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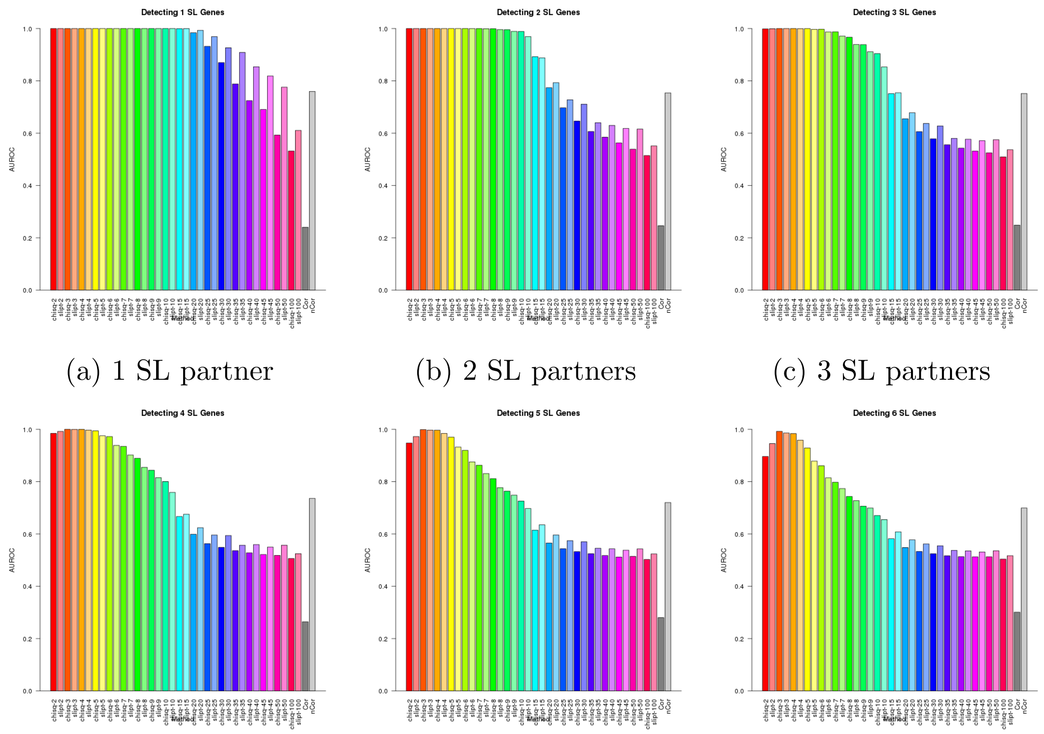
Appendix N

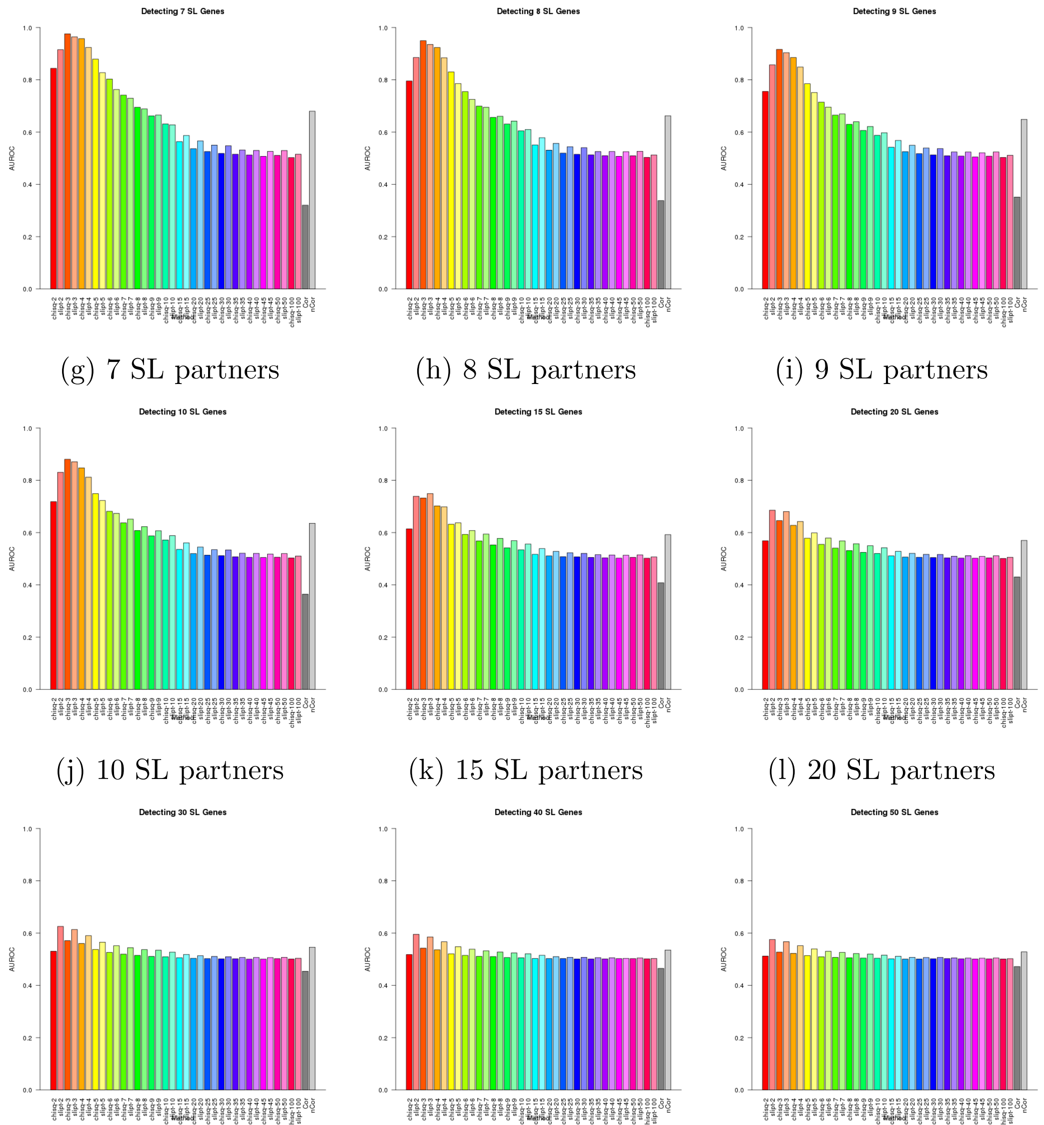
Performance of SLIPT and χ^2



(a) 1 SL partner (b) 2 SL partners (c) 3 SL partners

(d) 4 SL partners (e) 5 SL partners (f) 6 SL partners

Figure N.1: **Performance of χ^2 and SLIPT across quantiles**. (continued on next page)

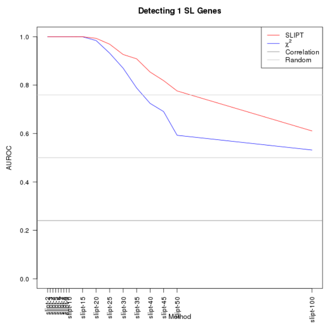


(g) 7 SL partners (h) 8 SL partners (i) 9 SL partners

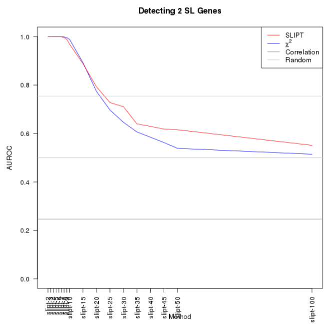
(j) 10 SL partners (k) 15 SL partners (l) 20 SL partners

(m) 30 SL partners (n) 40 SL partners (o) 50 SL partners

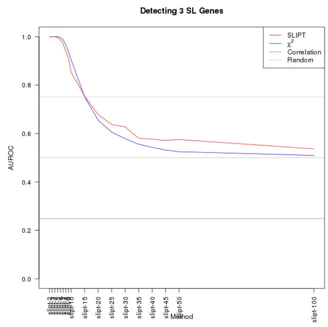
Figure N.1: **Performance of χ^2 and SLIPT across quantiles**. Synthetic lethal detection with quantiles as in axis labels. The barplot uses the same hues for each quantile (grey for correlation) and darker for χ^2 (and positive correlation). Synthetic Lethal Interaction Prediction Tool (SLIPT) and χ^2 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.



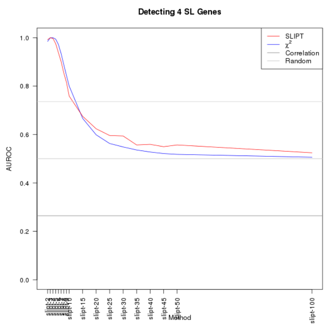
(a) 1 SL partner



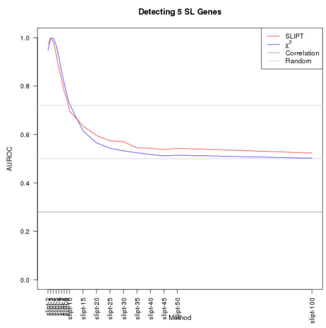
(b) 2 SL partners



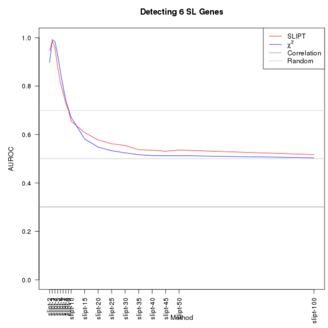
(c) 3 SL partners



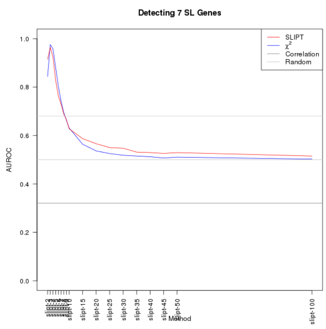
(d) 4 SL partners



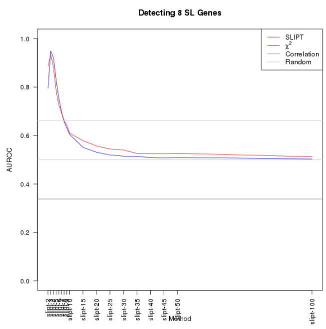
(e) 5 SL partners



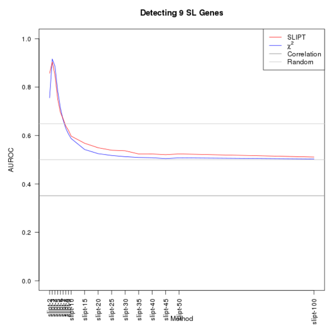
(f) 6 SL partners



(g) 7 SL partners

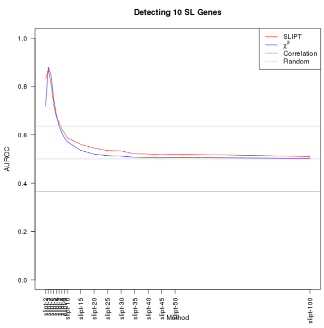


(h) 8 SL partners

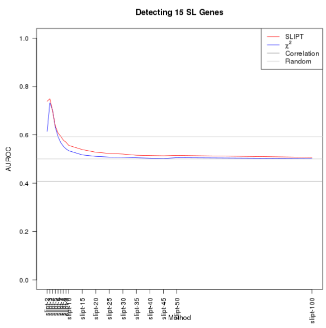


(i) 9 SL partners

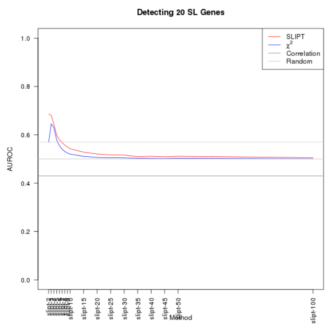
Figure N.2: **Performance of χ^2 and SLIPT across quantiles**. (continued on next page)



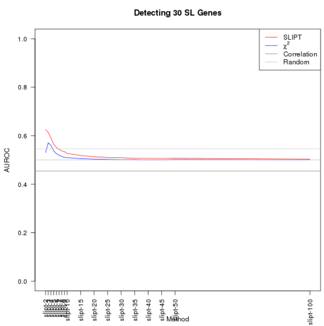
(j) 10 SL partners



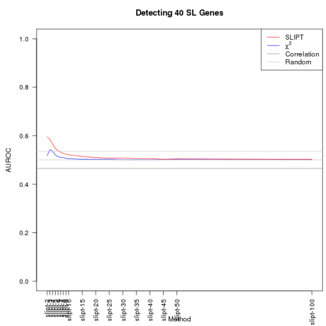
(k) 15 SL partners



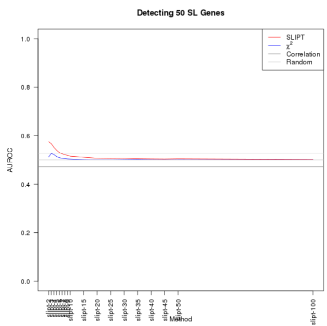
(l) 20 SL partners



(m) 30 SL partners

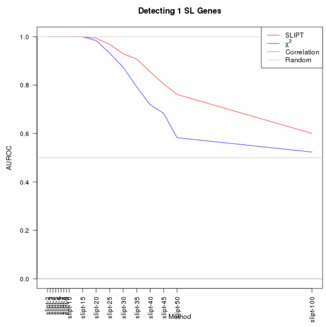


(n) 40 SL partners

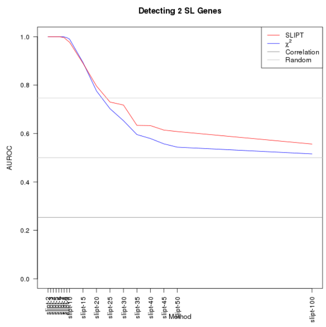


(o) 50 SL partners

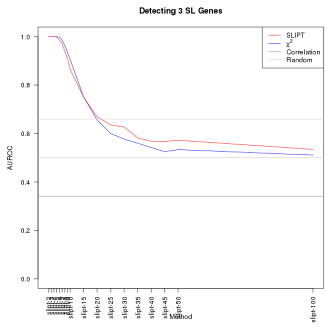
Figure N.2: **Performance of χ^2 and SLIPT across quantiles**. Synthetic lethal detection with quantiles as in axis labels. The line plots are coloured for SLIPT (red), χ^2 (blue) and correlation (grey) according to the legend. SLIPT and χ^2 perform similarly, peaking at $\frac{1}{3}$-quantiles and converging 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.



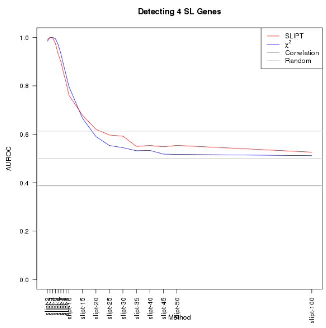
(a) 1 SL partner



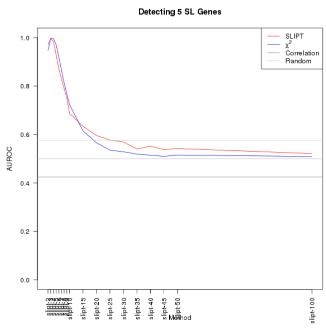
(b) 2 SL partners



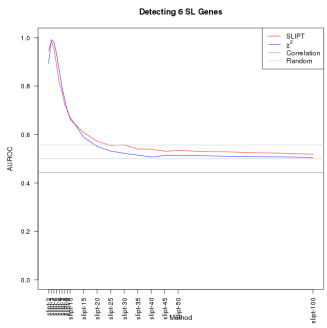
(c) 3 SL partners



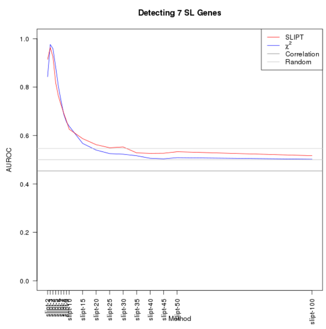
(d) 4 SL partners



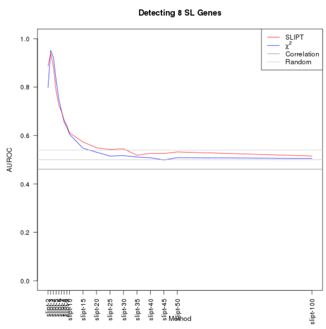
(e) 5 SL partners



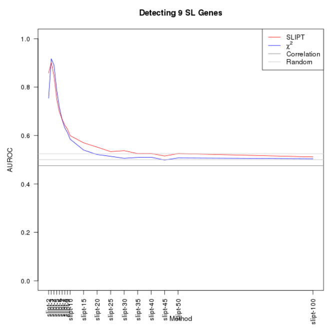
(f) 6 SL partners



(g) 7 SL partners

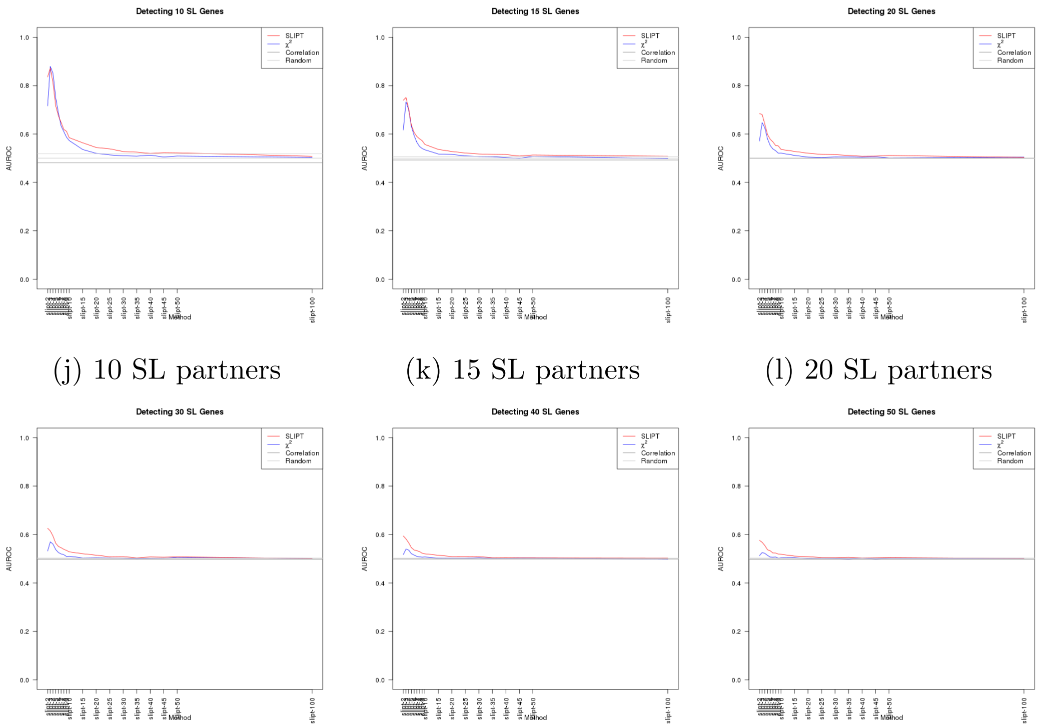


(h) 8 SL partners



(i) 9 SL partners

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

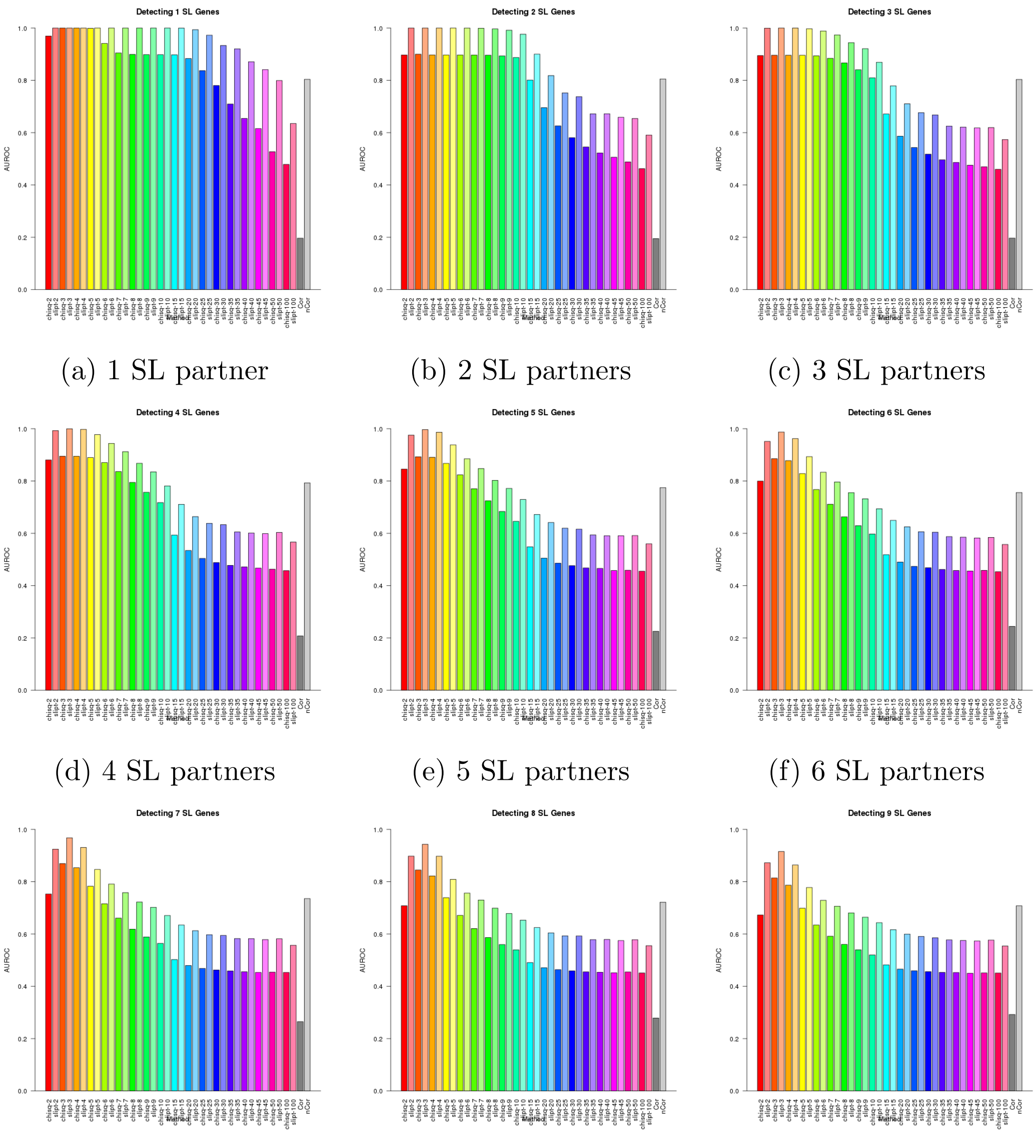


(j) 10 SL partners (k) 15 SL partners (l) 20 SL partners

(m) 30 SL partners (n) 40 SL partners (o) 50 SL partners

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

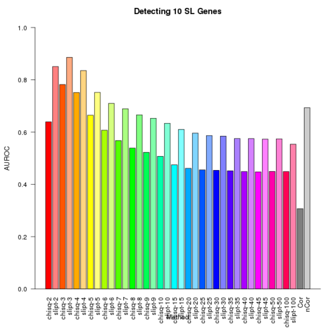


(a) 1 SL partner (b) 2 SL partners (c) 3 SL partners

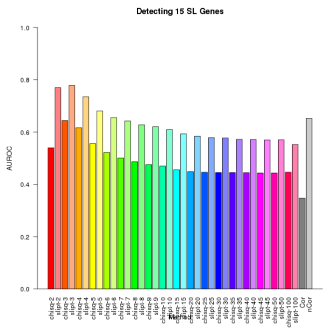
(d) 4 SL partners (e) 5 SL partners (f) 6 SL partners

(g) 7 SL partners (h) 8 SL partners (i) 9 SL partners

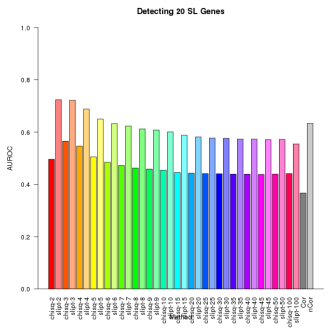
Figure N.4: **Performance of χ^2 and SLIPT across quantiles with query correlation**. (continued on next page)



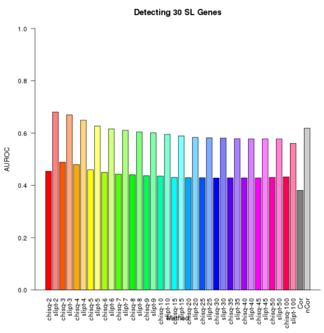
(j) 10 SL partners



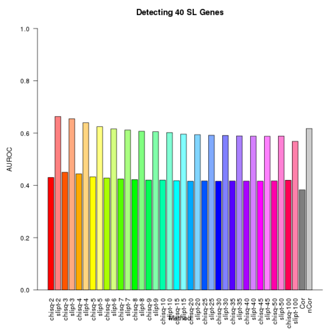
(k) 15 SL partners



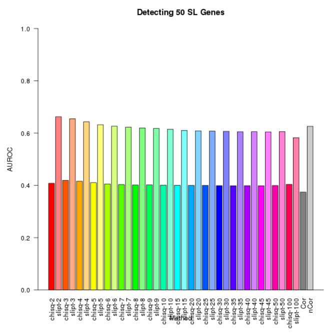
(l) 20 SL partners



(m) 30 SL partners

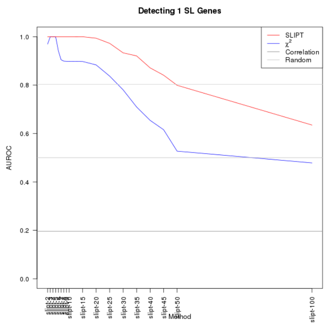


(n) 40 SL partners

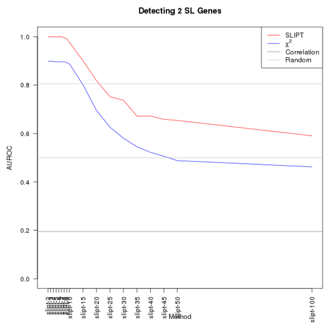


(o) 50 SL partners

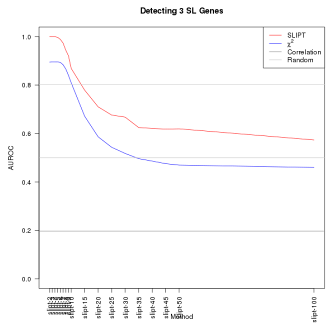
Figure N.4: **Performance of χ^2 and SLIPT across quantiles with query correlation**. Synthetic lethal detection with quantiles as in axis labels. The barplot uses the same hues for each quantile (grey for correlation) and darker for χ^2 (and positive correlation). SLIPT and χ^2 perform similarly, peaking 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.



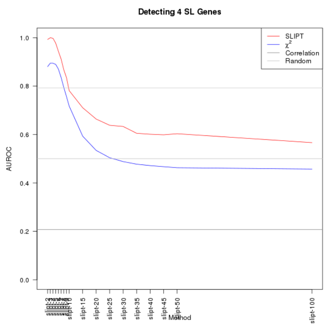
(a) 1 SL partner



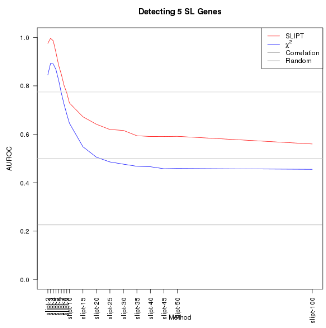
(b) 2 SL partners



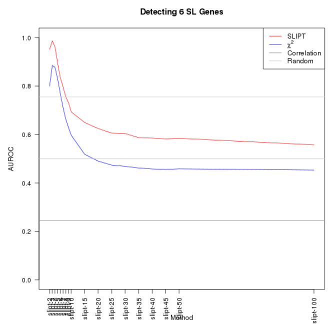
(c) 3 SL partners



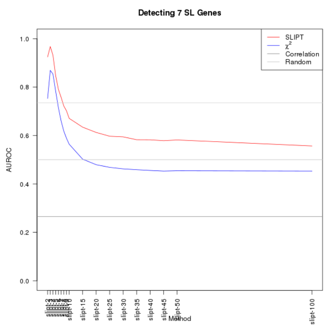
(d) 4 SL partners



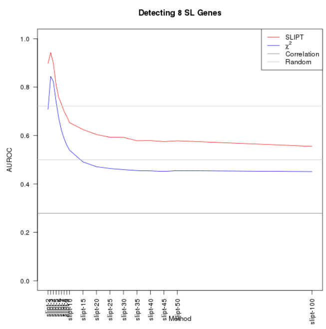
(e) 5 SL partners



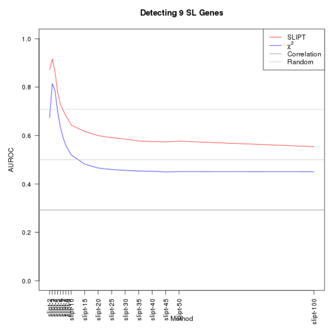
(f) 6 SL partners



(g) 7 SL partners

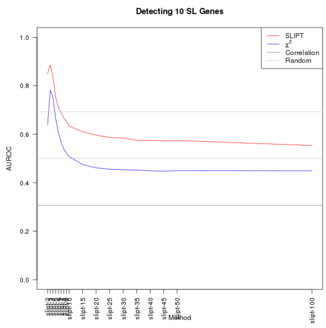


(h) 8 SL partners

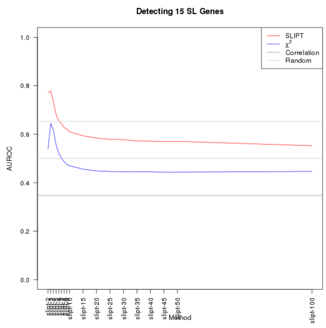


(i) 9 SL partners

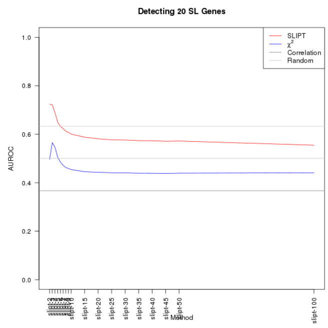
Figure N.5: **Performance of χ^2 and SLIPT across quantiles with query correlation**. (continued on next page)



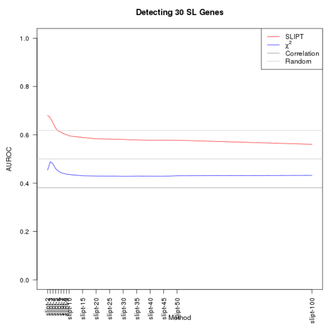
(j) 10 SL partners



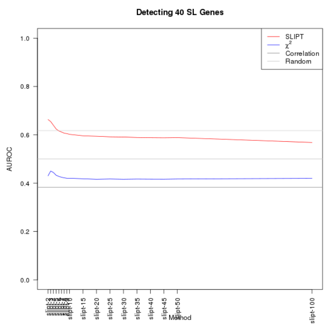
(k) 15 SL partners



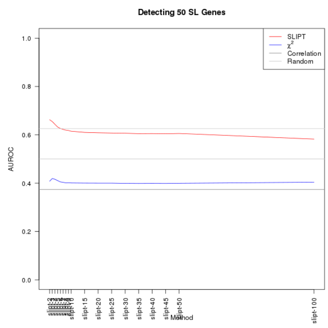
(l) 20 SL partners



(m) 30 SL partners

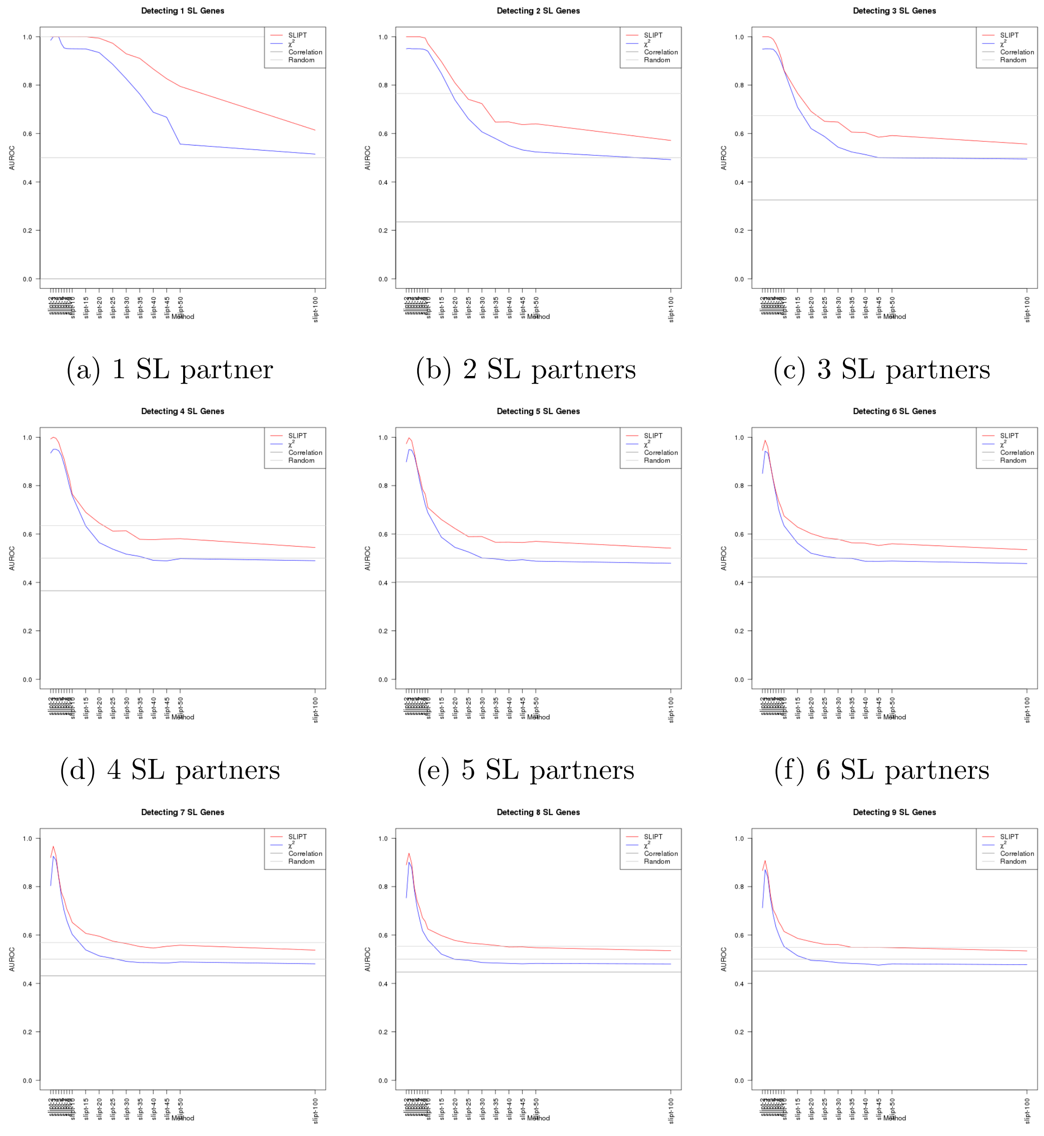


(n) 40 SL partners



(o) 50 SL partners

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.

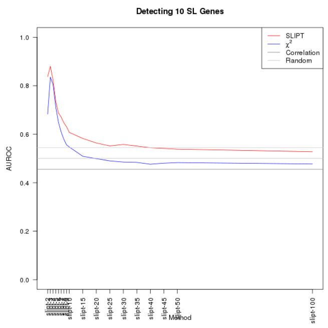


(a) 1 SL partner (b) 2 SL partners (c) 3 SL partners

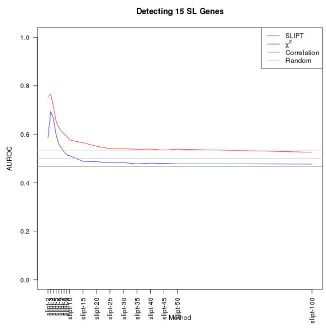
(d) 4 SL partners (e) 5 SL partners (f) 6 SL partners

(g) 7 SL partners (h) 8 SL partners (i) 9 SL partners

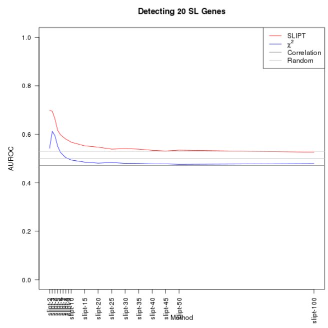
Figure N.6: **Performance of χ^2 and SLIPT across quantiles with query correlation and more genes**. (continued on next page)



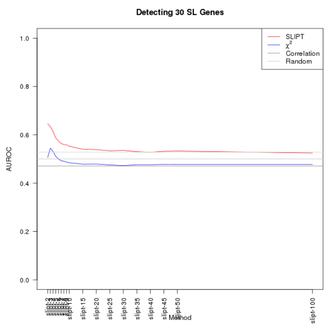
(j) 10 SL partners



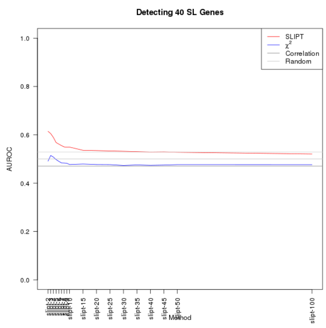
(k) 15 SL partners



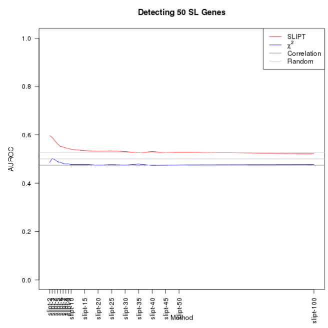
(l) 20 SL partners



(m) 30 SL partners



(n) 40 SL partners

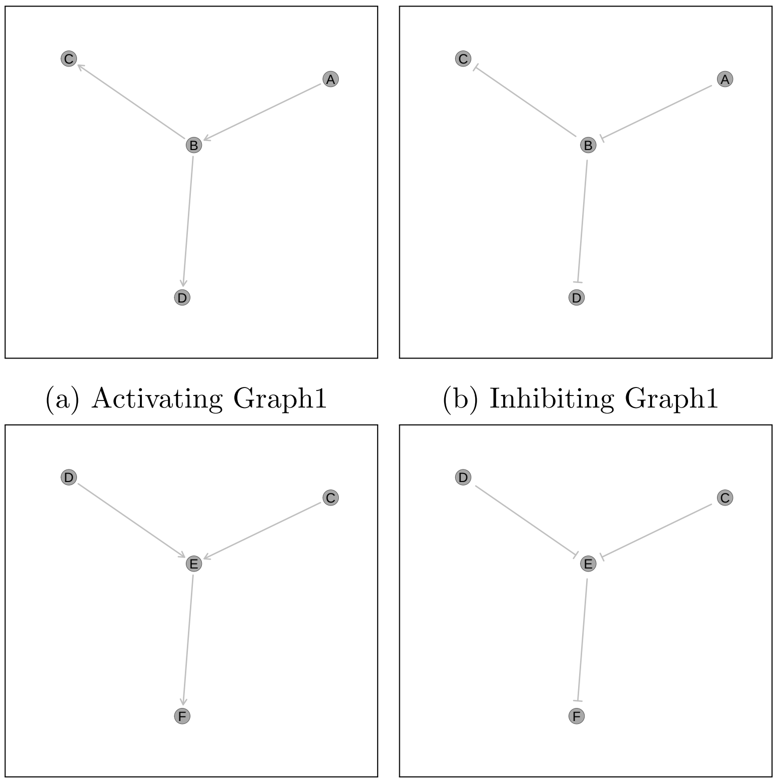


(o) 50 SL partners

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

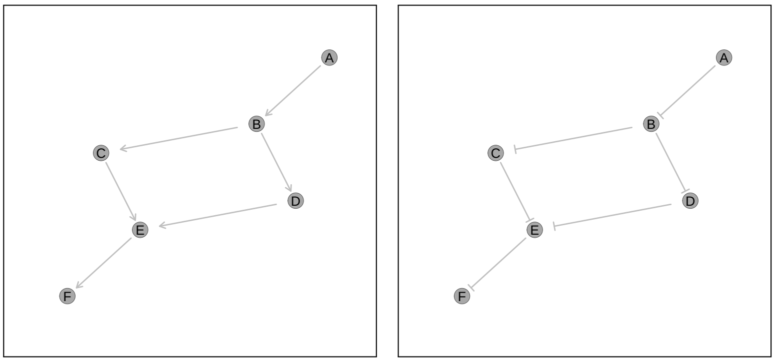
Graph Structures



(a) Activating Graph1 (b) Inhibiting Graph1

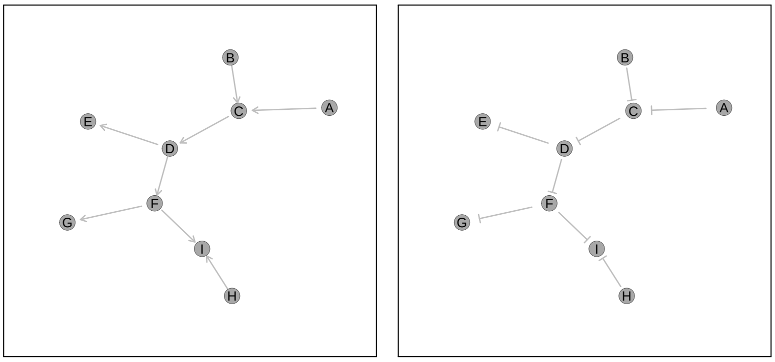
(c) Activating Graph2 (d) Inhibiting Graph2

Figure O.1: **Simple graph structures.** A simple graph structures used to demonstrate the simulation procedure. Graph1 and Graph2 are examples of a pathway converging or diverging respectively which enables testing the importance of direction in pathway structures. These are used with both activating and inhibiting relationships as shown.

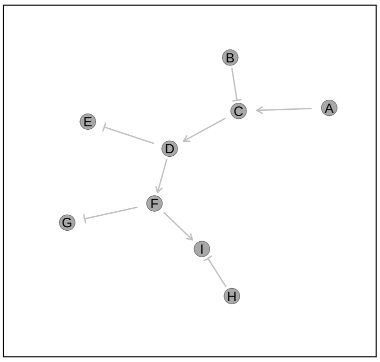


(a) Activating Graph3 (b) Inhibiting Graph3

Figure O.2: **Simple graph structure.** A constructed graph structure used for the simulation procedure. Graph3 combines the converging and diverging paths of a pathway. These are used with both activating and inhibiting relationships as shown.



(a) Activating Graph4 (b) Inhibiting Graph4



(c) Mixed Graph4

Figure O.3: **Constructed graph structure.** A constructed graph structure used for the simulation procedure. Graph4 is has a core cascade with branching signals. These are used with activating, inhibiting, and a combination of these relationships as shown.

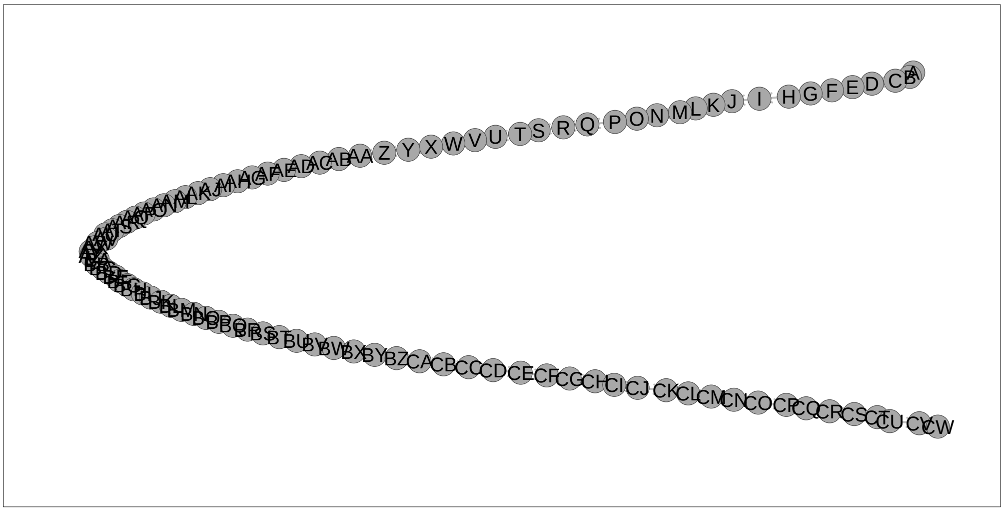
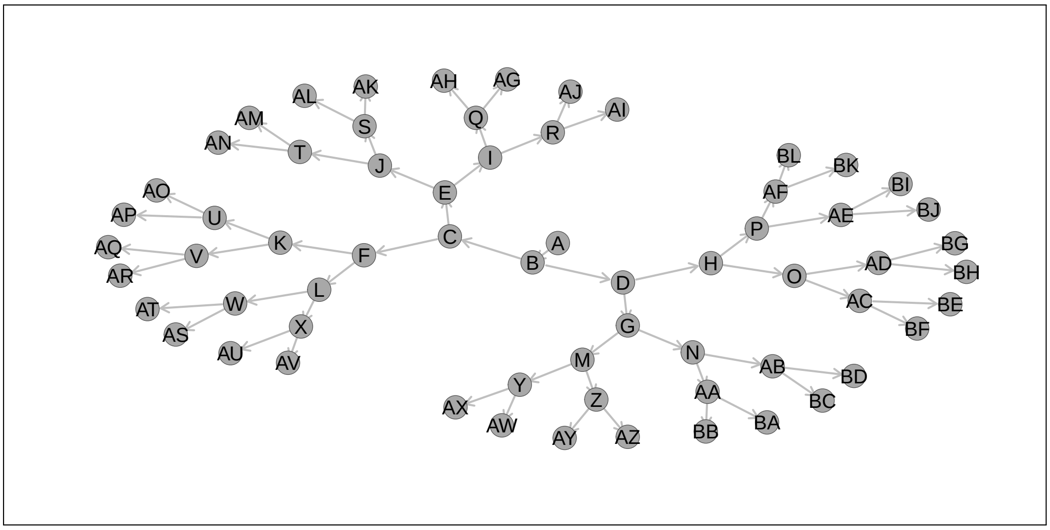
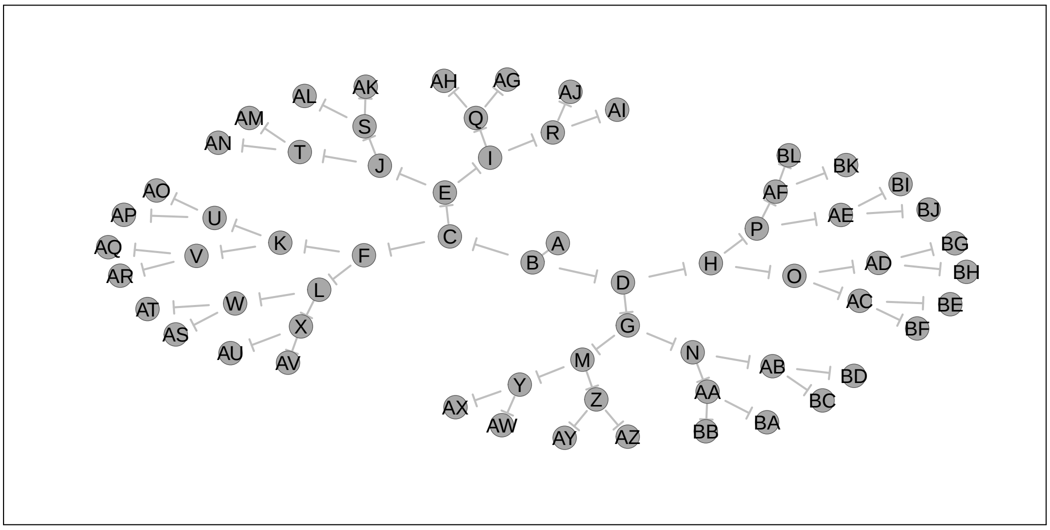


Figure O.4: **Large constructed graph structure.** A constructed graph structure used for the simulation procedure. Graph5 is an extended chain of 101 genes which are simulated with activating or inhibiting relations and these alternating along the chain.

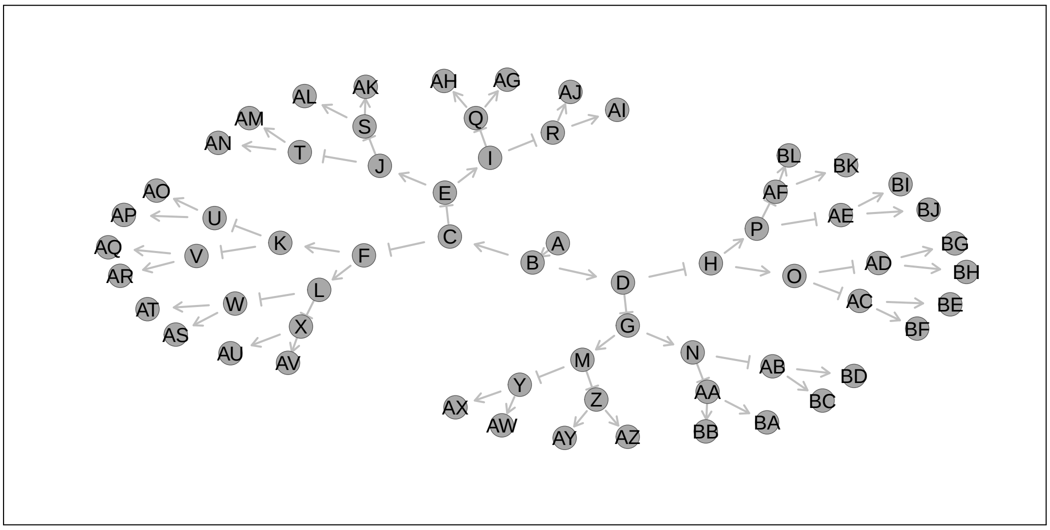


(a) Activating Graph6

Figure O.5: **Branching constructed graph structure.** (continued on next page)

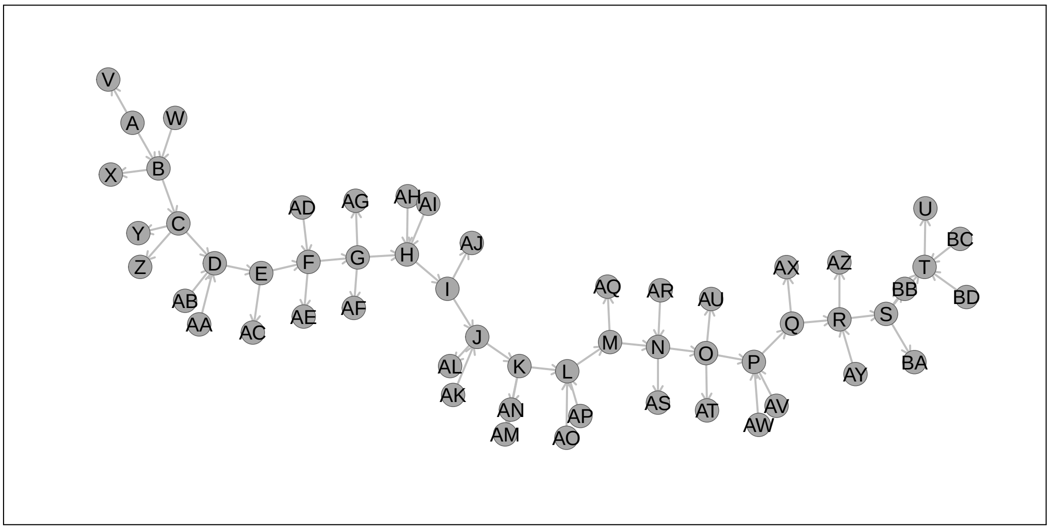


(b) Inhibiting Graph6

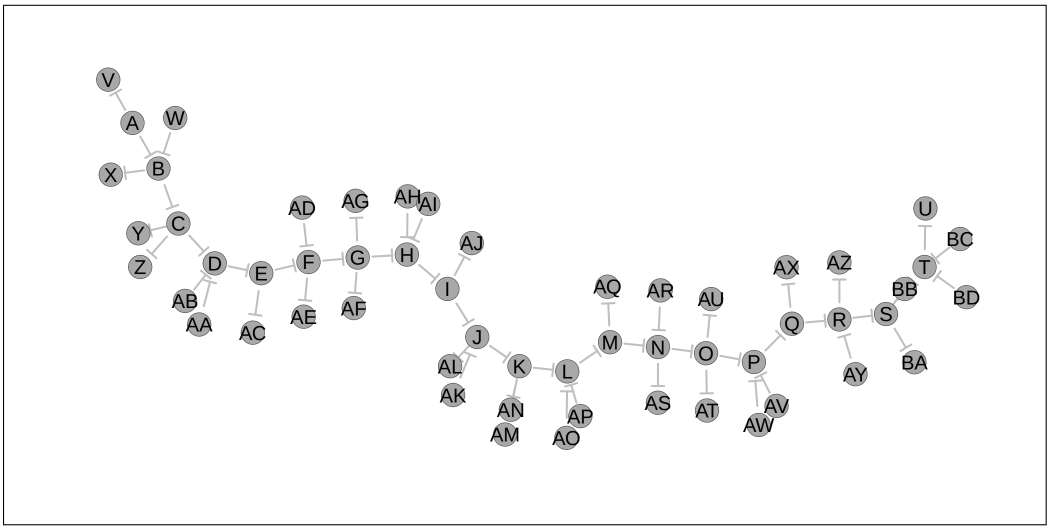


(c) Mixed Graph6

Figure O.5: **Branching constructed graph structure.** A constructed graph structure used for the simulation procedure. Graph6 is a branching signal cascade from a central hub. These are used with activating, inhibiting, and an alternating combination of these relationships as shown.

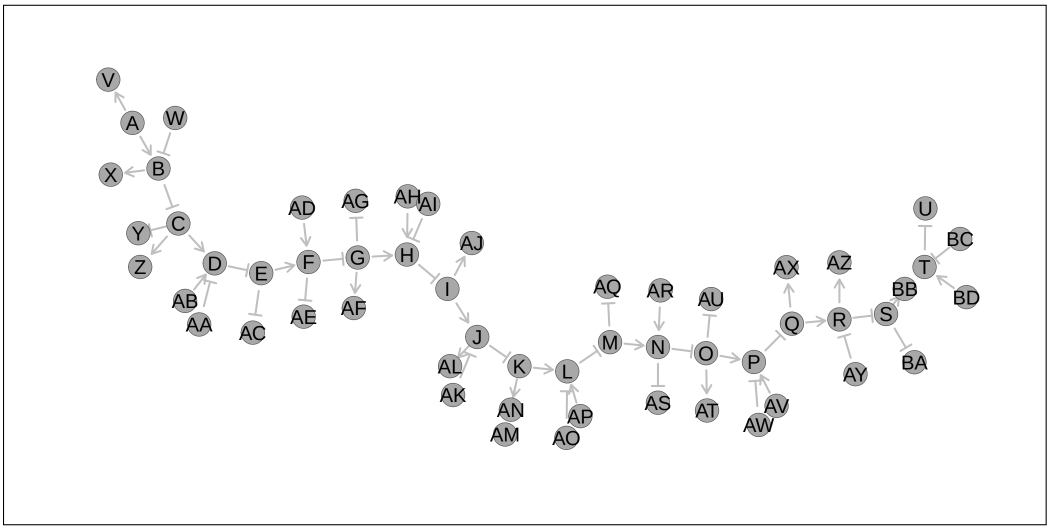


(a) Activating Graph7



(b) Inhibiting Graph7

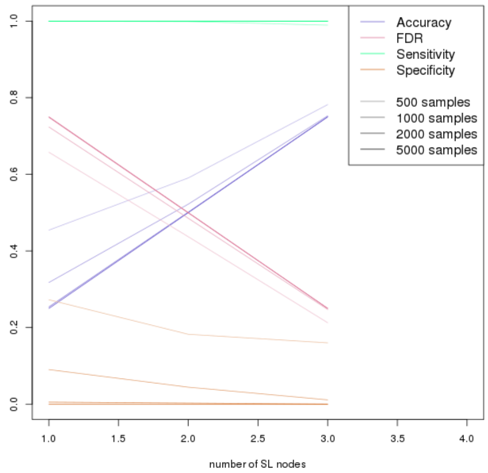
Figure O.6: **Complex constructed graph structure.** (continued on next page)



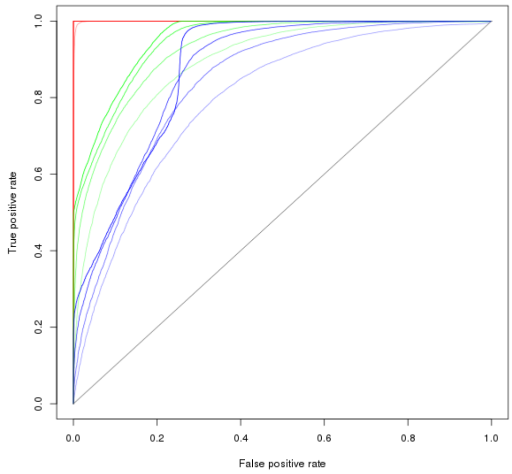
(c) Mixed Graph7

Figure O.6: **Complex constructed graph structure.** A constructed graph structure used for the simulation procedure. Graph7 is has a core cascade with branching signals in and out of the pathway. These are used with activating, inhibiting, and a combination of these relationships as shown.

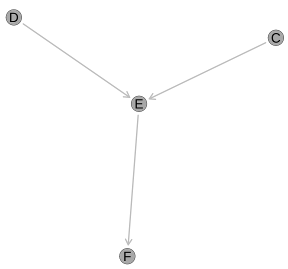
O.1 Simulations from Graph Structures



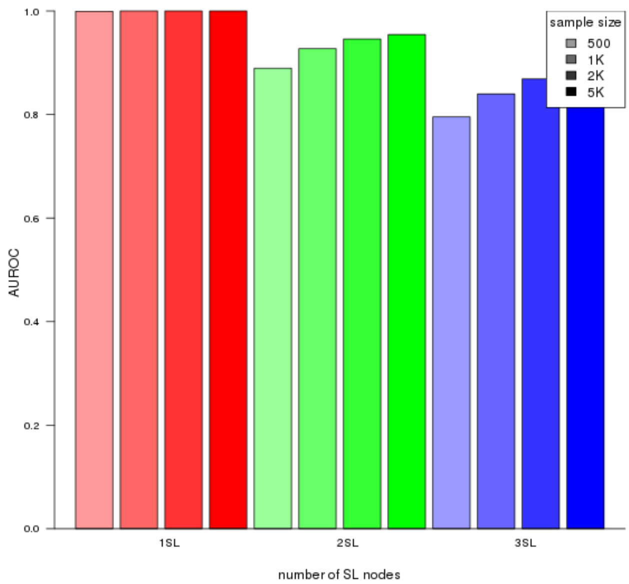
(a) Statistical evaluation



(b) Receiver operating characteristic

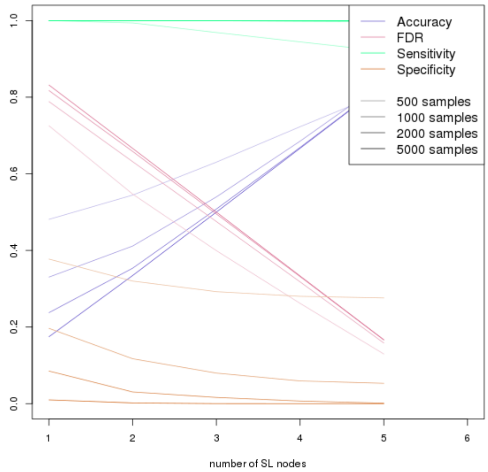


(c) Graph Structure

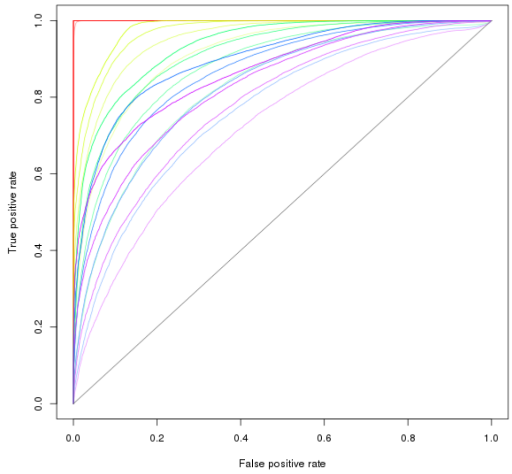


(d) Statistical performance

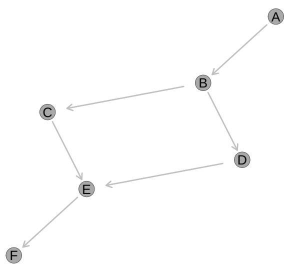
Figure O.7: **Performance of simulations on a simple graph.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph2. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



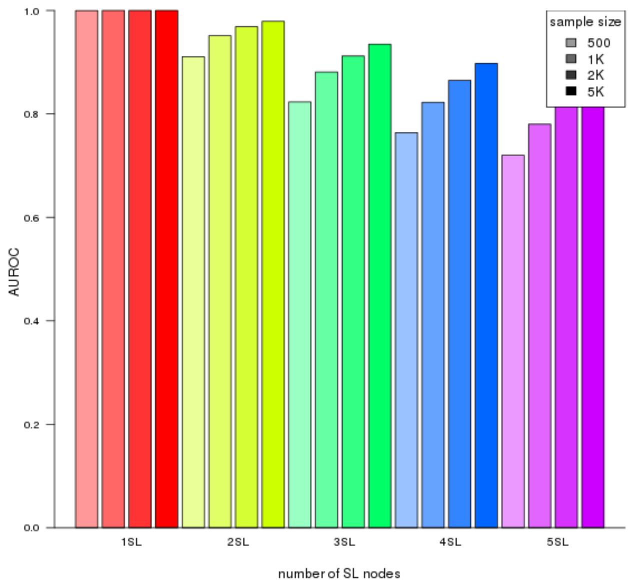
(a) Statistical evaluation



(b) Receiver operating characteristic

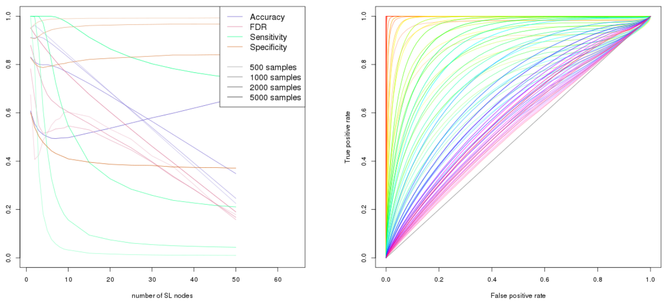


(c) Graph Structure

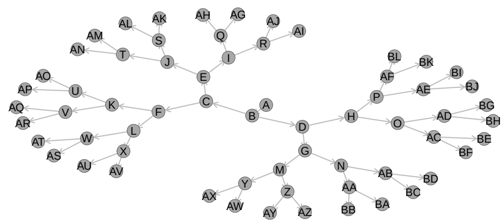


(d) Statistical performance

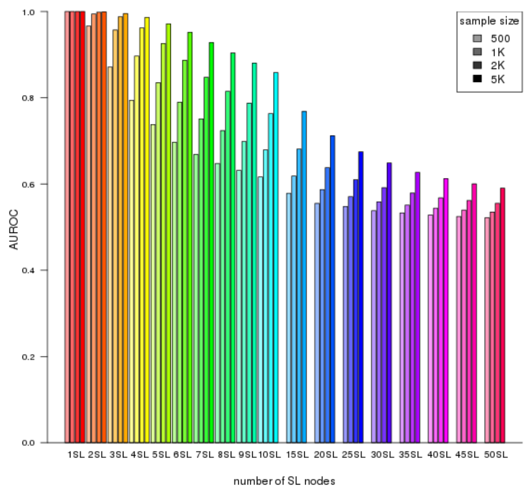
Figure O.8: **Performance of simulations on a constructed graph.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph3. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



(a) Statistical evaluation (b) Receiver operating characteristic

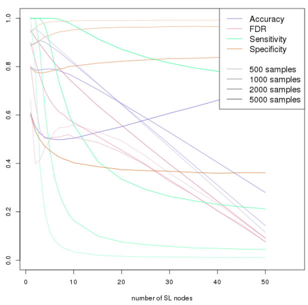


(c) Graph Structure

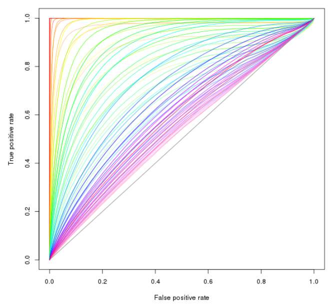


(d) Statistical performance

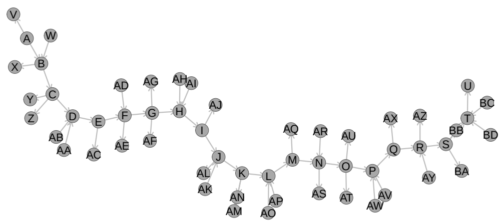
Figure O.9: **Performance of simulations on a branching graph.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph6. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



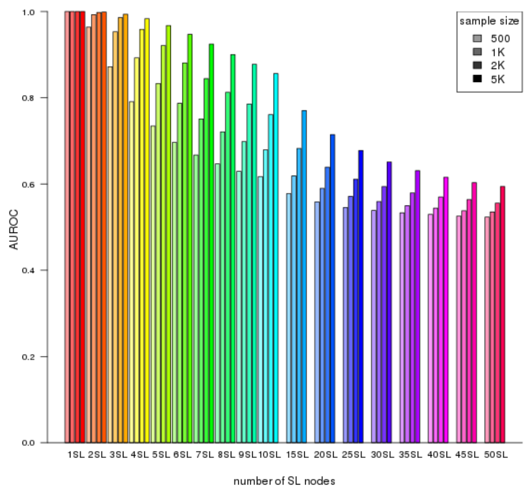
(a) Statistical evaluation



(b) Receiver operating characteristic



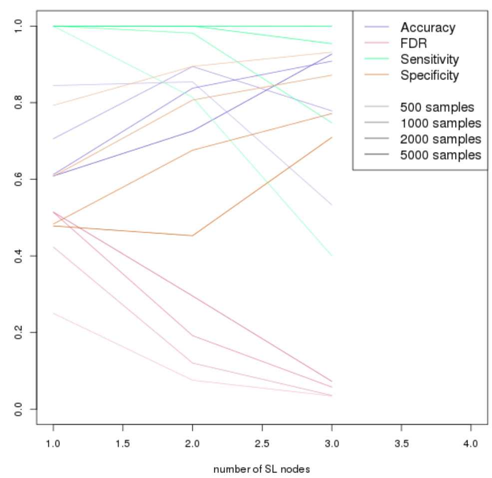
(c) Graph Structure



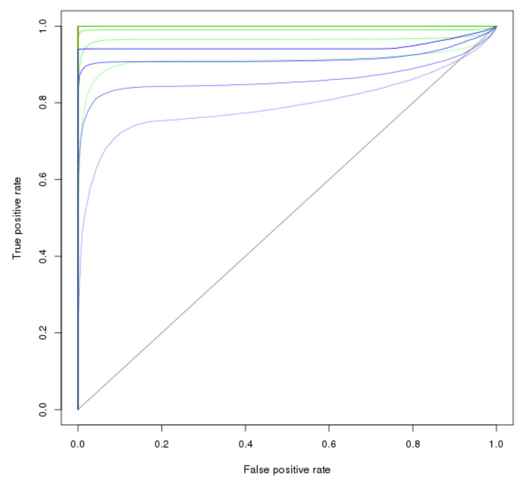
(d) Statistical performance

Figure O.10: **Performance of simulations on a complex graph.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph7. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.

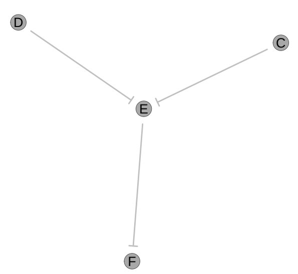
O.2 Simulations from Inhibiting Graph Structures



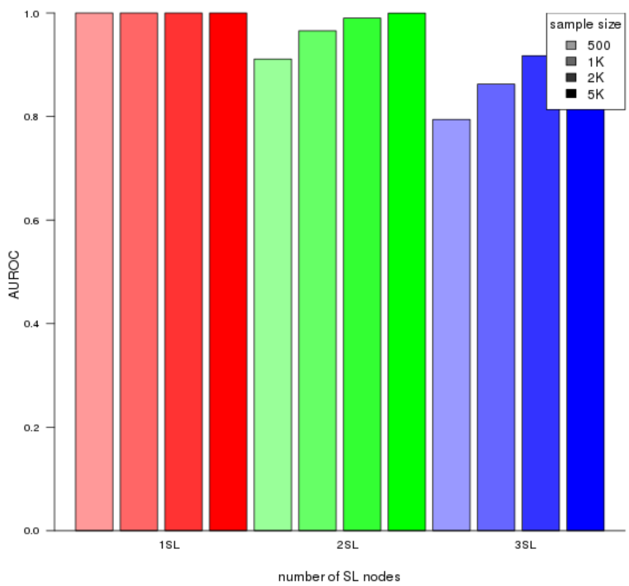
(a) Statistical evaluation



(b) Receiver operating characteristic

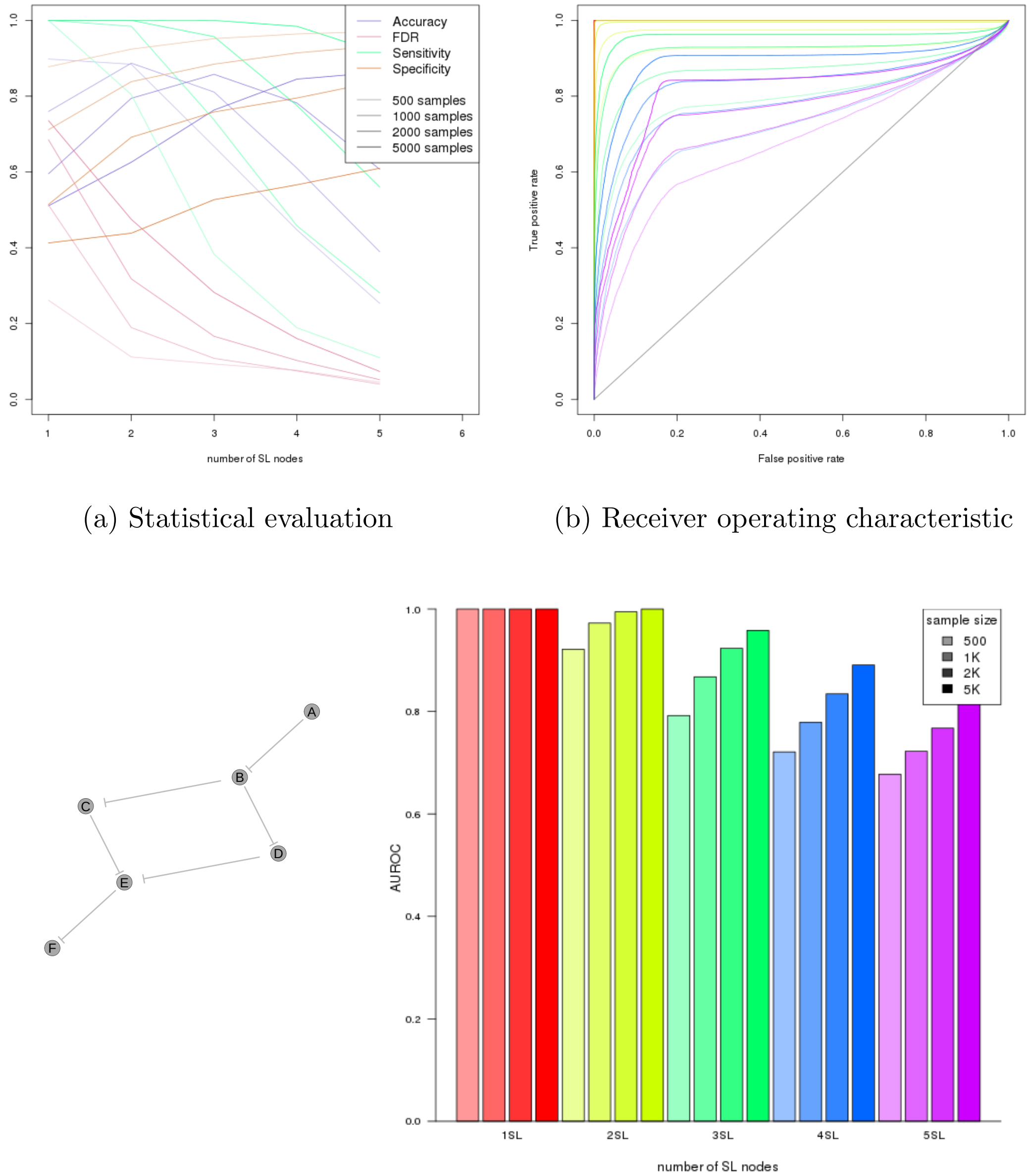


(c) Graph Structure



(d) Statistical performance

Figure O.11: **Performance of simulations on a simple graph with inhibition.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph2. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



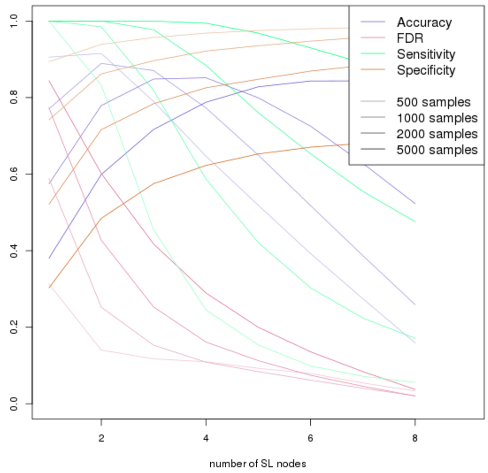
(a) Statistical evaluation

(b) Receiver operating characteristic

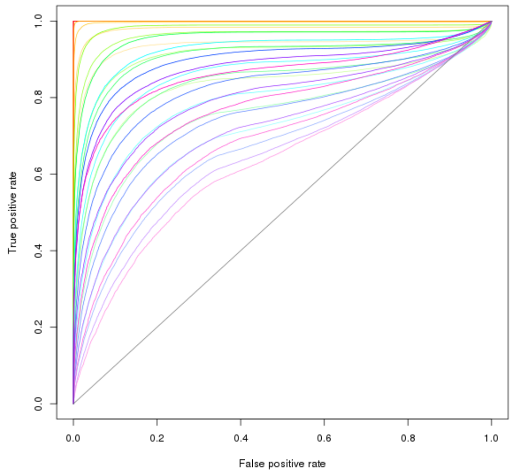
(c) Graph Structure

(d) Statistical performance

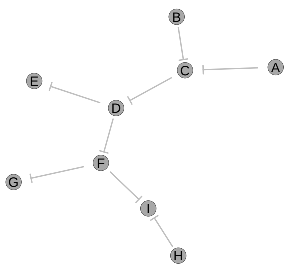
Figure O.12: **Performance of simulations on a simple graph with inhibition.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph3. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



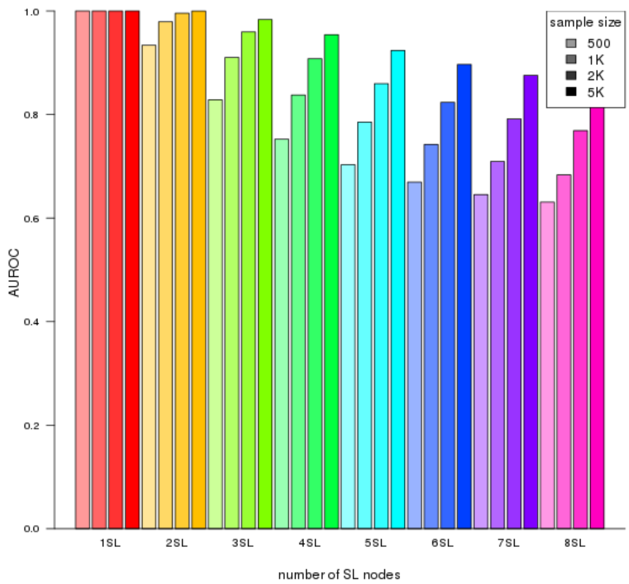
(a) Statistical evaluation



(b) Receiver operating characteristic

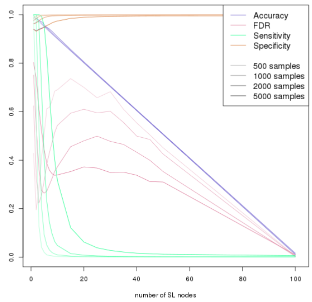


(c) Graph Structure

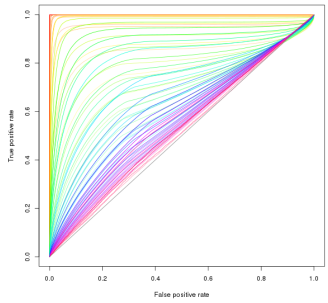


(d) Statistical performance

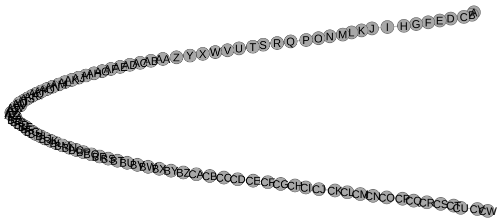
Figure O.13: **Performance of simulations on a constructed graph with inhibition.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph4 with only inhibitions. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



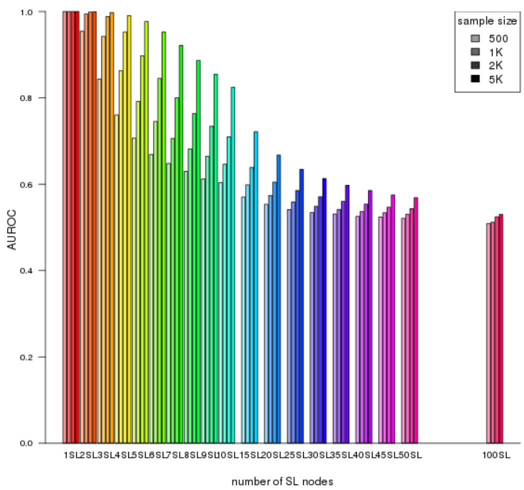
(a) Statistical evaluation



(b) Receiver operating characteristic

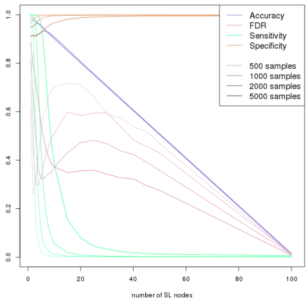


(c) Graph Structure

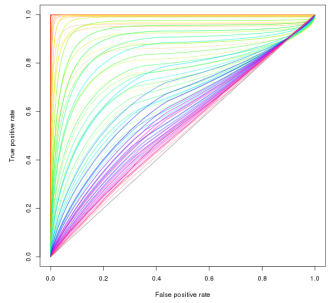


(d) Statistical performance

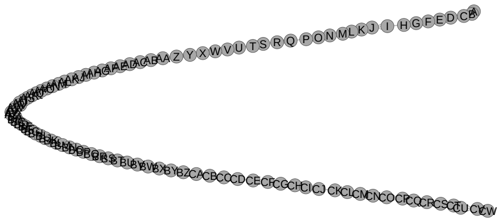
Figure O.14: **Performance of simulations on a large constructed graph with inhibition.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph5 with only inhibitions. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



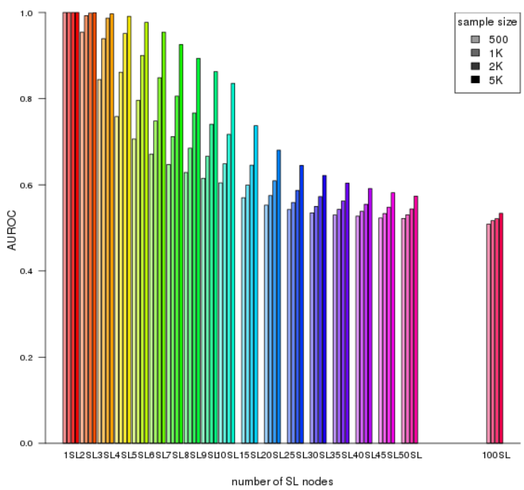
(a) Statistical evaluation



(b) Receiver operating characteristic

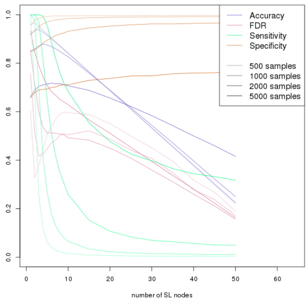


(c) Graph Structure

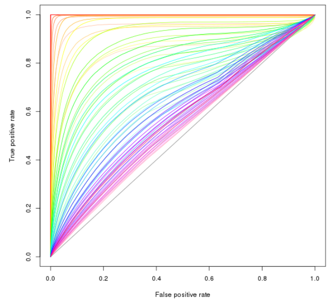


(d) Statistical performance

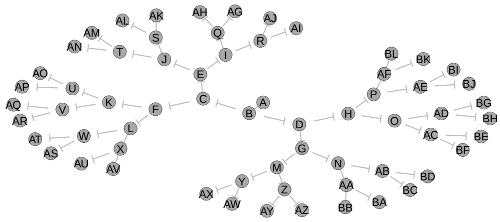
Figure O.15: **Performance of simulations on a large constructed graph with inhibition.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph5 with alternating inhibitions. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



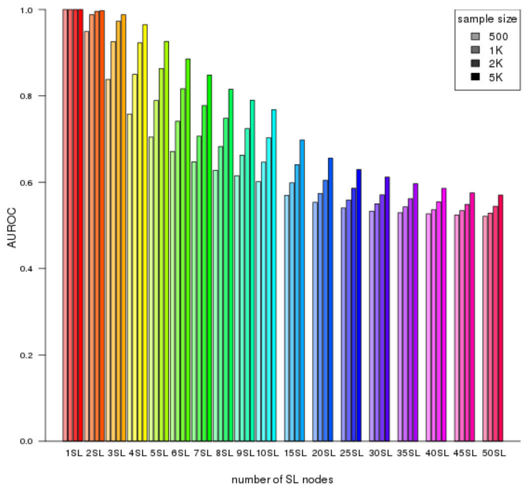
(a) Statistical evaluation



(b) Receiver operating characteristic

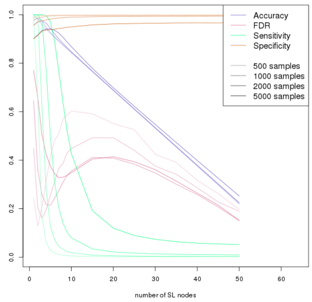


(c) Graph Structure

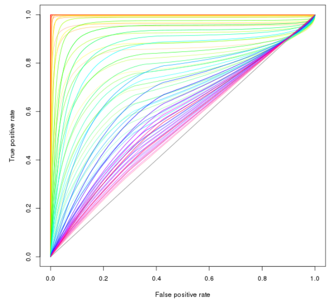


(d) Statistical performance

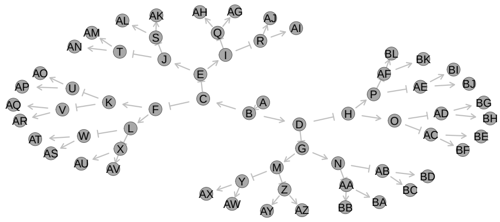
Figure O.16: **Performance of simulations on a branching graph with inhibition.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph6 with only inhibitions. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



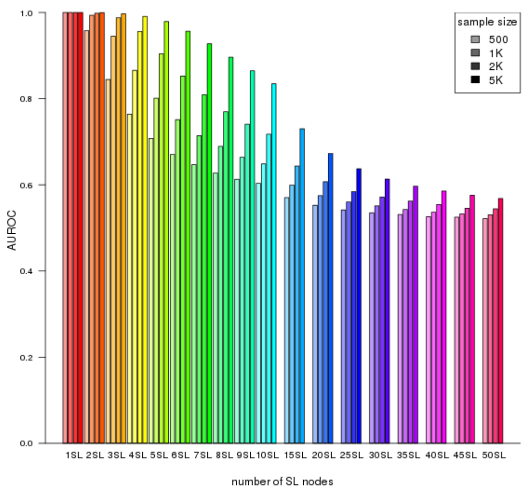
(a) Statistical evaluation



(b) Receiver operating characteristic

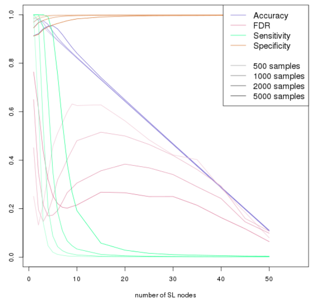


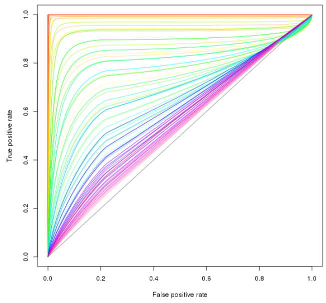
(c) Graph Structure



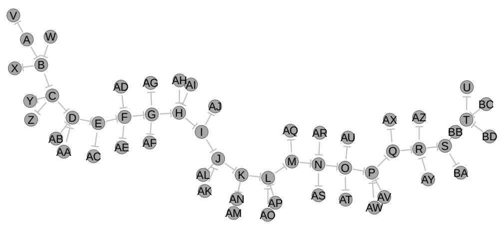
(d) Statistical performance

Figure O.17: **Performance of simulations on a branching graph with inhibition.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph6 with alternating inhibitions. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.

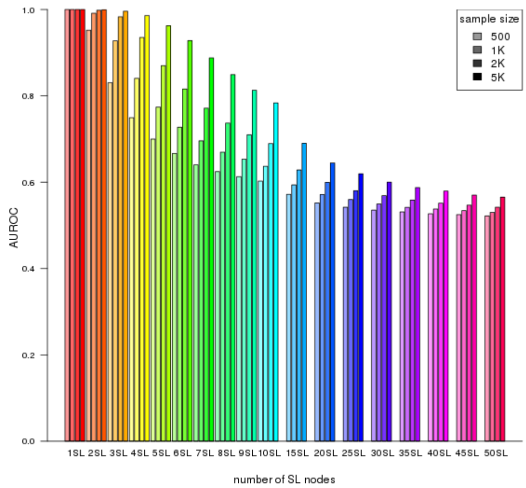




(a) Statistical evaluation (b) Receiver operating characteristic

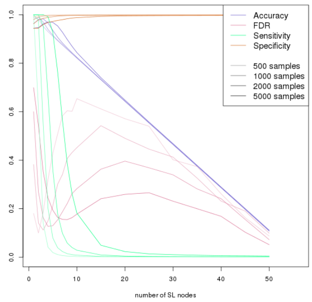


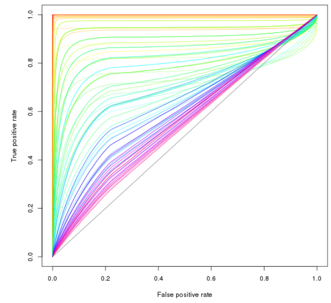
(c) Graph Structure



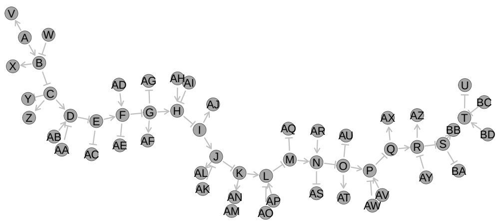
(d) Statistical performance

Figure O.18: **Performance of simulations on a complex graph with inhibition.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph7 with only inhibitions. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.

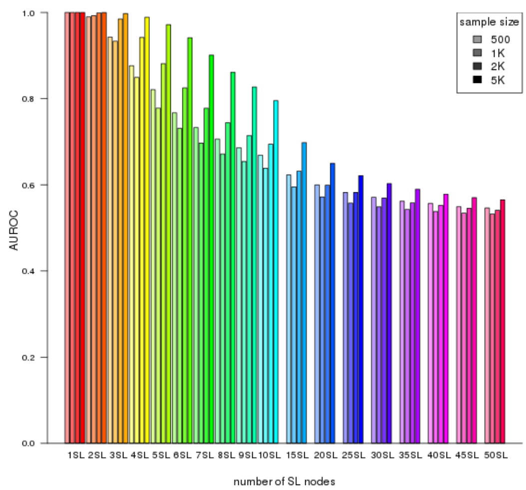




(a) Statistical evaluation (b) Receiver operating characteristic



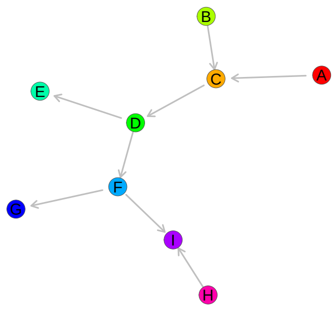
(c) Graph Structure



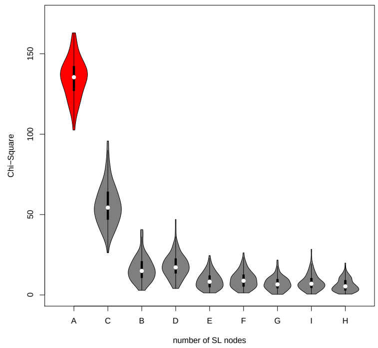
(d) Statistical performance

Figure O.19: **Performance of simulations on a complex graph with inhibition.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph7 with a combination of relationships. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.

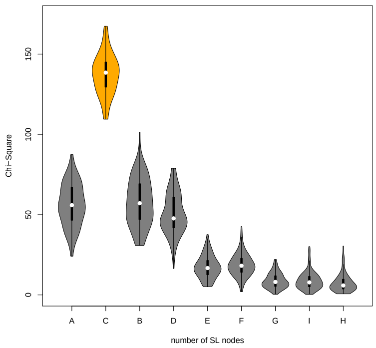
O.3 Simulation across Graph Structures



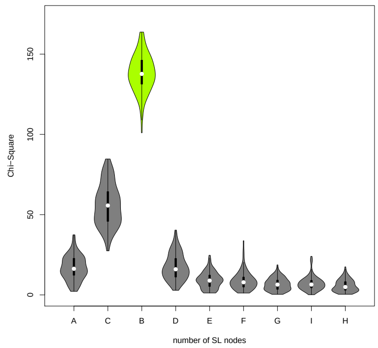
(a) Activating Graph Structure



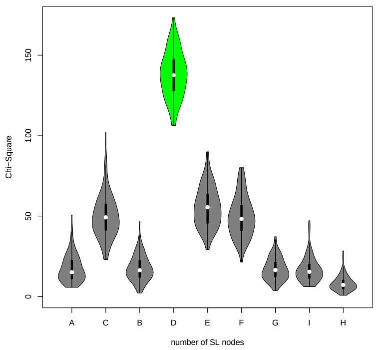
(b) χ^2 distribution for "A" SL



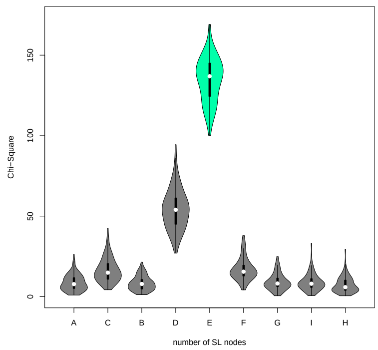
(c) Gene "B" SL



(d) Gene "C" SL

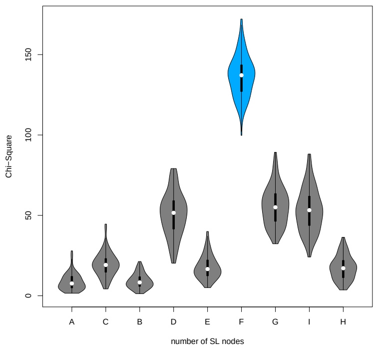


(e) Gene "D" SL

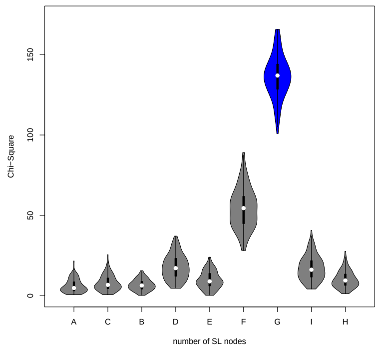


(f) Gene "E" SL

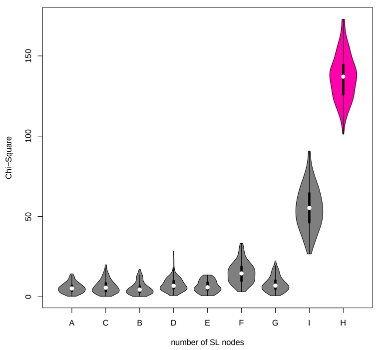
Figure O.20: **Detection of Synthetic Lethality within a Graph Structure.** (continued on next page)



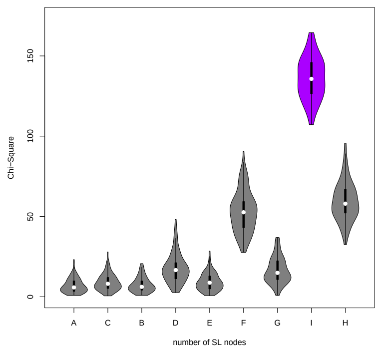
(g) Gene “F” SL



(h) Gene “G” SL

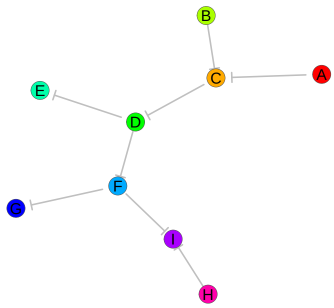


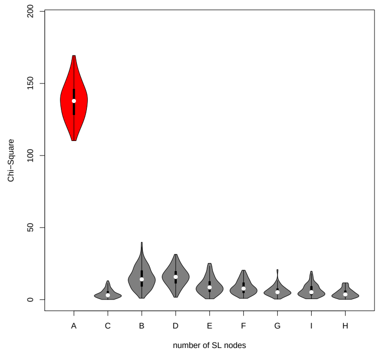
(i) Gene “H” SL



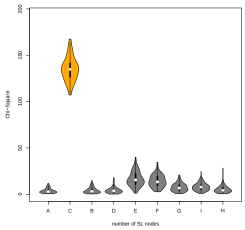
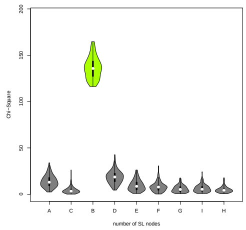
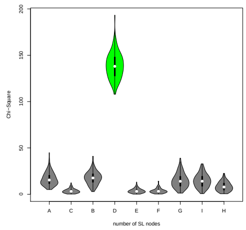
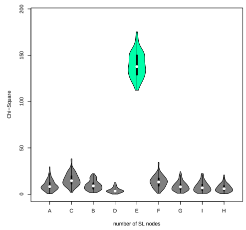
(j) Gene “I” SL

Figure O.20: **Detection of Synthetic Lethality within a Graph Structure.** Each gene was designated to be synthetic lethal separately and the χ^2 value from SLIPT was computed for each gene across the graph structure. For each synthetic lethal gene (highlighted in the respective colours), the χ^2 values were computed in 100 simulations of datasets of 20,000 genes including the graph structure and 1000 samples. For each synthetic lethal gene, the adjacent genes in the network also had elevated test statistics.

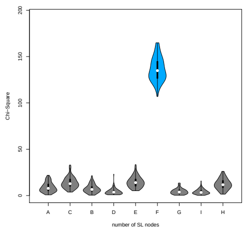
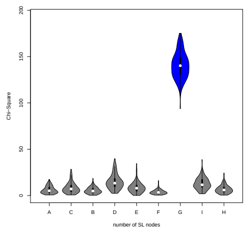
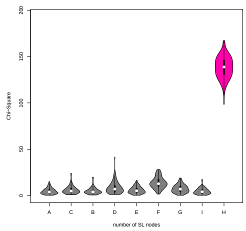
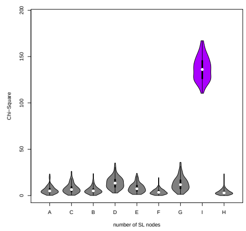




(a) Inhibiting Graph Structure (b) χ^2 distribution for "A" SL

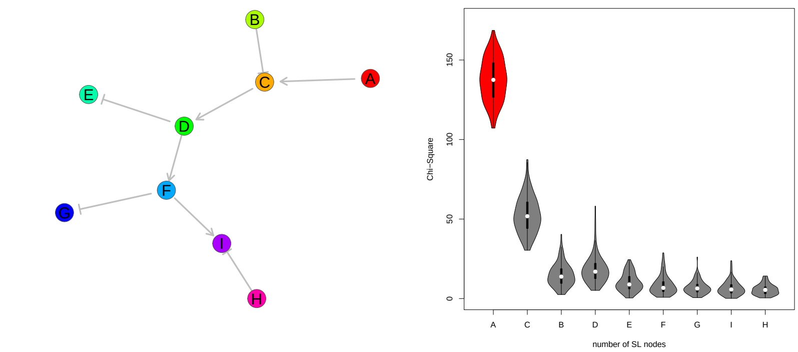





(c) Gene "B" SL (d) Gene "C" SL (e) Gene "D" SL (f) Gene "E" SL

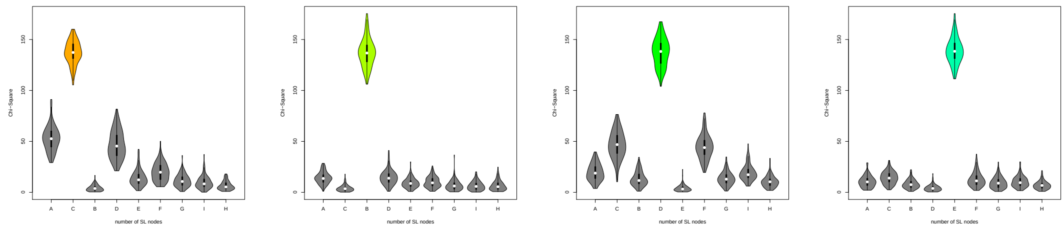





(g) Gene "F" SL (h) Gene "G" SL (i) Gene "H" SL (j) Gene "I" SL

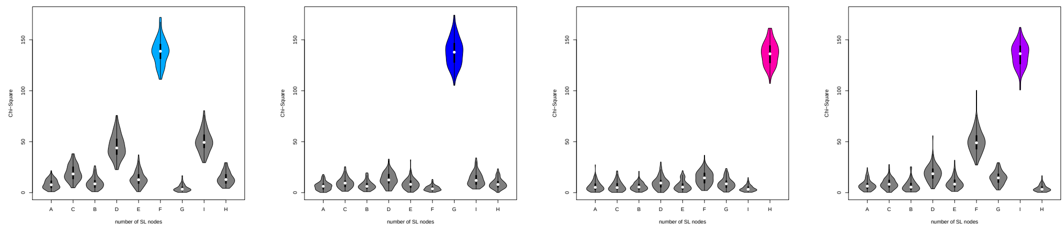
Figure O.21: **Detection of Synthetic Lethality within an Inhibiting Graph Structure.** Each gene was designated to be synthetic lethal separately and the χ^2 value from SLIPT was computed for each gene across the graph structure with inhibiting relationships. For each synthetic lethal gene (highlighted in the respective colours), the χ^2 values were computed in 100 simulations of datasets of 20,000 genes including the graph structure and 1000 samples. For each synthetic lethal gene, the adjacent genes exhibited lower χ values with inhibiting relationships.



(a) Inhibiting Graph Structure (b) χ^2 distribution for "A" SL



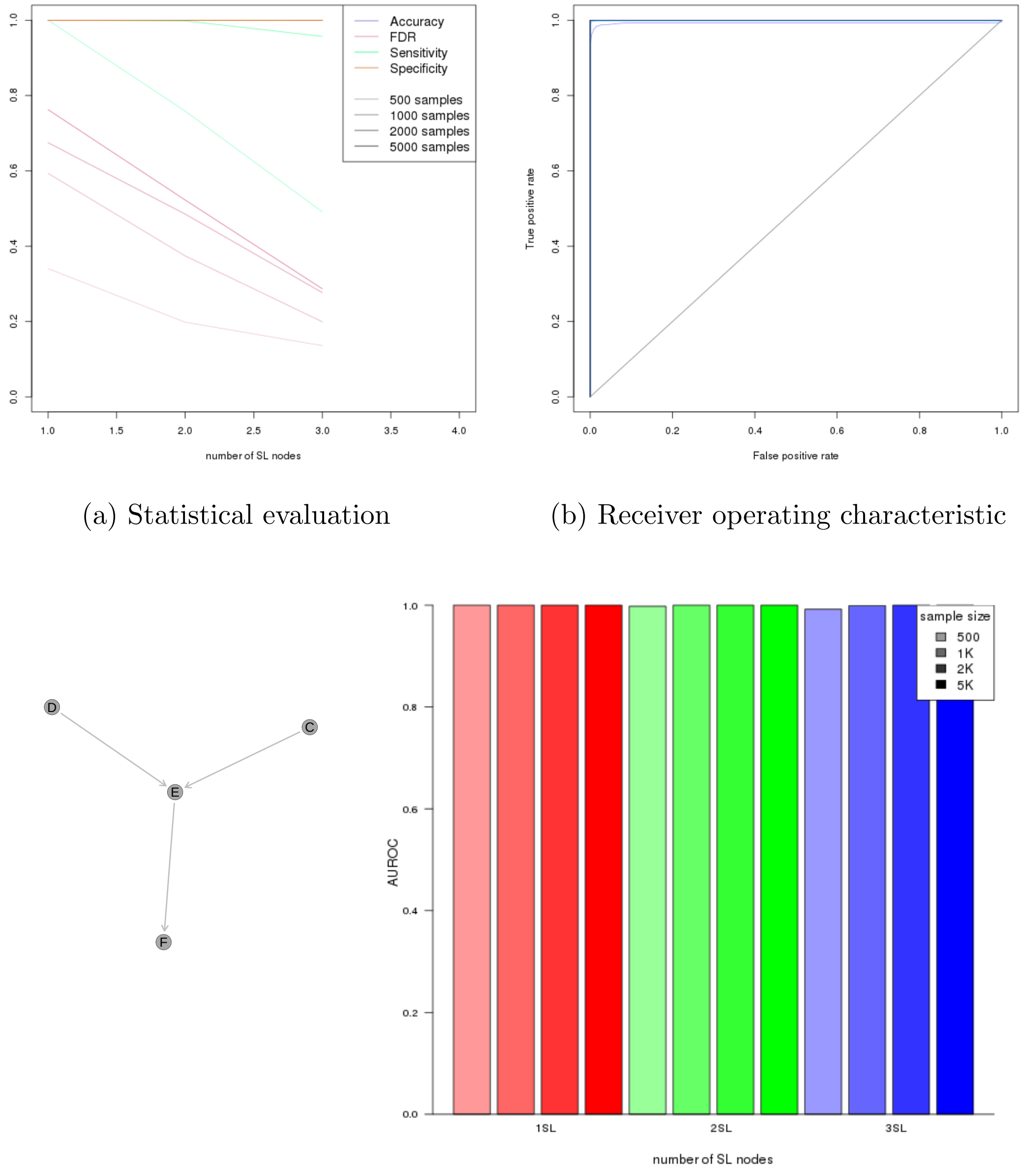
(c) Gene "B" SL (d) Gene "C" SL (e) Gene "D" SL (f) Gene "E" SL



(g) Gene "F" SL (h) Gene "G" SL (i) Gene "H" SL (j) Gene "I" SL

Figure O.22: **Detection of Synthetic Lethality within an Inhibiting Graph Structure.** Each gene was designated to be synthetic lethal separately and the χ^2 value from SLIPT was computed for each gene across the graph structure with inhibiting and relationships. For each synthetic lethal gene (highlighted in the respective colours), the χ^2 values were computed in 100 simulations of datasets of 20,000 genes including the graph structure and 1000 samples.

O.4 Simulations from Graph Structures with 20K genes



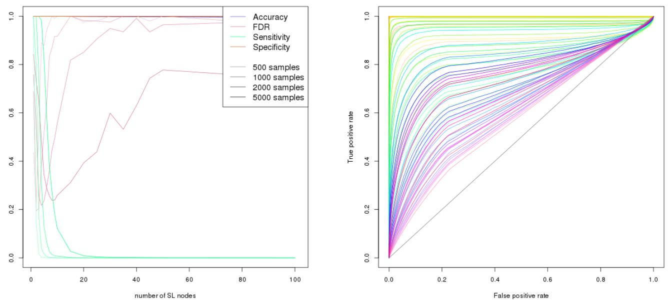
(a) Statistical evaluation

(b) Receiver operating characteristic

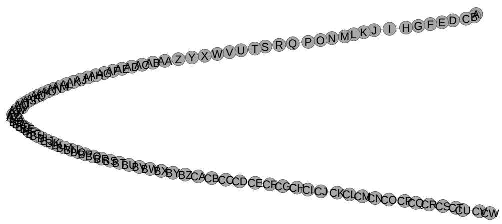
(c) Graph Structure

(d) Statistical performance

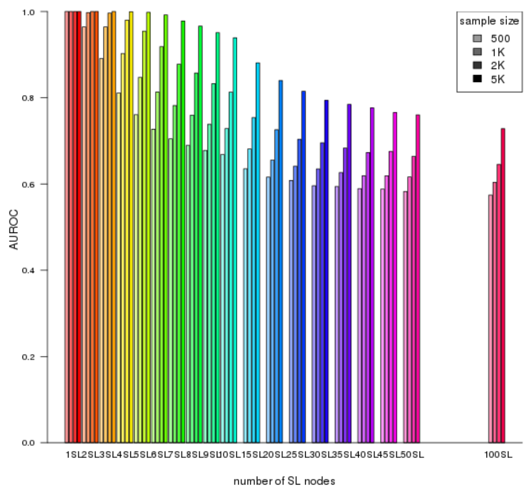
Figure O.23: **Performance of simulations on a simple graph with more genes.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph2. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



(a) Statistical evaluation (b) Receiver operating characteristic

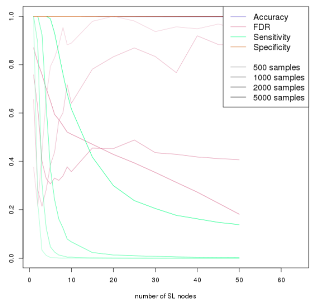


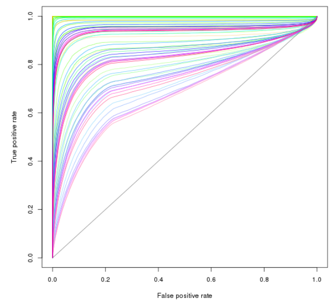
(c) Graph Structure



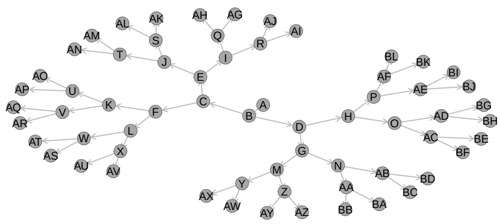
(d) Statistical performance

Figure O.24: **Performance of simulations on a simple graph with more genes.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph2. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.

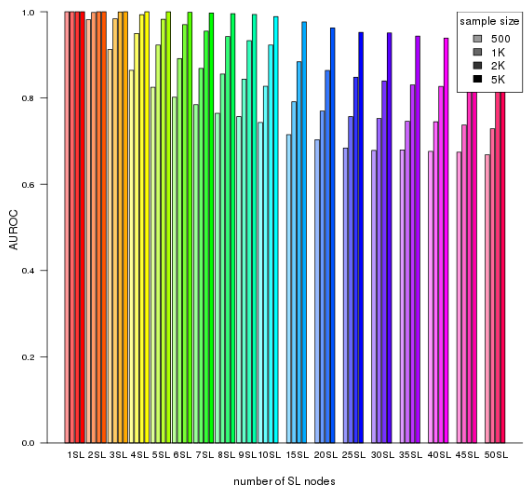




(a) Statistical evaluation (b) Receiver operating characteristic

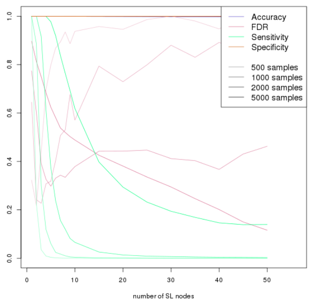


(c) Graph Structure

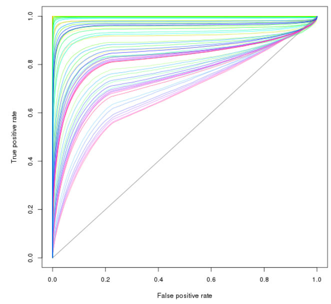


(d) Statistical performance

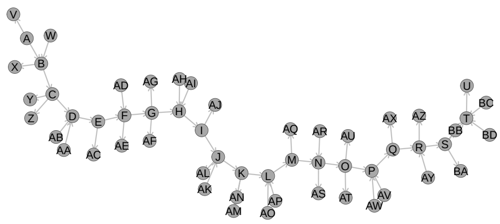
Figure O.25: **Performance of simulations on a simple graph with more genes.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph2. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.



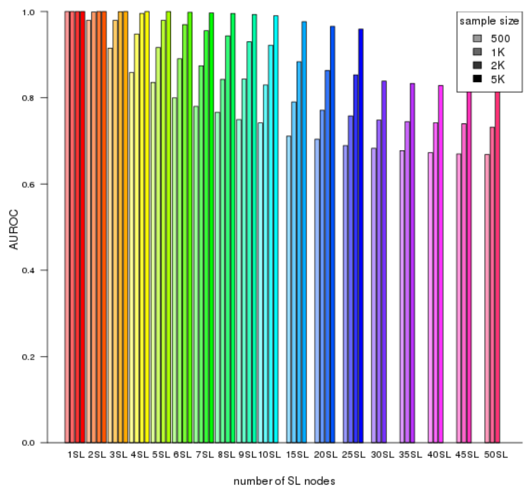
(a) Statistical evaluation



(b) Receiver operating characteristic



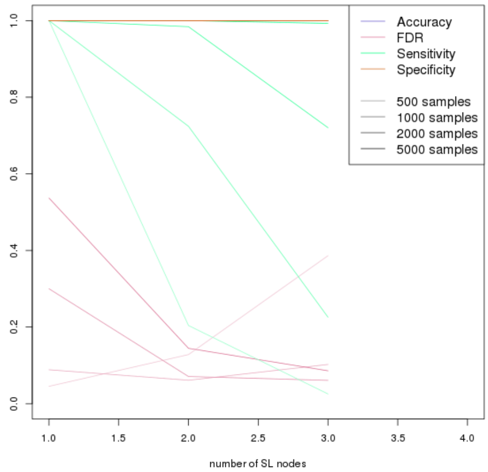
(c) Graph Structure



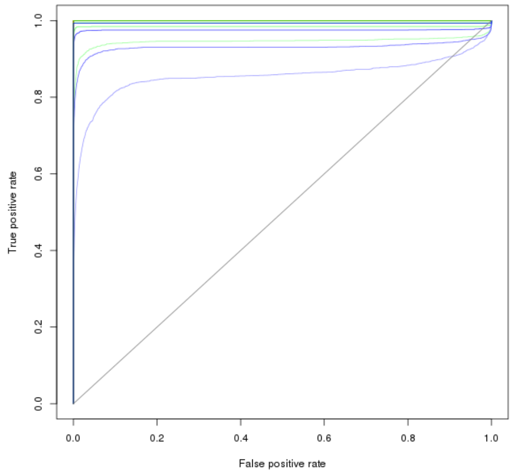
(d) Statistical performance

Figure O.26: **Performance of simulations on a simple graph with more genes.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution generated from Graph2. Performance of SLIPT declines for more synthetic partners and lower sample sizes. For each parameter value, 10,000 simulations were used.

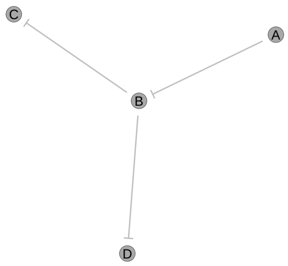
O.5 Simulations from Inhibiting Graph Structures with 20K genes



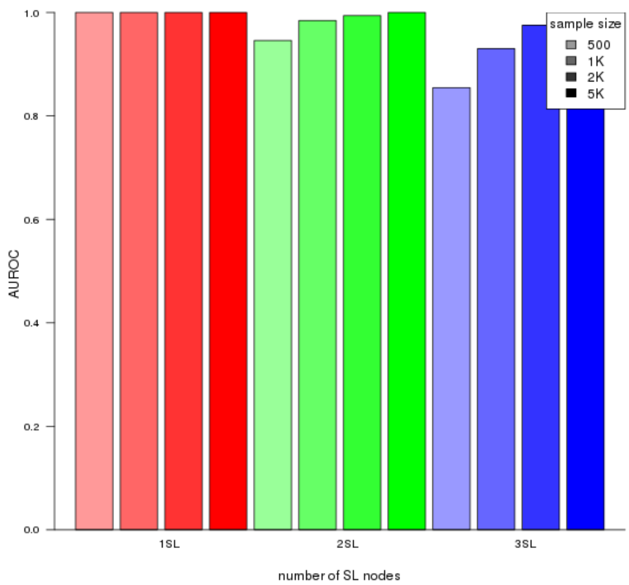
(a) Statistical evaluation



(b) Receiver operating characteristic

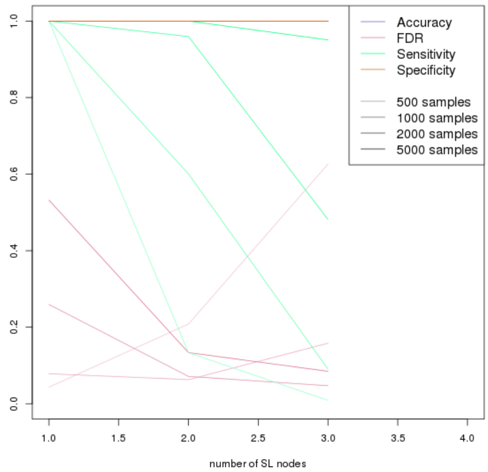


(c) Graph Structure

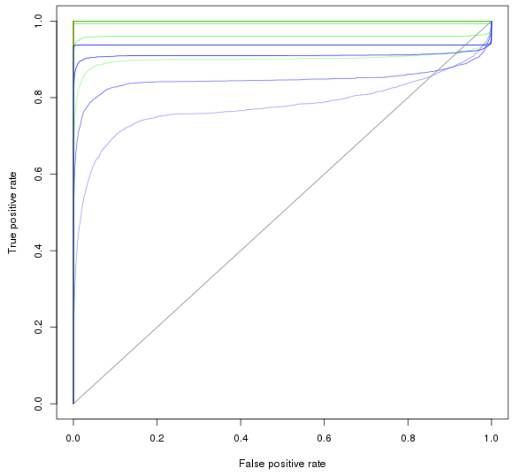


(d) Statistical performance

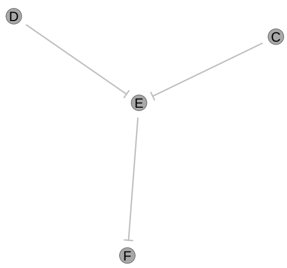
Figure O.27: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (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.



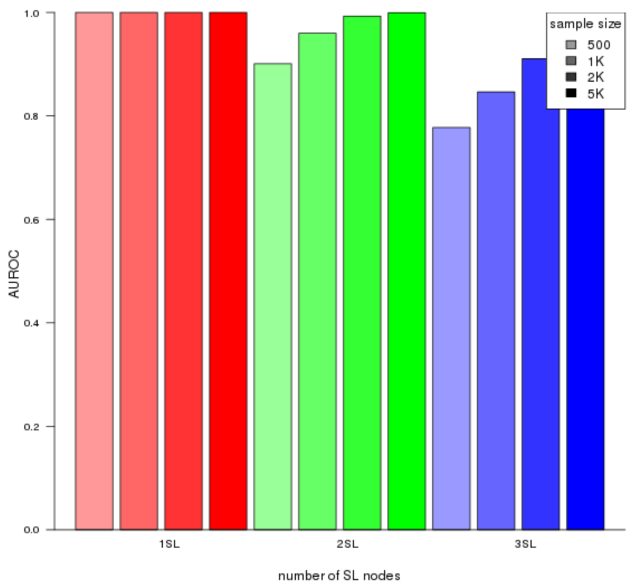
(a) Statistical evaluation



(b) Receiver operating characteristic

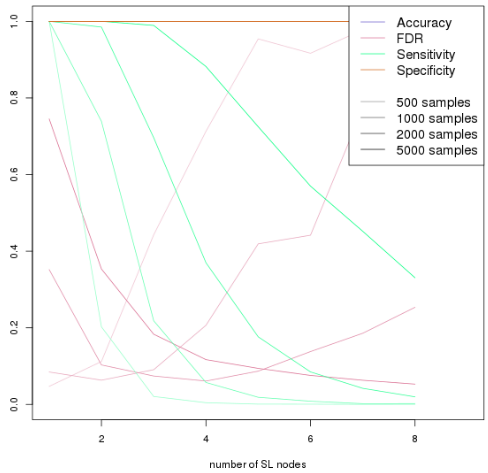


(c) Graph Structure

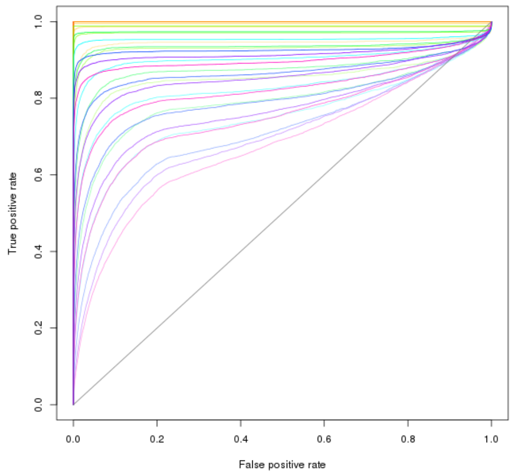


(d) Statistical performance

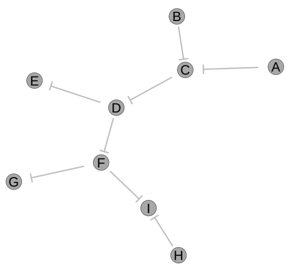
Figure O.28: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (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.



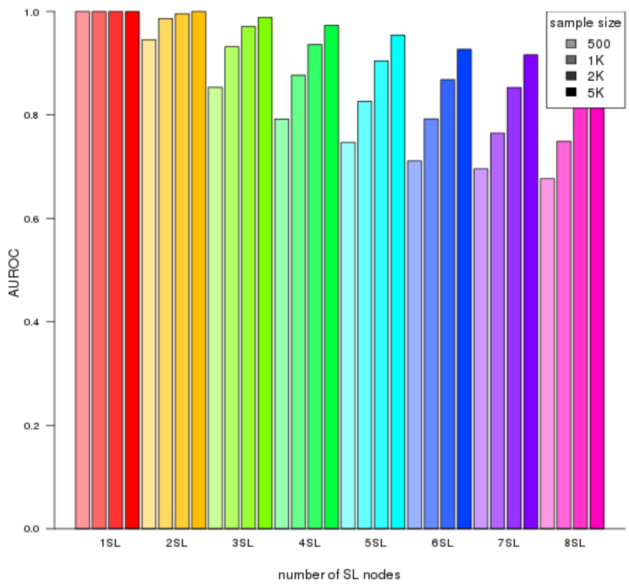
(a) Statistical evaluation



(b) Receiver operating characteristic

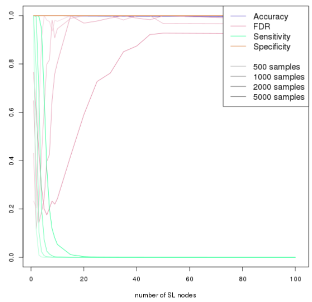


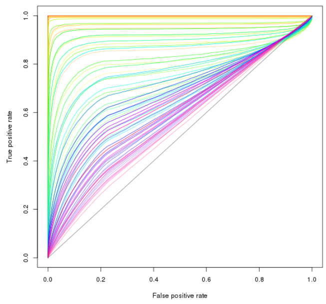
(c) Graph Structure



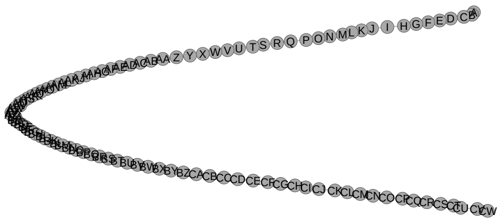
(d) Statistical performance

Figure O.29: **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.

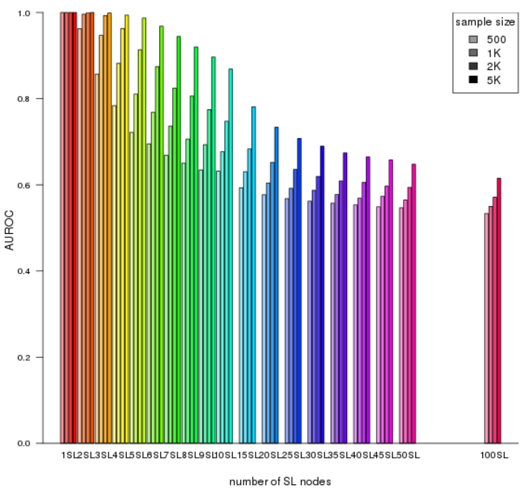




(a) Statistical evaluation (b) Receiver operating characteristic

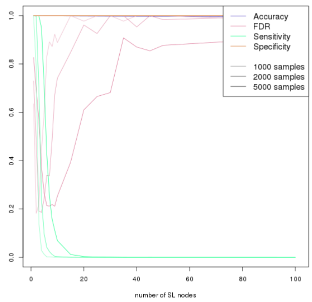


(c) Graph Structure

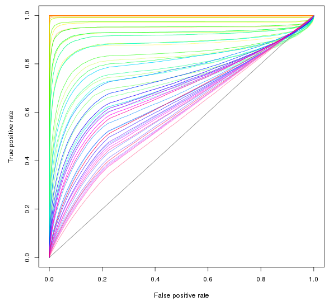


(d) Statistical performance

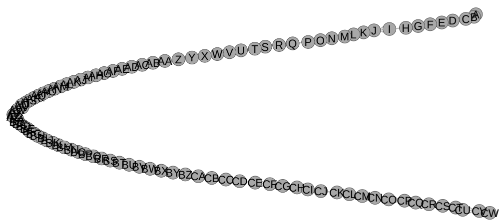
Figure O.30: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (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.



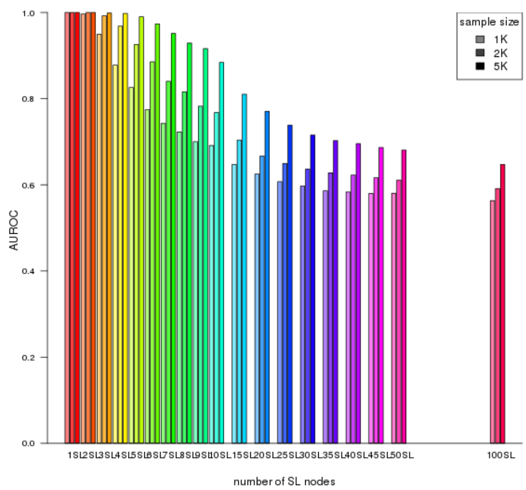
(a) Statistical evaluation



(b) Receiver operating characteristic

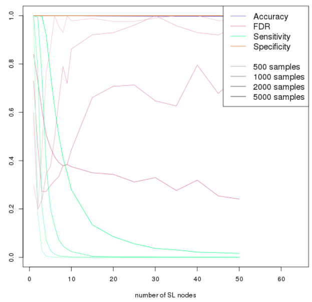


(c) Graph Structure

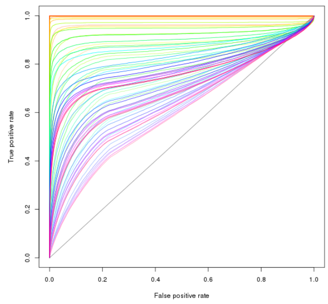


(d) Statistical performance

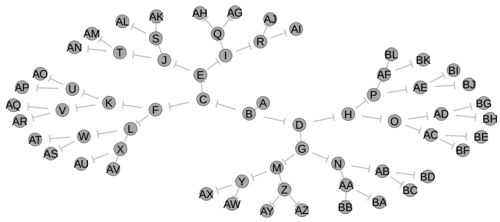
Figure O.31: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (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.



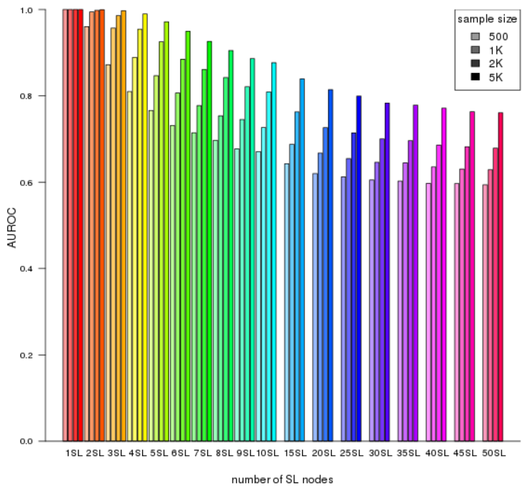
(a) Statistical evaluation



(b) Receiver operating characteristic

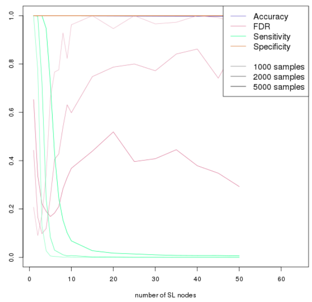


(c) Graph Structure

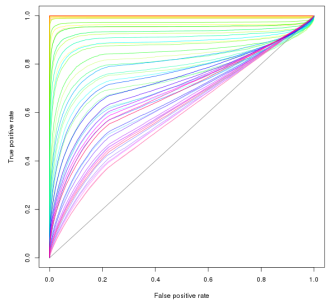


(d) Statistical performance

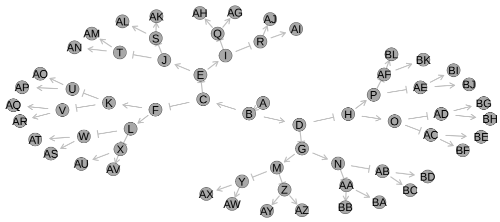
Figure O.32: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (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.



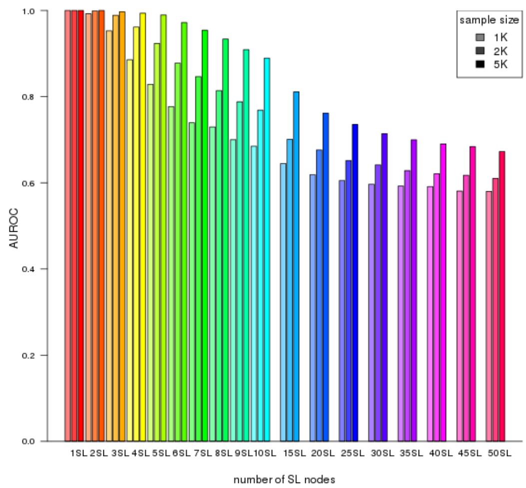
(a) Statistical evaluation



(b) Receiver operating characteristic

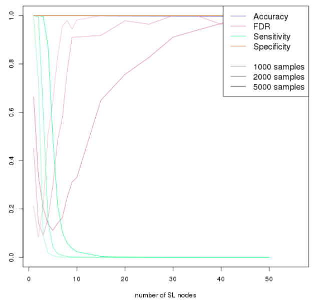


(c) Graph Structure

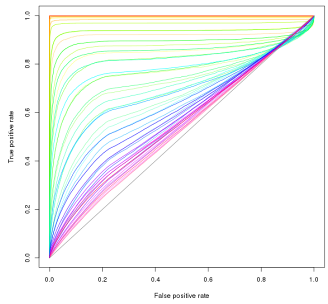


(d) Statistical performance

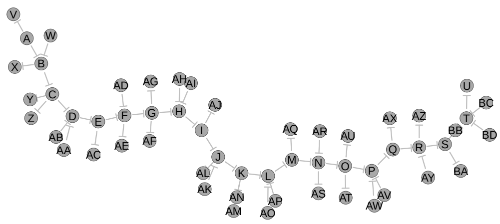
Figure O.33: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (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.



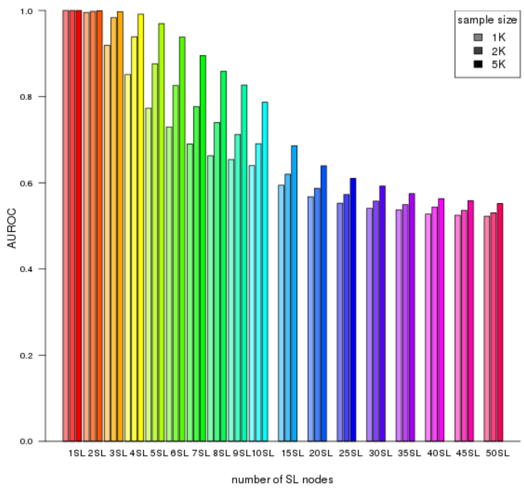
(a) Statistical evaluation



(b) Receiver operating characteristic

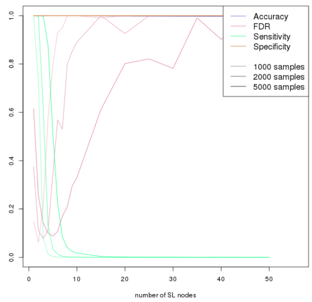


(c) Graph Structure

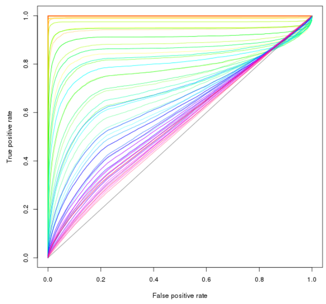


(d) Statistical performance

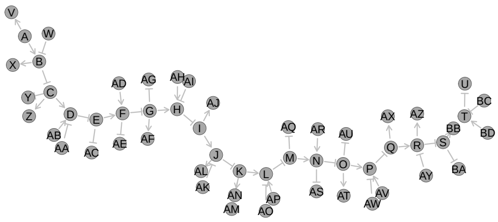
Figure O.34: **Performance of multivariate normal simulations.** Simulation of synthetic lethality was performed sampling from a multivariate normal distribution (without correlation structure). Performance of SLIPT declines for more synthetic partners but this is mitigated by increased sample sizes (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.



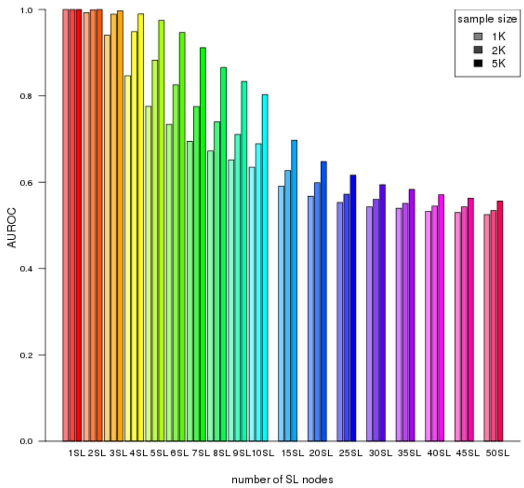
(a) Statistical evaluation



(b) Receiver operating characteristic



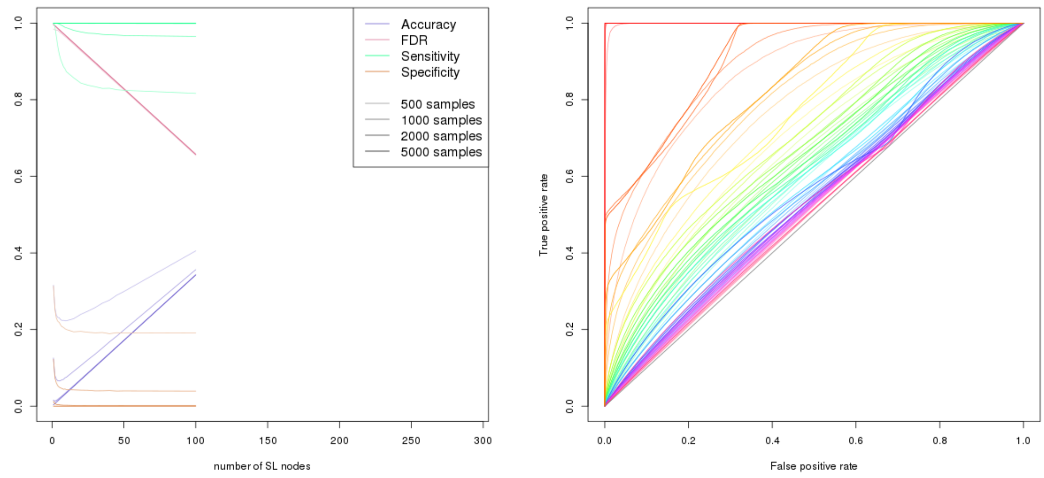
(c) Graph Structure



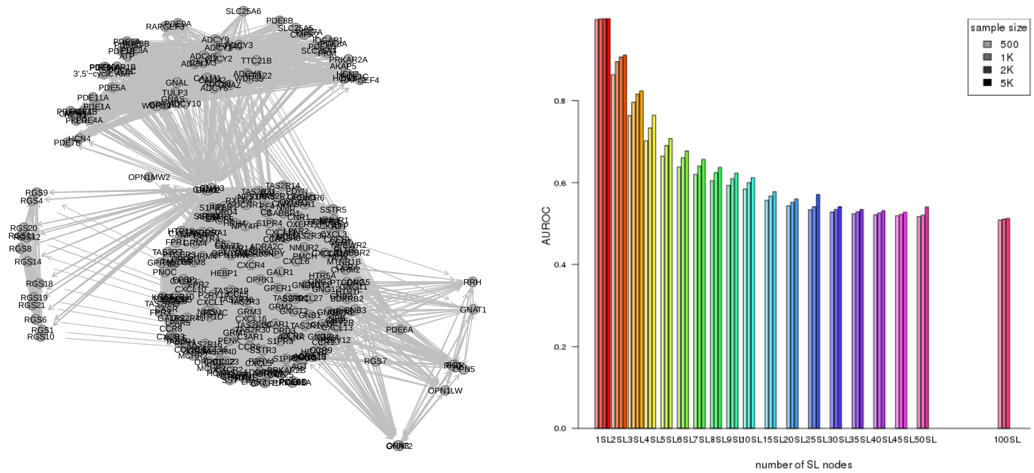
(d) Statistical performance

Figure O.35: **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.

O.6 Simations from Pathway Graph Structures

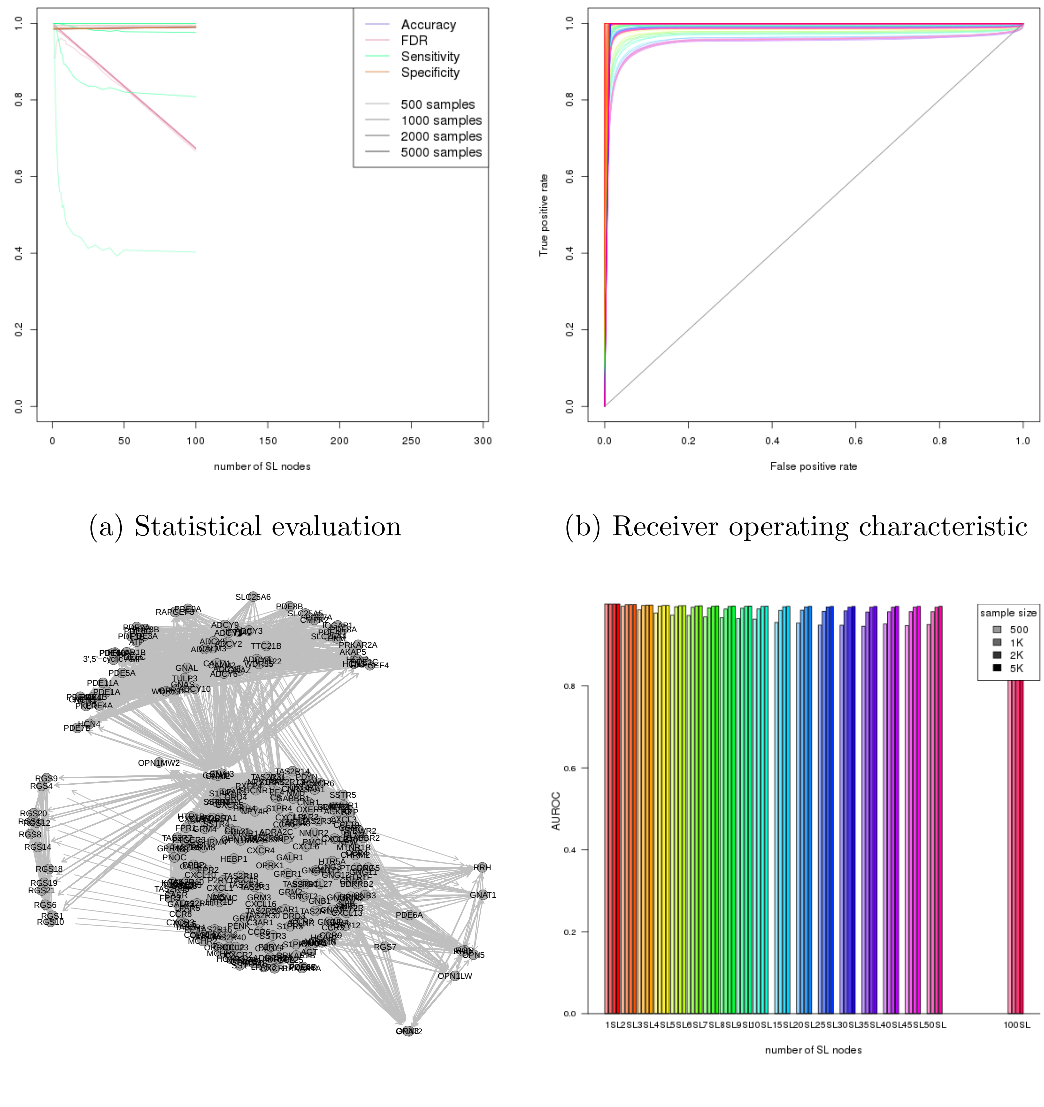


(a) Statistical evaluation (b) Receiver operating characteristic



(c) Graph Structure (d) Statistical performance

Figure O.36: **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 O.37: **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.