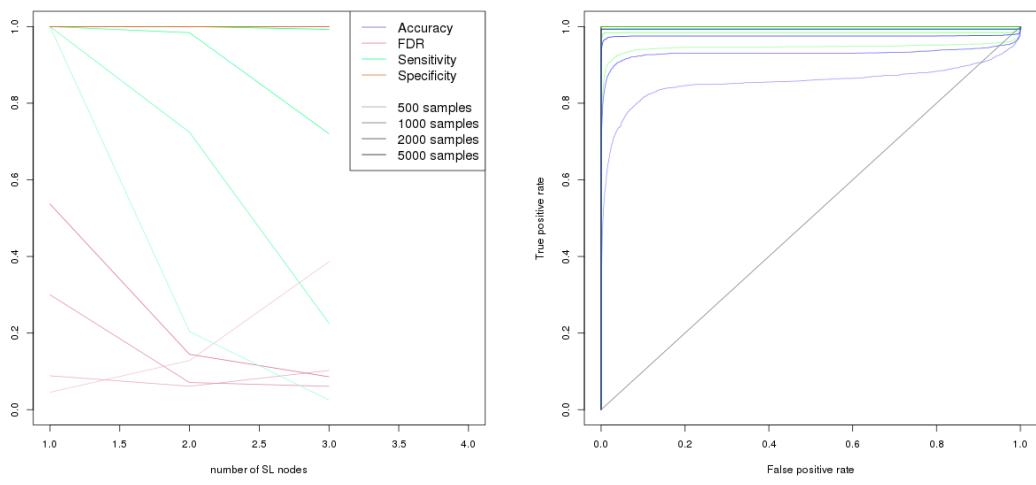


(d) Statistical performance

**Figure S.4: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.

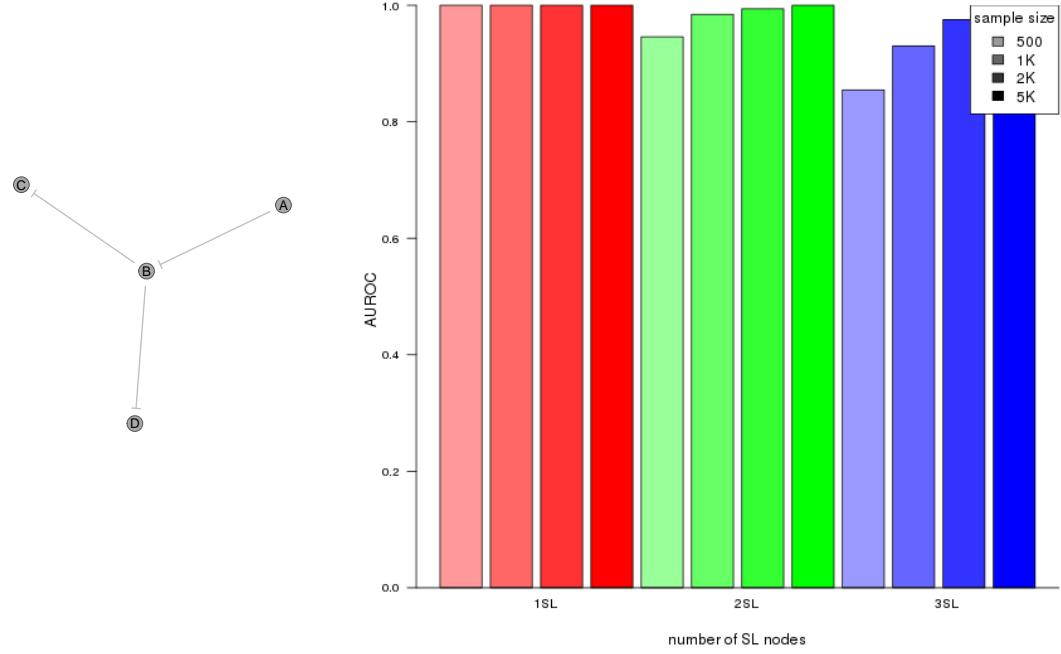
## **Appendix T**

### **Graph Simulations 20K genes with Inhibition**



(a) Statistical evaluation

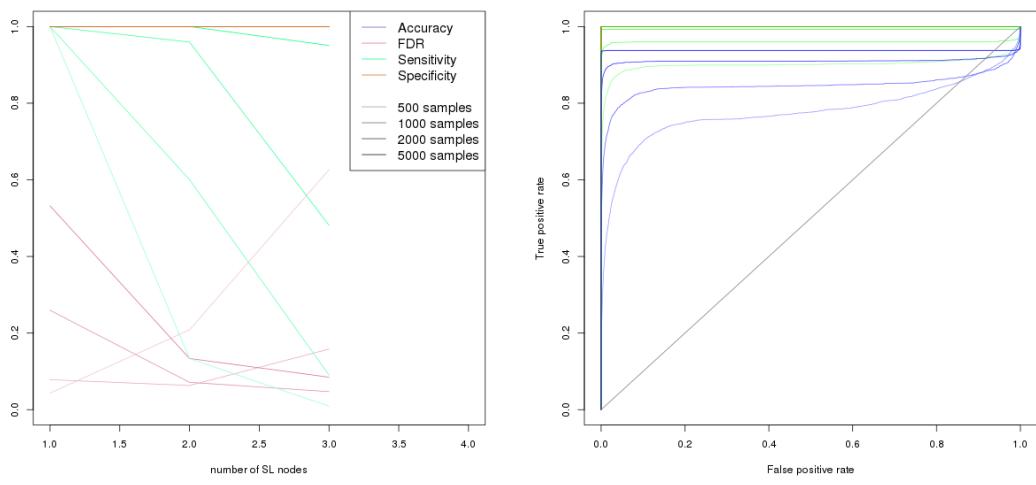
(b) Receiver operating characteristic



(c) Graph Structure

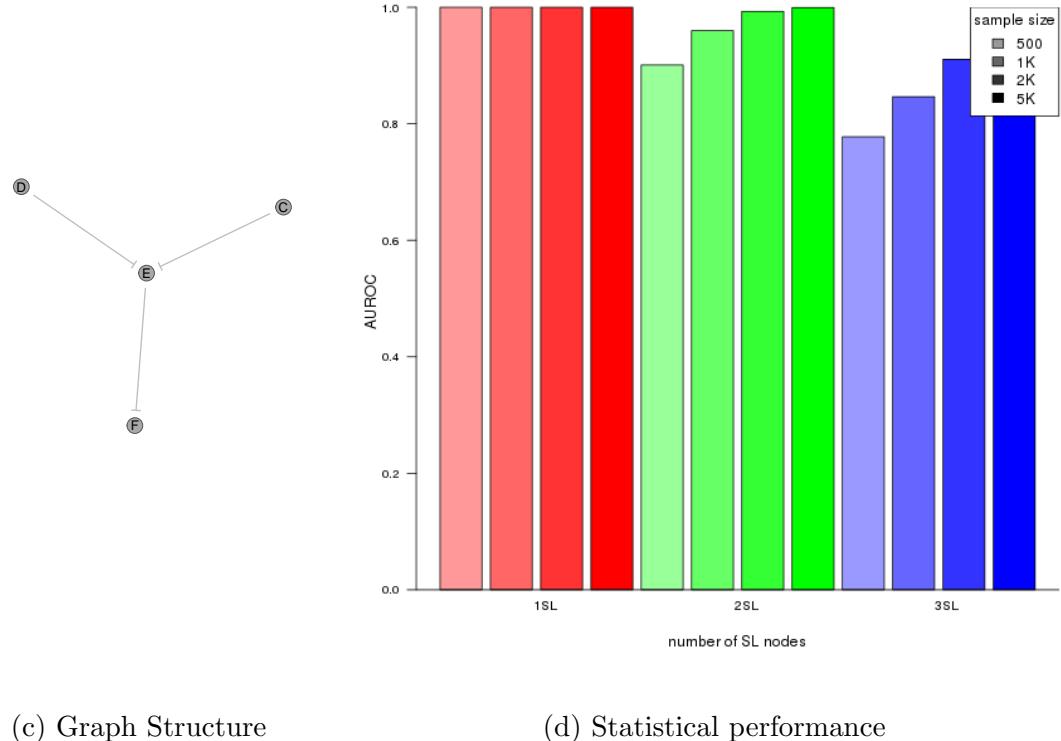
(d) Statistical performance

**Figure T.1: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation

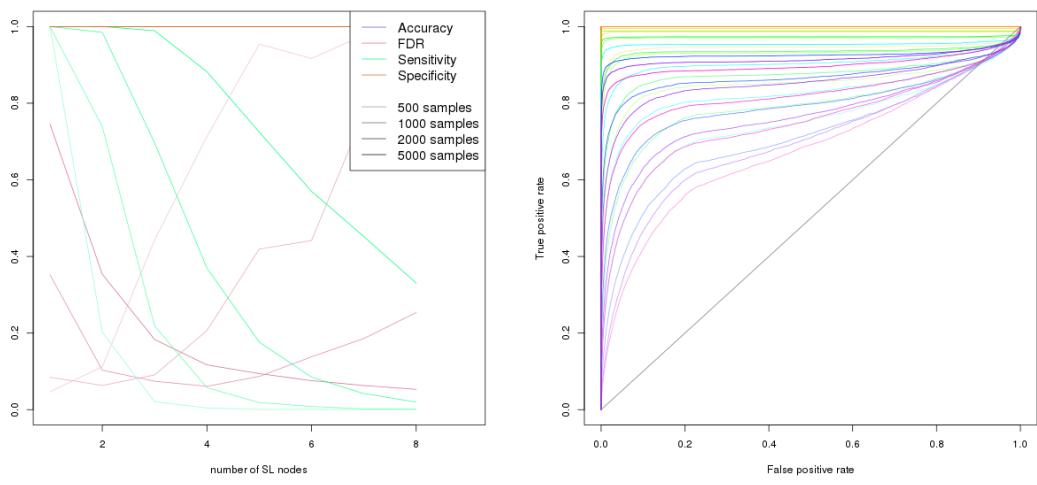
(b) Receiver operating characteristic



(c) Graph Structure

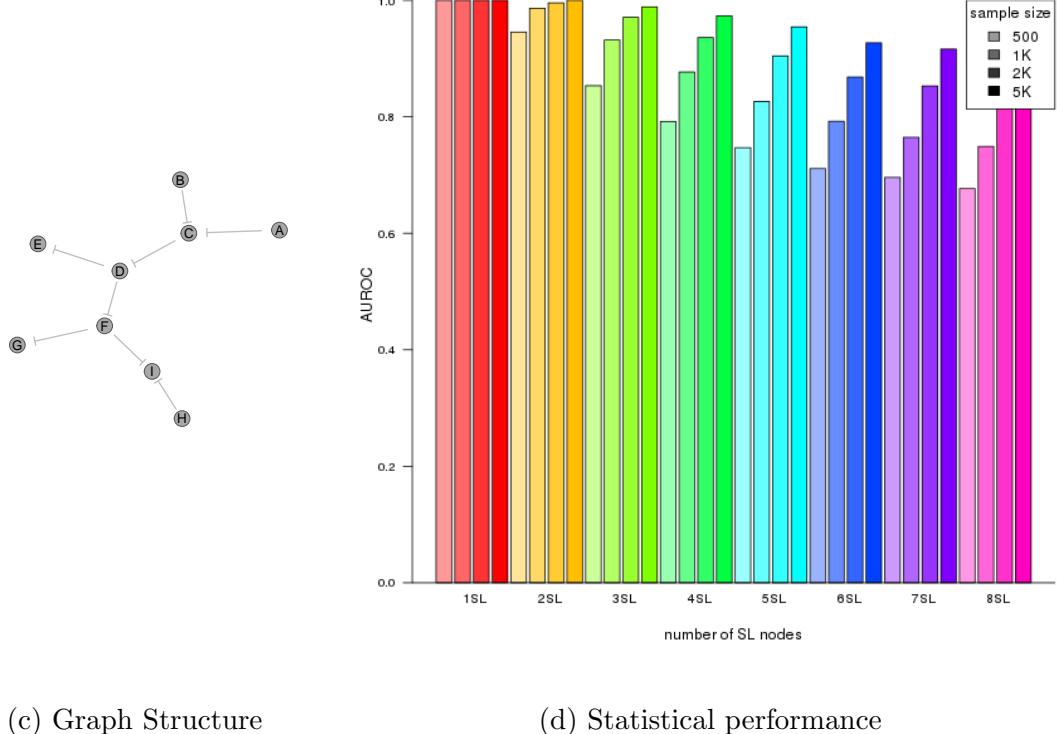
(d) Statistical performance

**Figure T.2: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation

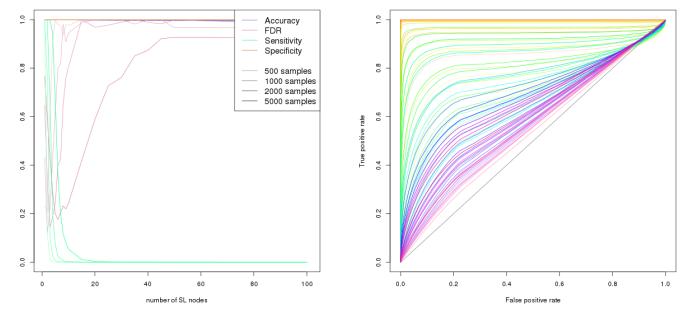
(b) Receiver operating characteristic



(c) Graph Structure

(d) Statistical performance

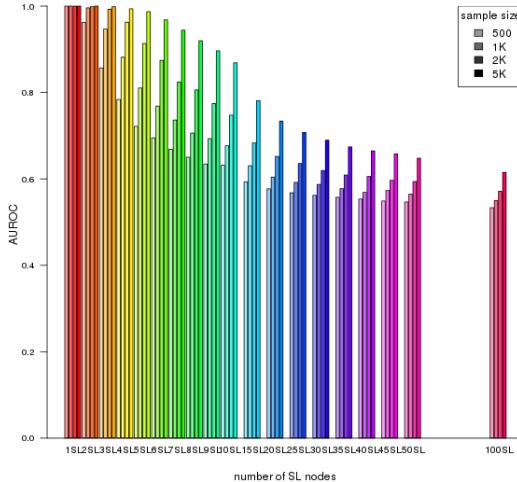
**Figure T.3: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation    (b) Receiver operating characteristic

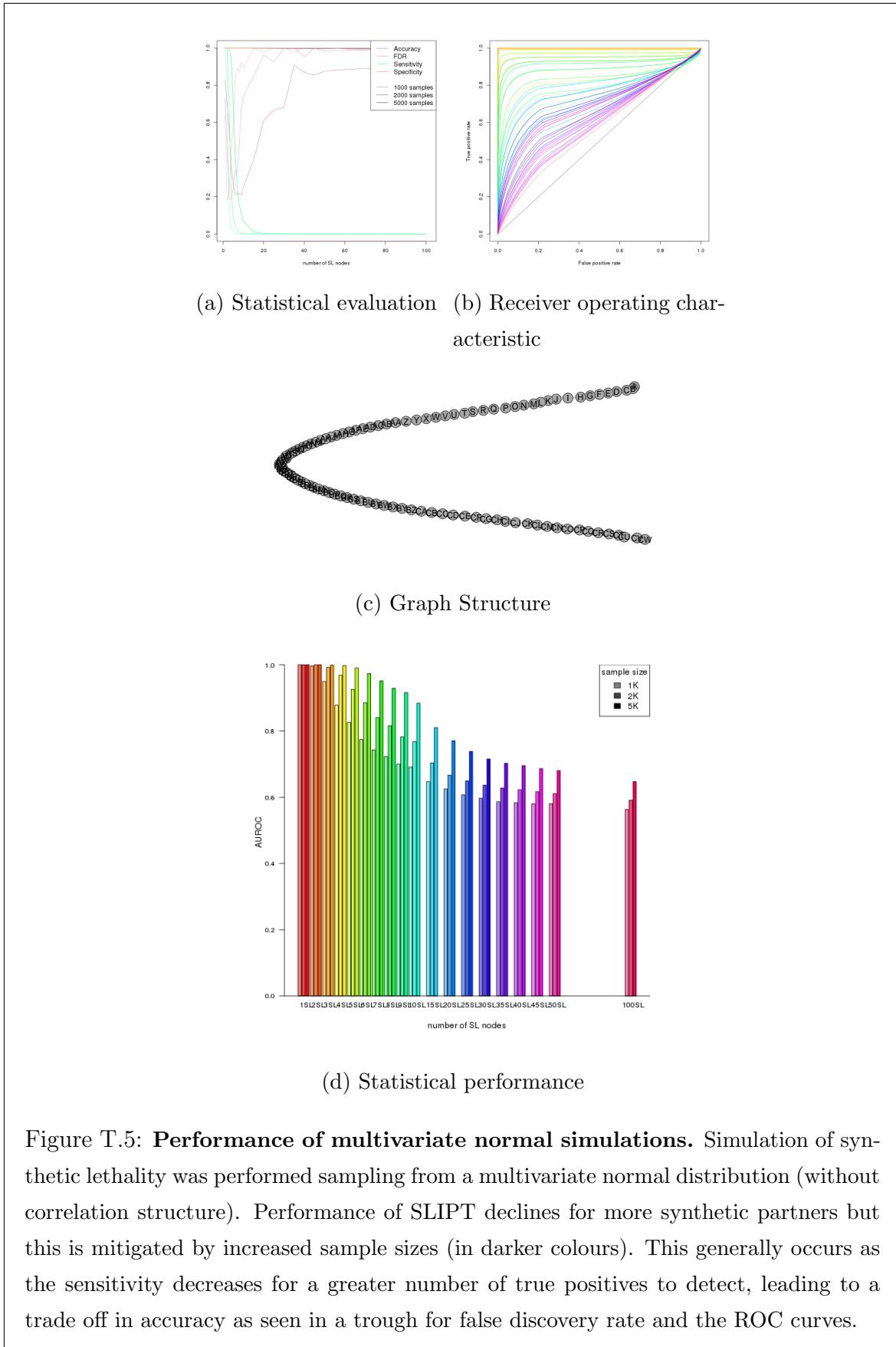


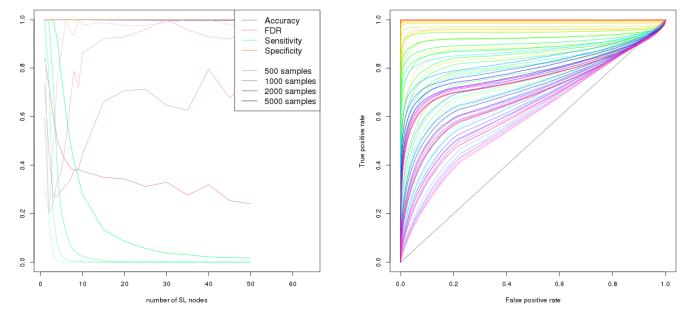
(c) Graph Structure



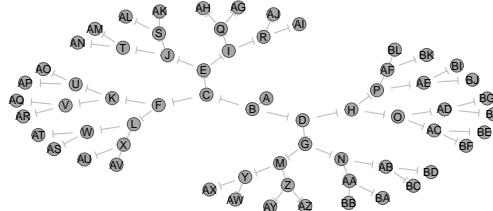
(d) Statistical performance

**Figure T.4: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.

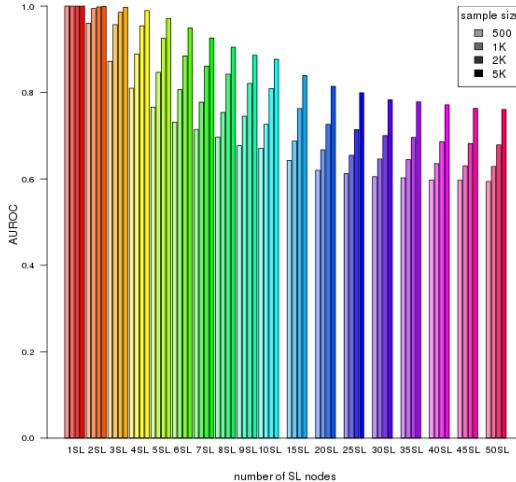




(a) Statistical evaluation    (b) Receiver operating characteristic

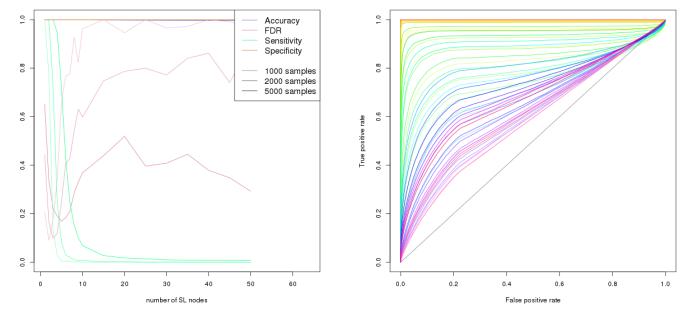


(c) Graph Structure

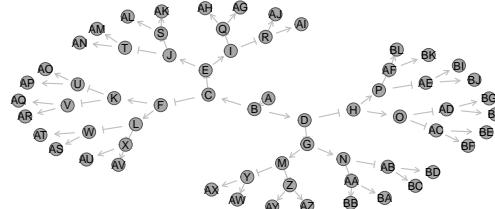


(d) Statistical performance

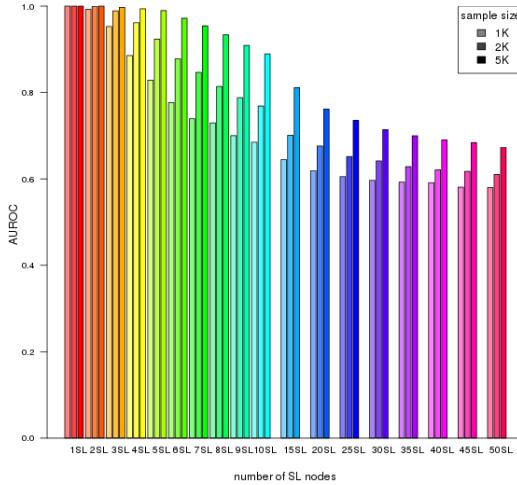
**Figure T.6: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation (b) Receiver operating characteristic

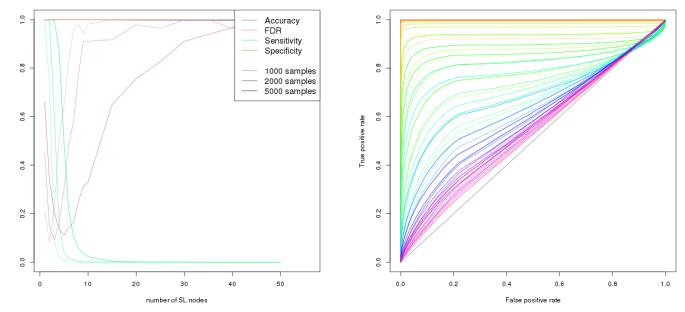


(c) Graph Structure

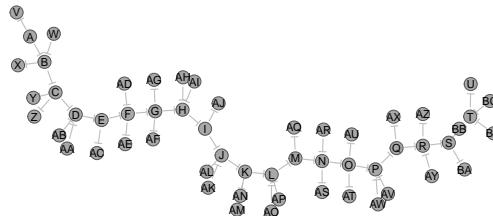


(d) Statistical performance

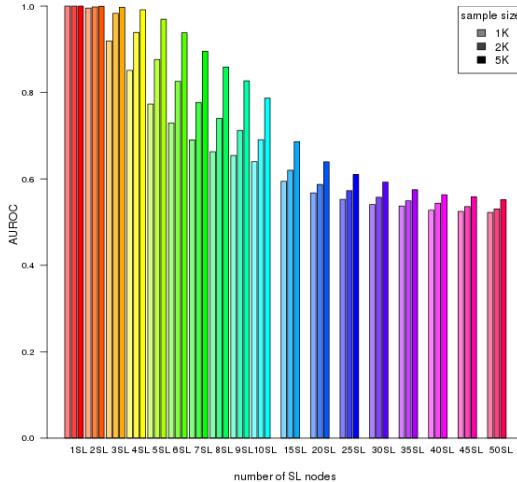
**Figure T.7: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation    (b) Receiver operating characteristic

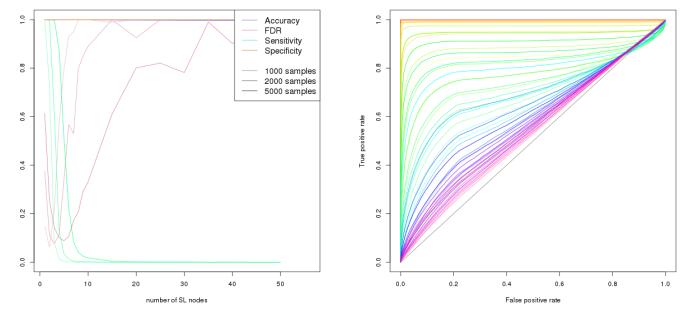


(c) Graph Structure

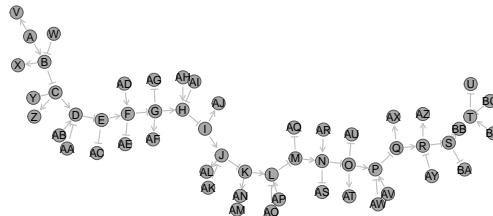


(d) Statistical performance

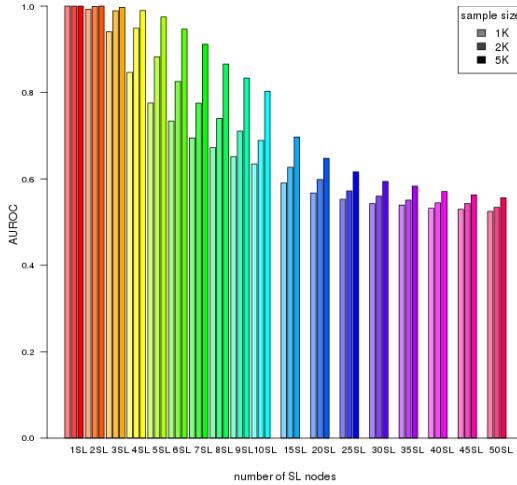
**Figure T.8: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



(a) Statistical evaluation    (b) Receiver operating characteristic



(c) Graph Structure

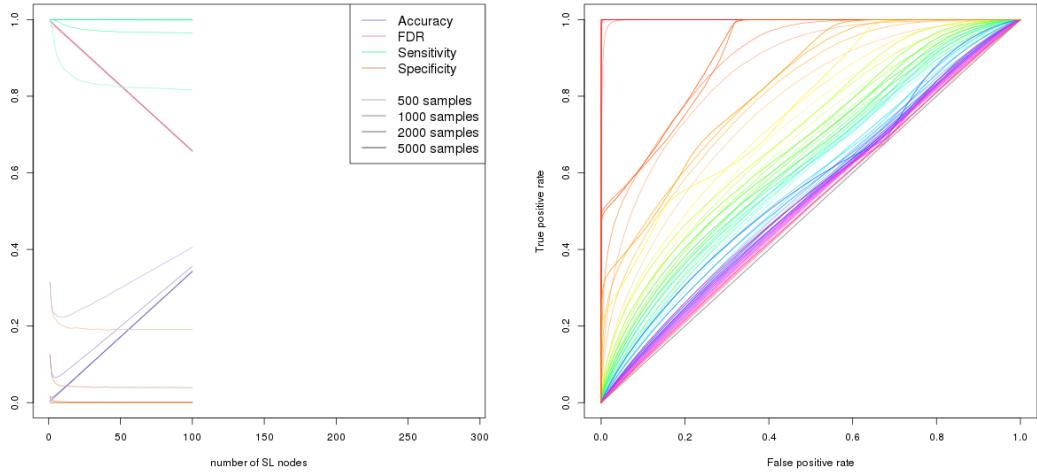


(d) Statistical performance

**Figure T.9: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.

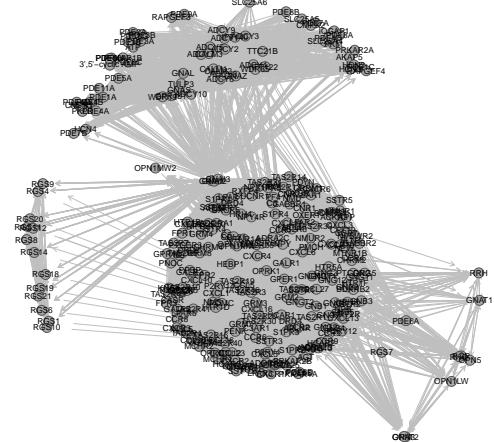
## Appendix U

### Pathway Simulations

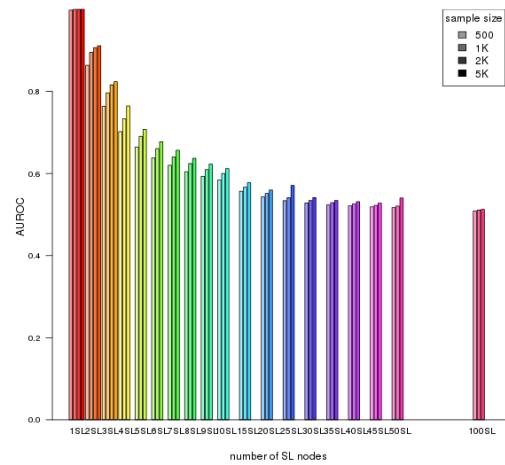


(a) Statistical evaluation

(b) Receiver operating characteristic

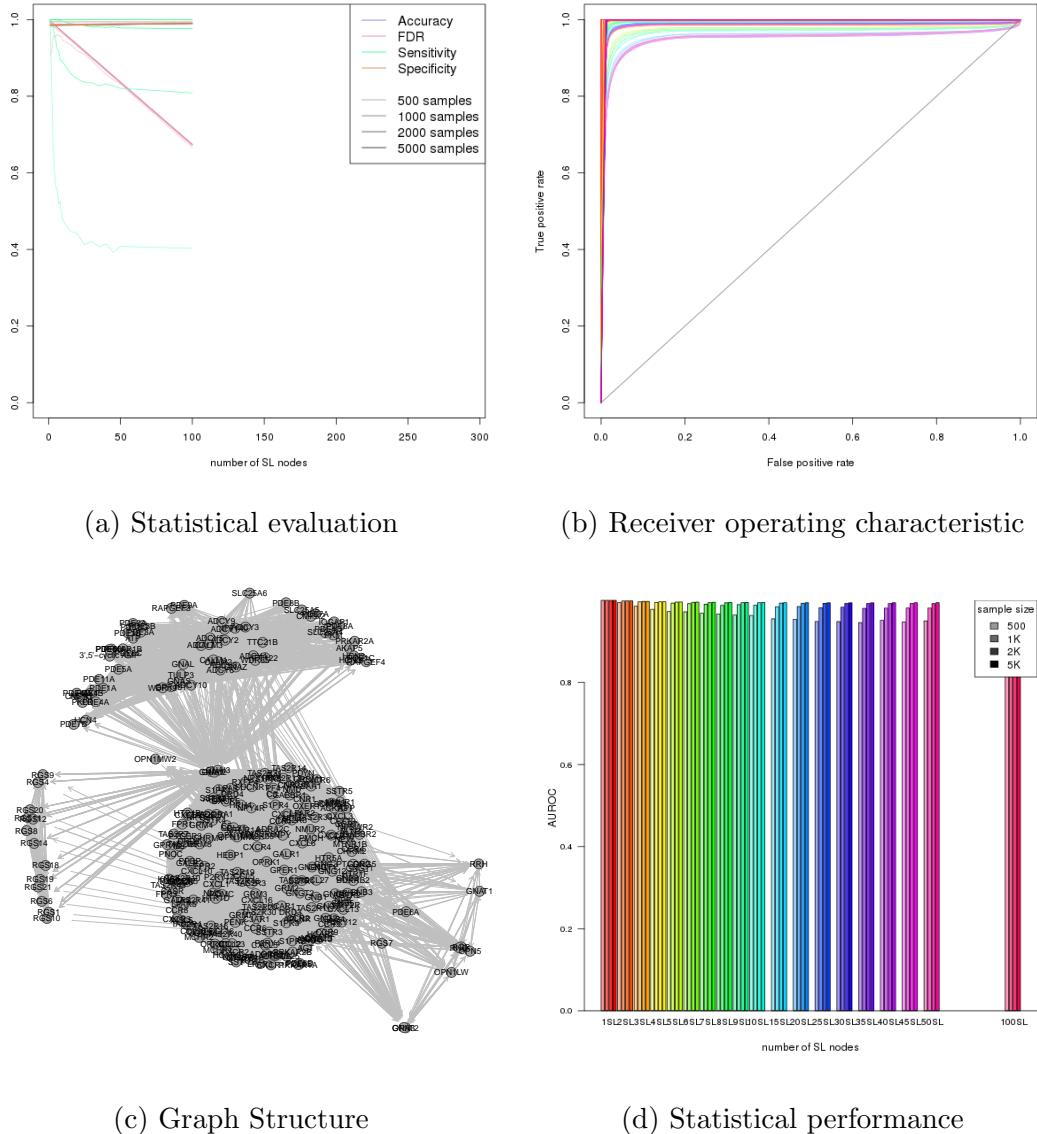


(c) Graph Structure



(d) Statistical performance

**Figure U.1: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.



**Figure U.2: Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker colours). This generally occurs as the sensitivity decreases for a greater number of true positives to detect, leading to a trade off in accuracy as seen in a trough for false discovery rate and the ROC curves.