

Contents

Glossary	xi
Acronyms	xii
1 Introduction and Literature Review	1
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	13
1.2.2 Synthetic Lethal Concepts in Genetics	13
1.2.3 Synthetic Lethality in Model Systems	15
1.2.3.1 Synthetic Lethal Pathways and Networks	15
1.2.3.2 Evolution of Synthetic Lethality	16
1.2.4 Synthetic Lethality in Cancer	17
1.2.5 Clinical Impact of Synthetic Lethality in Cancer	18
1.2.6 High-throughput Screening for Synthetic Lethality	20
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	32
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	34
1.3.1.1	Cytoskeleton	34
1.3.1.2	Extracellular and Tumour Micro-environment	34
1.3.1.3	Cell-Cell Adhesion and Signalling	35
1.3.2	<i>CDH1</i> as a Tumour (and Invasion) Suppressor	35
1.3.2.1	Breast Cancers and Invasion	35
1.3.3	Hereditary Diffuse Gastric (and Lobular Breast) Cancer	36
1.3.4	Cell Line Models of <i>CDH1</i> Null Mutations	37
1.4	Summary and Research Direction of Thesis	38
1.4.1	Thesis Aims	39
2	Methods and Resources	41
2.1	Bioinformatics Resources for Genomics Research	41
2.1.1	Public Data and Software Packages	41
2.1.1.1	Cancer Genome Atlas Data	42
2.1.1.2	Reactome and Annotation Data	43
2.2	Data Handling	43
2.2.1	Normalisation	43
2.2.2	Sample Triage	43
2.2.3	Metagenes and the Singular Value Decomposition	44
2.2.4	Candidate Triage and Integration with Screen Data	46
2.3	Techniques	46
2.3.1	Statistical Procedures and Tests	47
2.3.2	Gene Set Over-representation Analysis	48
2.3.3	Clustering	48
2.3.4	Heatmap	48
2.3.5	Modelling and Simulations	49
2.3.5.1	Receiver Operating Characteristic Curves	50
2.3.6	Resampling Analysis	50
2.4	Pathway Structure Methods	51
2.4.1	Network and Graph Analysis	51
2.4.2	Sourcing Graph Structure Data	52
2.4.3	Constructing Pathway Subgraphs	52
2.4.4	Network Analysis Metrics	53
2.5	Implementation	54
2.5.1	Computational Resources and Linux Utilities	54
2.5.2	R Language and Packages	55
2.5.3	High Performance and Parallel Computing	58
3	Methods Developed During Thesis	60
3.1	A Synthetic Lethal Detection Methodology	60
3.2	Synthetic Lethal Simulation and Modelling	62
3.2.1	A Model of Synthetic Lethality in Expression Data	63

3.2.2	Simulation Procedure	67
3.3	Detecting Simulated Synthetic Lethal Partners	70
3.3.1	Binomial Simulation of Synthetic Lethality	70
3.3.2	Multivariate Normal Simulation of Synthetic Lethality	72
3.3.2.1	Multivariate Normal Simulation with Correlated Genes	74
3.3.2.2	Specificity with Query-Correlated Pathways	82
3.4	Graph Structure Methods	84
3.4.1	Upstream and Downstream Gene Detection	84
3.4.1.1	Permutation Analysis for Statistical Significance	85
3.4.2	Simulating Gene Expression from Graph Structures	86
3.5	Customised Functions and Packages Developed	90
3.5.1	Synthetic Lethal Interaction Prediction Tool	90
3.5.2	Data Visualisation	91
3.5.3	Extensions to the iGraph Package	92
3.5.3.1	Sampling Simulated Data from Graph Structures	92
3.5.3.2	Plotting Directed Graph Structures	92
3.5.3.3	Computing Information Centrality	94
3.5.3.4	Testing Pathway Structure with Permutation Testing	94
3.5.3.5	Metapackage to Install iGraph Functions	95
4	Synthetic Lethal Analysis of Gene Expression Data	96
4.1	Synthetic Lethal Genes in Breast Cancer	97
4.1.1	Synthetic Lethal Pathways in Breast Cancer	98
4.1.2	Expression Profiles of Synthetic Lethal Partners	100
4.1.2.1	Subgroup Pathway Analysis	103
4.2	Comparing Synthetic Lethal Gene Candidates	105
4.2.1	Primary siRNA Screen Candidates	105
4.2.2	Comparison with Correlation	105
4.2.3	Comparison with Primary Screen Viability	108
4.2.4	Comparison with Secondary siRNA Screen Validation	110
4.2.5	Comparison to Primary Screen at Pathway Level	111
4.2.5.1	Resampling Genes for Pathway Enrichment	113
4.2.6	Integrating Synthetic Lethal Pathways and Screens	118
4.3	Synthetic Lethal Pathway Metagenes	119
4.4	Replication in Stomach Cancer	121
4.5	Discussion	122
4.5.1	Strengths of the SLIPT Methodology	122
4.5.2	Synthetic Lethal Pathways for E-cadherin	123
4.5.3	Replication and Validation	125
4.5.3.1	Integration with siRNA Screening	125
4.5.3.2	Replication across Tissues	126
4.6	Summary	126

5	Synthetic Lethal Pathway Structure	128
5.1	Synthetic Lethal Genes in Reactome Pathways	128
5.1.1	The PI3K/AKT Pathway	129
5.1.2	The Extracellular Matrix	131
5.1.3	G Protein Coupled Receptors	134
5.1.4	Gene Regulation and Translation	134
5.2	Network Analysis of Synthetic Lethal Genes	136
5.2.1	Gene Connectivity and Vertex Degree	137
5.2.2	Gene Importance and Centrality	138
5.2.2.1	Information Centrality	138
5.2.2.2	PageRank Centrality	140
5.3	Relationships between Synthetic Lethal Genes	141
5.3.1	Detecting Upstream or Downstream Synthetic Lethality	142
5.3.2	Resampling for Synthetic Lethal Pathway Structure	144
5.4	Discussion	146
5.5	Summary	148
6	Simulation and Modelling of Synthetic Lethal Pathways	149
6.1	Synthetic Lethal Detection Methods	150
6.1.1	Performance of SLIPT and χ^2 across Quantiles	151
6.1.1.1	Correlated Query Genes affects Specificity	154
6.1.2	Alternative Synthetic Lethal Detection Strategies	156
6.1.2.1	Correlation for Synthetic Lethal Detection	157
6.1.2.2	Testing for Bimodality with BiSEp	158
6.2	Simulations with Graph Structures	159
6.2.1	Performance over Graph Structures	160
6.2.1.1	Simple Graph Structures	160
6.2.1.2	Constructed Graph Structures	163
6.2.2	Performance with Inhibitions	165
6.2.3	Synthetic Lethality across Graph Structures	171
6.2.4	Performance within a Large Simulated Datasets	174
6.3	Simulations in More Complex Graph Structures	179
6.3.1	Simulations over Pathway-based Graphs	180
6.3.2	Pathway Structures in a Large Simulated Datasets	183
6.4	Discussion	186
6.4.1	Simulation Procedure	186
6.4.2	Comparing Methods with Simulated Data	187
6.4.3	Design and Performance of SLIPT	188
6.4.4	Simulations from Graph Structures	190
6.5	Summary	191
7	Discussion	192
7.1	Synthetic Lethality and <i>CDH1</i> Biology	192
7.1.1	Established Functions of <i>CDH1</i>	193
7.1.2	The Molecular Role of <i>CDH1</i> in Cancer	193
7.2	Significance	194

7.2.1	Synthetic Lethality in the Genomic Era	194
7.2.2	Clinical Interventions based on Synthetic Lethality	196
7.3	Future Directions	197
7.4	Conclusions	199
	Bibliography	201
A	Sample Quality	225
A.1	Sample Correlation	225
A.2	Replicate Samples in TCGA Breast Cancer Data	228
B	Software Used for Thesis	232
C	Mutation Analysis in Breast Cancer	240
C.1	Synthetic Lethal Genes and Pathways	240
C.2	Synthetic Lethal Expression Profiles	241
C.3	Comparison to Primary Screen	244
C.3.1	Resampling Analysis	246
C.4	Compare SLIPT genes	248
D	Metagene Analysis	250
D.1	Pathway Signature Expression	250
D.2	Synthetic Lethal Reactome Metagenes	254
E	Intrinsic Subtyping	255
F	Stomach Expression Analysis	257
F.1	Synthetic Lethal Genes and Pathways	257
F.2	Comparison to Primary Screen	261
F.2.1	Resampling Analysis	263
F.3	Metagene Analysis	265
G	Synthetic Lethal Genes in Pathways	266
H	Network Analysis for Mutation SLIPT	273
I	Pathway Structure for Mutation SLIPT	276
J	Performance of SLIPT and χ^2	278
J.1	Correlated Query Genes affects Specificity	284
K	Simulations on Graph Structures	290
K.0.1	Simulations from Inhibiting Graph Structures	291
K.1	Simulation across Graph Structures	294
K.2	Simulations from Complex Graph Structures	298
K.2.1	Simulations from Complex Inhibiting Graphs	301
K.3	Simulations from Pathway Graph Structures	307

List of Figures

1.1	Synthetic genetic interactions	14
1.2	Synthetic lethality in cancer	17
2.1	Read count density	45
2.2	Read count sample mean	45
3.1	Framework for synthetic lethal prediction	61
3.2	Synthetic lethal prediction adapted for mutation	62
3.3	A model of synthetic lethal gene expression	64
3.4	Modelling synthetic lethal gene expression	65
3.5	Synthetic lethality with multiple genes	66
3.6	Simulating gene function	68
3.7	Simulating synthetic lethal gene function	68
3.8	Simulating synthetic lethal gene expression	69
3.9	Performance of binomial simulations	71
3.10	Comparison of statistical performance	71
3.11	Performance of multivariate normal simulations	73
3.12	Simulating expression with correlated gene blocks	75
3.13	Simulating expression with correlated gene blocks	76
3.14	Synthetic lethal prediction across simulations	78
3.15	Performance with correlations	79
3.16	Comparison of statistical performance with correlation structure	80
3.17	Performance with query correlations	81
3.18	Statistical evaluation of directional criteria	82
3.19	Performance of directional criteria	83
3.20	Simulated graph structures	87
3.21	Simulating expression from a graph structure	88
3.22	Simulating expression from graph structure with inhibitions	89
3.23	Demonstration of violin plots with custom features	93
3.24	Demonstration of annotated heatmap	93
3.25	Simulating graph structures	94
4.1	Synthetic lethal expression profiles of analysed samples	101
4.2	Comparison of SLIPT with siRNA	106
4.3	Comparison of SLIPT and siRNA genes with correlation	106
4.4	Comparison of SLIPT and siRNA genes with correlation	108
4.5	Comparison of SLIPT and siRNA genes with screen viability	109

4.6	Comparison of SLIPT genes with siRNA screen viability	109
4.7	Resampled intersection of SLIPT and siRNA candidate genes	114
5.1	Synthetic lethality in the PI3K cascade	130
5.2	Synthetic lethality in Elastic Fibre Formation	132
5.3	Synthetic lethality in Fibrin Clot Formation	133
5.4	Synthetic lethality in the GPCRs	135
5.5	Synthetic lethality and vertex degree	137
5.6	Synthetic lethality and centrality	139
5.7	Synthetic lethality and PageRank	141
5.8	Structure of synthetic lethality resampling	143
6.1	Performance of χ^2 and SLIPT across quantiles	152
6.2	Performance of χ^2 and SLIPT across quantiles with more genes	153
6.3	Performance of χ^2 and SLIPT across quantiles with query correlation	154
6.4	Performance of χ^2 and SLIPT across quantiles with query correlation and more genes	155
6.5	Performance of negative correlation and SLIPT	158
6.6	Simple graph structures	161
6.7	Performance of simulations on a simple graph	162
6.8	Performance of simulations is similar in simple graphs	163
6.9	Performance of simulations on a pathway	164
6.10	Performance of simulations on a simple graph with inhibition	166
6.11	Performance is higher on a simple inhibiting graph	168
6.12	Performance of simulations on a constructed graph with inhibition	169
6.13	Performance is affected by inhibition in graphs	170
6.14	Detection of synthetic lethality within a graph structure	172
6.15	Performance of simulations including a simple graph	176
6.16	Performance on a simple graph improves with more genes	177
6.17	Performance on an inhibiting graph improves with more genes	178
6.18	Performance of simulations on the PI3K cascade	182
6.19	Performance of simulations including the PI3K cascade	184
6.20	Performance on pathways improves with more genes	185
A.1	Correlation profiles of removed samples	226
A.2	Correlation analysis and sample removal	227
A.3	Replicate excluded samples	228
A.4	Replicate samples with all remaining	229
A.5	Replicate samples with some excluded	230
C.1	Synthetic lethal expression profiles of analysed samples	242
C.2	Comparison of mtSLIPT to short interfering RNA (siRNA)	244
C.3	Compare mtSLIPT and siRNA genes with correlation	248
C.4	Compare mtSLIPT and siRNA genes with correlation	248
C.5	Compare mtSLIPT and siRNA genes with siRNA viability	249
D.1	Pathway metagene expression profiles	252

D.2	Expression profiles for estrogen receptor related genes	253
F.1	Synthetic lethal expression profiles of stomach samples	259
F.2	Comparison of SLIPT in stomach to siRNA	261
G.1	Synthetic lethality in the PI3K/AKT pathway	266
G.2	Synthetic lethality in the PI3K/AKT pathway in cancer	267
G.3	Synthetic lethality in the Extracellular Matrix	268
G.4	Synthetic lethality in the GPCR Downstream	269
G.5	Synthetic lethality in the Translation Elongation	270
G.6	Synthetic lethality in the Nonsense-mediated Decay	271
G.7	Synthetic lethality in the 3' UTR	272
H.1	Synthetic lethality and vertex degree	273
H.2	Synthetic lethality and centrality	274
H.3	Synthetic lethality and PageRank	274
I.1	Structure of synthetic lethality resampling	276
J.1	Performance of χ^2 and SLIPT across quantiles	278
J.2	Performance of χ^2 and SLIPT across quantiles	280
J.3	Performance of χ^2 and SLIPT across quantiles with more genes	282
J.4	Performance of χ^2 and SLIPT across quantiles with query correlation	284
J.5	Performance of χ^2 and SLIPT across quantiles with query correlation	286
J.6	Performance of χ^2 and SLIPT across quantiles with query correlation and more genes	288
K.1	Performance of simulations on a simple graph	290
K.2	Performance of simulations on an inhibiting graph	291
K.3	Performance of simulations on a constructed graph with inhibition	292
K.4	Performance of simulations on a constructed graph with inhibition	293
K.5	Detection of synthetic lethality within a graph structure	294
K.6	Detection of synthetic lethality within an inhibiting graph	296
K.7	Detection of synthetic lethality within an inhibiting graph	297
K.8	Performance of simulations on a branching graph	298
K.9	Performance of simulations on a complex graph	299
K.10	Performance of simulations on a large graph	300
K.11	Performance of simulations on a branching graph with inhibition	301
K.12	Performance of simulations on a branching graph with inhibition	302
K.13	Performance of simulations on a complex graph with inhibition	303
K.14	Performance of simulations on a complex graph with inhibition	304
K.15	Performance of simulations on a large constructed graph with inhibition	305
K.16	Performance of simulations on a large constructed graph with inhibition	306
K.17	Performance of simulations on the $G_{\alpha i}$ signalling pathway	307
K.18	Performance of simulations including the $G_{\alpha i}$ signalling pathway	308

List of Tables

1.1	Methods for predicting genetic interactions	23
1.2	Methods for predicting synthetic lethality in cancer	24
1.3	Methods used by Wu <i>et al.</i> (2014)	25
2.1	Excluded samples by batch and clinical characteristics.	44
2.2	Computers used during thesis	54
2.3	Linux utilities and applications used during thesis	55
2.4	R installations used during thesis	56
2.5	R Packages used during thesis	56
2.6	R packages developed during thesis	58
4.1	Candidate synthetic lethal gene partners of <i>CDH1</i> from SLIPT	98
4.2	Pathways for <i>CDH1</i> partners from SLIPT	99
4.3	Pathways for clusters of <i>CDH1</i> partners from SLIPT	104
4.4	ANOVA for synthetic lethality and correlation with <i>CDH1</i>	107
4.5	Comparison of Synthetic Lethal Interaction Prediction Tool (SLIPT) genes against secondary siRNA screen	111
4.6	Pathways for <i>CDH1</i> partners from SLIPT and siRNA	112
4.7	Pathways for <i>CDH1</i> partners from SLIPT	115
4.8	Pathways for <i>CDH1</i> partners from SLIPT and siRNA primary screen .	116
4.9	Examples of candidate metagenes synthetic lethal for <i>CDH1</i> from SLIPT	120
5.1	ANOVA for synthetic lethality and vertex degree	138
5.2	ANOVA for synthetic lethality and information centrality	139
5.3	ANOVA for synthetic lethality and PageRank centrality	140
5.4	Resampling for pathway structure of synthetic lethal detection methods	145
B.1	Complete list of R packages used during this thesis	232
C.1	Candidate synthetic lethal gene partners of <i>CDH1</i> from mtSLIPT . . .	240
C.2	Pathways for <i>CDH1</i> partners from mtSLIPT	241
C.3	Pathways for clusters of <i>CDH1</i> partners from mtSLIPT	243
C.4	Pathways for <i>CDH1</i> partners from mtSLIPT and siRNA	245
C.5	Pathways for <i>CDH1</i> partners from mtSLIPT	246
C.6	Pathways for <i>CDH1</i> partners from mtSLIPT and siRNA primary screen	247
D.1	Candidate synthetic lethal metagenes against <i>CDH1</i> from mtSLIPT . .	254

E.1	Comparison of intrinsic subtypes	255
F.1	Synthetic lethal gene partners of <i>CDH1</i> from SLIPT in stomach cancer	257
F.2	Pathways for <i>CDH1</i> partners from SLIPT in stomach cancer	258
F.3	Pathways for clusters of <i>CDH1</i> partners in stomach SLIPT	260
F.4	Pathways for <i>CDH1</i> partners from SLIPT and siRNA	262
F.5	Pathways for <i>CDH1</i> partners from SLIPT in stomach cancer	263
F.6	Pathways for <i>CDH1</i> partners from SLIPT in stomach and siRNA	264
F.7	Synthetic lethal metagenes against <i>CDH1</i> in stomach cancer	265
H.1	ANOVA for synthetic lethality and vertex degree	275
H.2	ANOVA for synthetic lethality and information centrality	275
H.3	ANOVA for synthetic lethality and PageRank centrality	275
I.1	Resampling for pathway structure of synthetic lethal detection methods	277

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

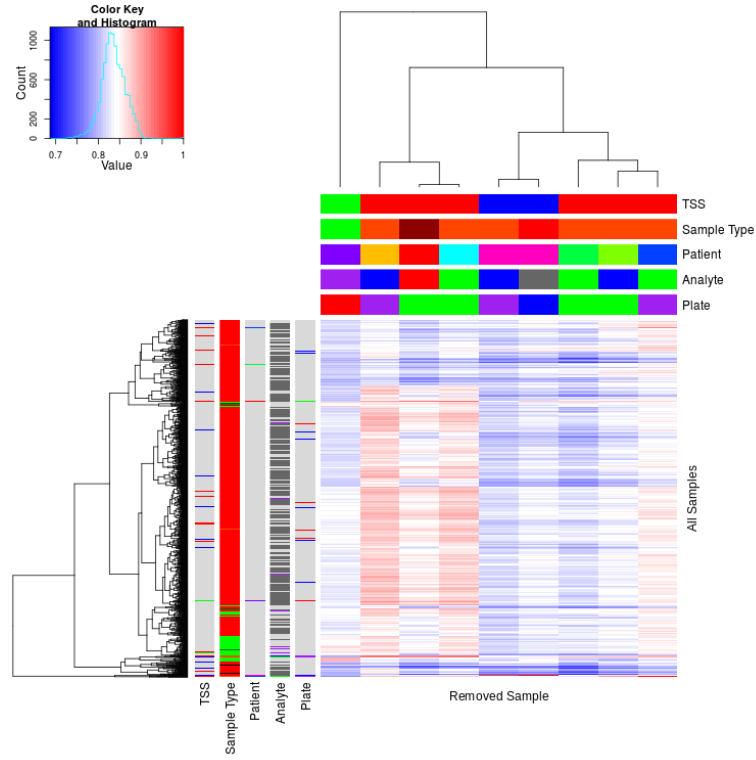


Figure A.1: **Correlation profiles of removed samples.** Heatmap (Euclidean distance) of samples in [The Cancer Genome Atlas \(TCGA\)](#) breast cancer dataset (left) clustered for all samples against removed samples (top): tissue source site (TSS), sample type with reds for tumour and greens for normal, 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.

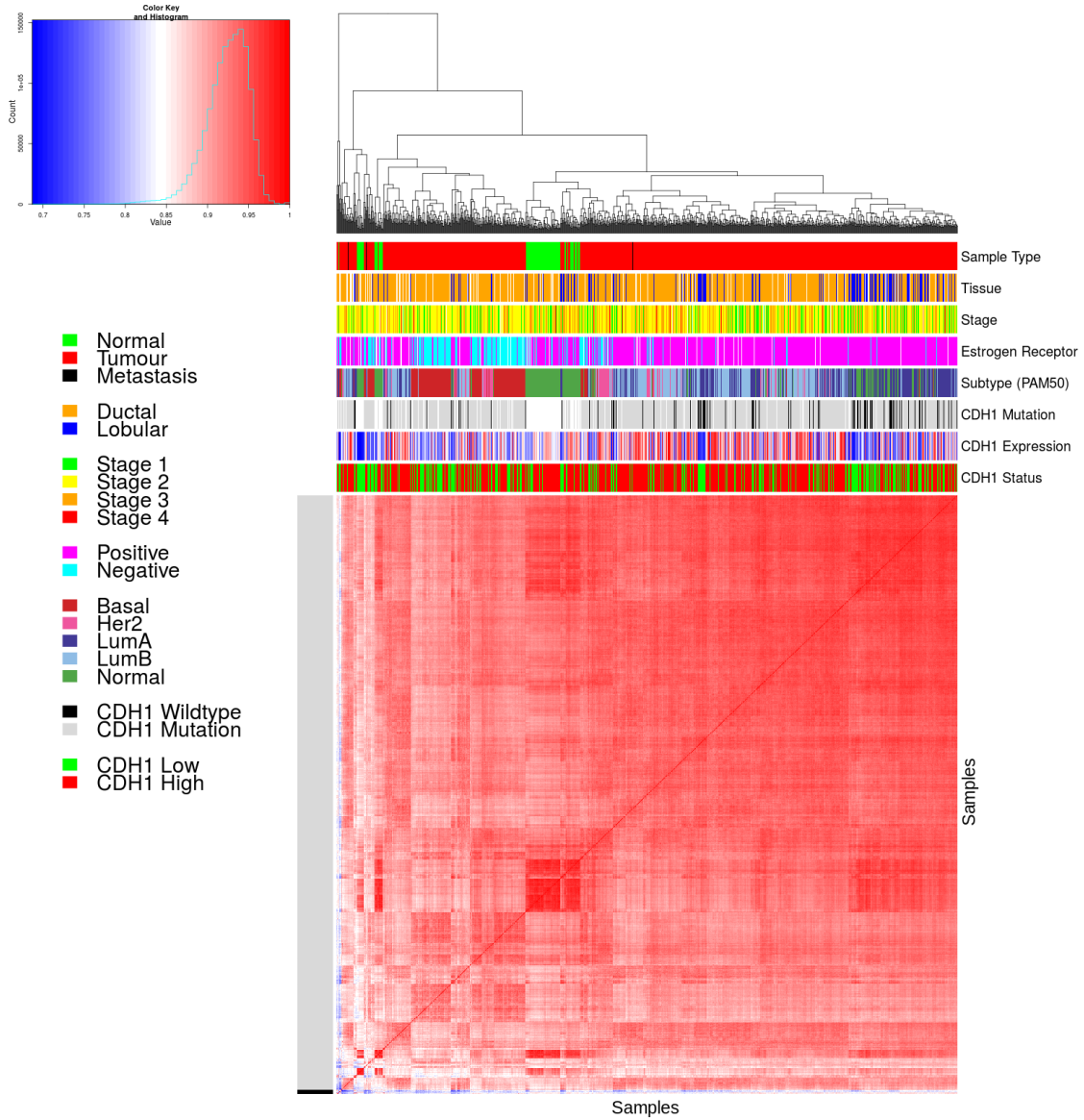


Figure A.2: **Correlation analysis and sample removal.** Correlation matrix heatmap (Euclidean distance) of all samples in [TCGA](#) breast cancer dataset against each other annotated for sample clinical data: sample type, tissue type, tumour stage, [Estrogen receptor \(ER\)](#) and intrinsic subtype (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.

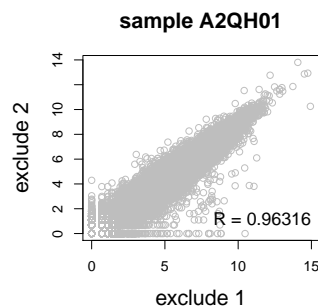


Figure A.3: **Replicate excluded samples.** Both tumour samples of patient A2QH were excluded as they were poorly correlated with other samples, although they were highly similar to each other as shown by Pearson correlation of log-raw counts.

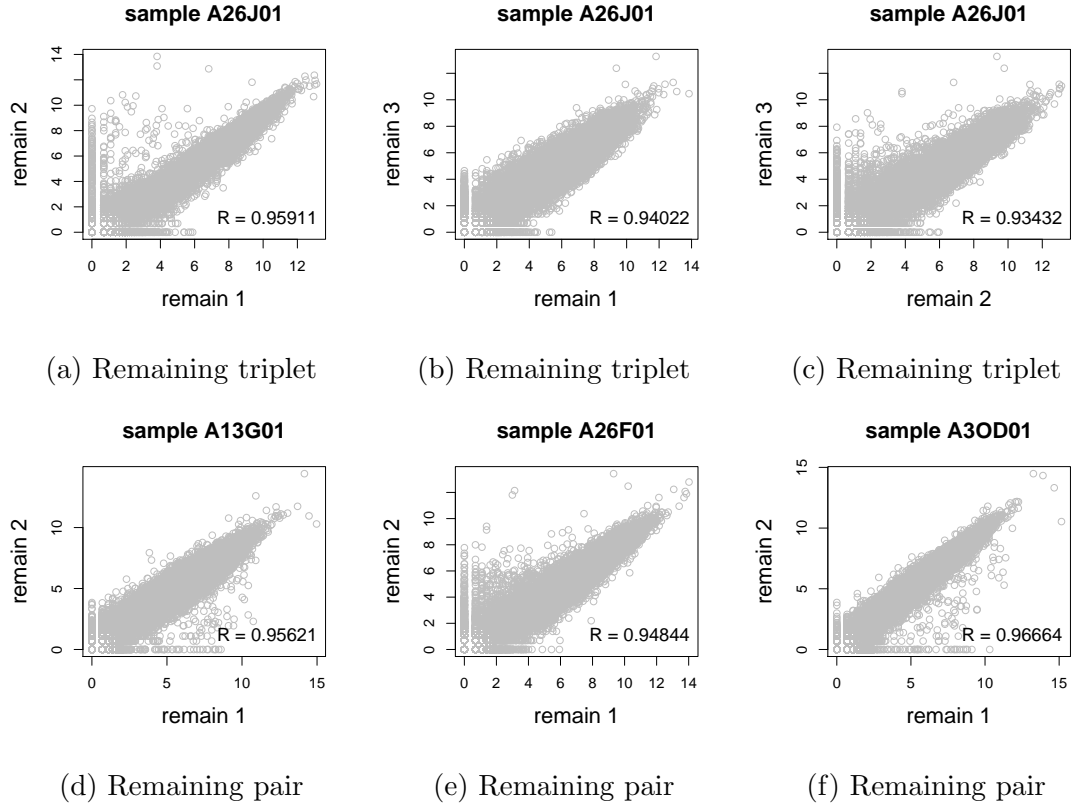


Figure A.4: **Replicate samples with all remaining.** Patient A26J was sampled 3 times and compared pairwise. Pairs of samples were also compared for other patients with replicate samples. In all cases, replicate samples remaining in the dataset were highly concordant, as shown by Pearson correlation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

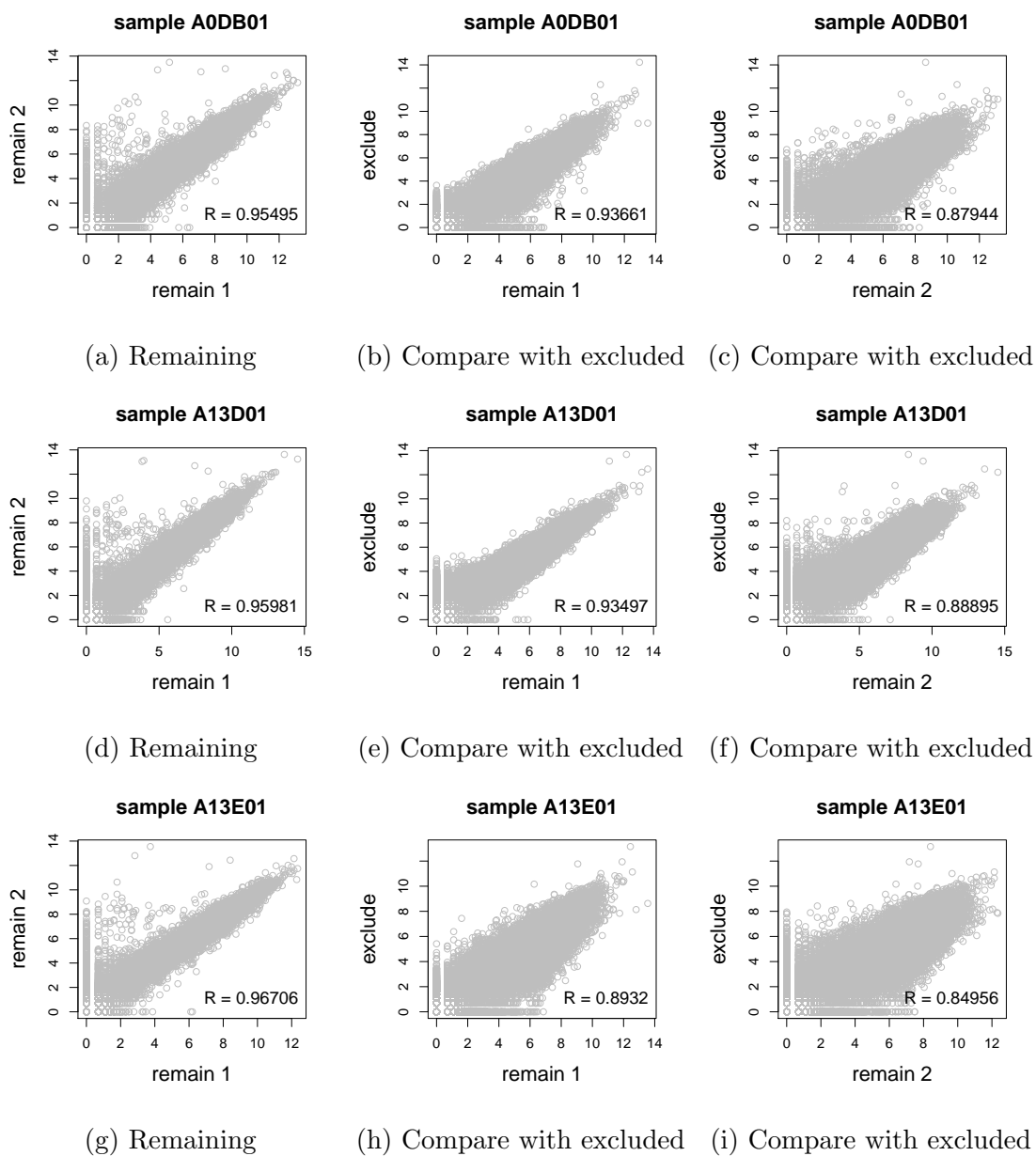


Figure A.5: **Replicate samples with some excluded.** (continued on next page)

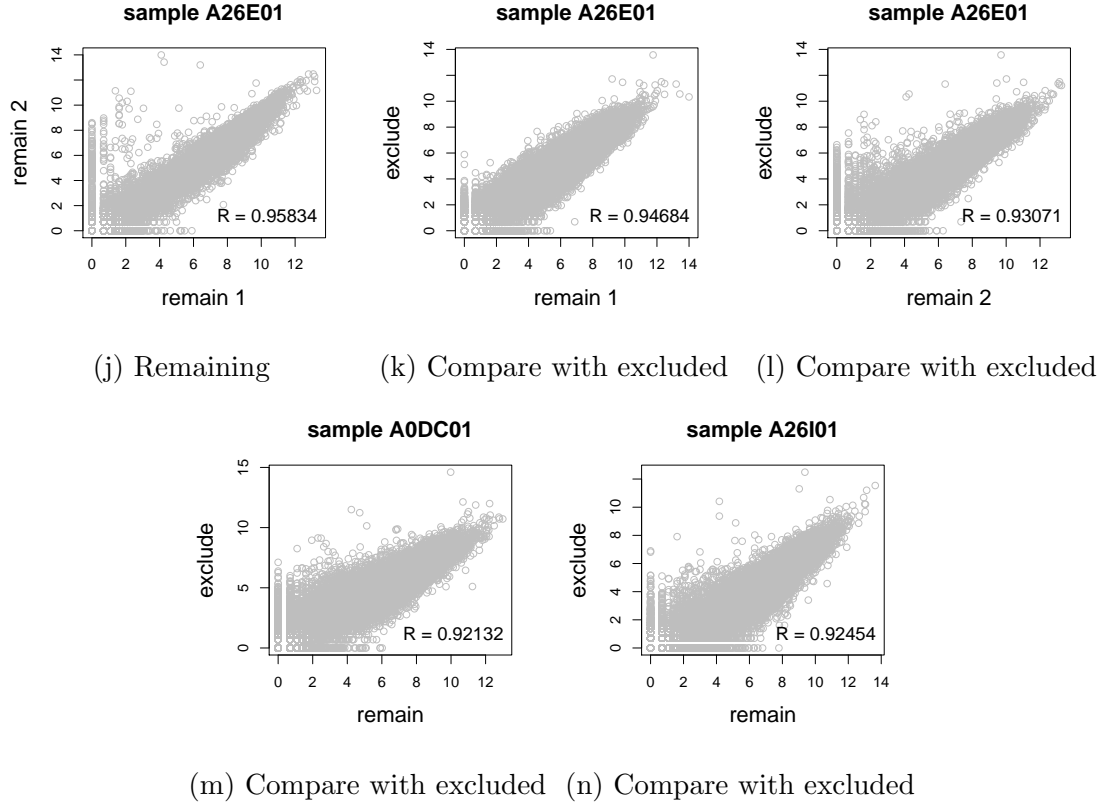


Figure A.5: **Replicate samples with some excluded.** Patients A0DB, A13D, A13E, and A26E were each sampled 3 times and compared pairwise. Pairs of samples were also compared for other patients with replicate samples. In all cases, the replicate samples remaining in the dataset more were highly concordant 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	CRAN		1.4-5		1.4-3
acepack	CRAN		1.4.1		1.3-3.3
ade4	CRAN		1.7-5		
annaffy	Bioconductor		1.46.0		
AnnotationDbi	Bioconductor		1.36.0	1.36.0	1.34.4
apComplex	CRAN		2.40.0		
ape	CRAN		4		3.4
arm	CRAN		1.9-3		
assertthat	CRAN	0.1	0.1	0.1	0.1
backports	CRAN	1.0.5	1.0.4	1.0.5	1.0.2
base64	CRAN			2	2
base64enc	CRAN		0.1-3		0.1-3
beanplot	CRAN		1.2	1.2	1.2
BH	CRAN	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	CRAN	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	CRAN	1.0-6	1.0-6	1.0-6	1.0-6
broom	CRAN	0.4.1			
caTools	CRAN	1.17.1	1.17.1	1.17.1	1.17.1
cgdsr	CRAN		1.2.5		
checkmate	CRAN		1.8.2		1.7.4
chron	CRAN	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	CRAN		0.19-1		0.18-1
codetools	base	0.2-15	0.2-15	0.2-15	0.2-14
colorRamps	CRAN		2.3		
colorspace	CRAN	1.2-6	1.3-2	1.3-2	1.2-6
commonmark	CRAN	1.1		1.2	
compiler	base	3.3.2	3.3.2	3.3.1	3.3.0
corpcor	CRAN		1.6.8	1.6.8	1.6.8
Cprob	CRAN		1.2.4		
crayon	CRAN	1.3.2	1.3.2	1.3.2	1.3.2
crop	CRAN		0.0-2	0.0-2	
curl	CRAN	1.2	2.3	2.3	0.9.7
d3Network	CRAN		0.5.2.1		
data.table	CRAN	1.9.6	1.10.0	1.10.1	1.9.6
data.tree	CRAN		0.7.0	0.7.0	
datasets	base	3.3.2	3.3.2	3.3.1	3.3.0
DBI	CRAN	0.5-1	0.5-1	0.5-1	0.5-1
dendextend	CRAN	1.4.0	1.4.0	1.4.0	
DEoptimR	CRAN	1.0-8	1.0-8	1.0-8	1.0-4
desc	CRAN	1.1.0		1.1.0	
devtools	CRAN	1.12.0	1.12.0	1.12.0	1.12.0
DiagrammeR	CRAN		0.9.0	0.9.0	
dichromat	CRAN	2.0-0	2.0-0	2.0-0	2.0-0
digest	CRAN	0.6.10	0.6.11	0.6.12	0.6.9
diptest	CRAN	0.75-7	0.75-7	0.75-7	
doParallel	CRAN	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	CRAN	1.1.1		1.1.1	1.0.0
xtable	CRAN	1.8-2	1.8-2	1.8-2	1.8-2
XVector	Bioconductor		0.14.0	0.14.0	
yaml	CRAN		2.1.14	2.1.14	2.1.13
zlibbioc	CRAN		1.20.0	1.20.0	
zoo	CRAN	1.7-13	1.7-14		1.7-13