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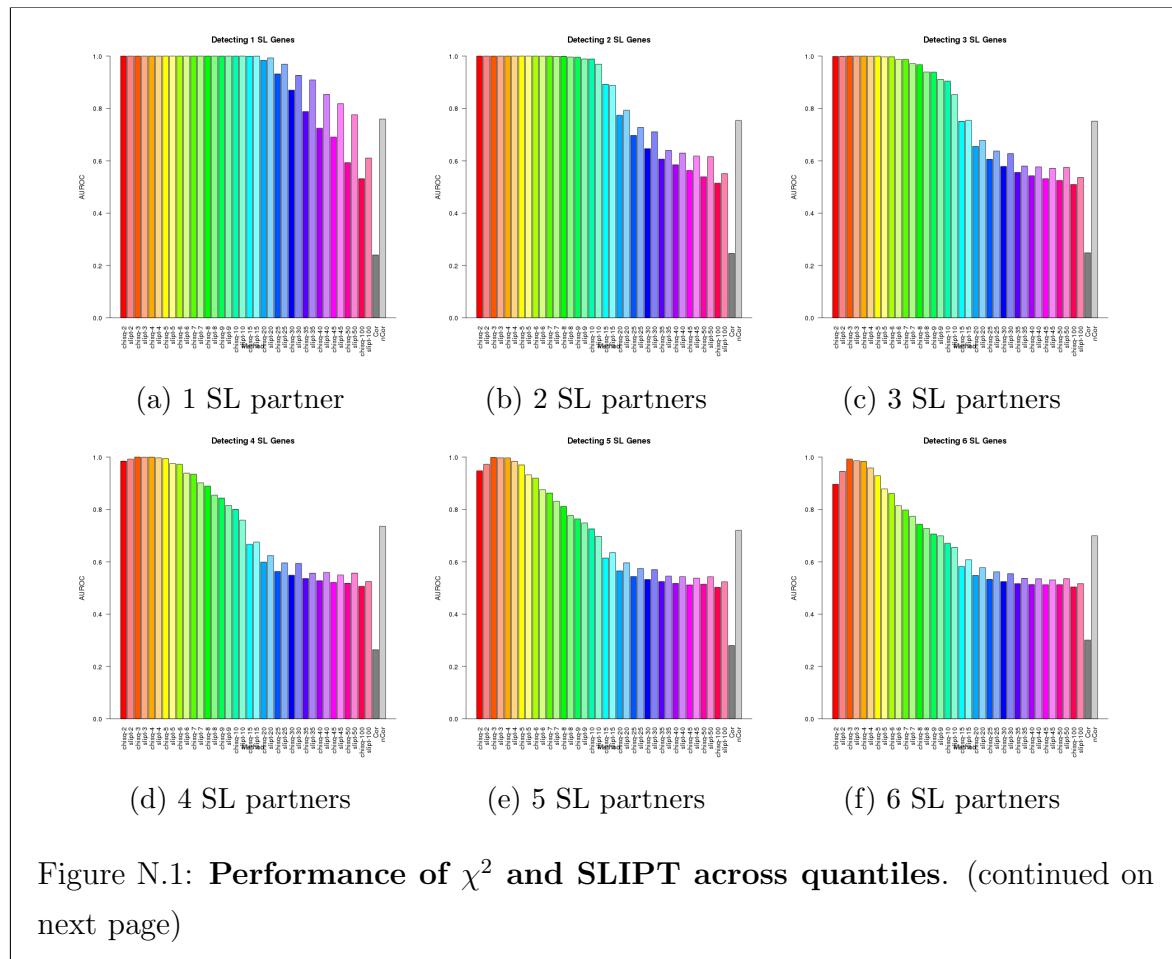
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Appendix N

Performance of SLIPT and χ^2



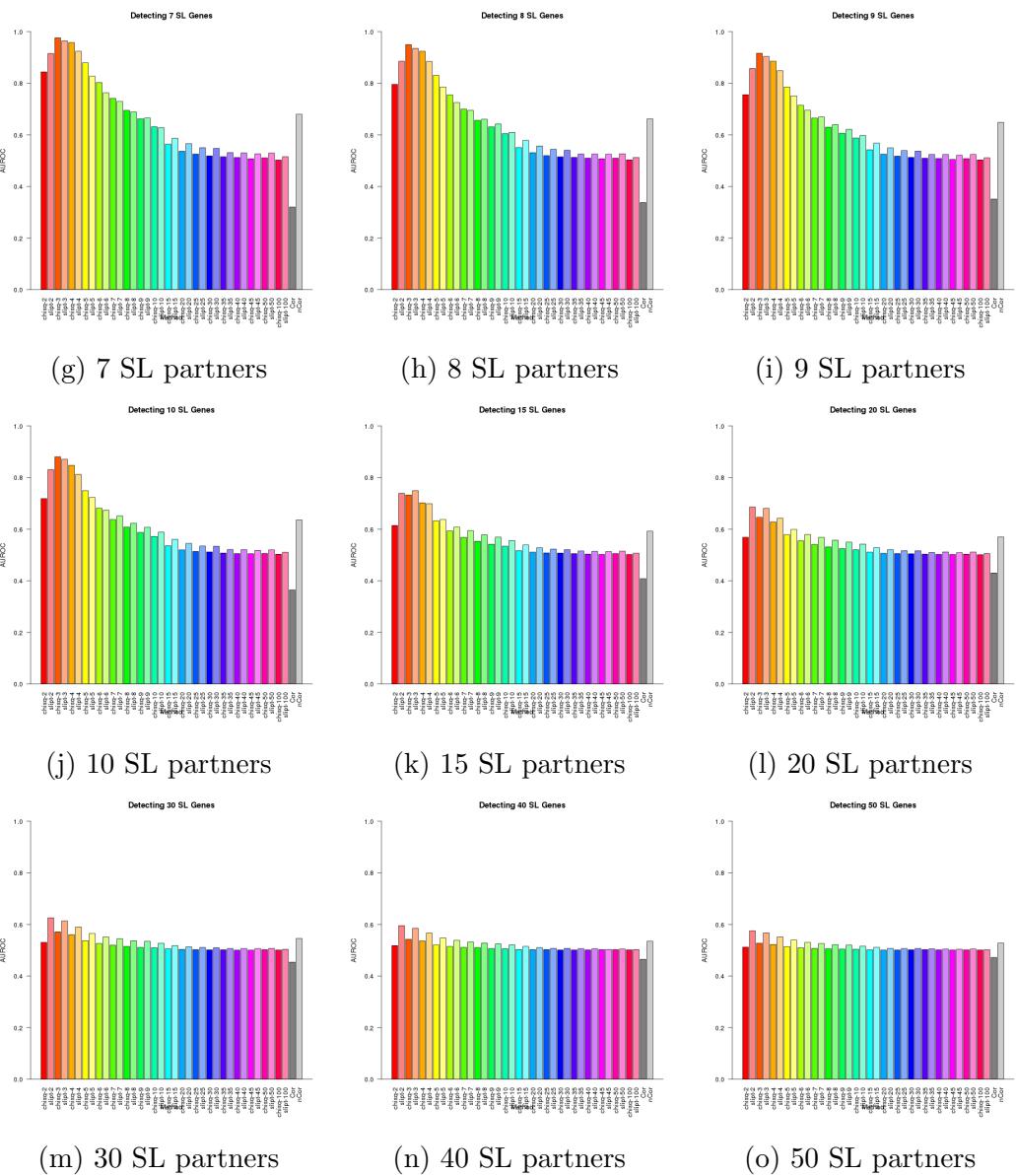


Figure N.1: Performance of χ^2 and SLIPT across quantiles. Synthetic lethal detection with quantiles as in axis labels. The barplot uses the same hues for each quantile (grey for correlation) and darker for χ^2 (and positive correlation). Synthetic Lethal Interaction Prediction Tool (SLIPT) and χ^2 perform similarly, peaking at $\frac{1}{3}$ -quantiles and converging to random (0.5). Negative correlation was higher than positive but not optimal quantiles for SLIPT or χ^2 . These findings are robust across different numbers of underlying synthetic lethal genes in 10,000 simulations of 100 genes and 1000 samples. SLIPT performs better than χ^2 for higher numbers of synthetic lethal genes and finer quantiles.

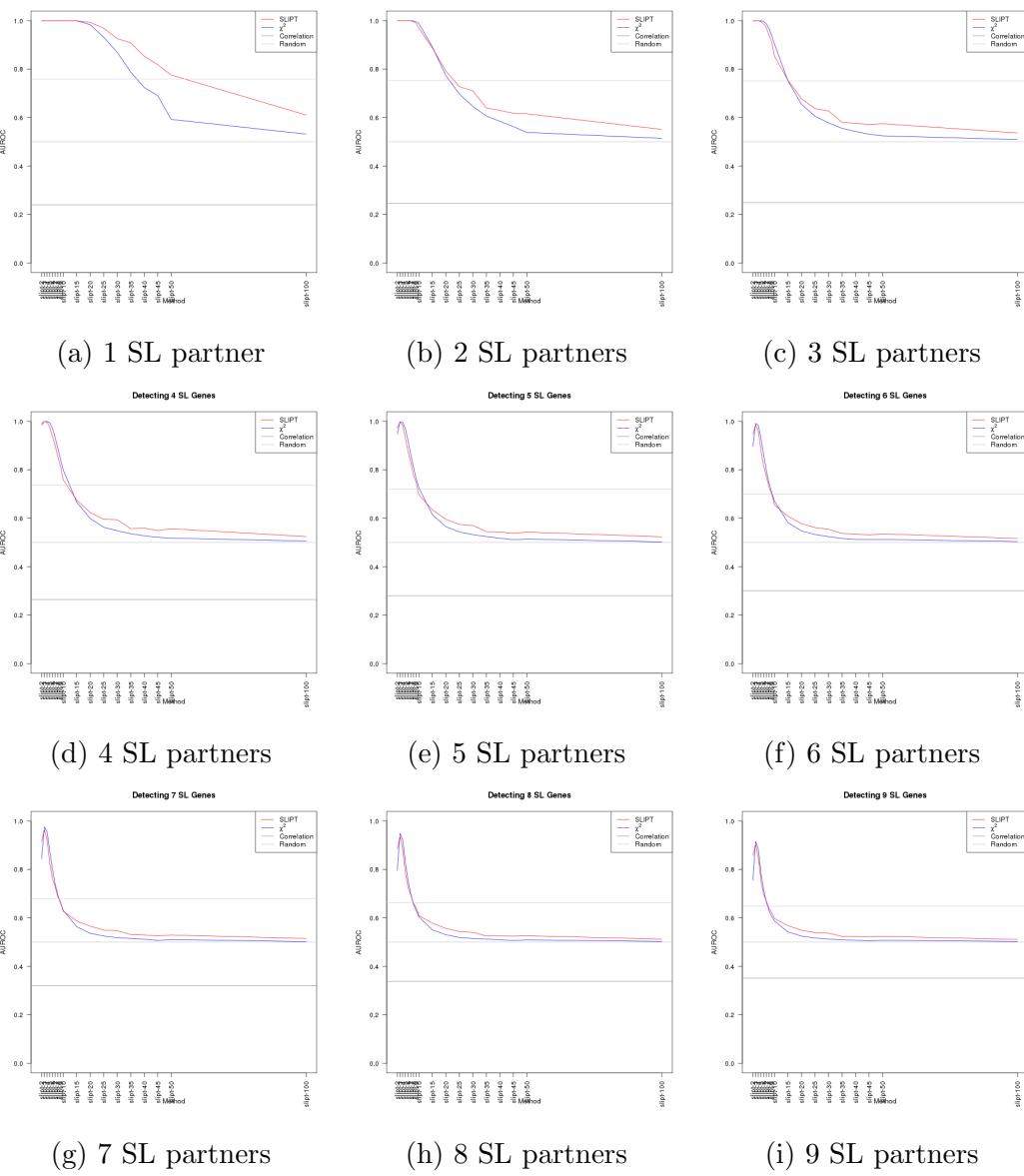


Figure N.2: **Performance of χ^2 and SLIPT across quantiles.** (continued on next page)

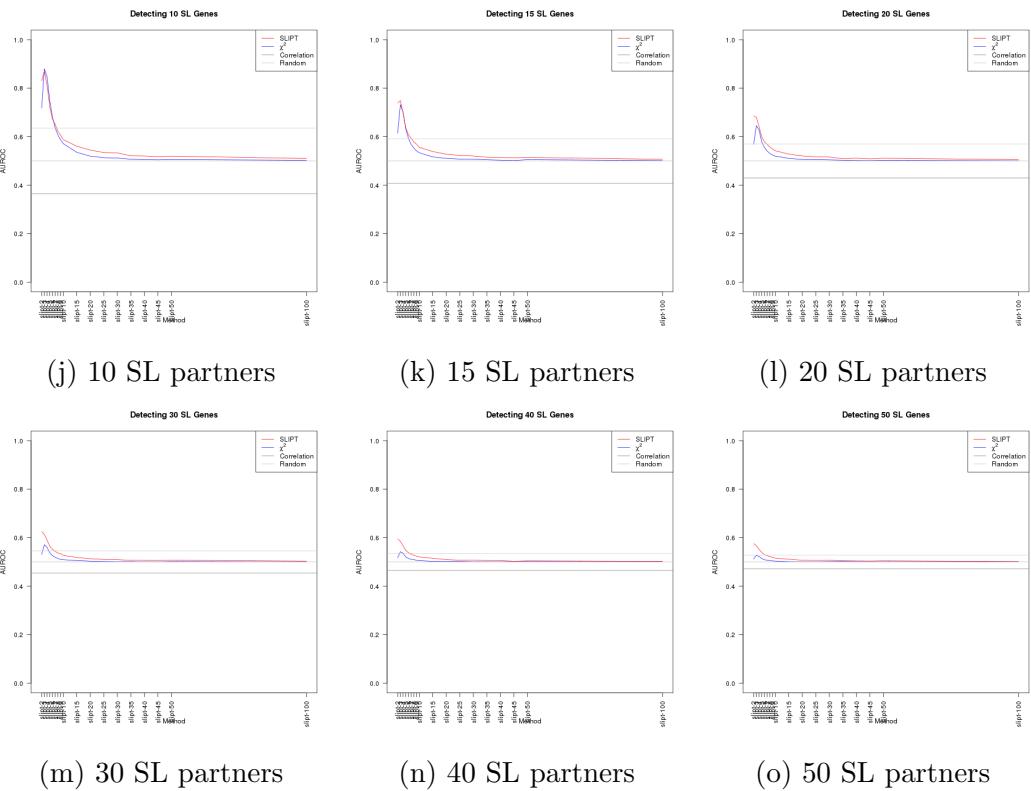


Figure N.2: Performance of χ^2 and SLIPT across quantiles. Synthetic lethal detection with quantiles as in axis labels. The line plots are coloured for SLIPT (red), χ^2 (blue) and correlation (grey) according to the legend. SLIPT and χ^2 perform similarly, peaking at $\frac{1}{3}$ -quantiles and converging to random (0.5). Negative correlation was higher than positive but not optimal quantiles for SLIPT or χ^2 . These findings are robust across different numbers of underlying synthetic lethal genes in 10,000 simulations of 100 genes and 1000 samples. SLIPT performs better than χ^2 for higher numbers of synthetic lethal genes and finer quantiles.

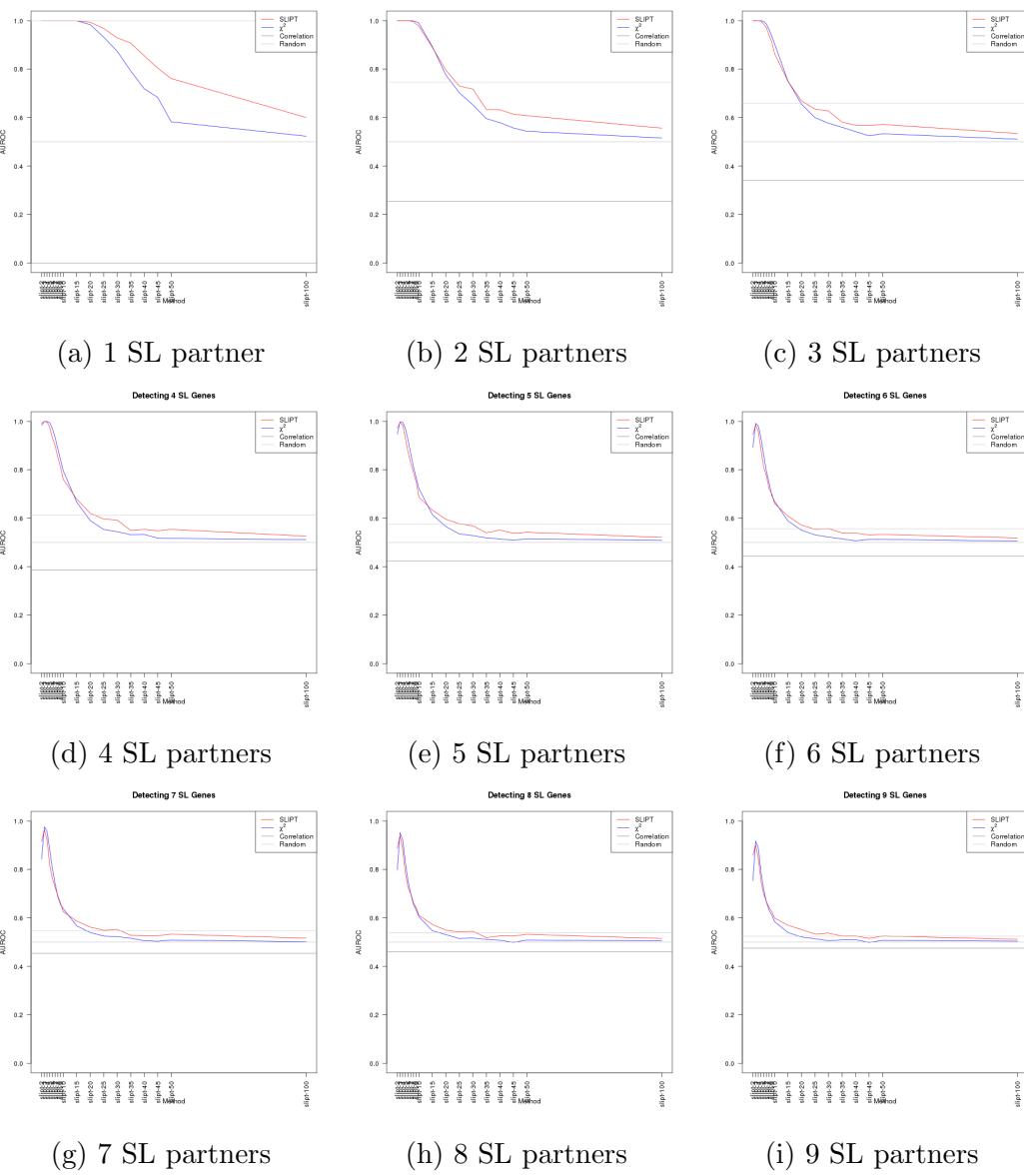


Figure N.3: Performance of χ^2 and SLIPT across quantiles with more genes. (continued on next page)

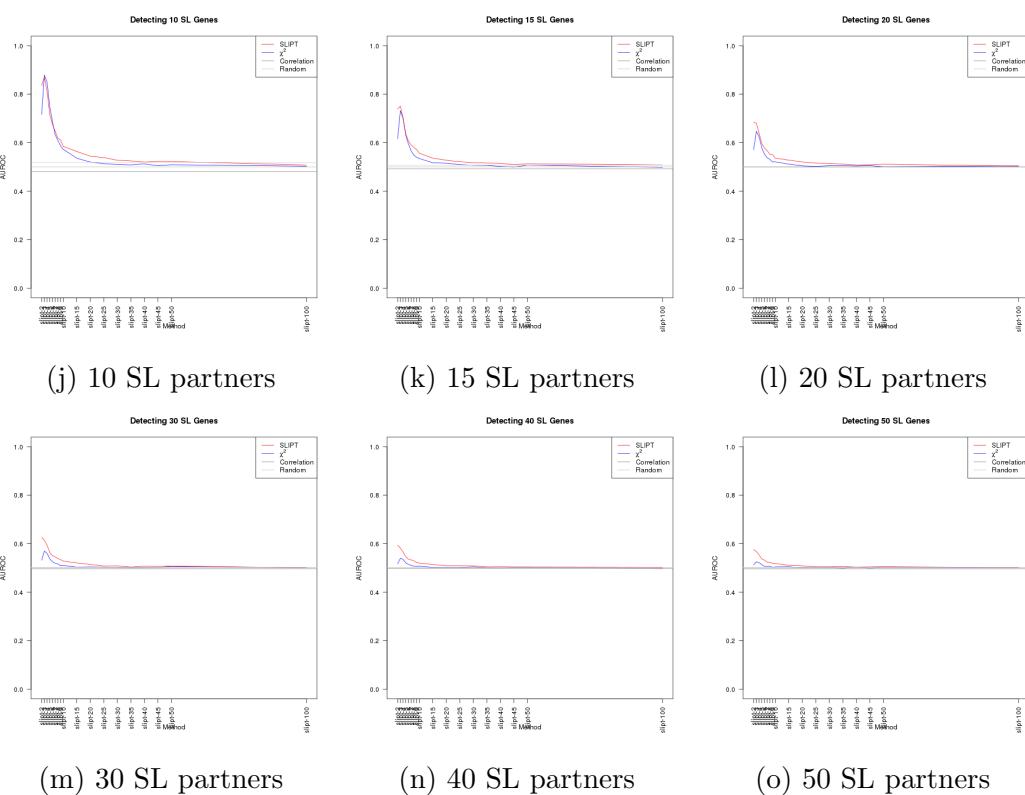


Figure N.3: Performance of χ^2 and SLIPT across quantiles with more genes. Synthetic lethal detection with quantiles as in axis labels. The line plots are coloured for SLIPT (red), χ^2 (blue) and correlation (grey) according to the legend. SLIPT and χ^2 perform similarly, peaking at $\frac{1}{3}$ -quantiles and converging to random (0.5). Negative correlation was higher than positive but not optimal quantiles for SLIPT or χ^2 . These findings are robust across different numbers of underlying synthetic lethal genes in 1000 simulations of 20,000 genes and 1000 samples. SLIPT performs better than χ^2 for higher numbers of synthetic lethal genes and finer quantiles.

N.0.1 Correlated Query Genes affects Specificity

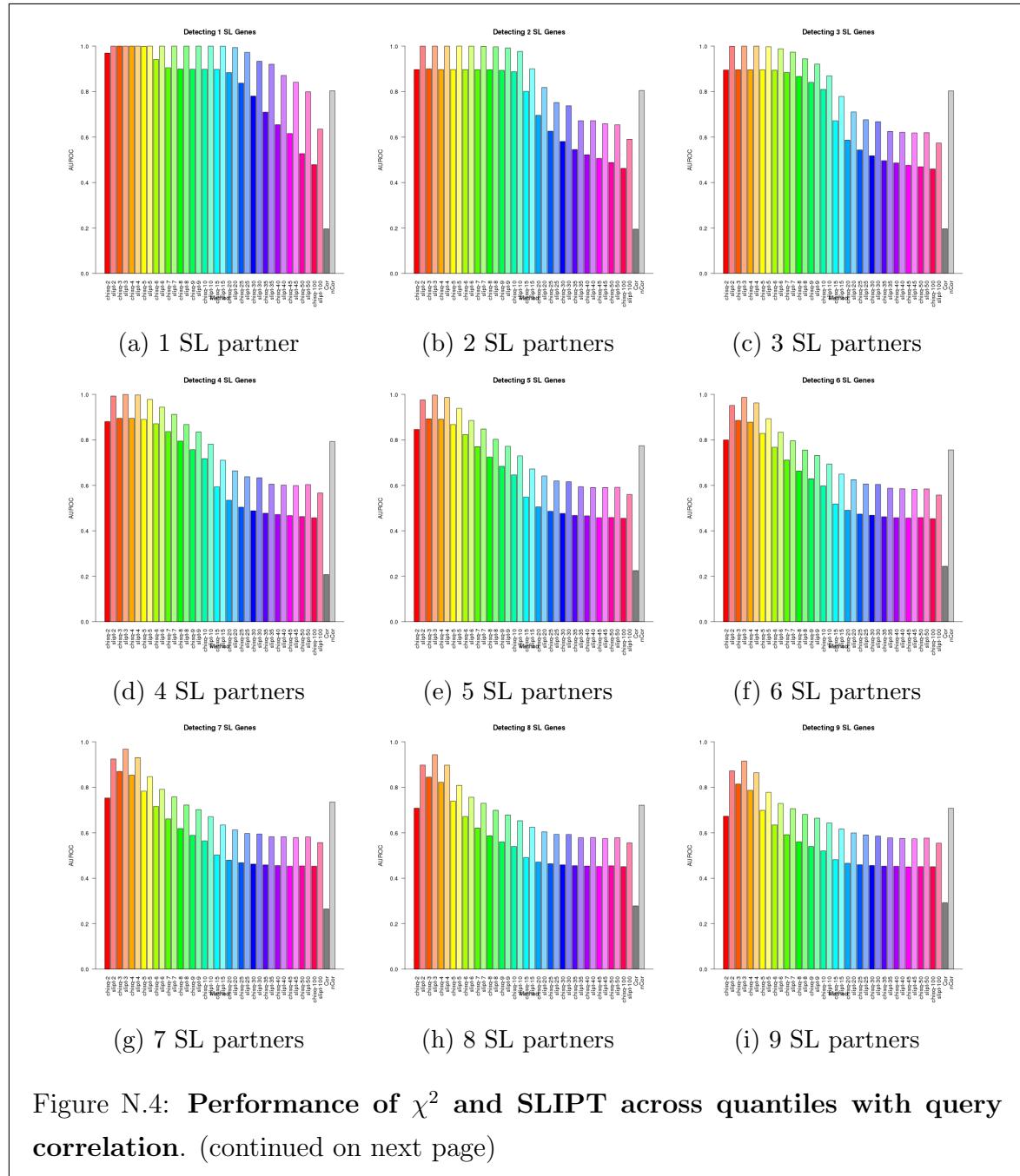


Figure N.4: **Performance of χ^2 and SLIPT across quantiles with query correlation.** (continued on next page)

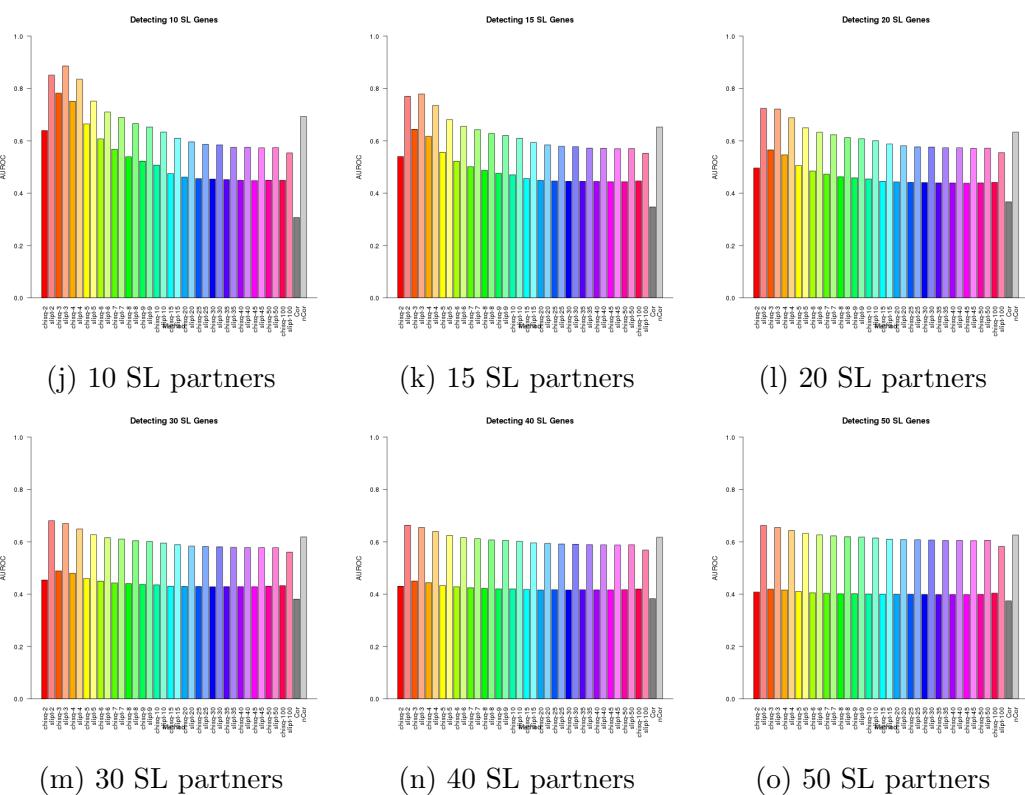


Figure N.4: Performance of χ^2 and SLIPT across quantiles with query correlation. Synthetic lethal detection with quantiles as in axis labels. The barplot uses the same hues for each quantile (grey for correlation) and darker for χ^2 (and positive correlation). SLIPT and χ^2 perform similarly, peaking at $\frac{1}{3}$ -quantiles and converging to random (0.5). Negative correlation was higher than positive but not optimal quantiles for SLIPT or χ^2 . These findings are robust across different numbers of underlying synthetic lethal genes in 10,000 simulations of 100 genes (including 10 correlated with the query) and 1000 samples. SLIPT performs consistently better than χ^2 with positively correlated genes.

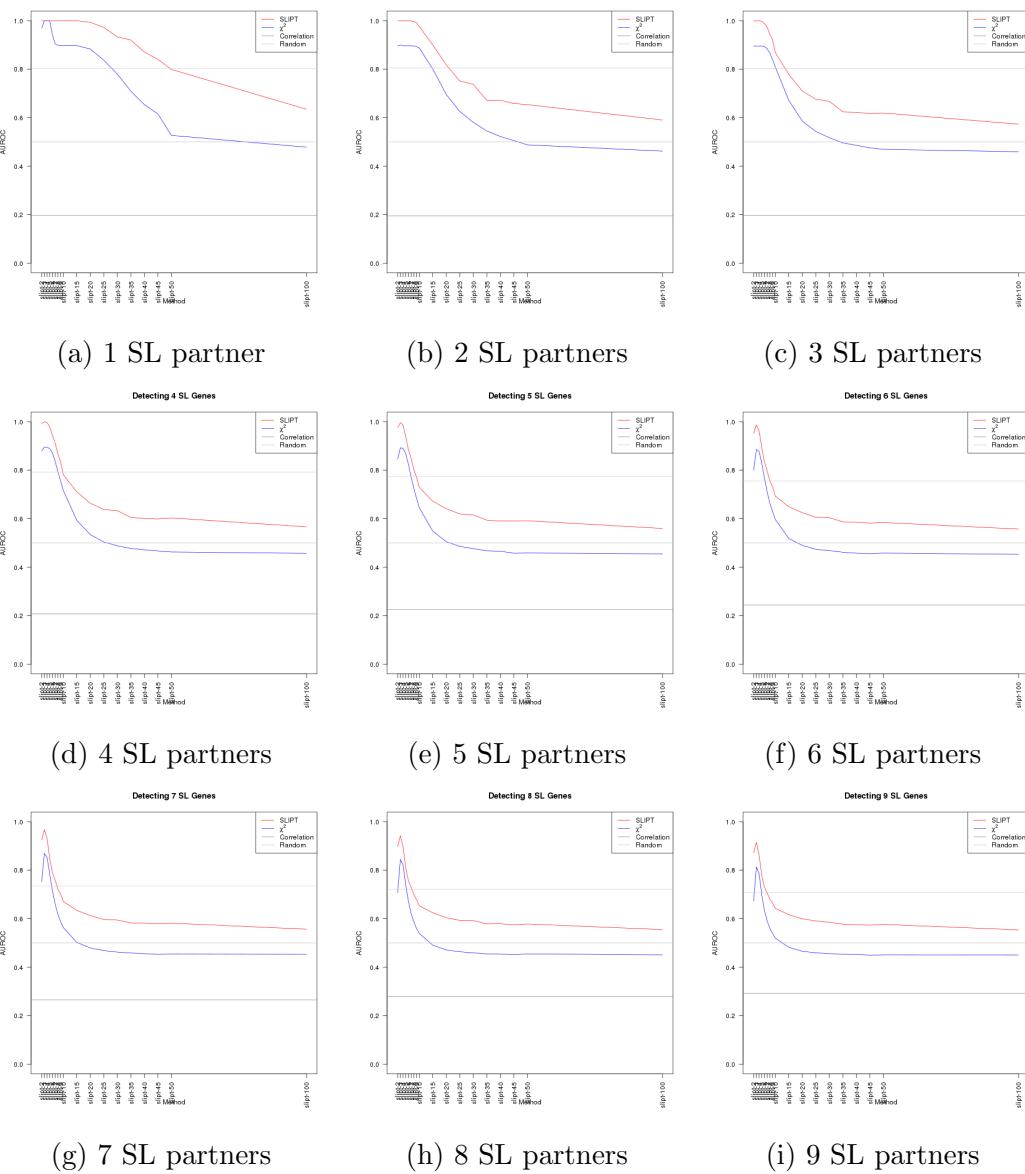


Figure N.5: **Performance of χ^2 and SLIPT across quantiles with query correlation.** (continued on next page)

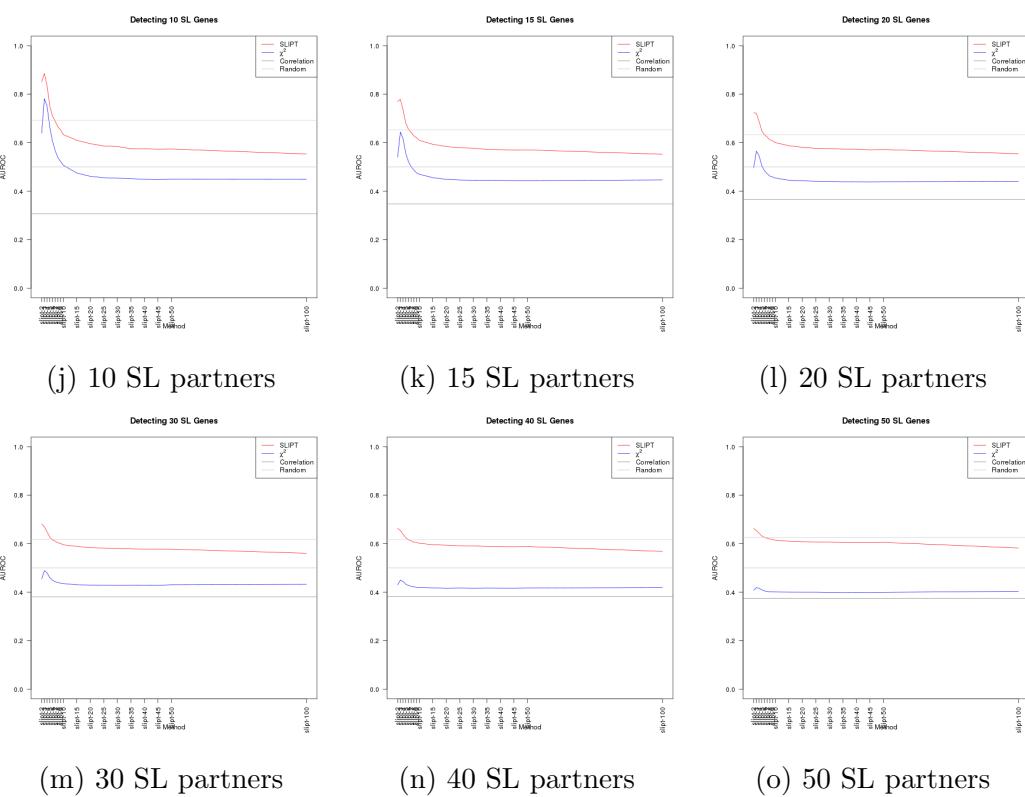


Figure N.5: Performance of χ^2 and SLIPT across quantiles with query correlation. Synthetic lethal detection with quantiles as in axis labels. The line plots are coloured for SLIPT (red), χ^2 (blue) and correlation (grey) according to the legend. SLIPT and χ^2 perform similarly, peaking at $\frac{1}{3}$ -quantiles and converging to random (0.5). Negative correlation was higher than positive but not optimal quantiles for SLIPT or χ^2 . These findings are robust across different numbers of underlying synthetic lethal genes in 10,000 simulations of 100 genes (including 10 correlated with the query) and 1000 samples. SLIPT performs consistently better than χ^2 with positively correlated genes.

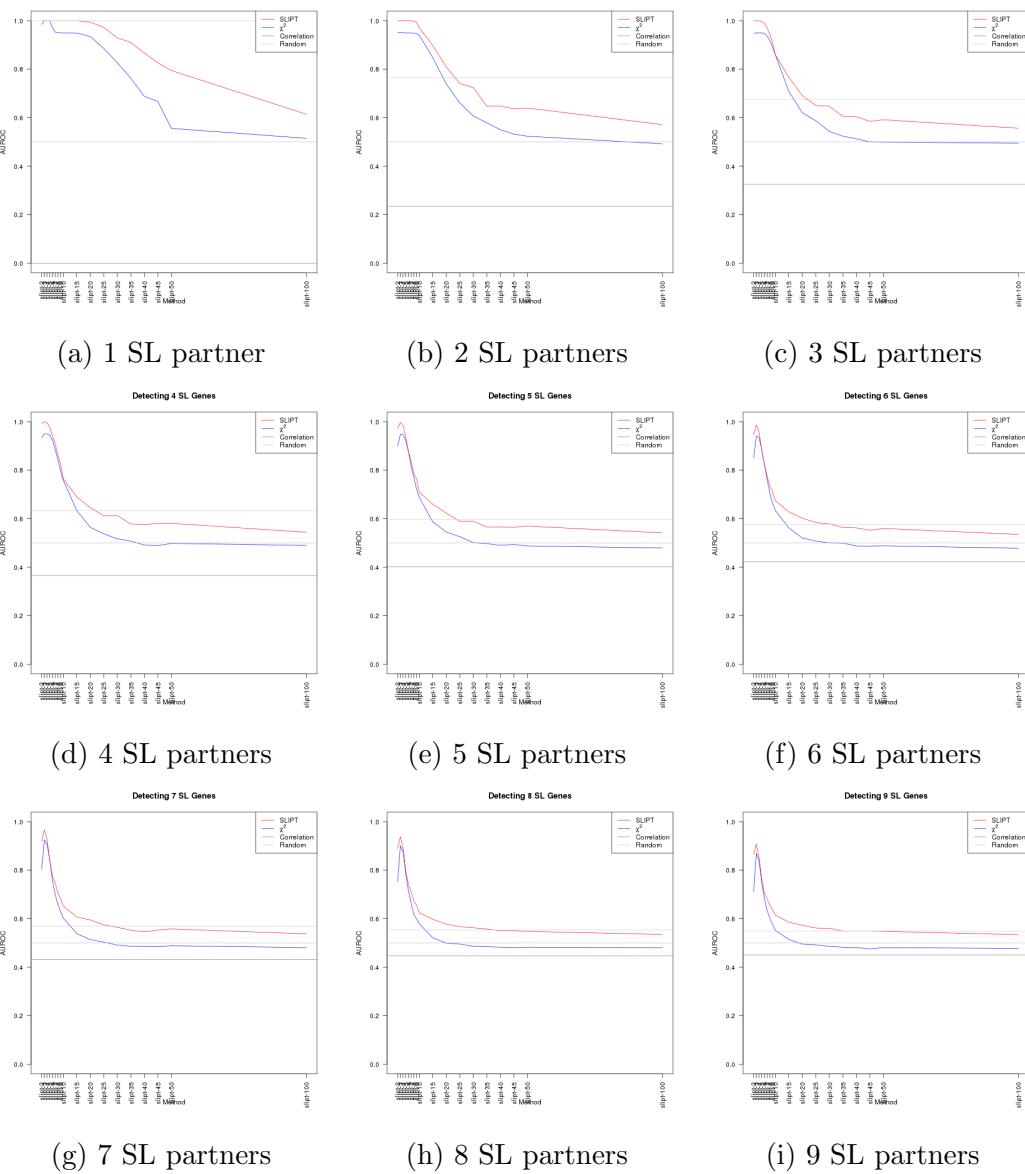


Figure N.6: Performance of χ^2 and SLIPT across quantiles with query correlation and more genes. (continued on next page)

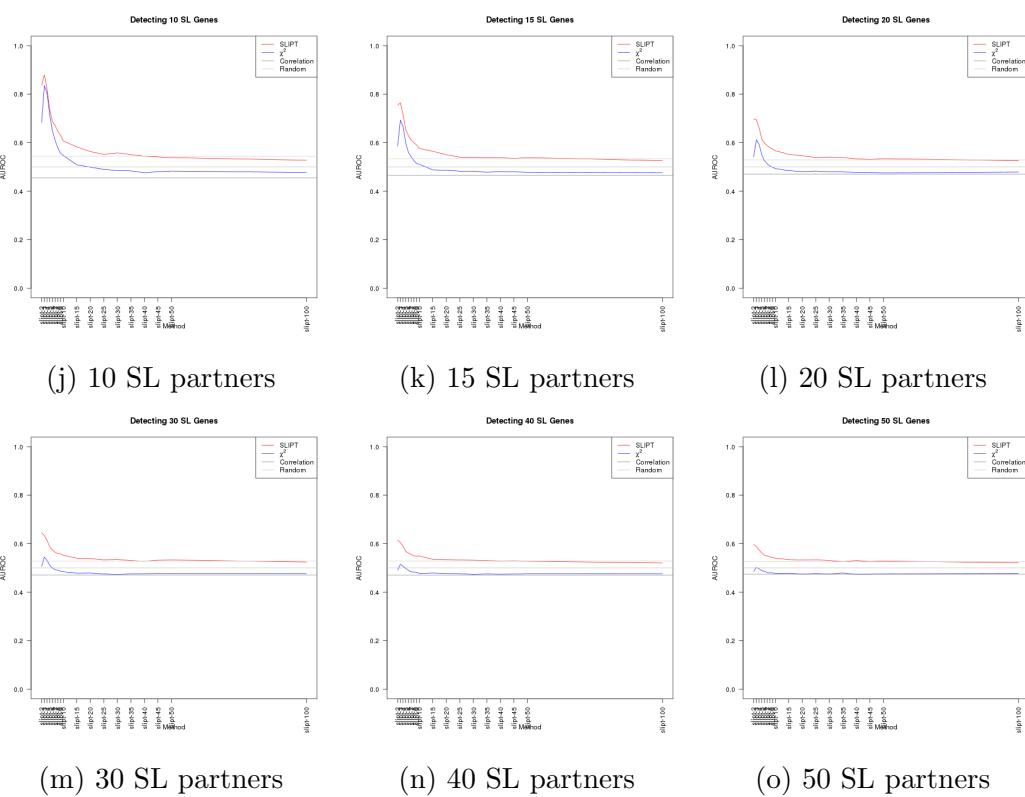


Figure N.6: Performance of χ^2 and SLIPT across quantiles with query correlation and more genes. Synthetic lethal detection with quantiles as in axis labels. The line plots are coloured for SLIPT (red), χ^2 (blue) and correlation (grey) according to the legend. SLIPT and χ^2 perform similarly, peaking at $\frac{1}{3}$ -quantiles and converging to random (0.5). Negative correlation was higher than positive but not optimal quantiles for SLIPT or χ^2 . These findings are robust across different numbers of underlying synthetic lethal genes in 1000 simulations of 20,000 genes (including 1000 correlated with the query) and 1000 samples. SLIPT performs consistently better than χ^2 with positively correlated genes.

Appendix O

Graph Structures

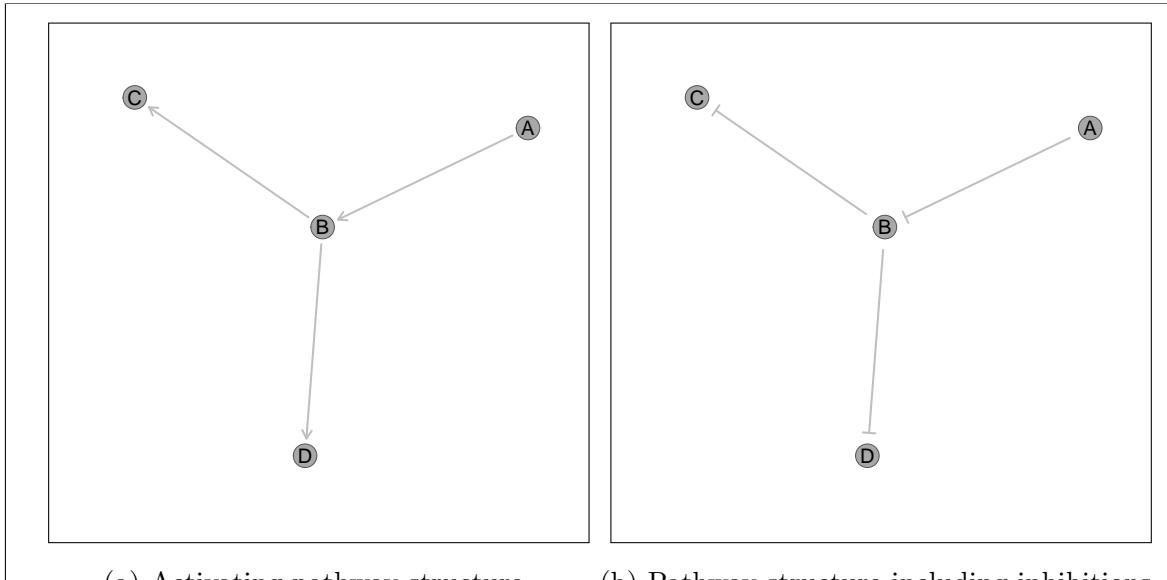
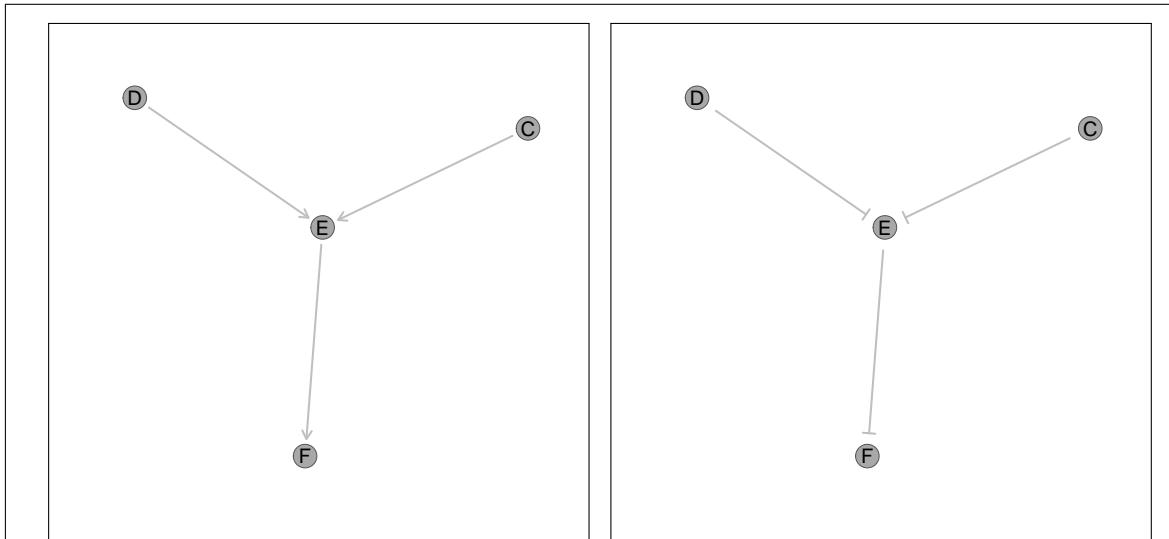
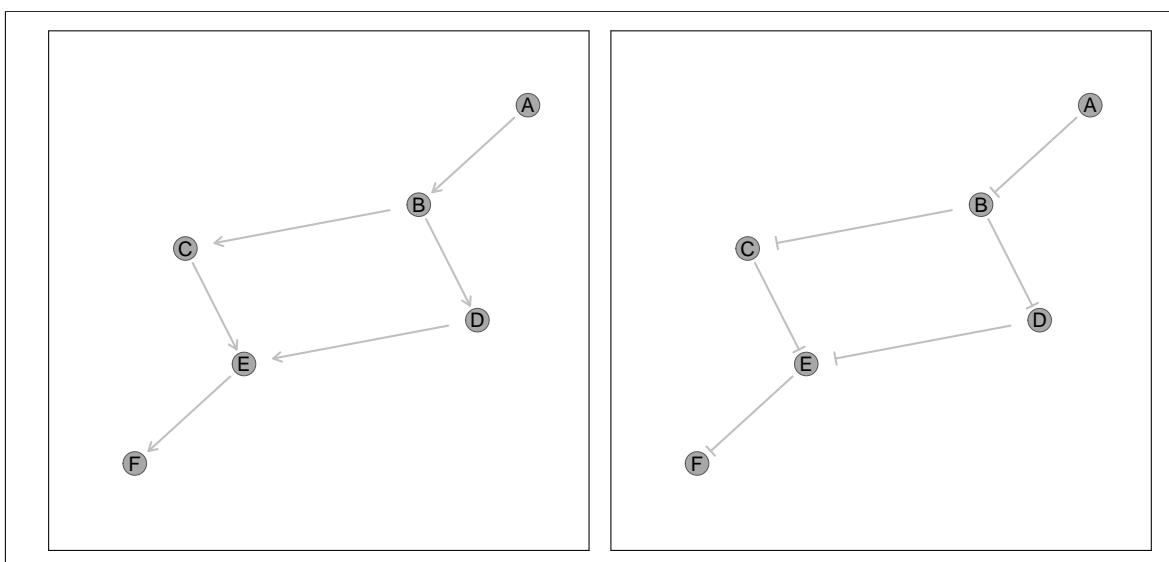


Figure O.1: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.



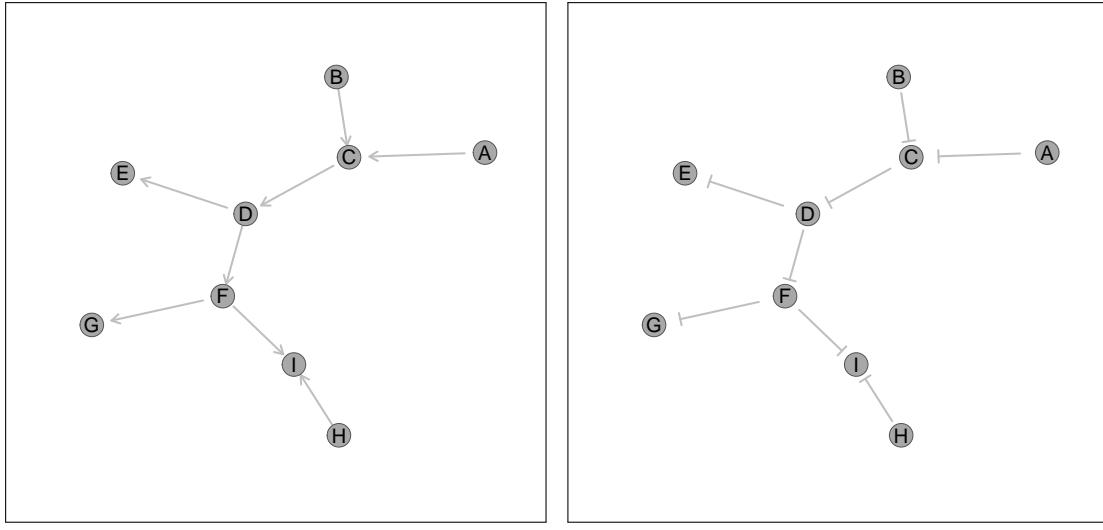
(a) Activating pathway structure (b) Pathway structure including inhibitions

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.

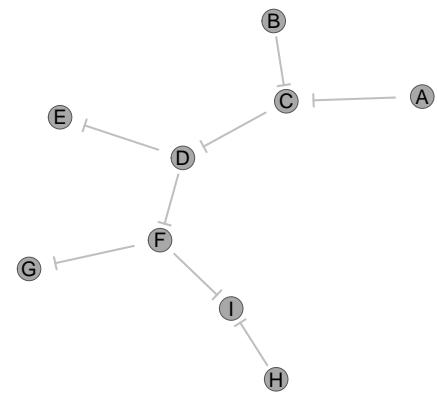


(a) Activating pathway structure (b) Pathway structure including inhibitions

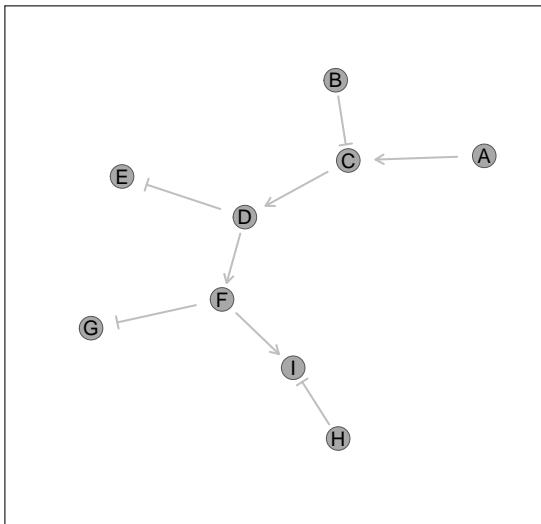
Figure O.3: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.



(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.

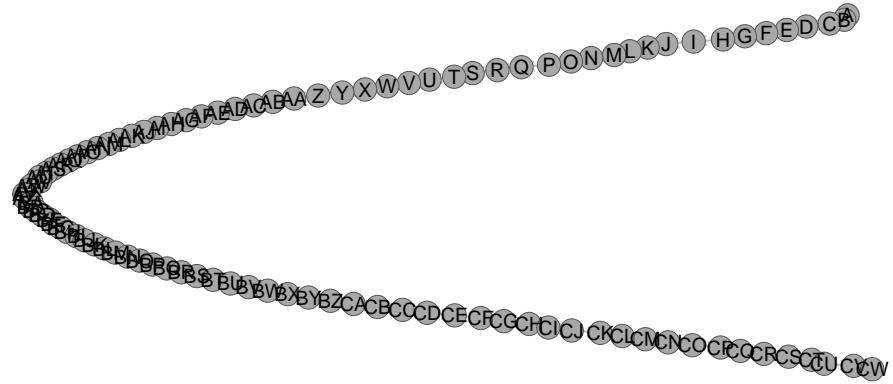


Figure O.5: Simulated graph structures. A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

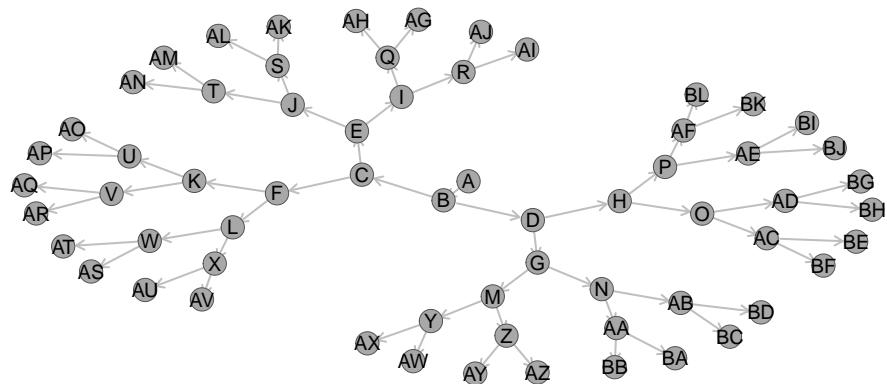


Figure O.6: Simulated graph structures. A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

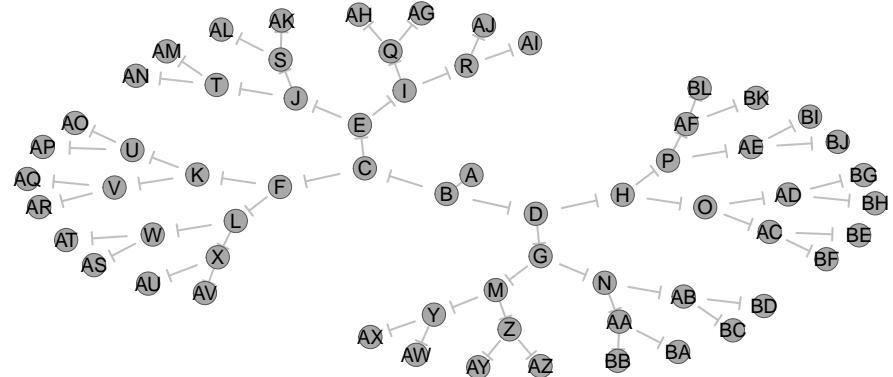


Figure O.7: Simulated graph structures. A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

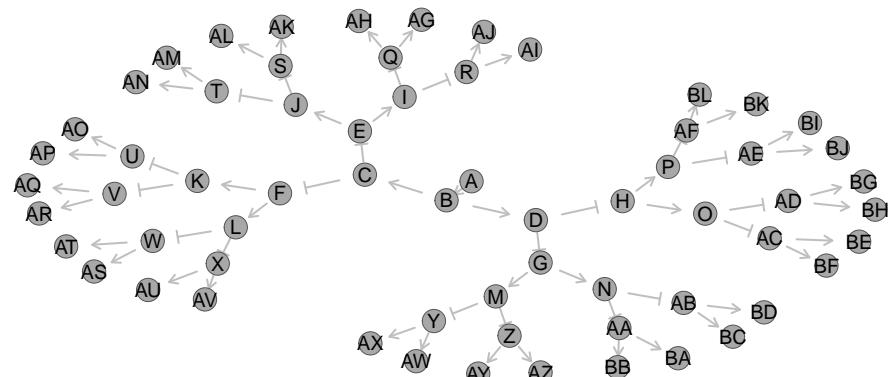


Figure O.8: Simulated graph structures. A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

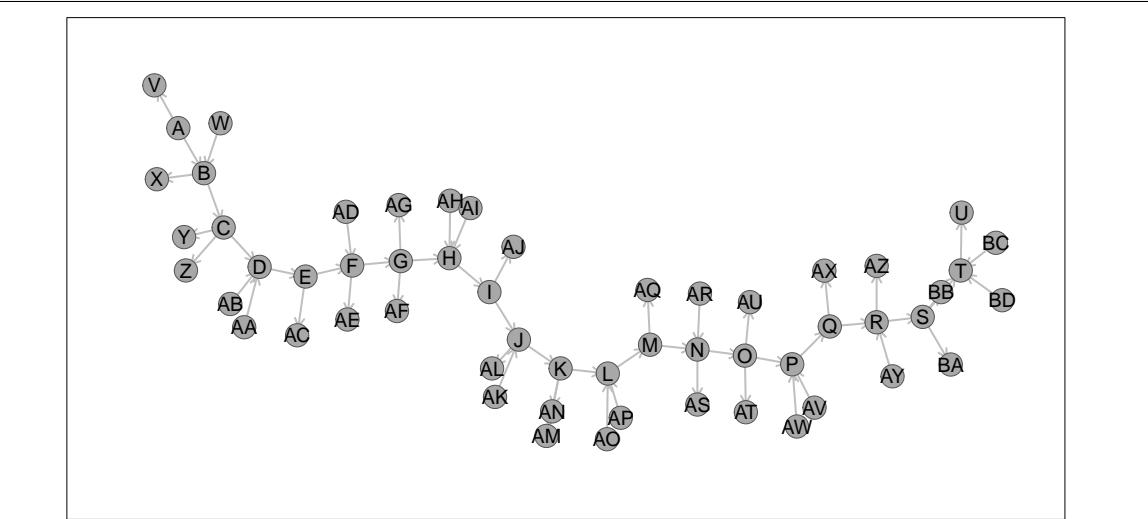


Figure O.9: Simulated graph structures. A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

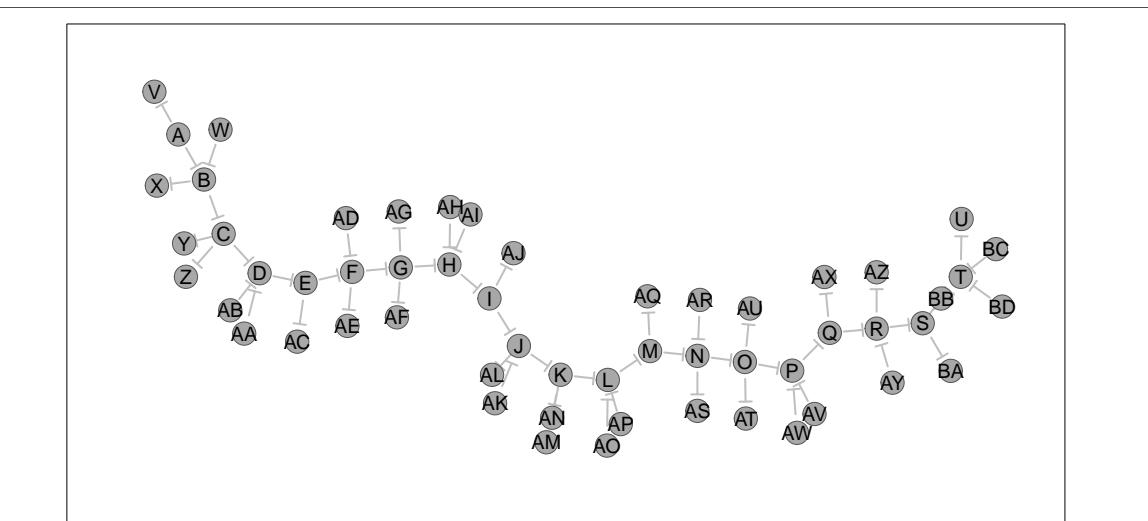


Figure O.10: Simulated graph structures. A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

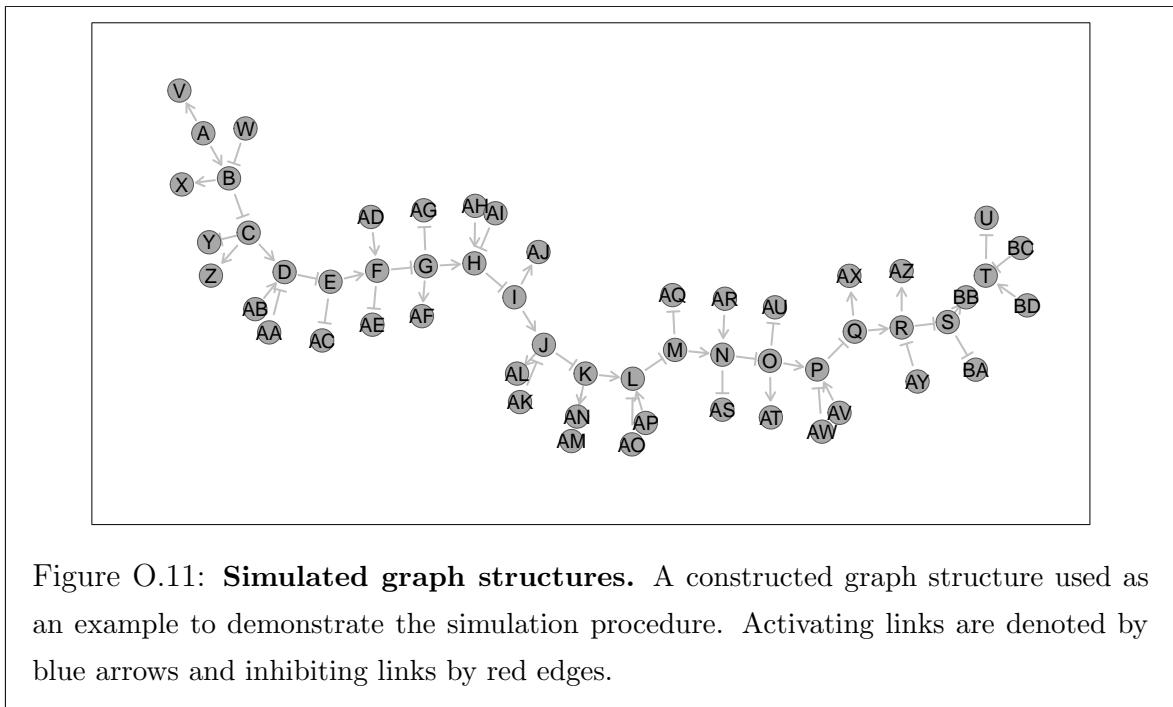
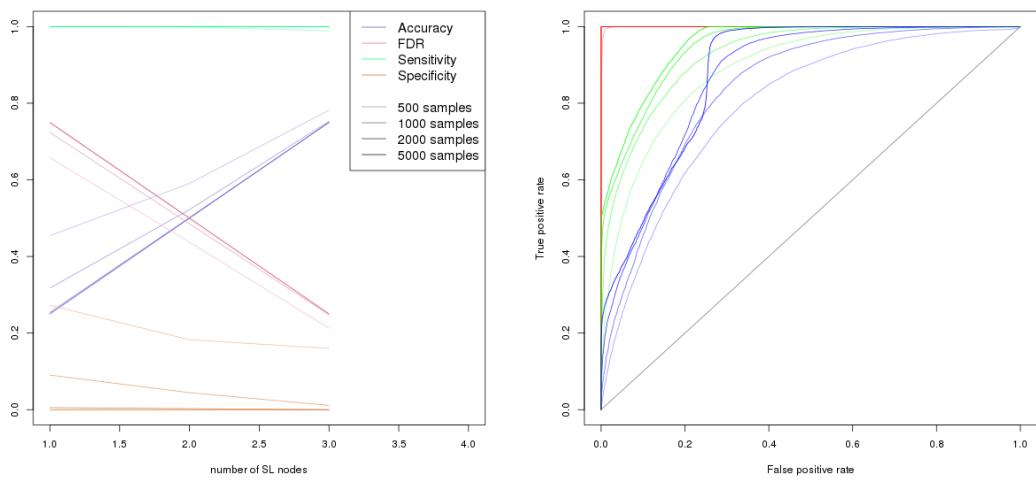


Figure O.11: **Simulated graph structures.** A constructed graph structure used as an example to demonstrate the simulation procedure. Activating links are denoted by blue arrows and inhibiting links by red edges.

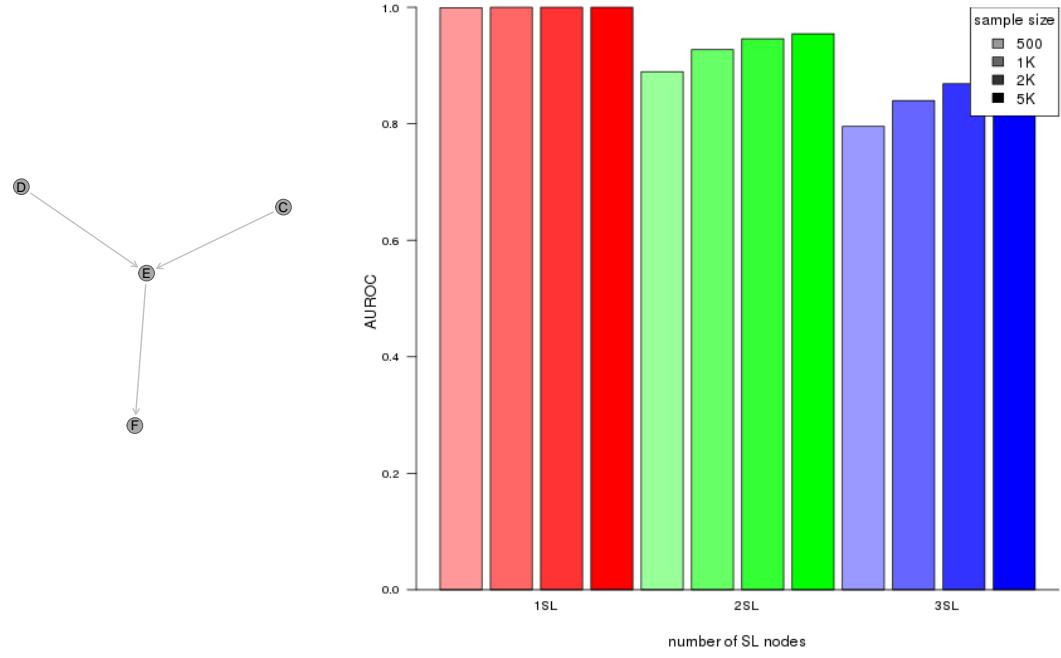
Appendix P

Graph Simulations



(a) Statistical evaluation

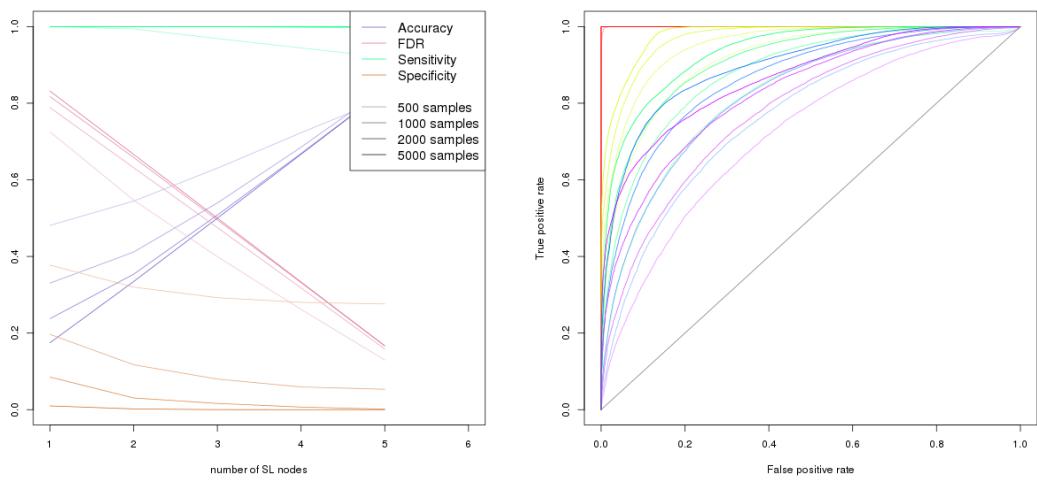
(b) Receiver operating characteristic



(c) Graph Structure

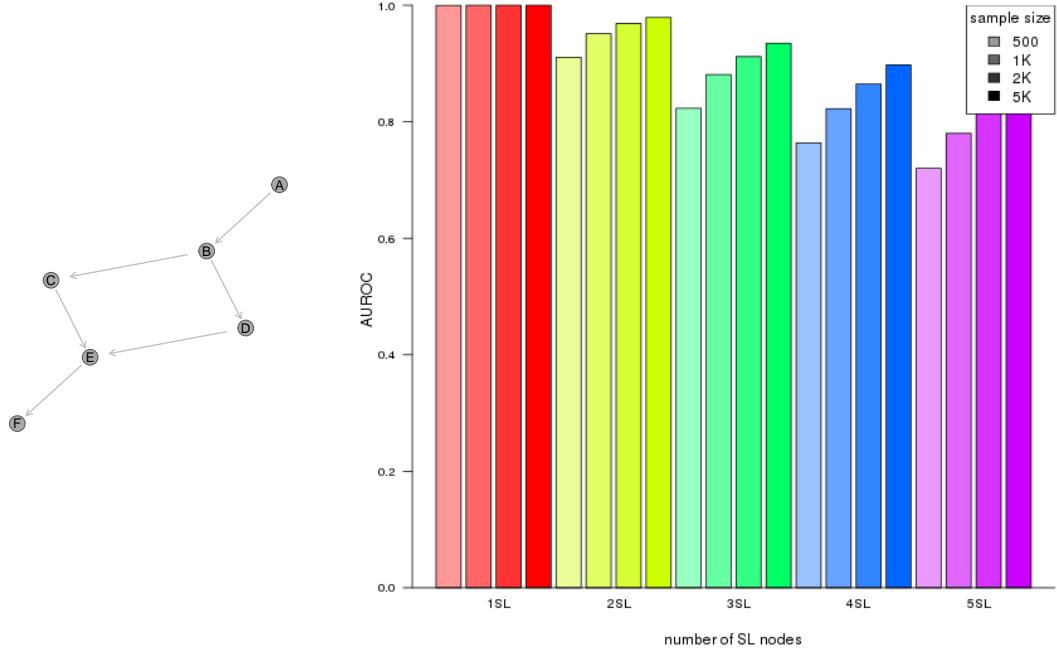
(d) Statistical performance

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

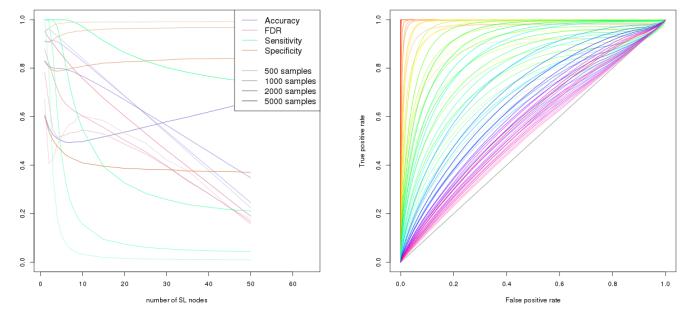
(b) Receiver operating characteristic



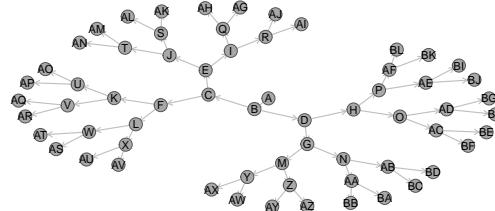
(c) Graph Structure

(d) Statistical performance

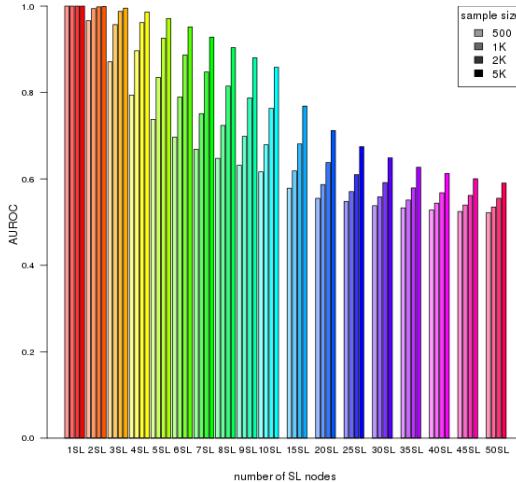
Figure P.2: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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

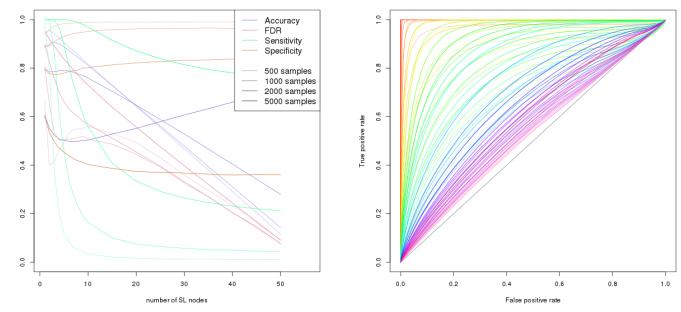


(c) Graph Structure

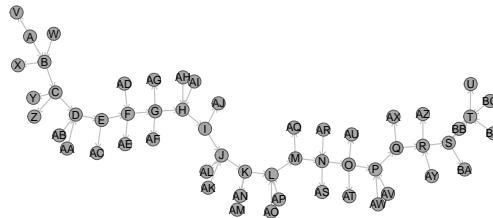


(d) Statistical performance

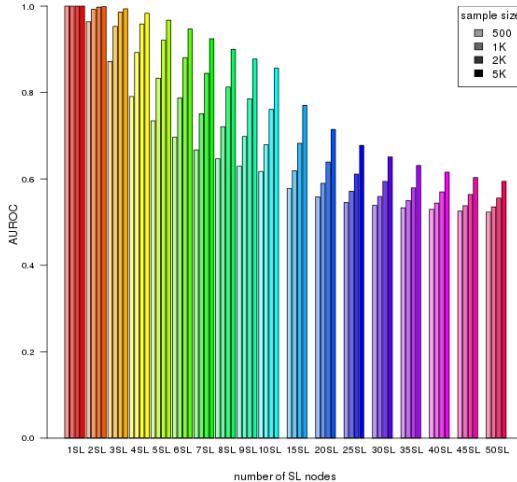
Figure P.3: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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

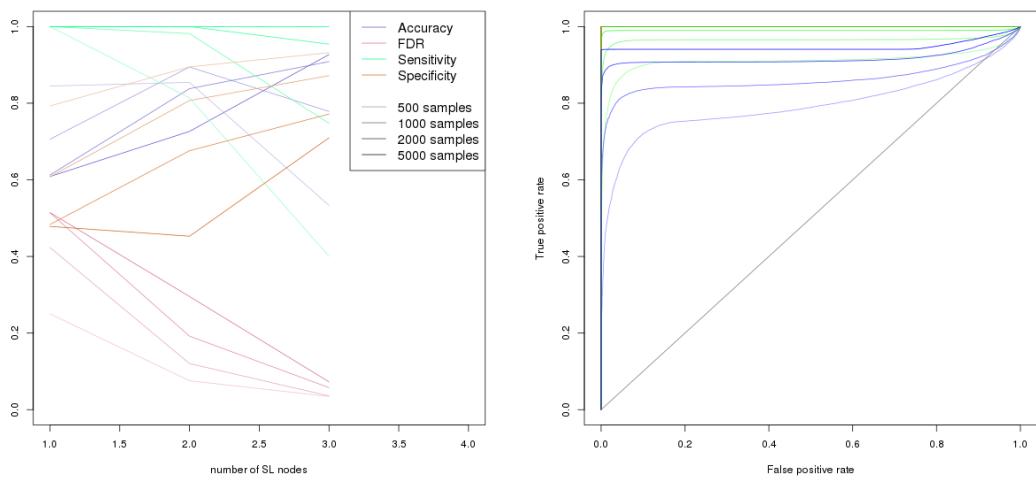


(d) Statistical performance

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.

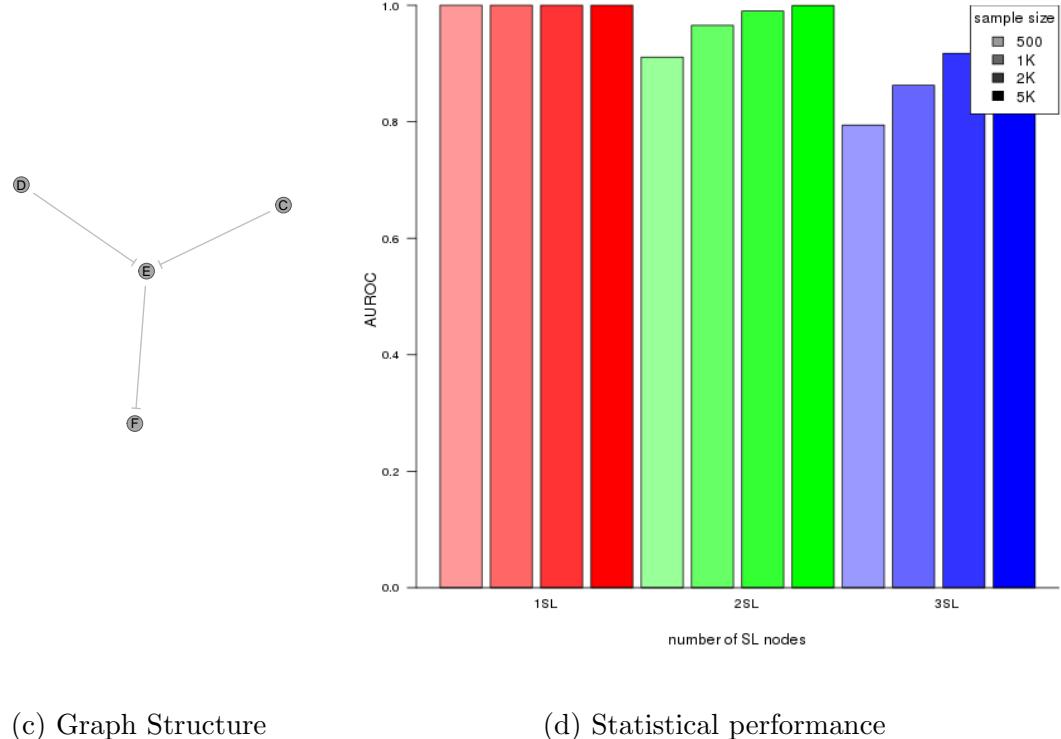
Appendix Q

Graph Simulations with Inhibition



(a) Statistical evaluation

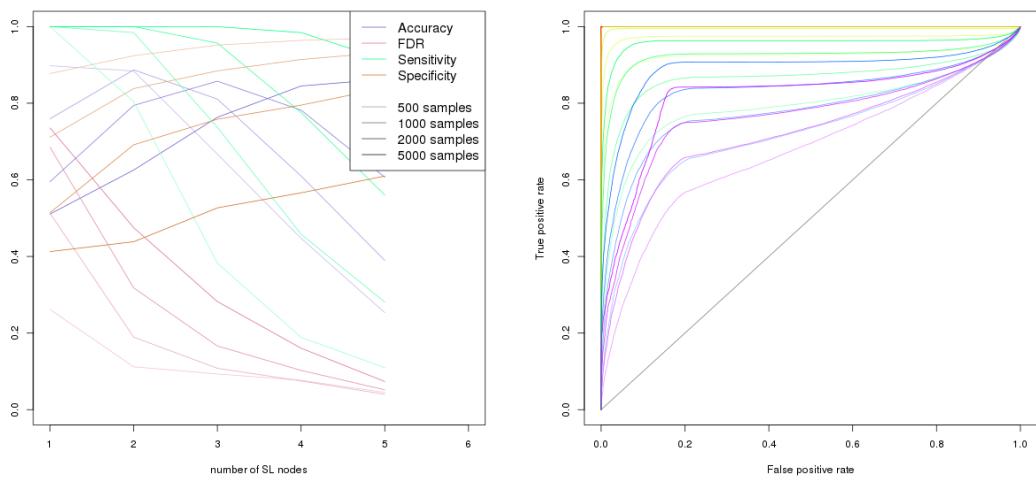
(b) Receiver operating characteristic



(c) Graph Structure

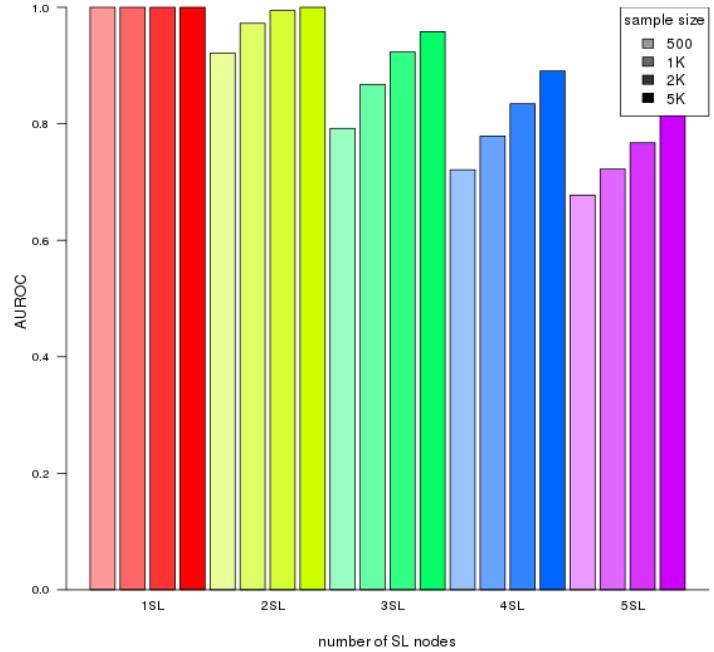
(d) Statistical performance

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

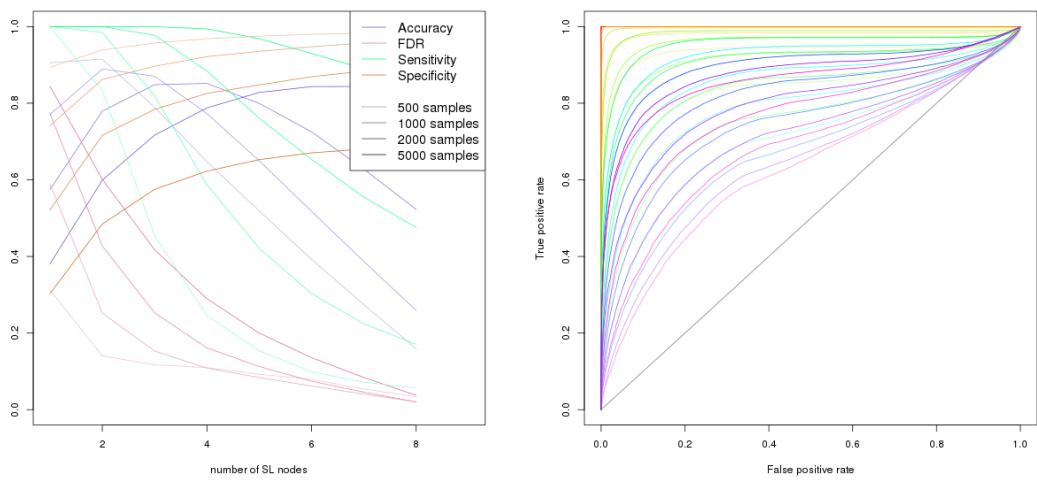
(b) Receiver operating characteristic



(c) Graph Structure

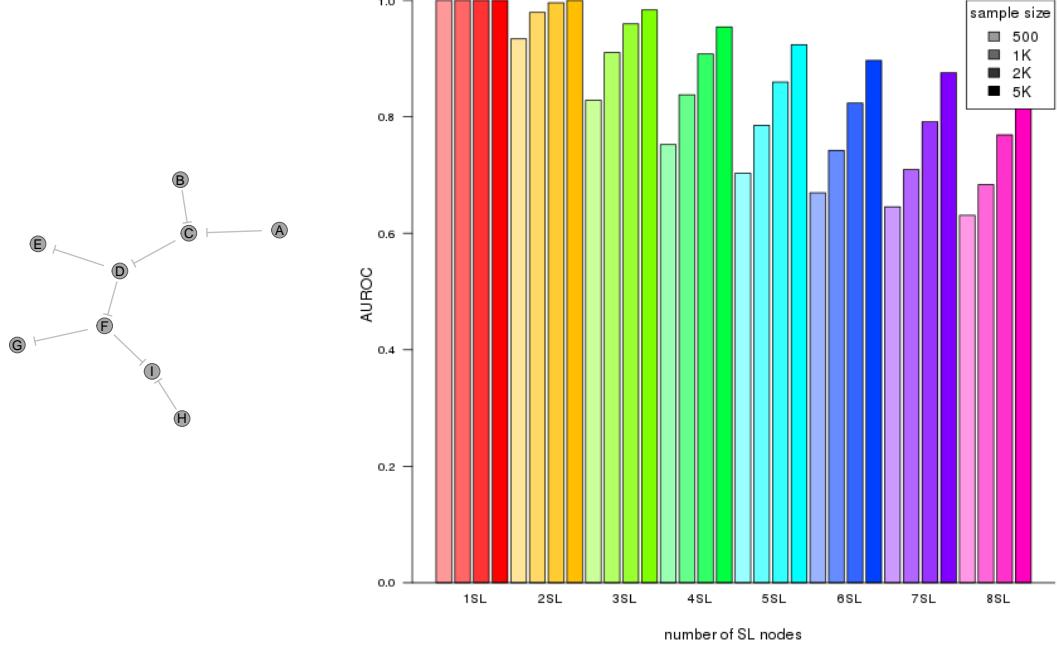
(d) Statistical performance

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

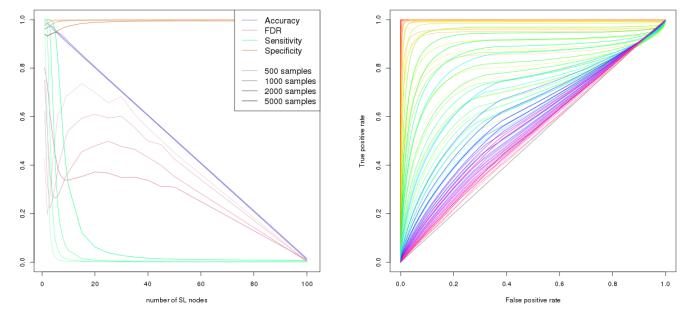
(b) Receiver operating characteristic



(c) Graph Structure

(d) Statistical performance

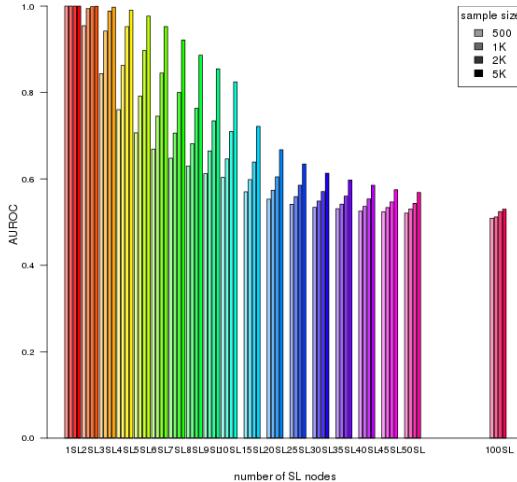
Figure Q.3: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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

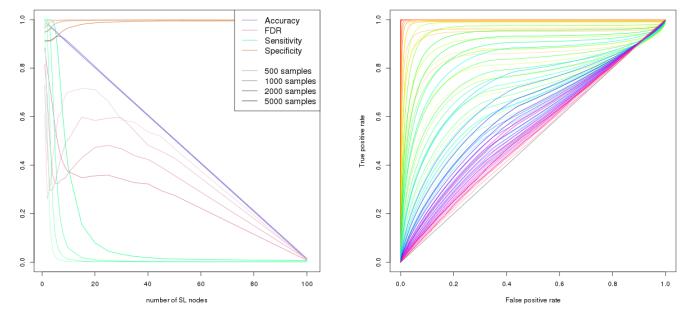


(c) Graph Structure



(d) Statistical performance

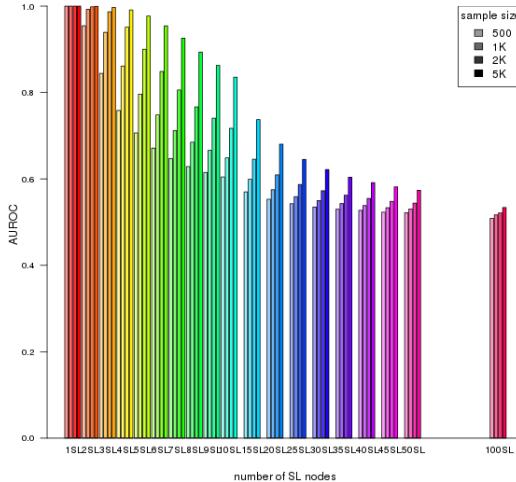
Figure Q.4: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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

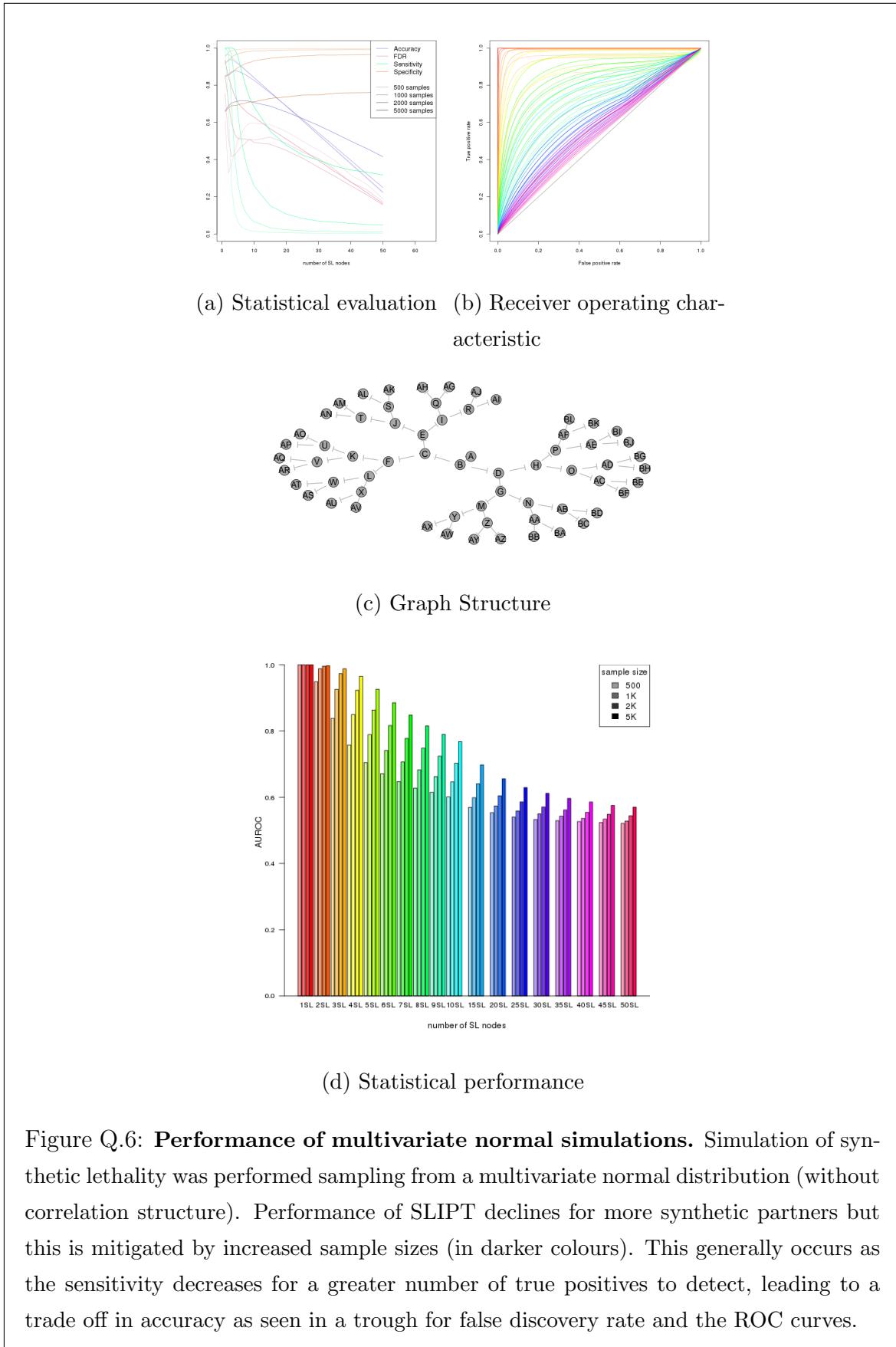


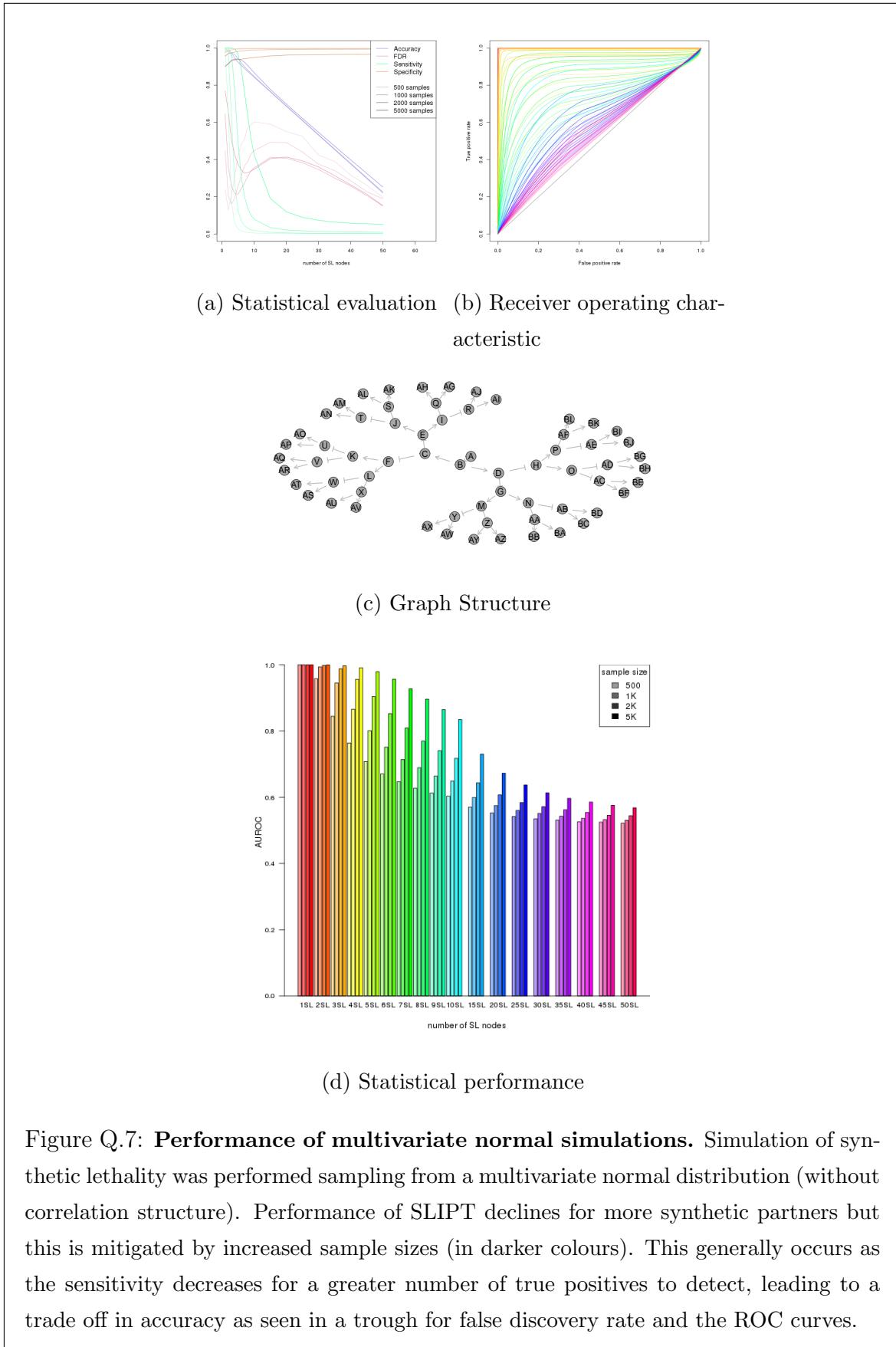
(c) Graph Structure

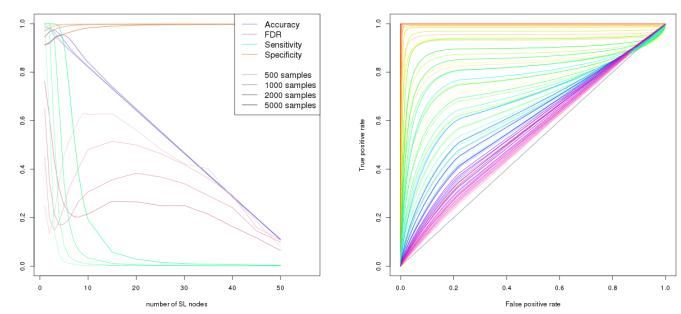


(d) Statistical performance

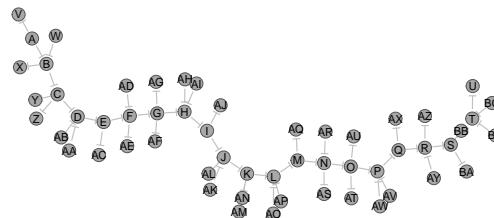
Figure Q.5: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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.



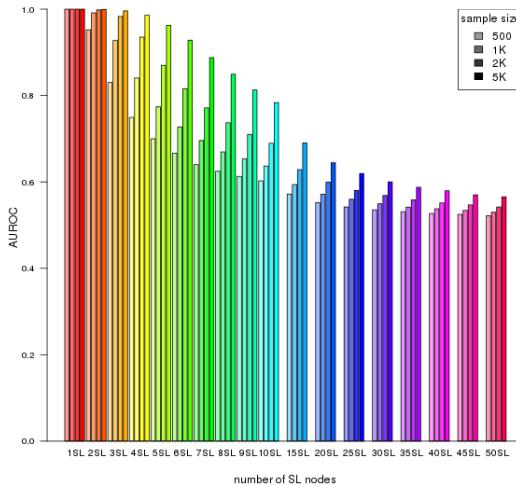




(a) Statistical evaluation (b) Receiver operating characteristic

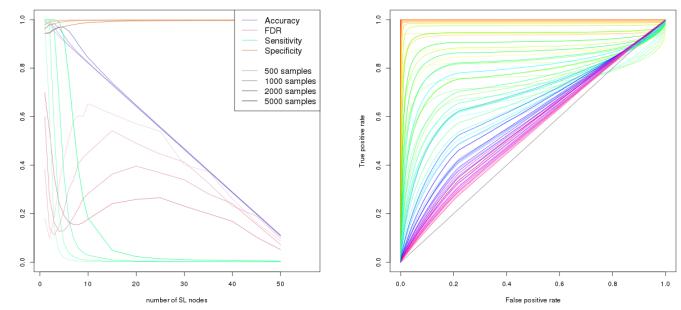


(c) Graph Structure

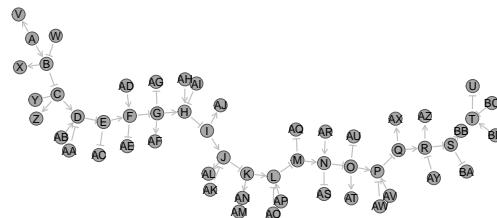


(d) Statistical performance

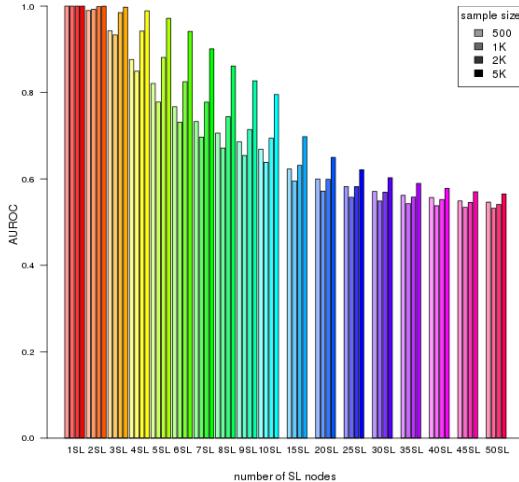
Figure Q.8: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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

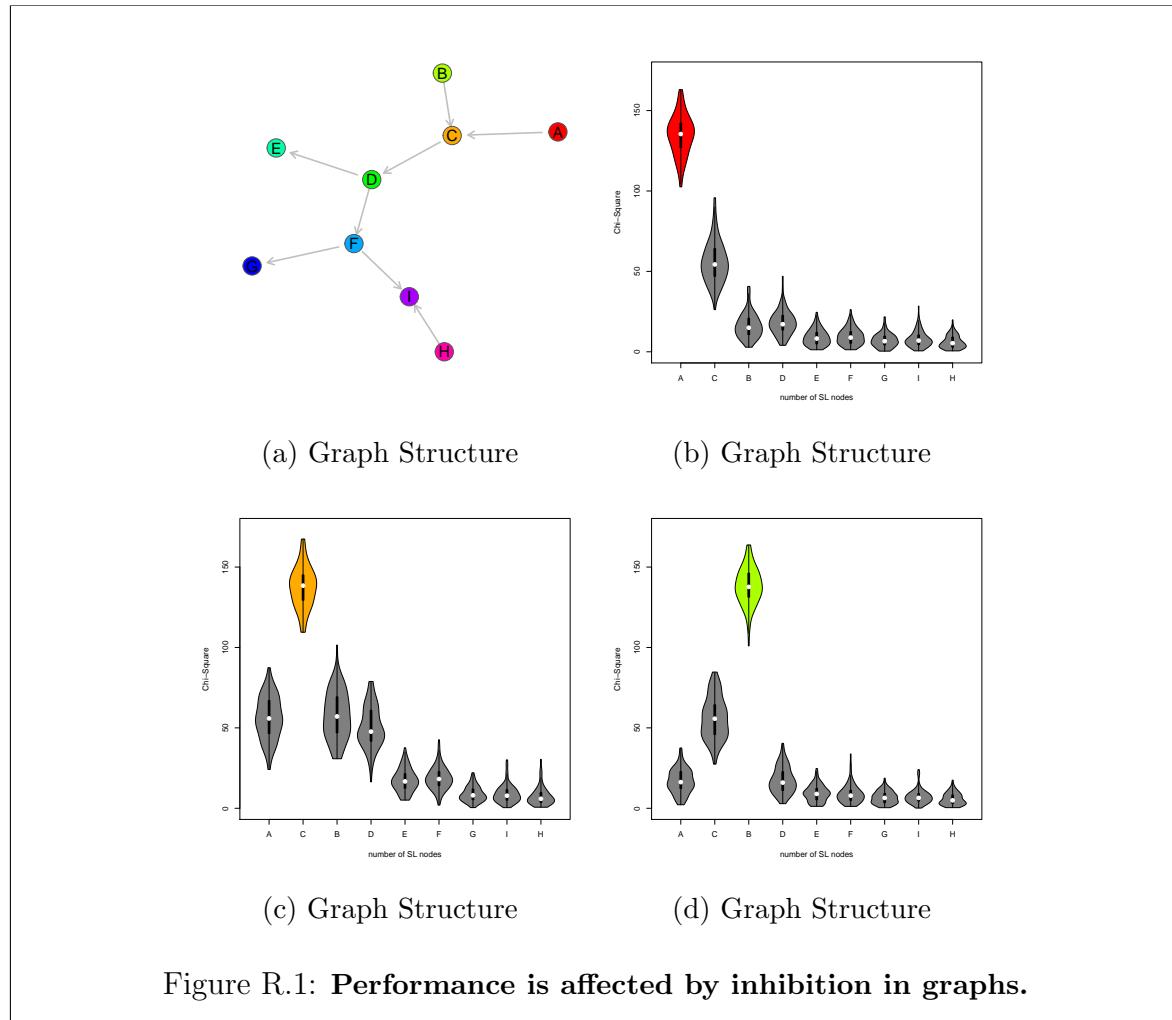


(d) Statistical performance

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

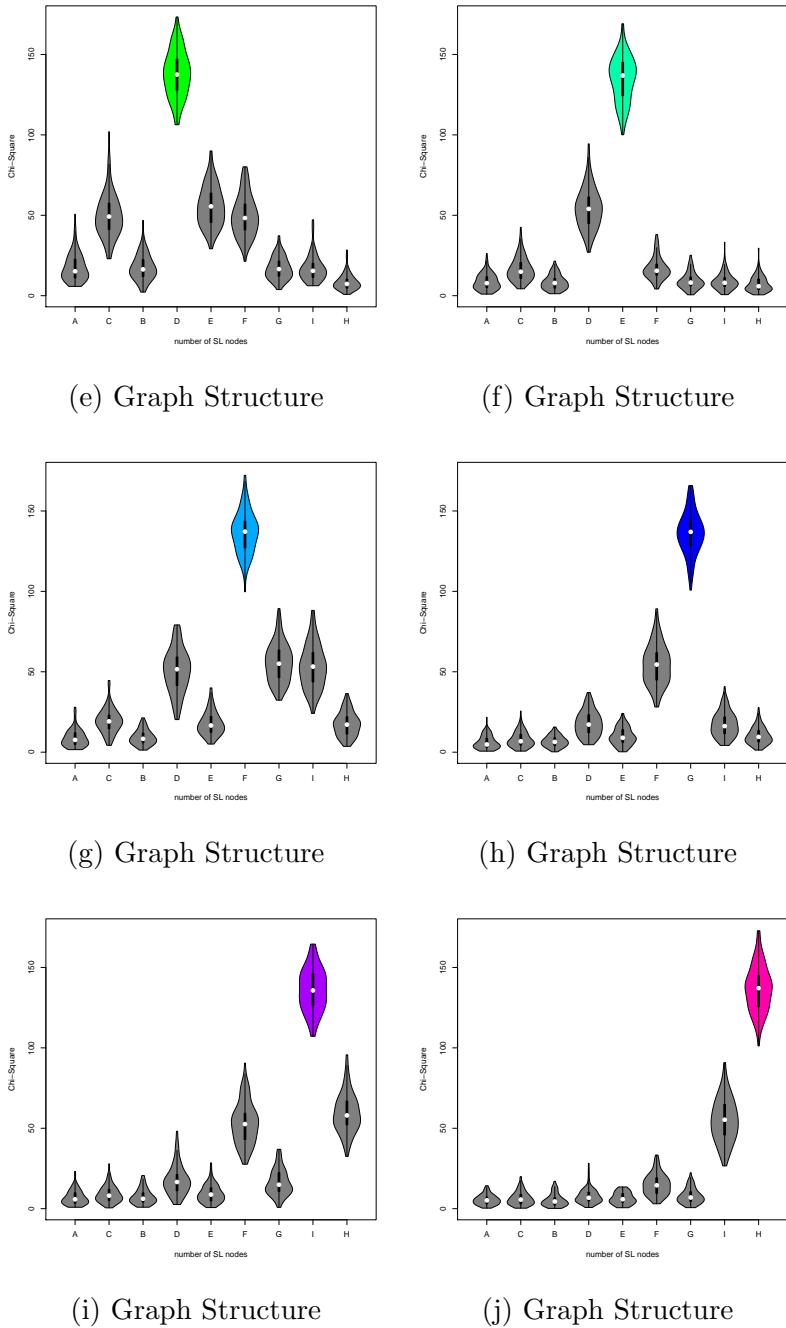
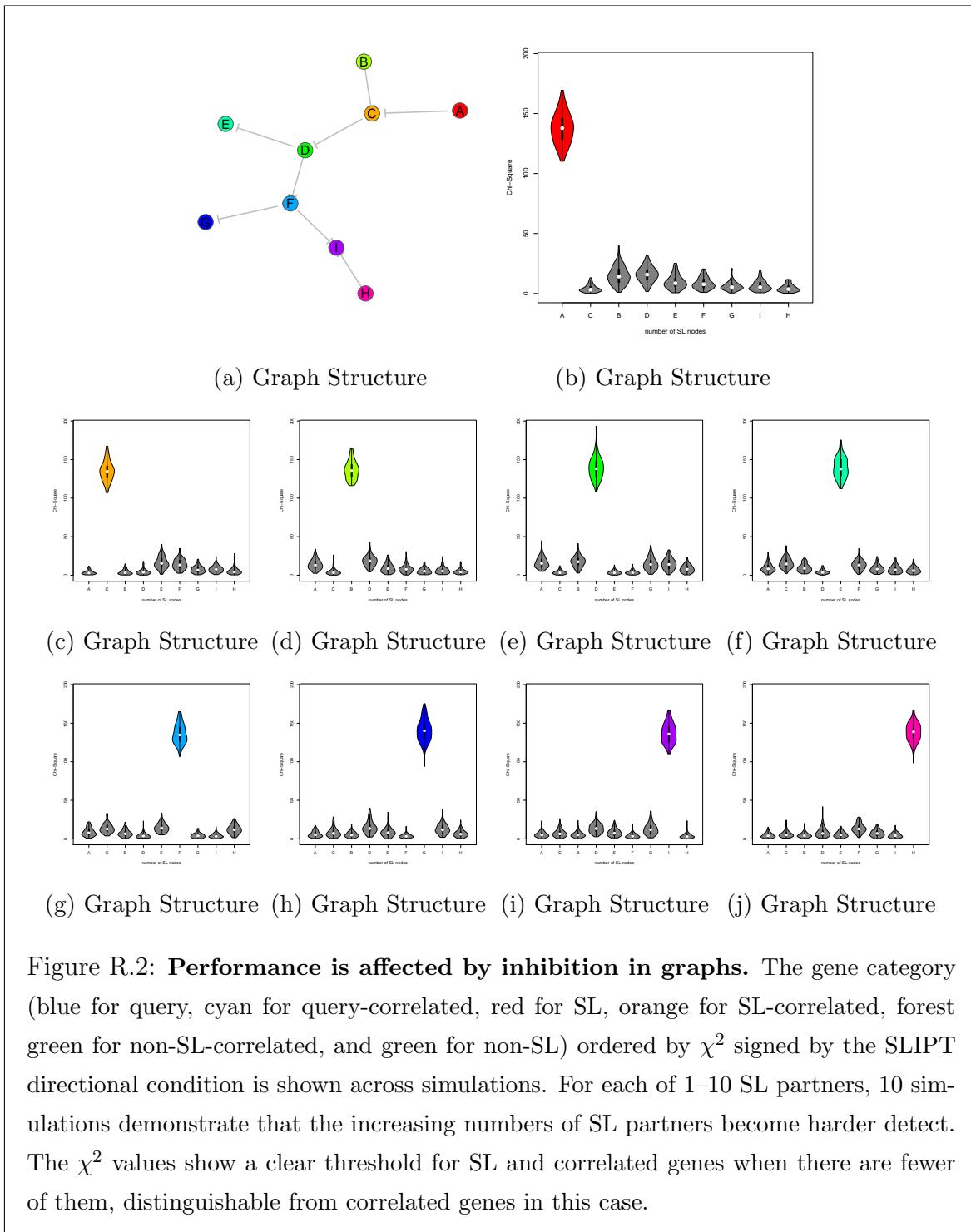
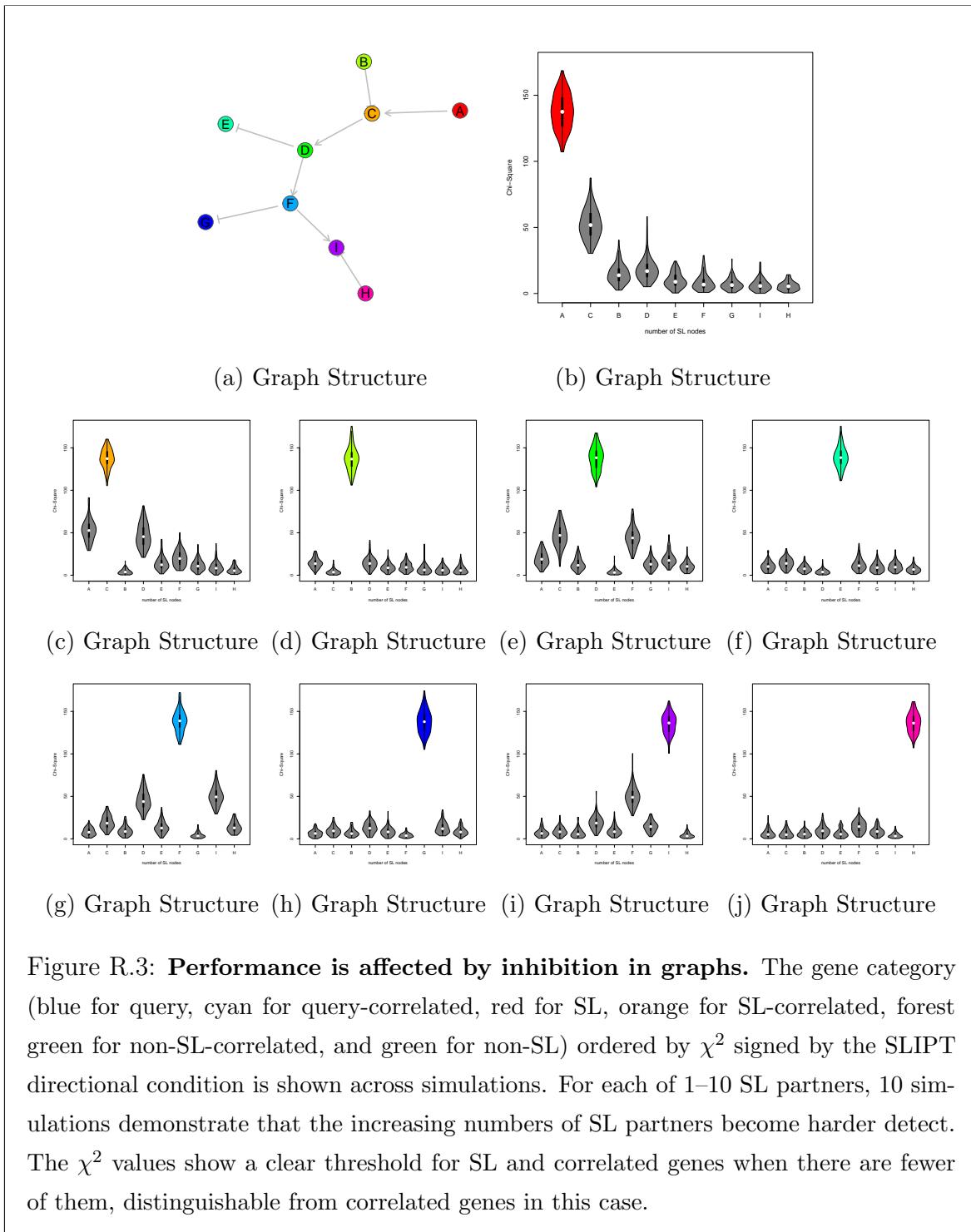


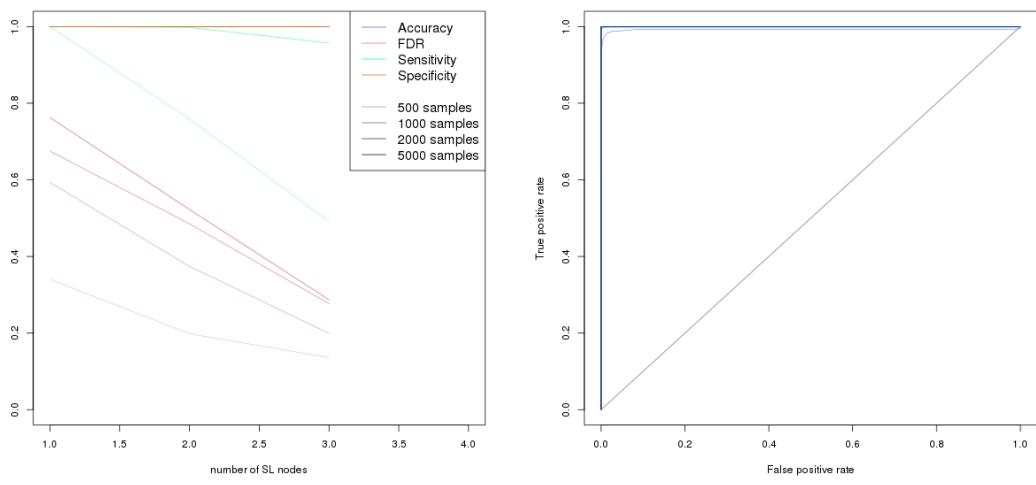
Figure R.1: Performance is affected by inhibition in graphs. The gene category (blue for query, cyan for query-correlated, red for SL, orange for SL-correlated, forest green for non-SL-correlated, and green for non-SL).





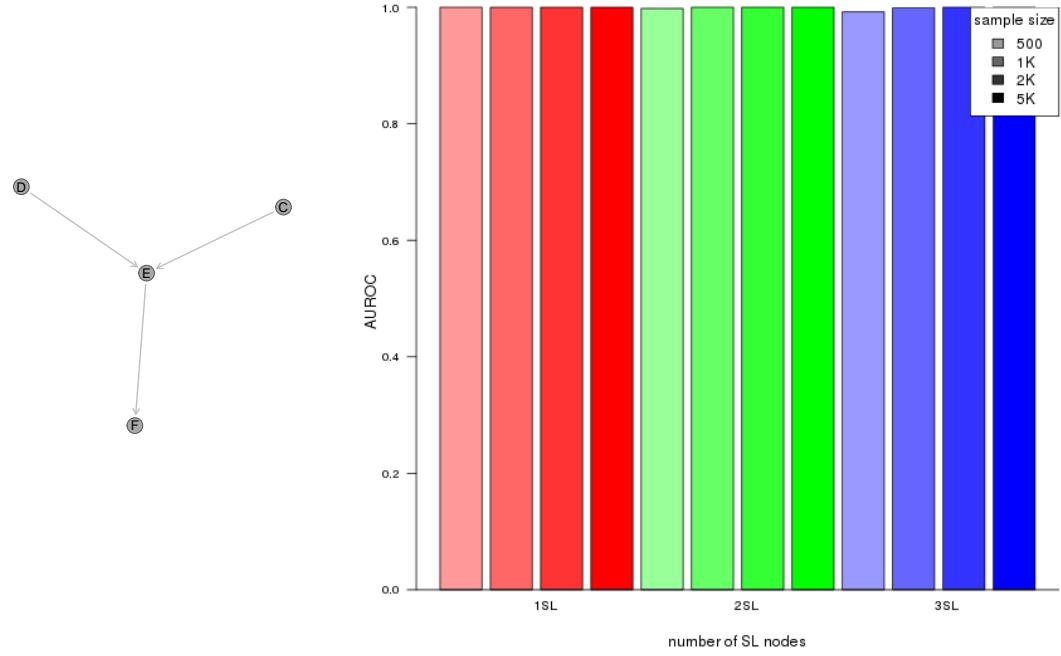
Appendix S

Graph Simulations 20K genes



(a) Statistical evaluation

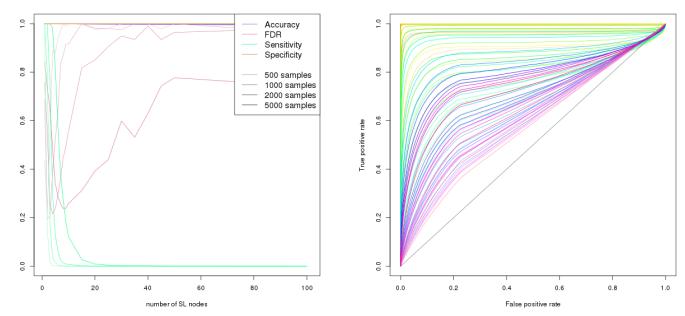
(b) Receiver operating characteristic



(c) Graph Structure

(d) Statistical performance

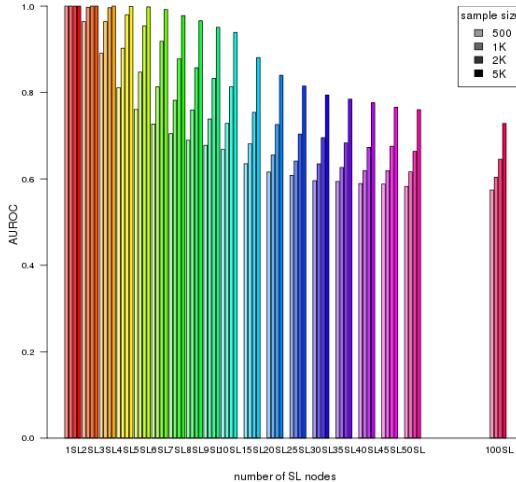
Figure S.1: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in 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

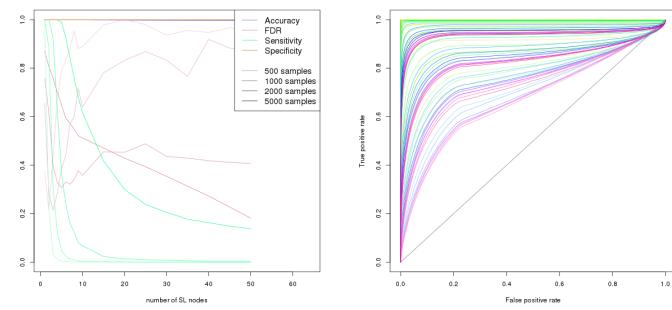


(c) Graph Structure

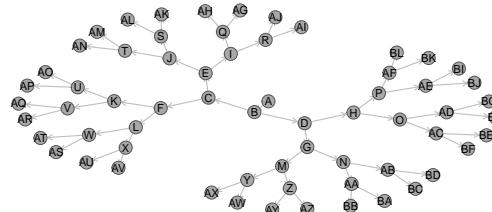


(d) Statistical performance

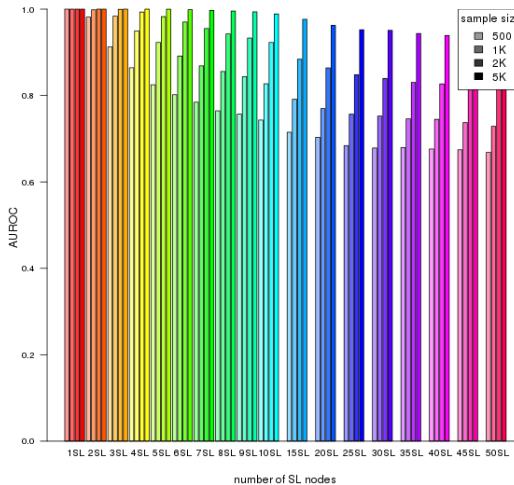
Figure S.2: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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

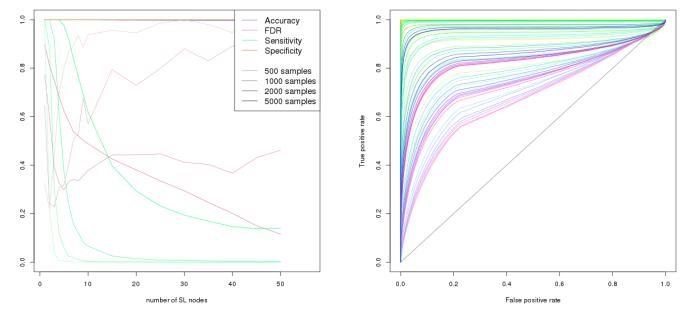


(c) Graph Structure

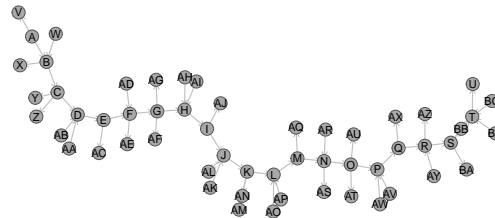


(d) Statistical performance

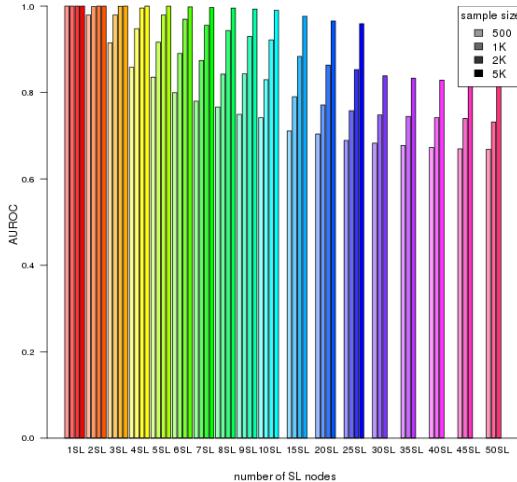
Figure S.3: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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

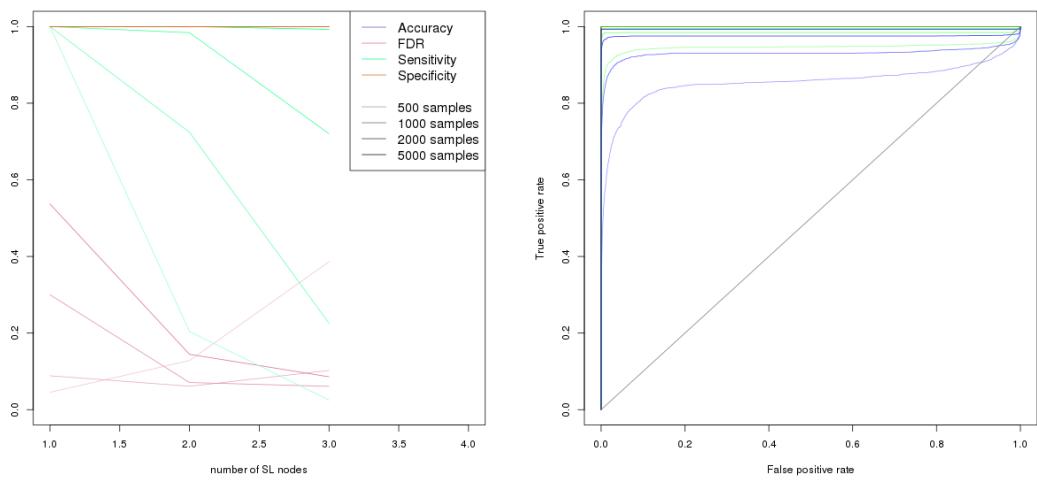


(d) Statistical performance

Figure 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.

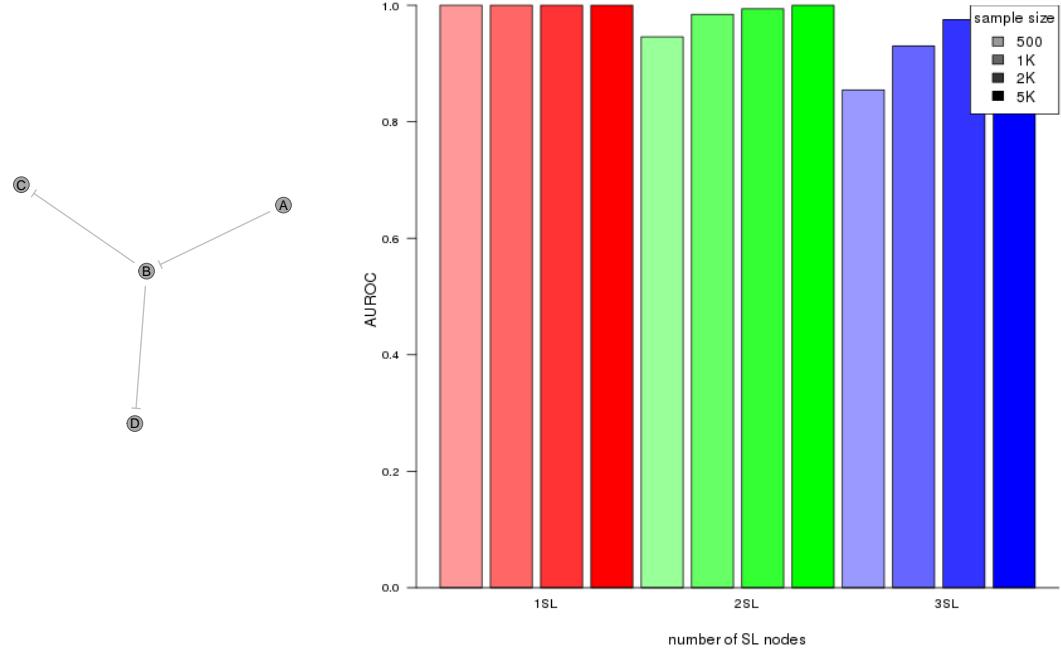
Appendix T

Graph Simulations 20K genes with Inhibition



(a) Statistical evaluation

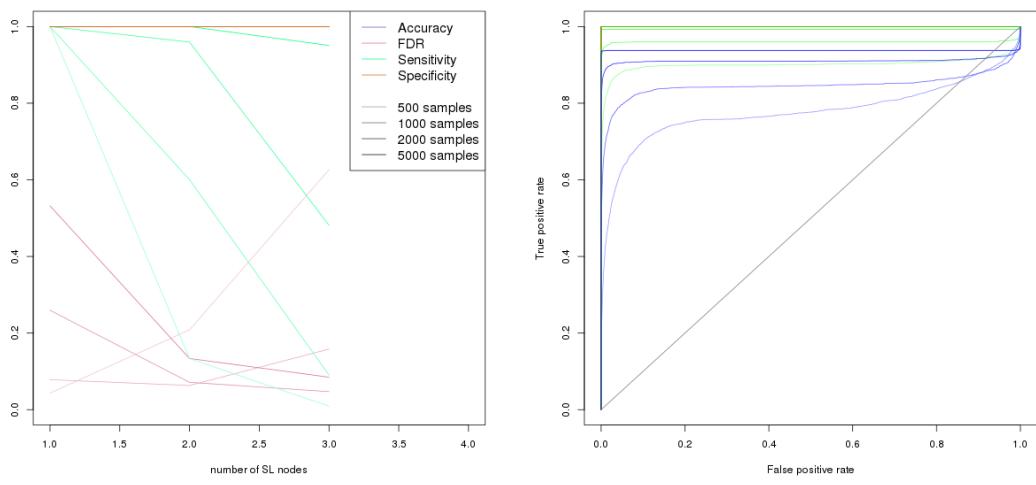
(b) Receiver operating characteristic



(c) Graph Structure

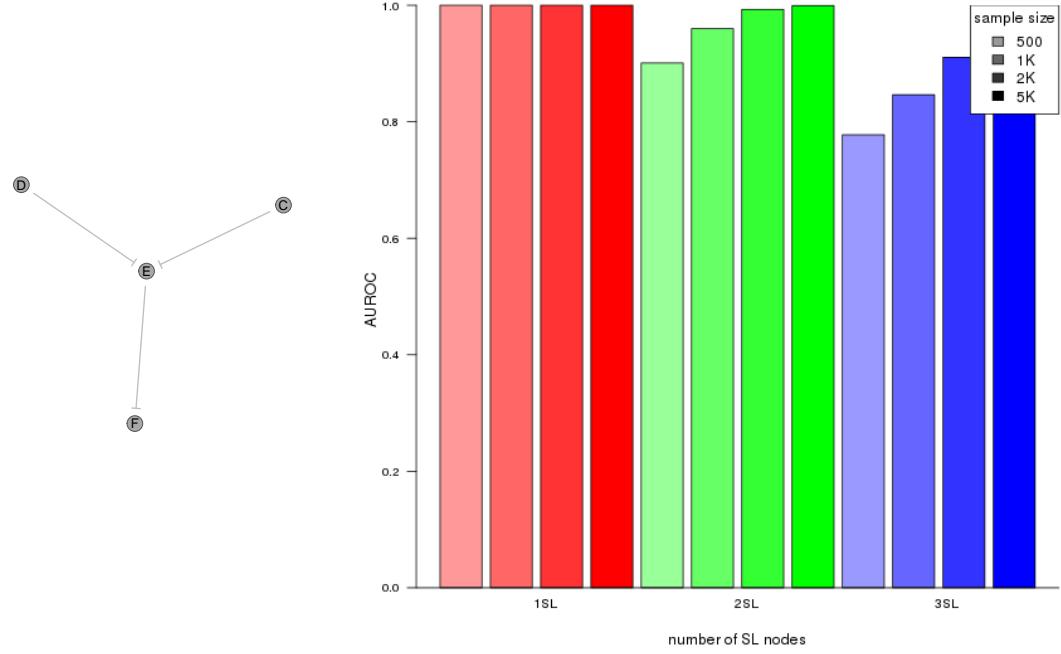
(d) Statistical performance

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

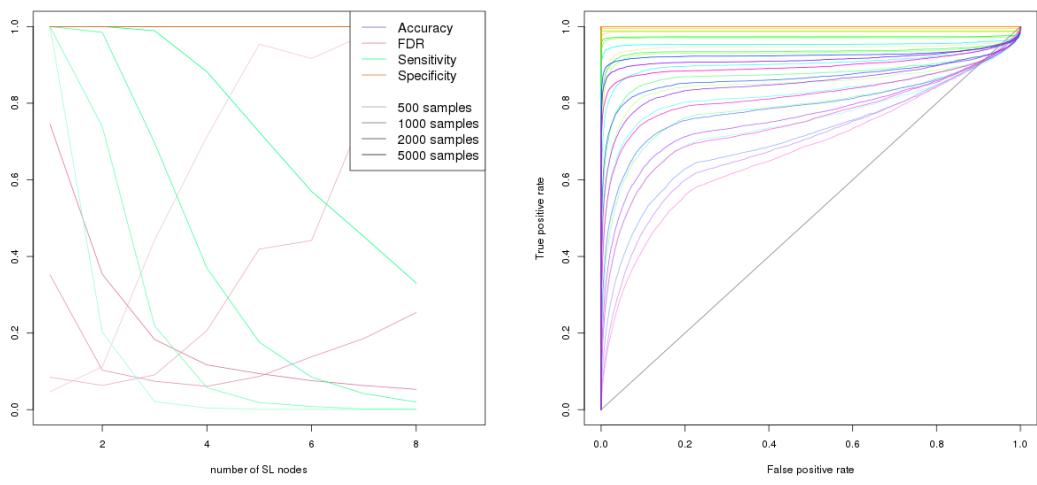
(b) Receiver operating characteristic



(c) Graph Structure

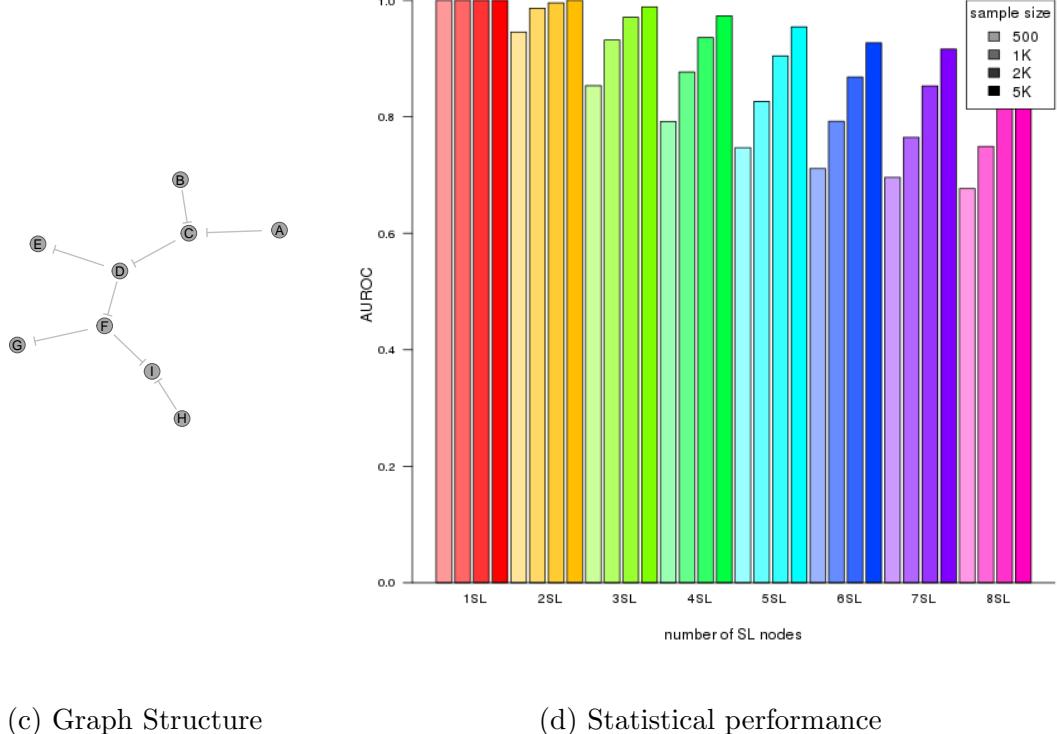
(d) Statistical performance

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

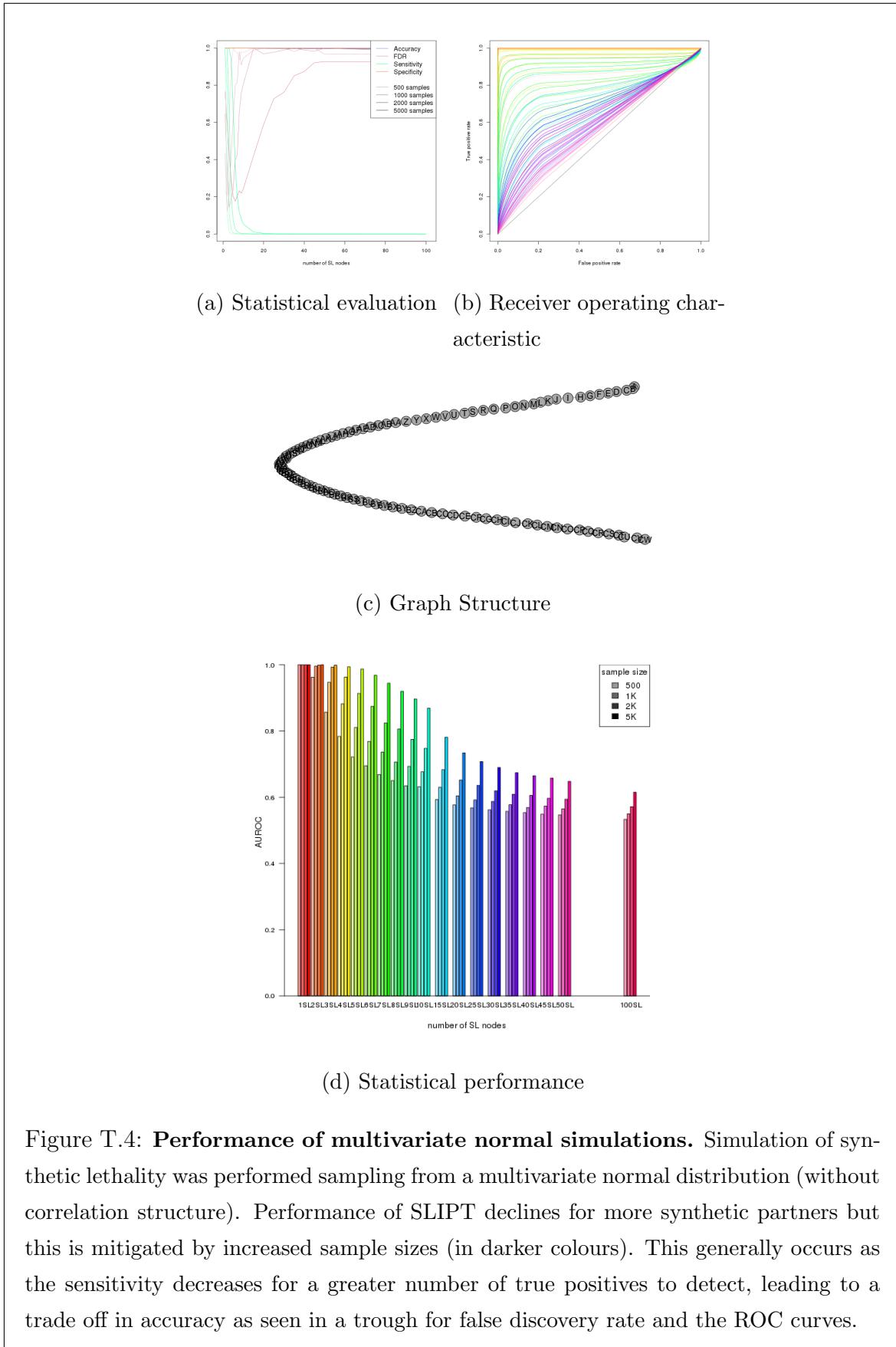
(b) Receiver operating characteristic

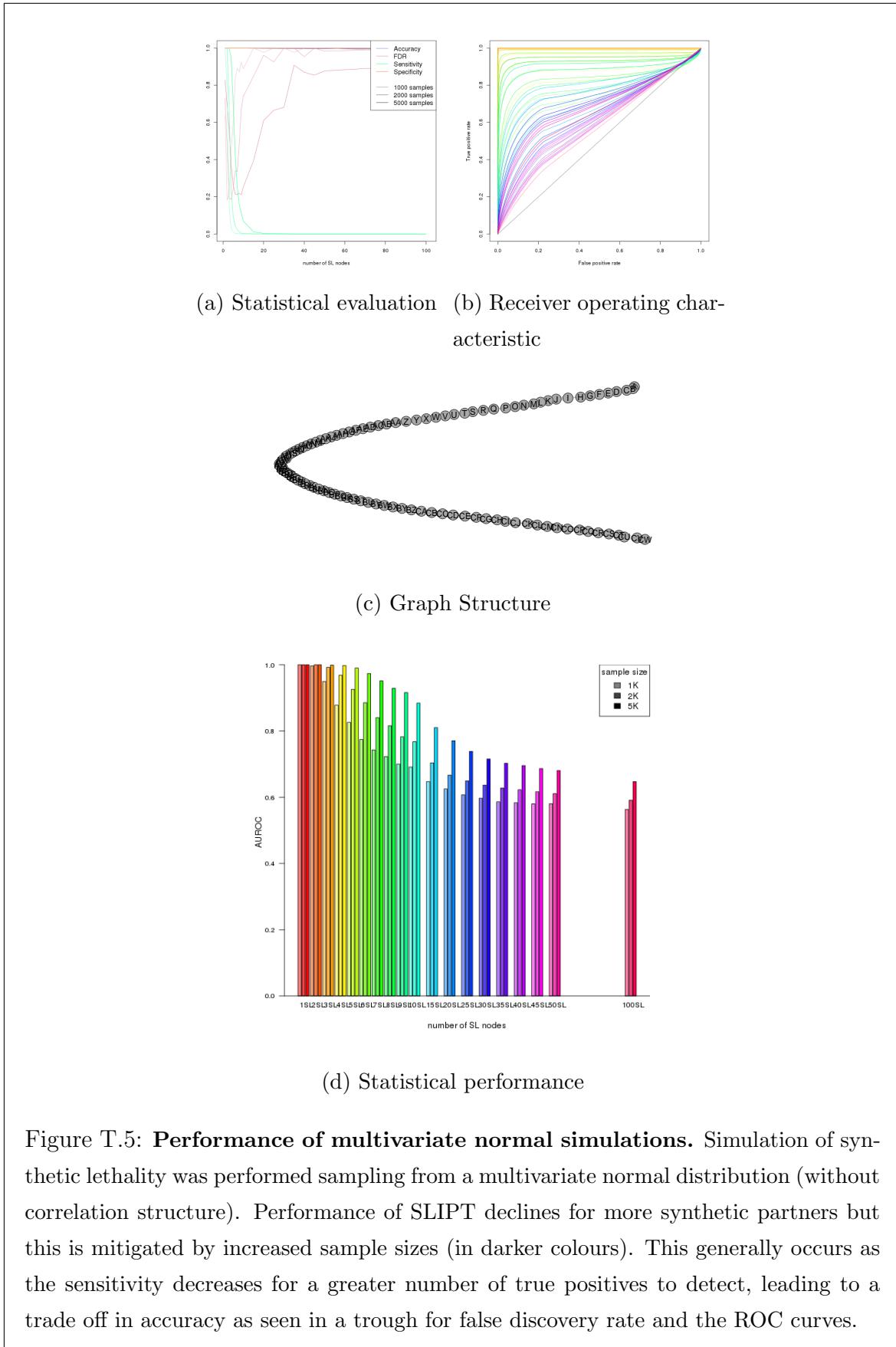


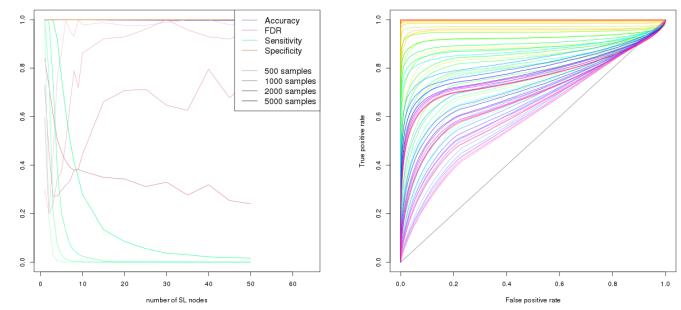
(c) Graph Structure

(d) Statistical performance

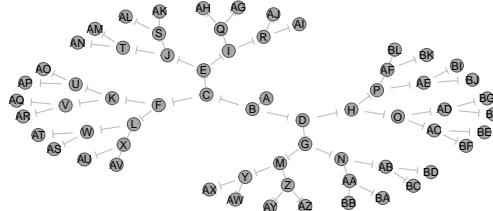
Figure T.3: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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.



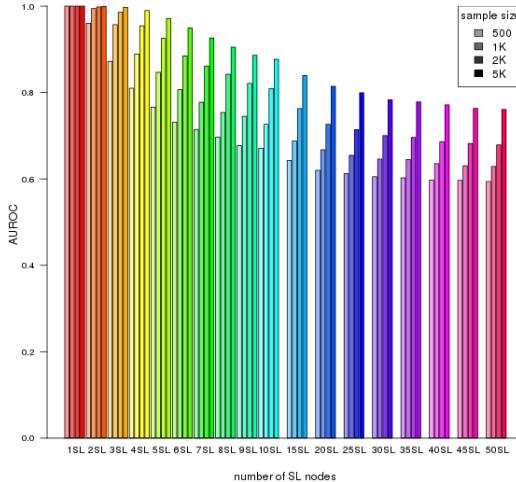




(a) Statistical evaluation (b) Receiver operating characteristic

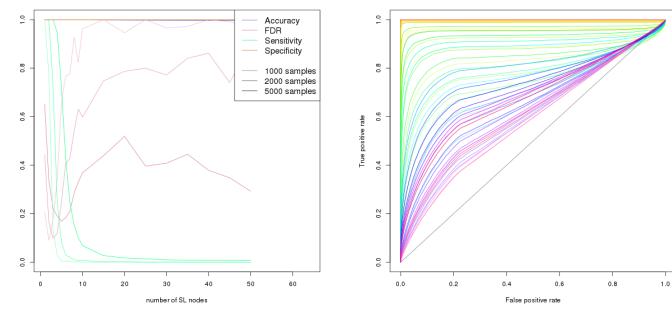


(c) Graph Structure

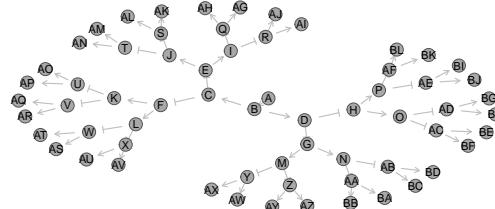


(d) Statistical performance

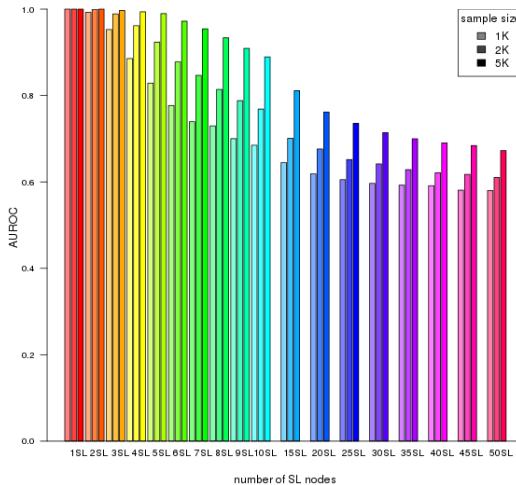
Figure T.6: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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

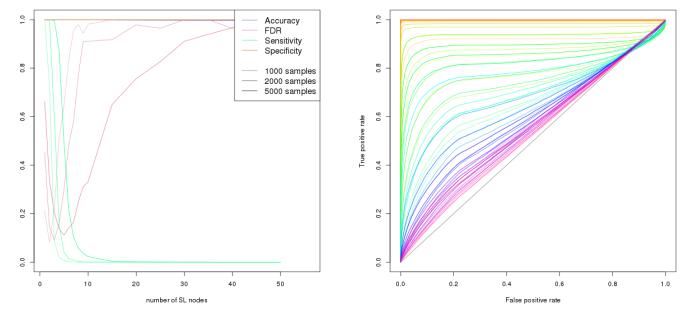


(c) Graph Structure

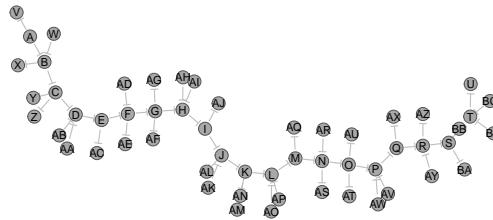


(d) Statistical performance

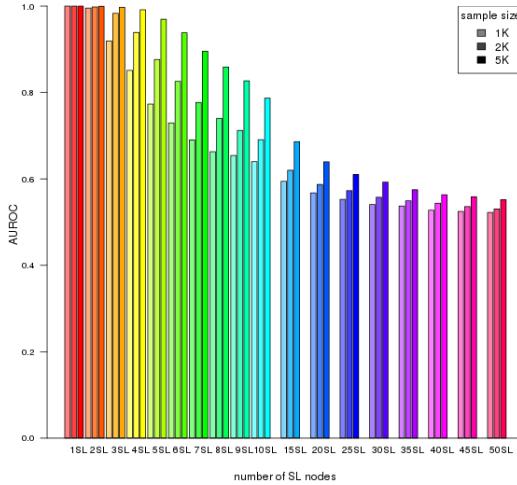
Figure T.7: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in 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

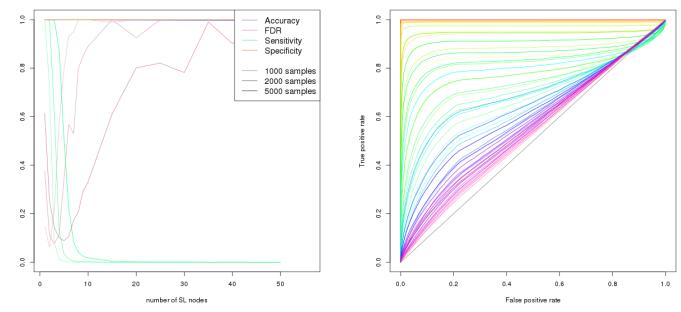


(c) Graph Structure

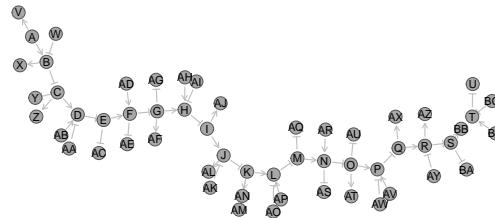


(d) Statistical performance

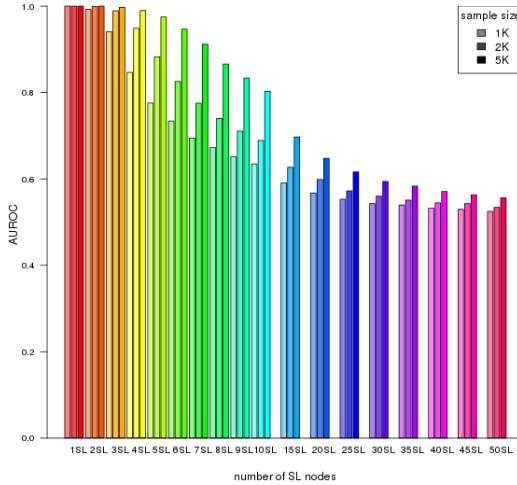
Figure T.8: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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

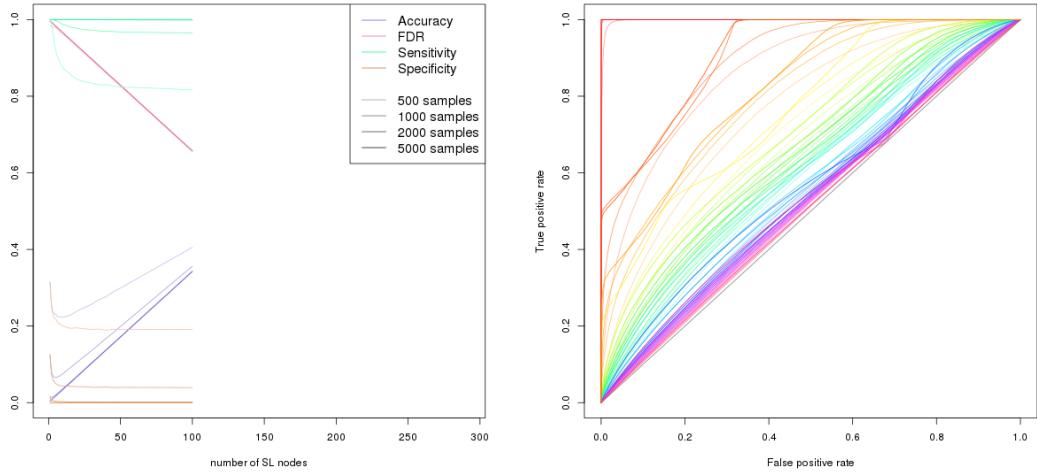


(d) Statistical performance

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.

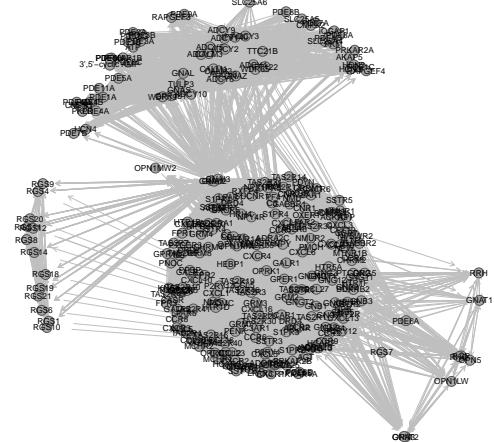
Appendix U

Pathway Simulations

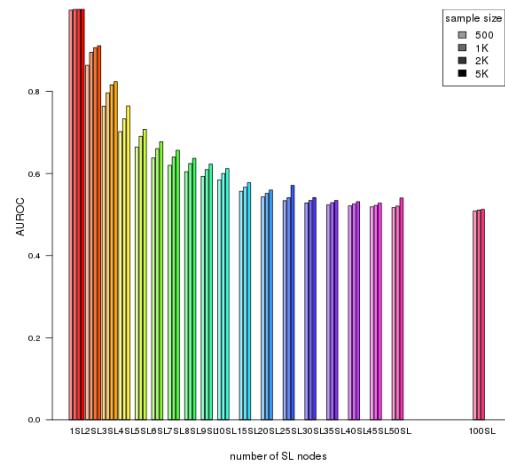


(a) Statistical evaluation

(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.

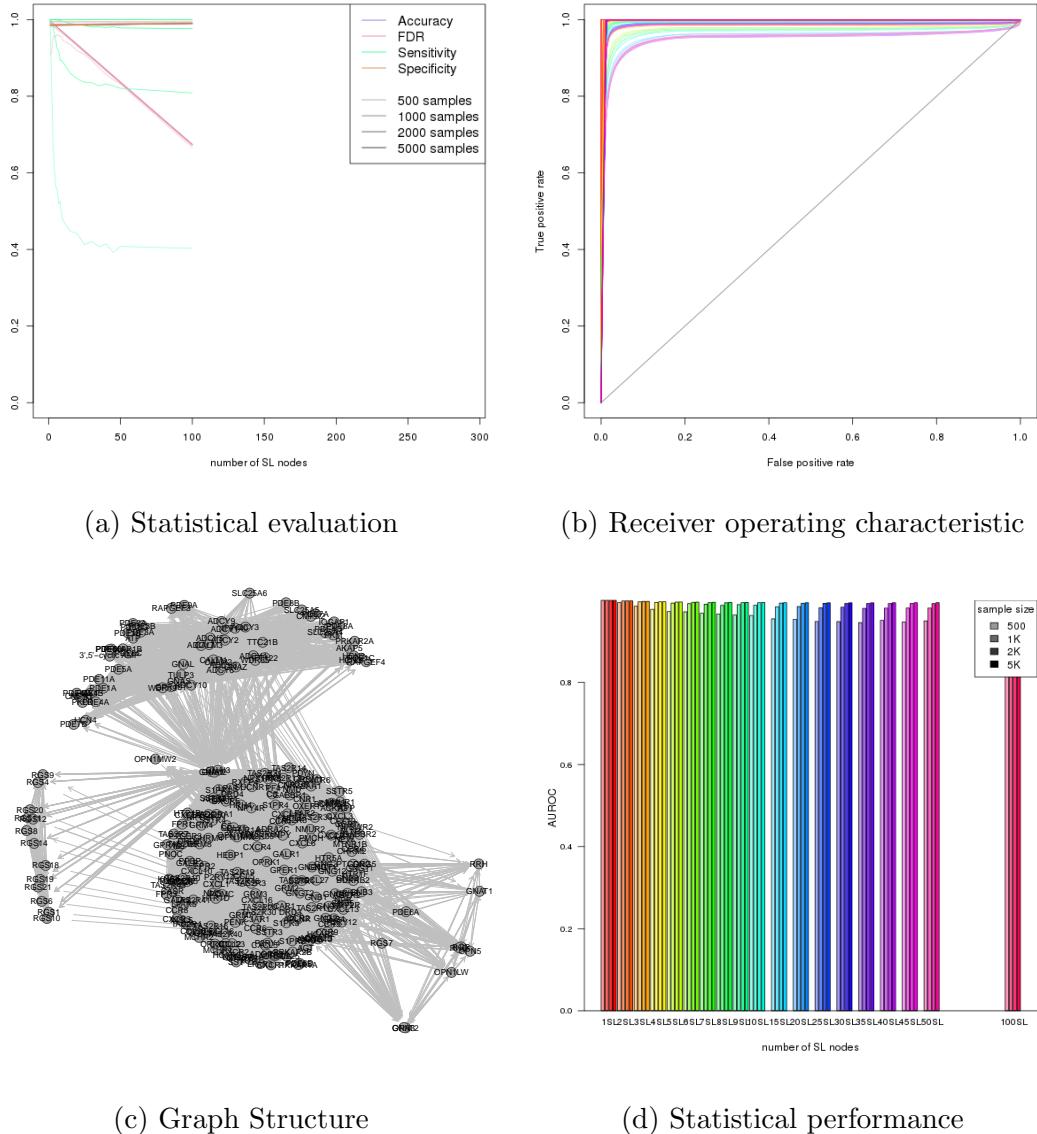


Figure U.2: Performance of multivariate normal simulations. Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (in darker 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.