

# Contents

<b>Glossary</b>	<b>xi</b>
<b>Acronyms</b>	<b>xii</b>
<b>1 Introduction and Literature Review</b>	<b>1</b>
1.1 Cancer Research in the Post-Genomic Era . . . . .	1
1.1.1 Cancer is a Global Health Issue . . . . .	2
1.1.1.1 The Genetics and Molecular Biology of Cancers . . . . .	3
1.1.2 The Genomics Revolution in Cancer Research . . . . .	3
1.1.2.1 High-Throughput Technologies . . . . .	4
1.1.2.2 Bioinformatics and Genomic Data . . . . .	5
1.1.3 Genomics Projects . . . . .	5
1.1.3.1 The Cancer Genome Project . . . . .	6
1.1.3.2 The Cancer Genome Atlas Project . . . . .	6
1.1.4 Genomic Cancer Medicine . . . . .	8
1.1.4.1 Cancer Genes and Driver Mutations . . . . .	8
1.1.4.2 Precision Cancer Medicine . . . . .	9
1.1.4.3 Molecular Diagnostics and Pan-Cancer Medicine . . . . .	9
1.1.4.4 Targeted Therapeutics and Pharmacogenomics . . . . .	10
1.1.5 Systems and Network Biology . . . . .	11
1.2 Synthetic Lethal Cancer Medicine . . . . .	12
1.2.1 Synthetic Lethal Genetic Interactions . . . . .	12
1.2.2 Synthetic Lethal Concepts in Genetics . . . . .	14
1.2.3 Synthetic Lethality in Model Systems . . . . .	14
1.2.3.1 Synthetic Lethal Pathways and Networks . . . . .	15
1.2.3.2 Evolution of Synthetic Lethality . . . . .	15
1.2.4 Synthetic Lethality in Cancer . . . . .	16
1.2.5 Clinical Impact of Synthetic Lethality in Cancer . . . . .	18
1.2.6 High-throughput Screening for Synthetic Lethality . . . . .	19
1.2.6.1 Synthetic Lethal Screens . . . . .	21
1.2.7 Computational Prediction of Synthetic Lethality . . . . .	22
1.2.7.1 Bioinformatics Approaches to Genetic Interactions . . . . .	22
1.2.7.2 Comparative Genomics . . . . .	23
1.2.7.3 Analysis and Modelling of Protein Data . . . . .	26
1.2.7.4 Differential Gene Expression . . . . .	28
1.2.7.5 Data Mining and Machine Learning . . . . .	29

1.2.7.6	Mutual Exclusivity and Bimodality . . . . .	31
1.2.7.7	Rationale for Further Development . . . . .	33
1.3	E-cadherin as a Synthetic Lethal Target . . . . .	33
1.3.1	The <i>CDH1</i> gene and its Biological Functions . . . . .	33
1.3.2	Hereditary Diffuse Gastric (and Lobular Breast) Cancer . . . . .	34
1.3.3	Cell Line Models of <i>CDH1</i> Null Mutations . . . . .	35
1.4	Summary and Research Direction of Thesis . . . . .	36
1.4.1	Thesis Aims . . . . .	37
<b>2</b>	<b>Methods and Resources</b>	<b>38</b>
2.1	Bioinformatics Resources for Genomics Research . . . . .	38
2.1.1	Public Data and Software Packages . . . . .	38
2.1.1.1	Cancer Genome Atlas Data . . . . .	39
2.1.1.2	Reactome and Annotation Data . . . . .	40
2.2	Data Handling . . . . .	40
2.2.1	Normalisation . . . . .	40
2.2.2	Sample Triage . . . . .	40
2.2.3	Metagenes and the Singular Value Decomposition . . . . .	41
2.2.4	Candidate Triage and Integration with Screen Data . . . . .	43
2.3	Techniques . . . . .	43
2.3.1	Statistical Procedures and Tests . . . . .	44
2.3.2	Gene Set Over-representation Analysis . . . . .	45
2.3.3	Clustering . . . . .	45
2.3.4	Heatmap . . . . .	45
2.3.5	Modelling and Simulations . . . . .	46
2.3.5.1	Receiver Operating Characteristic Curves . . . . .	47
2.3.6	Resampling Analysis . . . . .	47
2.4	Pathway Structure Methods . . . . .	48
2.4.1	Network and Graph Analysis . . . . .	48
2.4.2	Sourcing Graph Structure Data . . . . .	49
2.4.3	Constructing Pathway Subgraphs . . . . .	49
2.4.4	Network Analysis Metrics . . . . .	50
2.5	Implementation . . . . .	51
2.5.1	Computational Resources and Linux Utilities . . . . .	51
2.5.2	R Language and Packages . . . . .	52
2.5.3	High Performance and Parallel Computing . . . . .	55
<b>3</b>	<b>Methods Developed During Thesis</b>	<b>57</b>
3.1	A Synthetic Lethal Detection Methodology . . . . .	57
3.2	Synthetic Lethal Simulation and Modelling . . . . .	59
3.2.1	A Model of Synthetic Lethality in Expression Data . . . . .	60
3.2.2	Simulation Procedure . . . . .	64
3.3	Detecting Simulated Synthetic Lethal Partners . . . . .	67
3.3.1	Binomial Simulation of Synthetic Lethality . . . . .	67
3.3.2	Multivariate Normal Simulation of Synthetic Lethality . . . . .	69
3.3.2.1	Multivariate Normal Simulation with Correlated Genes . . . . .	71

3.3.2.2	Specificity with Query-Correlated Pathways . . . . .	79
3.4	Graph Structure Methods . . . . .	81
3.4.1	Upstream and Downstream Gene Detection . . . . .	81
3.4.1.1	Permutation Analysis for Statistical Significance . . . . .	82
3.4.2	Simulating Gene Expression from Graph Structures . . . . .	83
3.5	Customised Functions and Packages Developed . . . . .	87
3.5.1	Synthetic Lethal Interaction Prediction Tool . . . . .	87
3.5.2	Data Visualisation . . . . .	88
3.5.3	Extensions to the iGraph Package . . . . .	89
3.5.3.1	Sampling Simulated Data from Graph Structures . . . . .	89
3.5.3.2	Plotting Directed Graph Structures . . . . .	89
3.5.3.3	Computing Information Centrality . . . . .	91
3.5.3.4	Testing Pathway Structure with Permutation Testing . . . . .	91
3.5.3.5	Metapackage to Install iGraph Functions . . . . .	92
<b>4</b>	<b>Synthetic Lethal Analysis of Gene Expression Data</b>	<b>93</b>
4.1	Synthetic Lethal Genes in Breast Cancer . . . . .	94
4.1.1	Synthetic Lethal Pathways in Breast Cancer . . . . .	95
4.1.2	Expression Profiles of Synthetic Lethal Partners . . . . .	97
4.1.2.1	Subgroup Pathway Analysis . . . . .	100
4.2	Comparing Synthetic Lethal Gene Candidates . . . . .	102
4.2.1	Primary siRNA Screen Candidates . . . . .	102
4.2.2	Comparison with Correlation . . . . .	102
4.2.3	Comparison with Primary Screen Viability . . . . .	105
4.2.4	Comparison with Secondary siRNA Screen Validation . . . . .	107
4.2.5	Comparison to Primary Screen at Pathway Level . . . . .	108
4.2.5.1	Resampling Genes for Pathway Enrichment . . . . .	110
4.2.6	Integrating Synthetic Lethal Pathways and Screens . . . . .	115
4.3	Synthetic Lethal Pathway Metagenes . . . . .	116
4.4	Replication in Stomach Cancer . . . . .	118
4.5	Discussion . . . . .	119
4.5.1	Strengths of the SLIPT Methodology . . . . .	119
4.5.2	Synthetic Lethal Pathways for E-cadherin . . . . .	120
4.5.3	Replication and Validation . . . . .	122
4.5.3.1	Integration with siRNA Screening . . . . .	122
4.5.3.2	Replication across Tissues . . . . .	123
4.6	Summary . . . . .	123
<b>5</b>	<b>Synthetic Lethal Pathway Structure</b>	<b>125</b>
5.1	Synthetic Lethal Genes in Reactome Pathways . . . . .	125
5.1.1	The PI3K/AKT Pathway . . . . .	126
5.1.2	The Extracellular Matrix . . . . .	128
5.1.3	G Protein Coupled Receptors . . . . .	131
5.1.4	Gene Regulation and Translation . . . . .	131
5.2	Network Analysis of Synthetic Lethal Genes . . . . .	133
5.2.1	Gene Connectivity and Vertex Degree . . . . .	134

5.2.2	Gene Importance and Centrality . . . . .	135
5.2.2.1	Information Centrality . . . . .	135
5.2.2.2	PageRank Centrality . . . . .	137
5.3	Relationships between Synthetic Lethal Genes . . . . .	138
5.3.1	Detecting Upstream or Downstream Synthetic Lethality . . . . .	139
5.3.2	Resampling for Synthetic Lethal Pathway Structure . . . . .	141
5.4	Discussion . . . . .	143
5.5	Summary . . . . .	145
<b>6</b>	<b>Simulation and Modelling of Synthetic Lethal Pathways</b>	<b>147</b>
6.1	Synthetic Lethal Detection Methods . . . . .	148
6.1.1	Performance of SLIPT and $\chi^2$ across Quantiles . . . . .	149
6.1.1.1	Correlated Query Genes affects Specificity . . . . .	152
6.1.2	Alternative Synthetic Lethal Detection Strategies . . . . .	154
6.1.2.1	Correlation for Synthetic Lethal Detection . . . . .	155
6.1.2.2	Testing for Bimodality with BiSEp . . . . .	156
6.2	Simulations with Graph Structures . . . . .	157
6.2.1	Performance over Graph Structures . . . . .	158
6.2.1.1	Simple Graph Structures . . . . .	158
6.2.1.2	Constructed Graph Structures . . . . .	161
6.2.2	Performance with Inhibitions . . . . .	163
6.2.3	Synthetic Lethality across Graph Structures . . . . .	169
6.2.4	Performance within a Large Simulated Datasets . . . . .	172
6.3	Simulations in More Complex Graph Structures . . . . .	176
6.3.1	Simulations over Pathway-based Graphs . . . . .	177
6.3.2	Pathway Structures in a Large Simulated Datasets . . . . .	180
6.4	Discussion . . . . .	183
6.4.1	Simulation Procedure . . . . .	183
6.4.2	Comparing Methods with Simulated Data . . . . .	184
6.4.3	Design and Performance of SLIPT . . . . .	185
6.4.4	Simulations from Graph Structures . . . . .	187
6.5	Summary . . . . .	188
<b>7</b>	<b>Discussion</b>	<b>189</b>
7.1	Synthetic Lethality and <i>CDH1</i> Biology . . . . .	189
7.1.1	Established Functions of <i>CDH1</i> . . . . .	190
7.1.2	The Molecular Role of <i>CDH1</i> in Cancer . . . . .	190
7.2	Significance . . . . .	191
7.2.1	Synthetic Lethality in the Genomic Era . . . . .	191
7.2.2	Clinical Interventions based on Synthetic Lethality . . . . .	193
7.3	Future Directions . . . . .	194
7.4	Conclusions . . . . .	196
	<b>Bibliography</b>	<b>198</b>

<b>A</b>	<b>Sample Quality</b>	<b>222</b>
A.1	Sample Correlation . . . . .	222
A.2	Replicate Samples in TCGA Breast Cancer Data . . . . .	225
<b>B</b>	<b>Software Used for Thesis</b>	<b>229</b>
<b>C</b>	<b>Mutation Analysis in Breast Cancer</b>	<b>237</b>
C.1	Synthetic Lethal Genes and Pathways . . . . .	237
C.2	Synthetic Lethal Expression Profiles . . . . .	238
C.3	Comparison to Primary Screen . . . . .	241
C.3.1	Resampling Analysis . . . . .	243
C.4	Compare SLIPT genes . . . . .	245
<b>D</b>	<b>Metagene Analysis</b>	<b>247</b>
D.1	Pathway Signature Expression . . . . .	247
D.2	Synthetic Lethal Reactome Metagenes . . . . .	251
<b>E</b>	<b>Intrinsic Subtyping</b>	<b>252</b>
<b>F</b>	<b>Stomach Expression Analysis</b>	<b>254</b>
F.1	Synthetic Lethal Genes and Pathways . . . . .	254
F.2	Comparison to Primary Screen . . . . .	258
F.2.1	Resampling Analysis . . . . .	260
F.3	Metagene Analysis . . . . .	262
<b>G</b>	<b>Synthetic Lethal Genes in Pathways</b>	<b>263</b>
<b>H</b>	<b>Network Analysis for Mutation SLIPT</b>	<b>270</b>
<b>I</b>	<b>Pathway Structure for Mutation SLIPT</b>	<b>273</b>
<b>J</b>	<b>Performance of SLIPT and <math>\chi^2</math></b>	<b>275</b>
J.1	Correlated Query Genes affects Specificity . . . . .	281
<b>K</b>	<b>Simulations on Graph Structures</b>	<b>287</b>
K.0.1	Simulations from Inhibiting Graph Structures . . . . .	288
K.1	Simulation across Graph Structures . . . . .	291
K.2	Simulations from Complex Graph Structures . . . . .	295
K.2.1	Simulations from Complex Inhibiting Graphs . . . . .	298
K.3	Simulations from Pathway Graph Structures . . . . .	304

# List of Figures

1.1	Synthetic genetic interactions . . . . .	13
1.2	Synthetic lethality in cancer . . . . .	17
2.1	Read count density . . . . .	42
2.2	Read count sample mean . . . . .	42
3.1	Framework for synthetic lethal prediction . . . . .	58
3.2	Synthetic lethal prediction adapted for mutation . . . . .	59
3.3	A model of synthetic lethal gene expression . . . . .	61
3.4	Modelling synthetic lethal gene expression . . . . .	62
3.5	Synthetic lethality with multiple genes . . . . .	63
3.6	Simulating gene function . . . . .	65
3.7	Simulating synthetic lethal gene function . . . . .	65
3.8	Simulating synthetic lethal gene expression . . . . .	66
3.9	Performance of binomial simulations . . . . .	68
3.10	Comparison of statistical performance . . . . .	68
3.11	Performance of multivariate normal simulations . . . . .	70
3.12	Simulating expression with correlated gene blocks . . . . .	72
3.13	Simulating expression with correlated gene blocks . . . . .	73
3.14	Synthetic lethal prediction across simulations . . . . .	75
3.15	Performance with correlations . . . . .	76
3.16	Comparison of statistical performance with correlation structure . . . . .	77
3.17	Performance with query correlations . . . . .	78
3.18	Statistical evaluation of directional criteria . . . . .	79
3.19	Performance of directional criteria . . . . .	80
3.20	Simulated graph structures . . . . .	84
3.21	Simulating expression from a graph structure . . . . .	85
3.22	Simulating expression from graph structure with inhibitions . . . . .	86
3.23	Demonstration of violin plots with custom features . . . . .	90
3.24	Demonstration of annotated heatmap . . . . .	90
3.25	Simulating graph structures . . . . .	91
4.1	Synthetic lethal expression profiles of analysed samples . . . . .	98
4.2	Comparison of SLIPT with siRNA . . . . .	103
4.3	Comparison of SLIPT and siRNA genes with correlation . . . . .	103
4.4	Comparison of SLIPT and siRNA genes with correlation . . . . .	105
4.5	Comparison of SLIPT and siRNA genes with screen viability . . . . .	106

4.6	Comparison of SLIPT genes with siRNA screen viability . . . . .	106
4.7	Resampled intersection of SLIPT and siRNA candidate genes . . . . .	111
5.1	Synthetic lethality in the PI3K cascade . . . . .	127
5.2	Synthetic lethality in Elastic Fibre Formation . . . . .	129
5.3	Synthetic lethality in Fibrin Clot Formation . . . . .	130
5.4	Synthetic lethality in the GPCRs . . . . .	132
5.5	Synthetic lethality and vertex degree . . . . .	134
5.6	Synthetic lethality and centrality . . . . .	136
5.7	Synthetic lethality and PageRank . . . . .	138
5.8	Structure of synthetic lethality resampling . . . . .	140
6.1	Performance of $\chi^2$ and SLIPT across quantiles . . . . .	150
6.2	Performance of $\chi^2$ and SLIPT across quantiles with more genes . . . . .	151
6.3	Performance of $\chi^2$ and SLIPT across quantiles with query correlation . . . . .	152
6.4	Performance of $\chi^2$ and SLIPT across quantiles with query correlation and more genes . . . . .	153
6.5	Performance of negative correlation and SLIPT . . . . .	156
6.6	Simple graph structures . . . . .	159
6.7	Performance of simulations on a simple graph . . . . .	160
6.8	Performance of simulations is similar in simple graphs . . . . .	161
6.9	Performance of simulations on a pathway . . . . .	162
6.10	Performance of simulations on a simple graph with inhibition . . . . .	164
6.11	Performance is higher on a simple inhibiting graph . . . . .	166
6.12	Performance of simulations on a constructed graph with inhibition . . . . .	167
6.13	Performance is affected by inhibition in graphs . . . . .	168
6.14	Detection of synthetic lethality within a graph structure . . . . .	170
6.15	Performance of simulations including a simple graph . . . . .	173
6.16	Performance on a simple graph improves with more genes . . . . .	174
6.17	Performance on an inhibiting graph improves with more genes . . . . .	176
6.18	Performance of simulations on the PI3K cascade . . . . .	179
6.19	Performance of simulations including the PI3K cascade . . . . .	181
6.20	Performance on pathways improves with more genes . . . . .	182
A.1	Correlation profiles of removed samples . . . . .	223
A.2	Correlation analysis and sample removal . . . . .	224
A.3	Replicate excluded samples . . . . .	225
A.4	Replicate samples with all remaining . . . . .	226
A.5	Replicate samples with some excluded . . . . .	227
C.1	Synthetic lethal expression profiles of analysed samples . . . . .	239
C.2	Comparison of mtSLIPT to short interfering RNA (siRNA) . . . . .	241
C.3	Compare mtSLIPT and siRNA genes with correlation . . . . .	245
C.4	Compare mtSLIPT and siRNA genes with correlation . . . . .	245
C.5	Compare mtSLIPT and siRNA genes with siRNA viability . . . . .	246
D.1	Pathway metagene expression profiles . . . . .	249

D.2	Expression profiles for estrogen receptor related genes . . . . .	250
F.1	Synthetic lethal expression profiles of stomach samples . . . . .	256
F.2	Comparison of SLIPT in stomach to siRNA . . . . .	258
G.1	Synthetic lethality in the PI3K/AKT pathway . . . . .	263
G.2	Synthetic lethality in the PI3K/AKT pathway in cancer . . . . .	264
G.3	Synthetic lethality in the Extracellular Matrix . . . . .	265
G.4	Synthetic lethality in the GPCR Downstream . . . . .	266
G.5	Synthetic lethality in the Translation Elongation . . . . .	267
G.6	Synthetic lethality in the Nonsense-mediated Decay . . . . .	268
G.7	Synthetic lethality in the 3' UTR . . . . .	269
H.1	Synthetic lethality and vertex degree . . . . .	270
H.2	Synthetic lethality and centrality . . . . .	271
H.3	Synthetic lethality and PageRank . . . . .	271
I.1	Structure of synthetic lethality resampling . . . . .	273
J.1	Performance of $\chi^2$ and SLIPT across quantiles . . . . .	275
J.2	Performance of $\chi^2$ and SLIPT across quantiles . . . . .	277
J.3	Performance of $\chi^2$ and SLIPT across quantiles with more genes . . . . .	279
J.4	Performance of $\chi^2$ and SLIPT across quantiles with query correlation . . . . .	281
J.5	Performance of $\chi^2$ and SLIPT across quantiles with query correlation . . . . .	283
J.6	Performance of $\chi^2$ and SLIPT across quantiles with query correlation and more genes . . . . .	285
K.1	Performance of simulations on a simple graph . . . . .	287
K.2	Performance of simulations on an inhibiting graph . . . . .	288
K.3	Performance of simulations on a constructed graph with inhibition . . . . .	289
K.4	Performance of simulations on a constructed graph with inhibition . . . . .	290
K.5	Detection of synthetic lethality within a graph structure . . . . .	291
K.6	Detection of synthetic lethality within an inhibiting graph . . . . .	293
K.7	Detection of synthetic lethality within an inhibiting graph . . . . .	294
K.8	Performance of simulations on a branching graph . . . . .	295
K.9	Performance of simulations on a complex graph . . . . .	296
K.10	Performance of simulations on a large graph . . . . .	297
K.11	Performance of simulations on a branching graph with inhibition . . . . .	298
K.12	Performance of simulations on a branching graph with inhibition . . . . .	299
K.13	Performance of simulations on a complex graph with inhibition . . . . .	300
K.14	Performance of simulations on a complex graph with inhibition . . . . .	301
K.15	Performance of simulations on a large constructed graph with inhibition . . . . .	302
K.16	Performance of simulations on a large constructed graph with inhibition . . . . .	303
K.17	Performance of simulations on the $G_{\alpha i}$ signalling pathway . . . . .	304
K.18	Performance of simulations including the $G_{\alpha i}$ signalling pathway . . . . .	305



# List of Tables

1.1	Methods for predicting genetic interactions . . . . .	23
1.2	Methods for predicting synthetic lethality in cancer . . . . .	23
1.3	Methods used by Wu <i>et al.</i> (2014) . . . . .	25
2.1	Excluded samples by batch and clinical characteristics. . . . .	41
2.2	Computers used during thesis . . . . .	51
2.3	Linux utilities and applications used during thesis . . . . .	52
2.4	R installations used during thesis . . . . .	53
2.5	R Packages used during thesis . . . . .	53
2.6	R packages developed during thesis . . . . .	55
4.1	Candidate synthetic lethal gene partners of <i>CDH1</i> from SLIPT . . . . .	95
4.2	Pathways for <i>CDH1</i> partners from SLIPT . . . . .	96
4.3	Pathways for clusters of <i>CDH1</i> partners from SLIPT . . . . .	101
4.4	ANOVA for synthetic lethality and correlation with <i>CDH1</i> . . . . .	104
4.5	Comparison of Synthetic Lethal Interaction Prediction Tool (SLIPT) genes against secondary siRNA screen . . . . .	108
4.6	Pathways for <i>CDH1</i> partners from SLIPT and siRNA . . . . .	109
4.7	Pathways for <i>CDH1</i> partners from SLIPT . . . . .	112
4.8	Pathways for <i>CDH1</i> partners from SLIPT and siRNA primary screen .	113
4.9	Examples of candidate metagenes synthetic lethal for <i>CDH1</i> from SLIPT	117
5.1	ANOVA for synthetic lethality and vertex degree . . . . .	135
5.2	ANOVA for synthetic lethality and information centrality . . . . .	136
5.3	ANOVA for synthetic lethality and PageRank centrality . . . . .	137
5.4	Resampling for pathway structure of synthetic lethal detection methods	142
B.1	Complete list of R packages used during this thesis . . . . .	229
C.1	Candidate synthetic lethal gene partners of <i>CDH1</i> from mtSLIPT . . .	237
C.2	Pathways for <i>CDH1</i> partners from mtSLIPT . . . . .	238
C.3	Pathways for clusters of <i>CDH1</i> partners from mtSLIPT . . . . .	240
C.4	Pathways for <i>CDH1</i> partners from mtSLIPT and siRNA . . . . .	242
C.5	Pathways for <i>CDH1</i> partners from mtSLIPT . . . . .	243
C.6	Pathways for <i>CDH1</i> partners from mtSLIPT and siRNA primary screen	244
D.1	Candidate synthetic lethal metagenes against <i>CDH1</i> from mtSLIPT . .	251

E.1	Comparison of intrinsic subtypes . . . . .	252
F.1	Synthetic lethal gene partners of <i>CDH1</i> from SLIPT in stomach cancer	254
F.2	Pathways for <i>CDH1</i> partners from SLIPT in stomach cancer . . . . .	255
F.3	Pathways for clusters of <i>CDH1</i> partners in stomach SLIPT . . . . .	257
F.4	Pathways for <i>CDH1</i> partners from SLIPT and siRNA . . . . .	259
F.5	Pathways for <i>CDH1</i> partners from SLIPT in stomach cancer . . . . .	260
F.6	Pathways for <i>CDH1</i> partners from SLIPT in stomach and siRNA . . . .	261
F.7	Synthetic lethal metagenes against <i>CDH1</i> in stomach cancer . . . . .	262
H.1	ANOVA for synthetic lethality and vertex degree . . . . .	272
H.2	ANOVA for synthetic lethality and information centrality . . . . .	272
H.3	ANOVA for synthetic lethality and PageRank centrality . . . . .	272
I.1	Resampling for pathway structure of synthetic lethal detection methods	274

# Glossary

gene expression	A measure of the relative expression of each gene from the mRNA extracted from (pooled) cells.
graph or network	A mathematical structure modelling or depicting the relationships between elements.
metagene	A consistent signal of expression for a collection of genes such as a biological pathway, derived from singular value decomposition.
mutation	A change in DNA sequence that disrupts gene function.
synthetic lethal	Genetic interactions where inactivation of multiple genes is inviable (or deleterious) which are viable if inactivated separately.

# Acronyms

ANOVA	Analysis of Variance.
CRAN	comprehensive R archive network.
ER	Estrogen Receptor.
mtSLIPT	Synthetic Lethal Interaction Prediction Tool (against mutation).
PAM50	Prediction Analysis of Microarray 50.
siRNA	Short Interfering RNA.
SLIPT	Synthetic Lethal Interaction Prediction Tool.
TCGA	The Cancer Genome Atlas (genomics project).

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# Appendix A

## Sample Quality

### A.1 Sample Correlation

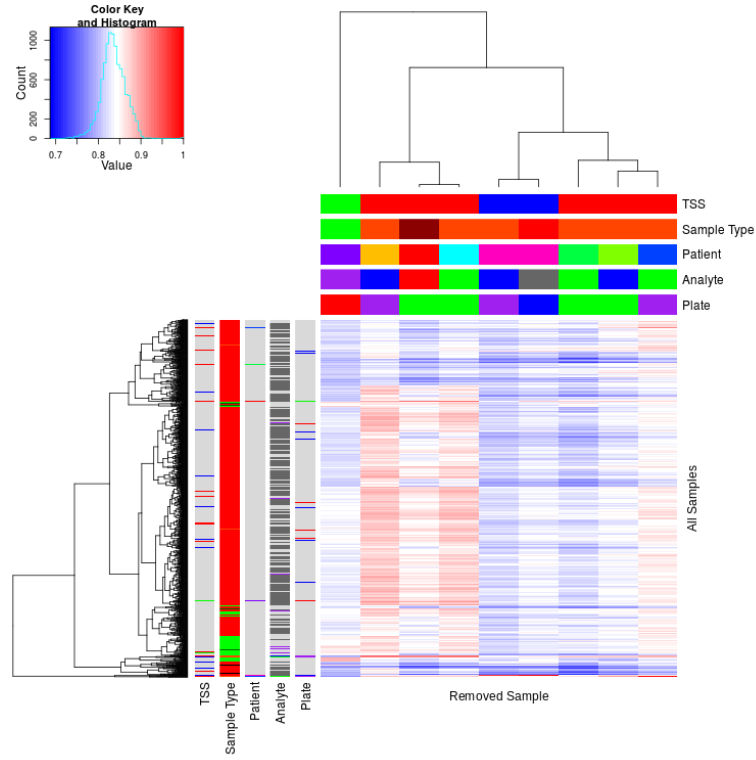


Figure A.1: **Correlation profiles of removed samples.** Heatmap (Euclidean distance) of samples in [The Cancer Genome Atlas \(TCGA\)](#) breast cancer dataset (left) clustered for all samples against removed samples (top): tissue source site (TSS), sample type with reds for tumour and greens for normal, patient (A2QH in pink), with varied analyte and plate. Excluded samples clustered at the bottom and annotation (left) show shared properties between samples in the dataset.

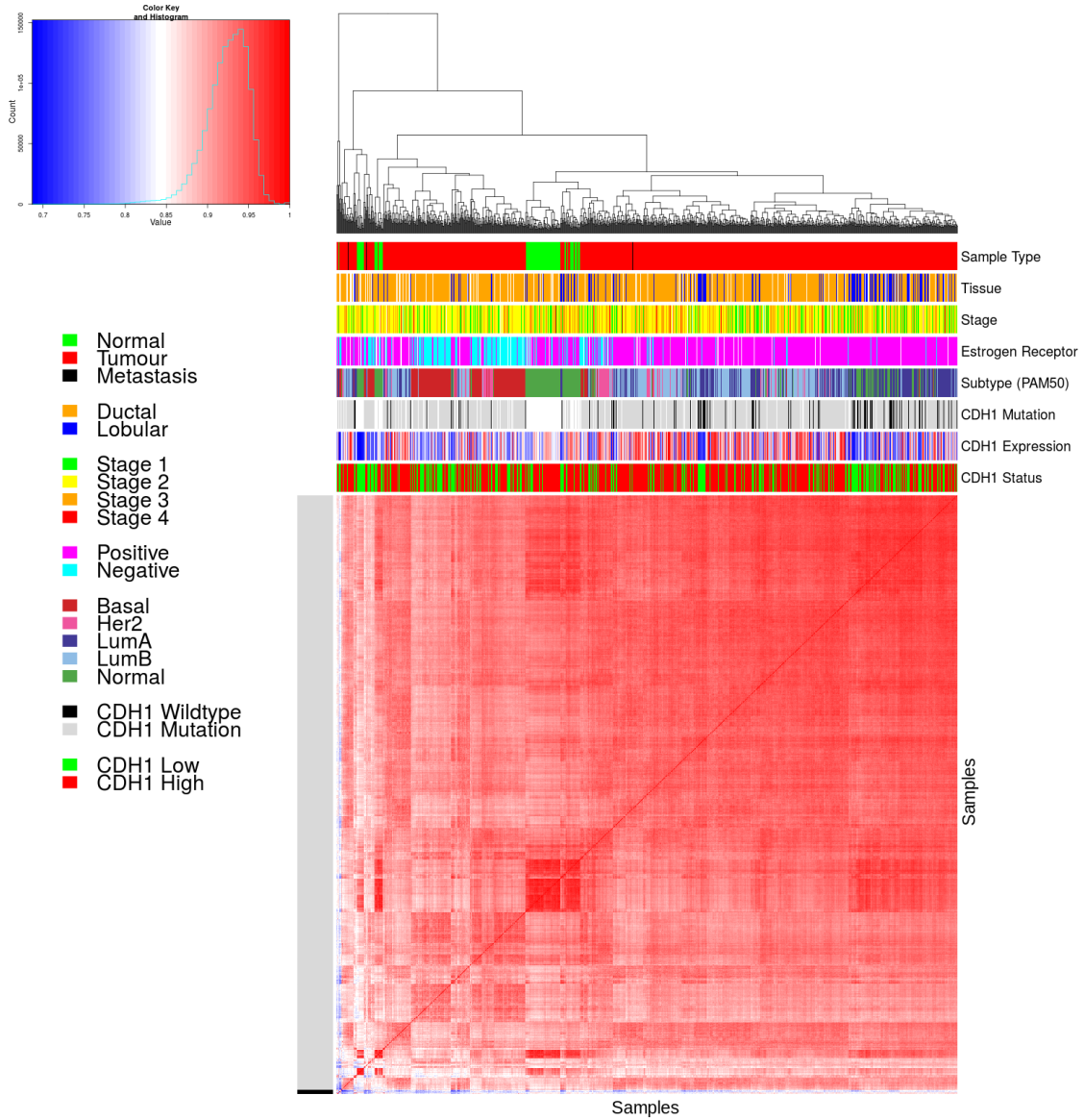


Figure A.2: **Correlation analysis and sample removal.** Correlation matrix heatmap (Euclidean distance) of all samples in [TCGA](#) breast cancer dataset against each other annotated for sample clinical data: sample type, tissue type, tumour stage, [Estrogen receptor \(ER\)](#) and intrinsic subtype (from the [PAM50](#) method). *CDH1* somatic mutation, gene expression, and status for [SLIPT](#) prediction were also annotated. Discrete variables were coloured as displayed in the legend and continuous variables on a blue–red scale as shown in the colour key. Trimmed samples cluster at the bottom of the heatmap and the colour bars of the left show which were removed for quality concerns.

## A.2 Replicate Samples in TCGA Breast Cancer Data

Replicate samples were picked where possible from the [TCGA](#) breast cancer gene expression data to examine for sample quality. Independent samples of the same tumour were expected to have very high Pearson correlation between their expression profiles unless there were issues with sample collection or preparation and were thus an indicator of sample quality. The log-transformed raw read counts for replicate samples were examined in Figures [A.3–A.5](#). These were examined before normalisation which would be expected to increase sample concordance.

Another consideration was the samples which were removed for quality concerns (in Section [2.2.2](#)). While these were selected by unbiased hierarchical clustering (See Figure [A.2](#)), many of the excluded (tumour) samples were performed in replicate despite relatively few replicate samples in the overall dataset. These samples correlate poorly with the rest of the dataset, in addition to correlation with replicate samples.

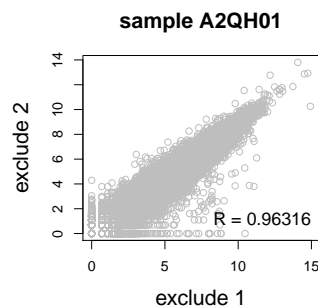


Figure A.3: **Replicate excluded samples.** Both tumour samples of patient A2QH were excluded as they were poorly correlated with other samples, although they were highly similar to each other as shown by Pearson correlation of log-raw counts.



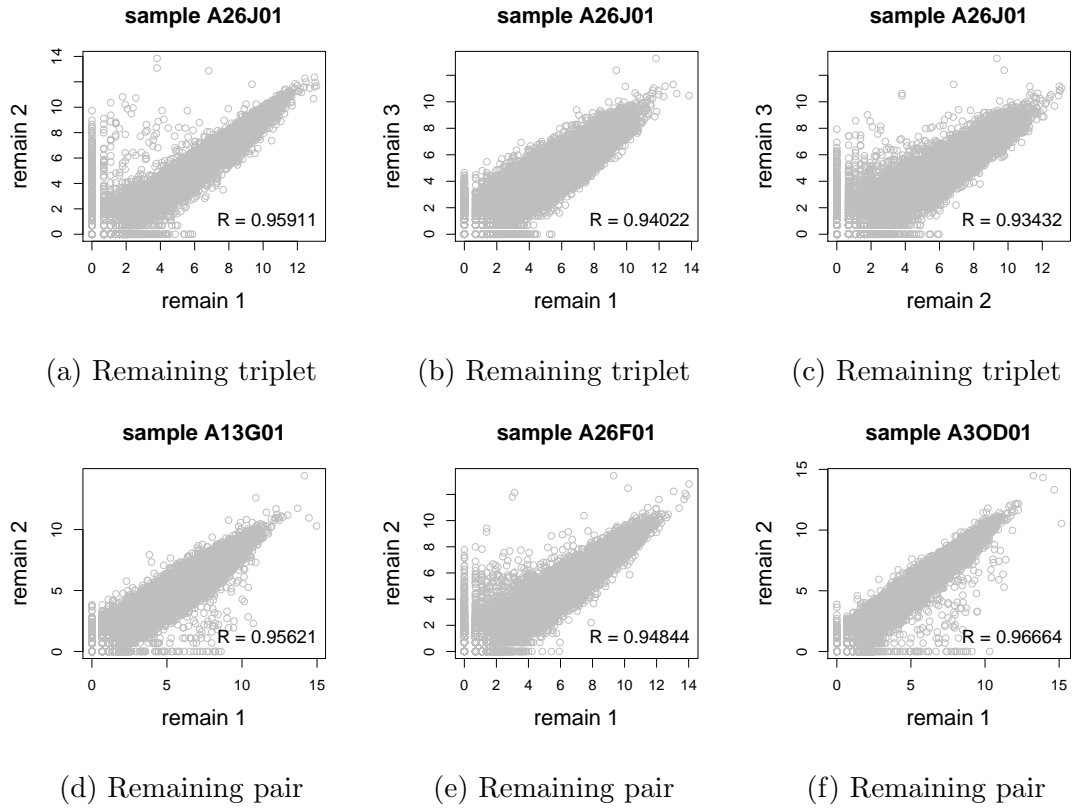


Figure A.4: **Replicate samples with all remaining.** Patient A26J was sampled 3 times and compared pairwise. Pairs of samples were also compared for other patients with replicate samples. In all cases, replicate samples remaining in the dataset were highly concordant, as shown by Pearson correlation of log-raw counts.

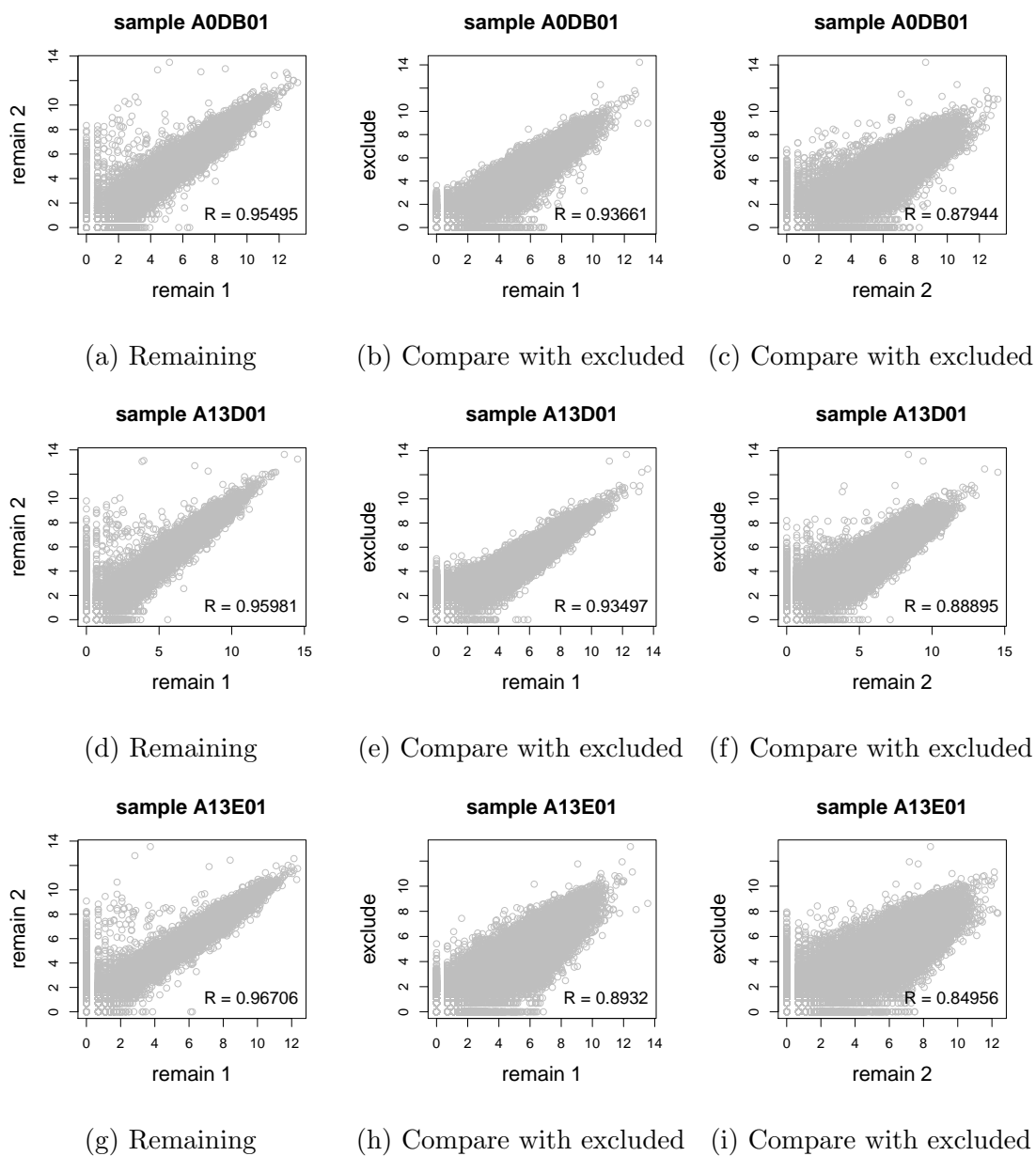


Figure A.5: **Replicate samples with some excluded.** (continued on next page)

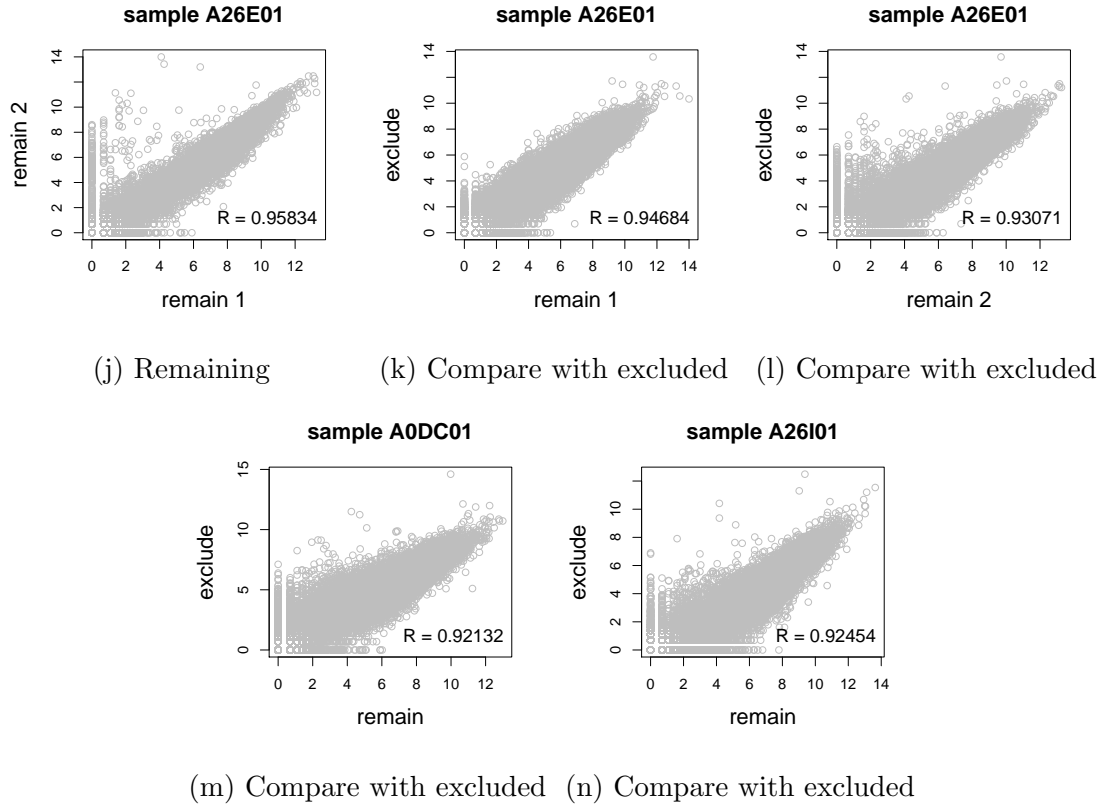


Figure A.5: **Replicate samples with some excluded.** Patients A0DB, A13D, A13E, and A26E were each sampled 3 times and compared pairwise. Pairs of samples were also compared for other patients with replicate samples. In all cases, the replicate samples remaining in the dataset more were highly concordant than those excluded from the analysis, as shown by Pearson correlation of log-raw counts.

# Appendix B

## Software Used for Thesis

Table B.1: Complete list of R packages used during this thesis

Package	Repository	Laptop	Lab	Server	NeSI
base	base	3.3.2	3.3.2	3.3.1	3.3.0
abind	<a href="#">CRAN</a>		1.4-5		1.4-3
acepack	<a href="#">CRAN</a>		1.4.1		1.3-3.3
ade4	<a href="#">CRAN</a>		1.7-5		
annaffy	Bioconductor		1.46.0		
AnnotationDbi	Bioconductor		1.36.0	1.36.0	1.34.4
apComplex	<a href="#">CRAN</a>		2.40.0		
ape	<a href="#">CRAN</a>		4		3.4
arm	<a href="#">CRAN</a>		1.9-3		
assertthat	<a href="#">CRAN</a>	0.1	0.1	0.1	0.1
backports	<a href="#">CRAN</a>	1.0.5	1.0.4	1.0.5	1.0.2
base64	<a href="#">CRAN</a>			2	2
base64enc	<a href="#">CRAN</a>		0.1-3		0.1-3
beanplot	<a href="#">CRAN</a>		1.2	1.2	1.2
BH	<a href="#">CRAN</a>	1.60.0-2	1.62.0-1	1.62.0-1	1.60.0-2
Biobase	Bioconductor		2.34.0	2.34.0	2.32.0
BiocGenerics	Bioconductor		0.20.0	0.20.0	0.18.0
BiocInstaller	Bioconductor		1.24.0	1.20.3	1.22.3
BiocParallel	Bioconductor		1.8.1	1.8.1	
Biostings	Bioconductor		2.42.1	2.42.0	
BiSEp	Bioconductor		2.0.1	2.0.1	2.0.1

bitops	<a href="#">CRAN</a>	1.0-6	1.0-6	1.0-6	1.0-6
boot	base	1.3-18	1.3-18	1.3-18	1.3-18
brew	<a href="#">CRAN</a>	1.0-6	1.0-6	1.0-6	1.0-6
broom	<a href="#">CRAN</a>	0.4.1			
caTools	<a href="#">CRAN</a>	1.17.1	1.17.1	1.17.1	1.17.1
cgdsr	<a href="#">CRAN</a>		1.2.5		
checkmate	<a href="#">CRAN</a>		1.8.2		1.7.4
chron	<a href="#">CRAN</a>	2.3-47	2.3-48	2.3-50	2.3-47
class	base	7.3-14	7.3-14	7.3-14	7.3-14
cluster	base	2.0.5	2.0.5	2.0.5	2.0.4
coda	<a href="#">CRAN</a>		0.19-1		0.18-1
codetools	base	0.2-15	0.2-15	0.2-15	0.2-14
colorRamps	<a href="#">CRAN</a>		2.3		
colorspace	<a href="#">CRAN</a>	1.2-6	1.3-2	1.3-2	1.2-6
commonmark	<a href="#">CRAN</a>	1.1		1.2	
compiler	base	3.3.2	3.3.2	3.3.1	3.3.0
corpcor	<a href="#">CRAN</a>		1.6.8	1.6.8	1.6.8
Cprob	<a href="#">CRAN</a>		1.2.4		
crayon	<a href="#">CRAN</a>	1.3.2	1.3.2	1.3.2	1.3.2
crop	<a href="#">CRAN</a>		0.0-2	0.0-2	
curl	<a href="#">CRAN</a>	1.2	2.3	2.3	0.9.7
d3Network	<a href="#">CRAN</a>		0.5.2.1		
data.table	<a href="#">CRAN</a>	1.9.6	1.10.0	1.10.1	1.9.6
data.tree	<a href="#">CRAN</a>		0.7.0	0.7.0	
datasets	base	3.3.2	3.3.2	3.3.1	3.3.0
DBI	<a href="#">CRAN</a>	0.5-1	0.5-1	0.5-1	0.5-1
dendextend	<a href="#">CRAN</a>	1.4.0	1.4.0	1.4.0	
DEoptimR	<a href="#">CRAN</a>	1.0-8	1.0-8	1.0-8	1.0-4
desc	<a href="#">CRAN</a>	1.1.0		1.1.0	
devtools	<a href="#">CRAN</a>	1.12.0	1.12.0	1.12.0	1.12.0
DiagrammeR	<a href="#">CRAN</a>		0.9.0	0.9.0	
dichromat	<a href="#">CRAN</a>	2.0-0	2.0-0	2.0-0	2.0-0
digest	<a href="#">CRAN</a>	0.6.10	0.6.11	0.6.12	0.6.9
diptest	<a href="#">CRAN</a>	0.75-7	0.75-7	0.75-7	
doParallel	<a href="#">CRAN</a>	1.0.10	1.0.10	1.0.10	1.0.10

dplyr	CRAN	0.5.0	0.5.0	0.5.0	0.5.0
ellipse	CRAN		0.3-8	0.3-8	0.3-8
evaluate	CRAN		0.1	0.1	0.9
fdrtool	CRAN		1.2.15		
fields	CRAN		8.1		
flexmix	CRAN	2.3-13	2.3-13	2.3-13	
forcats	CRAN	0.2.0			
foreach	CRAN	1.4.3	1.4.3	1.4.3	1.4.3
foreign	base	0.8-67	0.8-67	0.8-67	0.8-66
formatR	CRAN		1.4	1.4	1.4
Formula	CRAN		1.2-1		1.2-1
fpc	CRAN	2.1-10	2.1-10	2.1-10	
futile.logger	CRAN		1.4.3	1.4.3	1.4.1
futile.options	CRAN		1.0.0	1.0.0	1.0.0
gdata	CRAN	2.17.0	2.17.0	2.17.0	2.17.0
geepack	CRAN		1.2-1		
GenomeInfoDb	Bioconductor		1.10.2	1.10.1	
GenomicAlignments	Bioconductor		1.10.0	1.10.0	
GenomicRanges	Bioconductor		1.26.2	1.26.1	
ggm	CRAN		2.3		
ggplot2	CRAN	2.1.0	2.2.1	2.2.1	2.1.0
git2r	CRAN	0.15.0	0.18.0	0.16.0	0.15.0
glasso	CRAN		1.8		
GO.db	Bioconductor		3.4.0	3.2.2	3.3.0
GOSemSim	Bioconductor		2.0.3	1.28.2	1.30.3
gplots	CRAN	3.0.1	3.0.1	3.0.1	3.0.1
graph	Bioconductor		1.52.0		
graphics	base	3.3.2	3.3.2	3.3.1	3.3.0
graphsim	GitHub TomKellyGenetics	0.1.0	0.1.0	0.1.0	0.1.0
grDevices	base	3.3.2	3.3.2	3.3.1	3.3.0
grid	base	3.3.2	3.3.2	3.3.1	3.3.0
gridBase	CRAN	0.4-7	0.4-7	0.4-7	0.4-7
gridExtra	CRAN	2.2.1	2.2.1	2.2.1	2.2.1
gridGraphics	CRAN		0.1-5		

gtable	CRAN	0.2.0	0.2.0	0.2.0	0.2.0
gtools	CRAN	3.5.0	3.5.0	3.5.0	3.5.0
haven	CRAN	1.0.0			
heatmap.2x	GitHub TomKellyGenetics	0.0.0.9000	0.0.0.9000	0.0.0.9000	0.0.0.9000
hgu133plus2.db	Bioconductor		3.2.3		
highr	CRAN		0.6	0.6	0.6
Hmisc	CRAN		4.0-2	4.0-2	3.17-4
hms	CRAN	0.2	0.3		
htmlTable	CRAN		1.8	1.9	
htmltools	CRAN	0.3.5	0.3.5	0.3.5	0.3.5
htmlwidgets	CRAN		0.8	0.8	
httpuv	CRAN	1.3.3		1.3.3	
httr	CRAN	1.2.1	1.2.1	1.2.1	1.1.0
huge	CRAN		1.2.7		
hunspell	CRAN		2.3		2
hypergraph	CRAN		1.46.0		
igraph	CRAN	1.0.1	1.0.1	1.0.1	1.0.1
igraph.extensions	GitHub TomKellyGenetics	0.1.0.9001	0.1.0.9001	0.1.0.9001	0.1.0.9001
influenceR	CRAN		0.1.0	0.1.0	
info.centraliity	GitHub TomKellyGenetics	0.1.0	0.1.0	0.1.0	0.1.0
IRanges	Bioconductor		2.8.1	2.8.1	2.6.1
irlba	CRAN	2.1.1	2.1.2	2.1.2	2.0.0
iterators	CRAN	1.0.8	1.0.8	1.0.8	1.0.8
jpeg	CRAN		0.1-8		
jsonlite	CRAN	1.1	1.2	1.3	0.9.20
KEGG.db	Bioconductor		3.2.3		
kernlab	CRAN	0.9-25	0.9-25	0.9-25	
KernSmooth	base	2.23-15	2.23-15	2.23-15	2.23-15
knitr	CRAN		1.15.1	1.15.1	1.14
labeling	CRAN	0.3	0.3	0.3	0.3
lambda.r	CRAN		1.1.9	1.1.9	1.1.7
lattice	base	0.20-34	0.20-34	0.20-34	0.20-33

latticeExtra	CRAN		0.6-28		0.6-28
lava	CRAN		1.4.6		
lavaan	CRAN		0.5-22		
lazyeval	CRAN	0.2.0	0.2.0	0.2.0	0.2.0
les	CRAN		1.24.0		
lgtdl	CRAN		1.1.3		
limma	Bioconductor		3.30.7	3.30.3	
lme4	CRAN		1.1-12		1.1-12
lubridate	CRAN	1.6.0			
magrittr	CRAN	1.5	1.5	1.5	1.5
maps	CRAN		3.1.1		
markdown	CRAN		0.7.7	0.7.7	0.7.7
MASS	base	7.3-45	7.3-45	7.3-45	7.3-45
Matrix	base	1.2-7.1	1.2-7.1	1.2-8	1.2-6
matrixcalc	CRAN	1.0-3	1.0-3	1.0-3	1.0-3
mclust	CRAN	5.2	5.2.1	5.2.2	5.2
memoise	CRAN	1.0.0	1.0.0	1.0.0	1.0.0
methods	base	3.3.2	3.3.2	3.3.1	3.3.0
mgcv	base	1.8-16	1.8-16	1.8-17	1.8-12
mi	CRAN		1		
mime	CRAN	0.5	0.5	0.5	0.4
minqa	CRAN		1.2.4		1.2.4
mnormt	CRAN	1.5-5	1.5-5		1.5-4
modelr	CRAN	0.1.0			
modeltools	CRAN	0.2-21	0.2-21	0.2-21	
multtest	Bioconductor		2.30.0	2.30.0	
munsell	CRAN	0.4.3	0.4.3	0.4.3	0.4.3
mvtnorm	CRAN	1.0-5	1.0-5	1.0-6	1.0-5
network	CRAN		1.13.0		
nlme	base	3.1-128	3.1-128	3.1-131	3.1-128
nloptr	CRAN		1.0.4		1.0.4
NMF	CRAN	0.20.6	0.20.6	0.20.6	0.20.6
nnet	base	7.3-12	7.3-12	7.3-12	7.3-12
numDeriv	CRAN		2016.8-1		2014.2-1
openssl	CRAN	0.9.4	0.9.6	0.9.6	0.9.4



org.Hs.eg.db	Bioconductor		3.1.2		3.3.0
org.Sc.sgd.db	Bioconductor		3.4.0		
parallel	base	3.3.2	3.3.2	3.3.1	3.3.0
pathway.structure	GitHub				
.permutation	TomKellyGenetics	0.1.0	0.1.0	0.1.0	0.1.0
pbivnorm	CRAN		0.6.0		
PGSEA	Bioconductor		1.48.0		
pkgmaker	CRAN	0.22	0.22	0.22	0.22
PKI	CRAN		0.1-3		
plogr	CRAN		0.1-1	0.1-1	
plot.igraph	GitHub				
	TomKellyGenetics	0.0.0.9001	0.0.0.9001	0.0.0.9001	0.0.0.9001
plotrix	CRAN		3.6-4		
plyr	CRAN	1.8.4	1.8.4	1.8.4	1.8.3
png	CRAN		0.1-7		0.1-7
prabclus	CRAN	2.2-6	2.2-6	2.2-6	
praise	CRAN	1.0.0	1.0.0		1.0.0
pROC	CRAN		1.8	1.9.1	
prodlim	CRAN		1.5.7		
prof.tree	CRAN		0.1.0		
proftools	CRAN		0.99-2		
progress	CRAN			1.1.2	
psych	CRAN	1.6.12	1.6.12		
purrr	CRAN	0.2.2	0.2.2	0.2.2	0.2.2
qgraph	CRAN		1.4.1		
quadprog	CRAN		1.5-5	1.5-5	1.5-5
R.methodsS3	CRAN		1.7.1		1.7.1
R.oo	CRAN		1.21.0		1.20.0
R.utils	CRAN		2.5.0		
R6	CRAN	2.1.3	2.2.0	2.2.0	2.1.3
RBGL	CRAN		1.50.0		
RColorBrewer	CRAN	1.1-2	1.1-2	1.1-2	1.1-2
Rcpp	CRAN	0.12.7	0.12.9	0.12.9	0.12.7
RcppArmadillo	CRAN			0.7.700.0.0	0.6.700.6.0
RcppEigen	CRAN		0.3.2.9.0		0.3.2.8.1

RCurl	CRAN		1.95-4.8	1.95-4.8	1.95-4.8
reactome.db	Bioconductor		1.52.1	1.52.1	
reactometree	GitHub TomKellyGenetics		0.1		
readr	CRAN	1.0.0	1.0.0		
readxl	CRAN	0.1.1			
registry	CRAN	0.3	0.3	0.3	0.3
reshape2	CRAN	1.4.1	1.4.2	1.4.2	1.4.1
rgexf	CRAN		0.15.3	0.15.3	
rgl	CRAN			0.97.0	0.95.1441
Rgraphviz	CRAN		2.18.0		
rjson	CRAN		0.2.15		
RJSONIO	CRAN		1.3-0		
rmarkdown	CRAN		1.3	1.3	1
Rmpi	CRAN		0.6-6		0.6-5
rngtools	CRAN	1.2.4	1.2.4	1.2.4	1.2.4
robustbase	CRAN	0.92-7	0.92-7	0.92-7	0.92-5
ROCR	CRAN	1.0-7	1.0-7	1.0-7	1.0-7
Rook	CRAN		1.1-1	1.1-1	
roxygen2	CRAN	6.0.1	5.0.1	6.0.1	5.0.1
rpart	base	4.1-10	4.1-10	4.1-10	4.1-10
rprojroot	CRAN	1.2	1.1	1.2	
Rsamtools	Bioconductor		1.26.1	1.26.1	
rsconnect	CRAN		0.7		
RSQLite	CRAN		1.1-2	1.1-2	1.0.0
rstudioapi	CRAN	0.6	0.6	0.6	0.6
rvest	CRAN	0.3.2			
S4Vectors	Bioconductor		0.12.1	0.12.0	0.10.3
safe	Bioconductor		3.14.0	3.10.0	
scales	CRAN	0.4.0	0.4.1	0.4.1	0.4.0
selectr	CRAN	0.3-1			
sem	CRAN		3.1-8		
shiny	CRAN	0.14		1.0.0	
slipt	GitHub TomKellyGenetics	0.1.0	0.1.0	0.1.0	0.1.0

sm	CRAN	2.2-5.4	2.2-5.4		
sna	CRAN		2.4		
snow	CRAN	0.4-1	0.4-2	0.4-2	0.3-13
sourcetools	CRAN	0.1.5		0.1.5	
SparseM	CRAN		1.74		1.7
spatial	base	7.3-11	7.3-11	7.3-11	7.3-11
splines	base	3.3.2	3.3.2	3.3.1	3.3.0
statnet.common	CRAN		3.3.0		
stats	base	3.3.2	3.3.2	3.3.1	3.3.0
stats4	base	3.3.2	3.3.2	3.3.1	3.3.0
stringi	CRAN	1.1.1	1.1.2	1.1.2	1.0-1
stringr	CRAN	1.1.0	1.1.0	1.2.0	1.0.0
Summarized Experiment	Bioconductor		1.4.0	1.4.0	
survival	base	2.39-4	2.40-1	2.40-1	2.39-4
tcltk	base	3.3.2	3.3.2	3.3.1	3.3.0
testthat	CRAN	1.0.2	1.0.2		1.0.2
tibble	CRAN	1.2	1.2	1.2	1.2
tidyr	CRAN	0.6.1	0.6.1	0.6.1	
tidyverse	GitHub hadley	1.1.1			
timeline	CRAN		0.9		
tools	base	3.3.2	3.3.2	3.3.1	3.3.0
tpr	CRAN		0.3-1		
trimcluster	CRAN	0.1-2	0.1-2	0.1-2	
Unicode	CRAN	9.0.0-1	9.0.0-1	9.0.0-1	
utils	base	3.3.2	3.3.2	3.3.1	3.3.0
vioplot	CRAN		0.2		
vioplotx	GitHub TomKellyGenetics	0.0.0.9000	0.0.0.9000		
viridis	CRAN	0.3.4	0.3.4	0.3.4	
visNetwork	CRAN		1.0.3	1.0.3	
whisker	CRAN	0.3-2	0.3-2	0.3-2	0.3-2
withr	CRAN	1.0.2	1.0.2	1.0.2	1.0.2
XML	base	3.98-1.3	3.98-1.1	3.98-1.5	3.98-1.4

xml2	<a href="#">CRAN</a>	1.1.1		1.1.1	1.0.0
xtable	<a href="#">CRAN</a>	1.8-2	1.8-2	1.8-2	1.8-2
XVector	Bioconductor		0.14.0	0.14.0	
yaml	<a href="#">CRAN</a>		2.1.14	2.1.14	2.1.13
zlibbioc	<a href="#">CRAN</a>		1.20.0	1.20.0	
zoo	<a href="#">CRAN</a>	1.7-13	1.7-14		1.7-13