

Bibliography

- [1] Alfred V. Aho, M.R. Garey, and Jeffrey D. Ullman. The transitive reduction of a directed graph. *SIAM J. Comput.*, 1(2):131 – 137, 1972.
- [2] Tatsuya Akutsu, Satoru Kuhara, Osamu Maruyama, and Satoru Miyano. Identification of gene regulatory networks by strategic gene disruptions and gene overexpressions. In *Proc. 9th Annual ACM-SIAM Symposium on Discrete Algorithms*, pages 695–702, 1998.
- [3] Tatsuya Akutsu, Satoru Kuhara, Osamu Maruyama, and Satoru Miyano. A system for identifying genetic networks from gene expression patterns produced by gene disruptions and overexpressions. In Satoru Miyano and T. Takagi, editors, *Genome Informatics 9*, pages 151–160, Tokyo, 1998. Universal Academy Press.
- [4] Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, and Peter Walter. *Molecular Biology of the Cell*. Garland Science, New York, 4 edition, 2002.
- [5] M Ashburner, CA Ball, JA Blake, D Botstein, H Butler, JM Cherry, AP Davis, K Dolinski, SS Dwight, JT Eppig, MA Harris, DP Hill, L Issel-Tarver, A Kasarskis, S Lewis, JC Matese, JE Richardson, M Ringwald, GM Rubin, and G Sherlock. Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. *Nat Genet*, 25(1):25–9, May 2000.
- [6] L Avery and S Wasserman. Ordering gene function: the interpretation of epistasis in regulatory hierarchies. *Trends Genet*, 8(9):312–6, Sep 1992.
- [7] Katia Basso, Adam A Margolin, Gustavo Stolovitzky, Ulf Klein, Riccardo Dalla-Favera, and Andrea Califano. Reverse engineering of regulatory networks in human B cells. *Nat Genet*, Mar 2005.
- [8] Matthew J. Beal, Francesco Falciani, Zoubin Ghahramani, Claudia Rangel, and David L. Wild. A Bayesian approach to reconstructing genetic regulatory networks with hidden factors. *Bioinformatics*, 21(3):349–356, 2005.
- [9] Allister Bernard and Alexander J Hartemink. Informative structure priors: joint learning of dynamic regulatory networks from multiple types of data. *Pac Symp Biocomput*, pages 459–70, 2005.

- [10] David R Bickel. Probabilities of spurious connections in gene networks: application to expression time series. *Bioinformatics*, 21(7):1121–8, Apr 2005.
- [11] Susanne G. Böttcher. *Learning Bayesian Networks with Mixed Variables*. PhD thesis, Aalborg University, Denmark, 2004.
- [12] Michael Boutros, Hervé Agaisse, and Norbert Perrimon. Sequential activation of signaling pathways during innate immune responses in *Drosophila*. *Dev Cell*, 3(5):711–22, Nov 2002.
- [13] Michael Boutros, Amy A. Kiger, Susan Armknecht, Kim Kerr, Marc Hild, Britta Koch, Stefan A. Haas, Heidelberg Fly Array Consortium, Renato Paro, and Norbert Perrimon. Genome-Wide RNAi Analysis of Growth and Viability in *Drosophila* Cells. *Science*, 303(5659):832–835, 2004. DOI: 10.1126/science.1091266.
- [14] C.T. Brown, A.G. Rust, P.J.C. Clarke, Z. Pan, M.J. Schilstra, T.D. Buysscher, G. Griffin, B.J. Wold, R.A. Cameron, E.H. Davidson, and H. Bolouri. New computational approaches for analysis of cis-regulatory networks. *Developmental Biology*, (246):86–102, 2002.
- [15] Thijn R. Brummelkamp and René Bernards. Innovation: New tools for functional mammalian cancer genetics. *Nature Reviews Cancer*, 3(10):781–789, 2003.
- [16] Svetlana Bulashevskaya and Roland Eils. Inferring genetic regulatory logic from expression data. *Bioinformatics*, Mar 2005.
- [17] Wray L. Buntine. Theory refinement of Bayesian networks. In *Uncertainty in Artificial Intelligence*, 1991.
- [18] AJ Butte and IS Kohane. Mutual information relevance networks: functional genomic clustering using pairwise entropy measurements. *Pac Symp Biocomput*, pages 418–29, 2000.
- [19] Anne E Carpenter and David M Sabatini. Systematic genome-wide screens of gene function. *Nat Rev Genet*, 5(1):11–22, Jan 2004.
- [20] David M. Chickering. Learning equivalence classes of Bayesian network structures. In *Proceedings of Twelfth Conference on Uncertainty in Artificial Intelligence, Portland, OR*, pages 150–157. Morgan Kaufmann, August 1996.
- [21] David M. Chickering, David Heckerman, and Christopher Meek. A Bayesian approach to learning Bayesian networks with local structure. In *Proceedings of Thirteenth Conference on Uncertainty in Artificial Intelligence*, Providence, RI, 1997. Morgan Kaufmann.
- [22] Gregory F. Cooper. A Bayesian Method for Causal Modeling and Discovery Under Selection. In C. Boutilier and M. Goldszmidt, editors, *Uncertainty in Artificial Intelligence; Proceedings of the Sixteenth Conference*, pages 98–106, San Mateo, California, 2000. Morgan Kaufmann.

-
- [23] Gregory F. Cooper and Edward Herskovits. A Bayesian Method for the Induction of Probabilistic Networks from Data. *Machine Learning*, 9:309–347, 1992.
- [24] Gregory F. Cooper and Changwon Yoo. Causal discovery from a mixture of experimental and observational data. In K. Laskey and H. Prade, editors, *Proc. Fifteenth Conference on Uncertainty in Artificial Intelligence (UAI '99)*, pages 116–125, San Francisco, Calif., 1999. Morgan Kaufman.
- [25] Eric H. Davidson, Jonathan P. Rast, Paola Oliveri, Andrew Ransick, Cristina Calestani, Chiou-Hwa Yuh, Takuya Minokawa, Gabriele Amore, Veronica Hinman, Cesar Arenas-Mena, Ochan Otim, C. Titus Brown, Carolina B. Livi, Pei Yun Lee, Roger Revilla, Alistair G. Rust, Zheng jun Pan, Maria J. Schilstra, Peter J. C. Clarke, Maria I. Arnone, Lee Rowen, R. Andrew Cameron, David R. McClay, Leroy Hood, and Hamid Bolouri. A Genomic Regulatory Network for Development. *Science*, 295(5560):1669–1678, 2002.
- [26] Armaity P Davierwala, Jennifer Haynes, Zhijian Li, Rene L Brost, Mark D Robinson, Lisa Yu, Sanie Mnaimneh, Huiming Ding, Hongwei Zhu, Yiqun Chen, Xin Cheng, Grant W Brown, Charles Boone, Brenda J Andrews, and Timothy R Hughes. The synthetic genetic interaction spectrum of essential genes. *Nat Genet*, 37(10):1147–52, Oct 2005.
- [27] Alberto de la Fuente, Nan Bing, Ina Hoeschele, and Pedro Mendes. Discovery of meaningful associations in genomic data using partial correlation coefficients. *Bioinformatics*, 20(18):3565–3574, 2004.
- [28] Diego di Bernardo, Gardner Timothy S, and James J Collins. Robust identification of large genetic networks. *Pac Symp Biocomput*, pages 486–97, 2004.
- [29] Diego di Bernardo, Michael J Thompson, Timothy S Gardner, Sarah E Chobot, Erin L Eastwood, Andrew P Wojtovich, Sean J Elliott, Scott E Schaus, and James J Collins. Chemogenomic profiling on a genome-wide scale using reverse-engineered gene networks. *Nat Biotechnol*, 23(3):377–83, Mar 2005.
- [30] Adrian Dobra, Chris Hans, Beatrix Jones, Joseph R. Nevins, Guang Yao, and Mike West. Sparse graphical models for exploring gene expression data. *Journal of Multivariate Analysis*, 90(1):196–212, July 2004.
- [31] Nancy Van Driessche, Janez Demsar, Ezgi O Booth, Paul Hill, Peter Juvan, Blaz Zupan, Adam Kuspa, and Gad Shaulsky. Epistasis analysis with global transcriptional phenotypes. *Nat Genet*, 37(5):471–7, May 2005.
- [32] Mathias Drton and Michael D. Perlman. Model selection for gaussian concentration graphs. *Biometrika*, 91(3), 2004.
- [33] Mathias Drton and Michael D. Perlman. A SINful approach to gaussian graphical model selection. *Submitted to special issue of Statistical Science*, 2004.

- [34] Richard Durbin, Sean Eddy, Anders Krogh, and Graeme Mitchison. *Biological sequence analysis*. Cambridge University Press, 1998.
- [35] David Edwards. *Introduction to Graphical Modelling*. Springer, 2000.
- [36] Bradley Efron and Robert J. Tibshirani. *An introduction to the bootstrap*. Chapman and Hall, 1993.
- [37] MB Eisen, PT Spellman, PO Brown, and D Botstein. Cluster analysis and display of genome-wide expression patterns. *Proc Natl Acad Sci U S A*, 95(25):14863–8, Dec 1998.
- [38] Andrew Fire, SiQun Xu, Mary K. Montgomery, Steven A. Kostas, Samuel E. Driver, and Craig C. Mello. Potent and specific genetic interference by double-stranded RNA in *caenorhabditis elegans*. *Nature*, 391(6669):806 – 811, Feb 1998.
- [39] Nir Friedman. Learning belief networks in the presence of missing values and hidden variables. In D. Fisher, editor, *Proc. of the Fourteenth Inter. Conf. on Machine Learning (ICML97)*, pages 125–133, San Francisco, CA, 1997. Morgan Kaufmann.
- [40] Nir Friedman. The Bayesian Structural EM Algorithm. In G. F. Cooper and S. Moral, editors, *Proc. of the Fourteenth Conf. on Uncertainty in Artificial Intelligence (UAI'98)*, pages 129–138, San Francisco, CA, 1998. Morgan Kaufmann.
- [41] Nir Friedman. Inferring Cellular Networks Using Probabilistic Graphical Models. *Science*, 303(5659):799–805, 2004.
- [42] Nir Friedman and Moises Goldszmidt. Learning Bayesian networks with local structure. In Michael I. Jordan, editor, *Learning in Graphical Models*, pages 421–459. MIT Press, Cambridge, MA, 1998.
- [43] Nir Friedman and Daphne Koller. Being Bayesian about network structure: A Bayesian approach to structure discovery in Bayesian networks. *Machine Learning*, 50:95–126, 2003.
- [44] Nir Friedman, Michal Linial, Iftach Nachman, and Dana Pe'er. Using Bayesian networks to analyze expression data. *Journal of Computational Biology*, 7(3):601–620, August 2000.
- [45] Nir Friedman, Kevin Murphy, and Stuart Russell. Learning the structure of dynamic probabilistic networks. In *Proceedings of the 14th Annual Conference on Uncertainty in Artificial Intelligence (UAI-98)*, pages 139–147, San Francisco, CA, 1998. Morgan Kaufmann Publishers.
- [46] Nir Friedman, Iftach Nachman, and Dana Peer. Learning bayesian network structures from massive datasets: The sparse candidate algorithm. In *Proc. of Uncertainty in Artificial Intelligence*, 1999.

-
- [47] Timothy S. Gardner, Diego di Bernardo, David Lorenz, and James J. Collins. Inferring genetic networks and identifying compound mode of action via expression profiling. *Science*, 301(5629):102–105, 2003.
- [48] Dan Geiger and David Heckerman. Learning Gaussian Networks. In Ramon López de Mántaras and David Poole, editors, *Proceedings of the Tenth Annual Conference on Uncertainty in Artificial Intelligence*, pages 235–243, Seattle, Washington, USA, July 29-31 1994. Morgan Kaufmann.
- [49] Andrew Gelman, John B. Carlin, Hal S. Stern, and Donald B. Rubin. *Bayesian Data Analysis*. Chapman and Hall-CRC, 1996.
- [50] Viola Gesellchen, David Kuttenukeuler, Michael Steckel, Nadge Pelte, and Michael Boutros. An RNA interference screen identifies Inhibitor of Apoptosis Protein 2 as a regulator of innate immune signalling in *Drosophila*. *EMBO Rep*, 6(10):979–84, Oct 2005.
- [51] Marian A. C. Groenenboom, Athanasius F. M. Marée, Paulien Hogeweg, and Simon Levin. The RNA Silencing Pathway: The Bits and Pieces That Matter. *PLoS Computational Biology*, 1(2):e21, 2005.
- [52] Kristin C Gunsalus, Hui Ge, Aaron J Schetter, Debra S Goldberg, Jing-Dong J Han, Tong Hao, Gabriel F Berriz, Nicolas Bertin, Jerry Huang, Ling-Shiang Chuang, Ning Li, Ramamurthy Mani, Anthony A Hyman, Birte Snnichsen, Christophe J Echeverri, Frederick P Roth, Marc Vidal, and Fabio Piano. Predictive models of molecular machines involved in *Caenorhabditis elegans* early embryogenesis. *Nature*, 436(7052):861–5, Aug 2005.
- [53] Kristin C Gunsalus, Wan-Chen Yueh, Philip MacMenamin, and Fabio Piano. RNAiDB and PhenoBlast: web tools for genome-wide phenotypic mapping projects. *Nucleic Acids Res*, 32(Database issue):D406–10, Jan 2004.
- [54] SP Gygi, Y Rochon, BR Franza, and R Aebersold. Correlation between protein and mRNA abundance in yeast. *Mol Cell Biol*, 19(3):1720–30, Mar 1999.
- [55] Alexander J. Hartemink. Reverse engineering gene regulatory networks. *Nat Biotechnol*, 23(5):554–5, May 2005.
- [56] Alexander J. Hartemink, Daniel K. Gifford, Tommi S. Jaakkola, and Richard A. Young. Combining location and expression data for principled discovery of genetic regulatory network models. In *Proceedings of Pacific Symposium on Biocomputing 7:437-449*, 2002.
- [57] W.K. Hastings. Monte carlo sampling methods using markov chains and their applications. *Biometrika*, 57:97–109, 1970.
- [58] David Heckerman, Dan Geiger, and David Maxwell Chickering. Learning Bayesian Networks: The Combination of Knowledge and Statistical Data. *Machine Learning*, 20(3):197–243, Sep. 1995.

- [59] Jules A Hoffmann. The immune response of *Drosophila*. *Nature*, 426(6962):33–8, Nov 2003.
- [60] Wolfgang Huber, Anja von Heydebreck, Holger Sltmann, Annemarie Poustka, and Martin Vingron. Variance stabilization applied to microarray data calibration and to the quantification of differential expression. *Bioinformatics*, 18(Suppl 1):S96–104, 2002.
- [61] Timothy R. Hughes, Matthew J. Marton, Allan R. Jones, Christopher J. Roberts, Roland Stoughton, Christopher D. Armour, Holly A. Bennett, Ernest Coffey, Hongyue Dai, Yudong D. He, Matthew J. Kidd, Amy M. King, Michael R. Meyer, David Slade, Pek Y. Lum, Sergey B. Stepaniants, Daniel D. Shoemaker, Daniel Gachotte, Kalpana Chakraburttty, Julian Simon, Martin Bard, and Stephen H. Friend. Functional discovery via a compendium of expression profiles. *Cell*, 102:109–126, July 2000.
- [62] Dirk Husmeier. Sensitivity and specificity of inferring genetic regulatory interactions from microarray experiments with dynamic Bayesian networks. *Bioinformatics*, 19(17):2271–2282, 2003.
- [63] Trey Ideker, Vesteynn Thorsson, and Richard M. Karp. Discovery of regulatory interactions through perturbation: inference and experimental design. In *Proc. of the Pacic Symp. on Biocomputing*, volume 5, pages 302–313, 2000.
- [64] Seiya Imoto, T. Goto, and S. Miyano. Estimation of genetic networks and functional structures between genes by using Bayesian network and nonparametric regression. In *Pacific Symposium on Biocomputing*, volume 7, pages 175–186, 2002.
- [65] Seiya Imoto, T. Higuchi, T. Goto, K. Tashiro, S. Kuhara, and S. Miyano. Combining microarrays and biological knowledge for estimating gene networks via Bayesian networks. In *Proc. 2nd Computational Systems Bioinformatics*, pages 104–113, 2003.
- [66] Seiya Imoto, Sunyong Kim, Takao Goto, Satoru Miyano, Sachiyo Aburatani, Kousuke Tashiro, and Satoru Kuhara. Bayesian network and nonparametric heteroscedastic regression for nonlinear modeling of genetic network. *J Bioinform Comput Biol*, 1(2):231–52, Jul 2003.
- [67] Rafael A Irizarry, Benjamin M Bolstad, Francois Collin, Leslie M Cope, Bridget Hobbs, and Terence P Speed. Summaries of Affymetrix GeneChip probe level data. *Nucleic Acids Res*, 31(4):e15, Feb 2003.
- [68] Tsuyoshi Kato, Koji Tsuda, and Kiyoshi Asai. Selective integration of multiple biological data for supervised network inference. *Bioinformatics*, Feb 2005.
- [69] Hirohisa Kishino and Peter J. Waddell. Correspondence analysis of genes and tissue types and finding genetic links from microarray data. In A.K. Dunker, A. Konagaya, S. Miyano, and T. Takagi, editors, *Genome Informatics*, Tokyo, 2000. Universal Academy Press.

-
- [70] Dennis Kostka and Rainer Spang. Finding disease specific alterations in the co-expression of genes. *Bioinformatics*, 20 Suppl 1:I194–I199, Aug 2004.
- [71] David Latchman. *Gene regulation – A eukaryotic perspective*. Stanley Thornes, 2002.
- [72] Steffen L. Lauritzen. *Graphical Models*. Clarendon Press, Oxford, 1996.
- [73] Steffen L. Lauritzen. Causal inference from graphical models, 1999.
- [74] Tong Ihn Lee, Nicola J Rinaldi, Francois Robert, Duncan T Odom, Ziv Bar-Joseph, Georg K Gerber, Nancy M Hannett, Christopher T Harbison, Craig M Thompson, Itamar Simon, Julia Zeitlinger, Ezra G Jennings, Heather L Murray, D Benjamin Gordon, Bing Ren, John J Wyrick, Jean-Bosco Tagne, Thomas L Volkert, Ernest Fraenkel, David K Gifford, and Richard A Young. Transcriptional regulatory networks in *Saccharomyces cerevisiae*. *Science*, 298(5594):799–804, Oct 2002.
- [75] Jan van Leeuwen. Graph algorithms, 1990. in: *Handbook of Theoretical Computer Science*, Elsevier, 525–632.
- [76] Shoudan Liang, Stefanie Fuhrmann, and Roland Somogyi. REVEAL, a general reverse engineering algorithm for inference of genetic network architectures. In *Proc. of Pacific Symposium on Biocomputing*, number 3, pages 18–29, 1998.
- [77] Lennard Ljung. *System Identification – Theory for the User*. Prentice Hall, 2nd edition, 1999.
- [78] D. Madigan, S. Andersson, M. Perlman, and C. Volinsky. Bayesian model averaging and model selection for markov equivalence classes of acyclic graphs. *Communications in Statistics: Theory and Methods*, 25:2493–2519, 1996.
- [79] Paul M Magwene and Junhyong Kim. Estimating genomic coexpression networks using first-order conditional independence. *Genome Biol*, 5(12):R100, 2004.
- [80] Florian Markowetz, Jacques Bloch, and Rainer Spang. Non-transcriptional pathway features reconstructed from secondary effects of RNA interference. *Bioinformatics*, 21(21):4026–4032, 2005.
- [81] Florian Markowetz, Steffen Grossmann, and Rainer Spang. Probabilistic soft interventions in conditional Gaussian networks. In Robert Cowell and Zoubin Ghahramani, editors, *Proc. Tenth International Workshop on Artificial Intelligence and Statistics*, Jan 2005.
- [82] Florian Markowetz and Rainer Spang. Evaluating the effect of perturbations in reconstructing network topologies. In Kurt Hornik, Friedrich Leisch, and Achim Zeileis, editors, *Proceedings of the 3rd International Workshop on Distributed Statistical Computing (DSC 2003)*, 2003.

- [83] Florian Markowetz and Rainer Spang. Molecular diagnosis: classification, model selection, and performance evaluation. *Methods of Information in Medicine*, 44(3):438–43, 2005.
- [84] Nicolai Meinshausen and Peter Bühlmann. High dimensional graphs and variable selection with the lasso. *Annals of Statistics*, ?(?):?, 2005.
- [85] Gunter Meister and Thomas Tuschl. Mechanisms of gene silencing by double-stranded RNA. *Nature*, 431(7006):343–9, Sep 2004.
- [86] Ron Milo, Shai S. Shen-Orr, Shalev Itzkovitz, Nadav Kashtan, Dmitri Chklovskii, and Uri Alon. Network Motifs: Simple Building Blocks of Complex Networks. *Science*, 298(5594):824–827, 2002.
- [87] K. Murphy and S. Mian. Modelling gene expression data using dynamic Bayesian networks. Technical report, Computer Science Division, University of California, Berkeley, CA, 1999.
- [88] Kevin P. Murphy. Active Learning of Causal Bayes Net Structure, 2001.
- [89] I. Nachman, A. Regev, and N. Friedman. Inferring quantitative models of regulatory networks from expression data. *Bioinformatics*, 20(suppl.1):i248–256, 2004.
- [90] Iftach Nachman, Gal Elidan, and Nir Friedman. "ideal parent" structure learning for continuous variable networks. In *AUAI '04: Proceedings of the 20th conference on Uncertainty in artificial intelligence*, pages 400–409, Arlington, Virginia, United States, 2004. AUAI Press.
- [91] Yuki Naito, Tomoyuki Yamada, Takahiro Matsumiya, Kumiko Ui-Tei, Kaoru Saigo, and Shinichi Morishita. dsCheck: highly sensitive off-target search software for double-stranded RNA-mediated RNA interference. *Nucleic Acids Res*, 33(Web Server issue):W589–91, Jul 2005.
- [92] Carl D Novina and Phillip A Sharp. The RNAi revolution. *Nature*, 430(6996):161–4, Jul 2004.
- [93] Irene M Ong, Jeremy D Glasner, and David Page. Modelling regulatory pathways in E. coli from time series expression profiles. *Bioinformatics*, 18 Suppl 1:S241–8, 2002.
- [94] George Orphanides and Danny Reinberg. A unified theory of gene expression. *Cell*, 108(4):439–51, Feb 2002.
- [95] Jason A. Papin, Tony Hunter, Bernhard O. Palsson, and Shankar Subramaniam. Reconstruction of cellular signalling networks and analysis of their properties. *Nat Rev Mol Cell Biol*, 6(2):99–111, 2005.
- [96] Judea Pearl. *Probabilistic Reasoning in Intelligent Systems: networks of plausible inference*. Morgan Kaufmann, 1988.

-
- [97] Judea Pearl. *Causality: Models, Reasoning and Inference*. Cambridge University Press, Cambridge, 2000.
- [98] Juan M Pedraza and Alexander van Oudenaarden. Noise propagation in gene networks. *Science*, 307(5717):1965–9, Mar 2005.
- [99] Dana Pe’er, Aviv Regev, Gal Elidan, and Nir Friedman. Inferring subnetworks from perturbed expression profiles. *Bioinformatics*, 17(90001):S215–S224, 2001.
- [100] JM Peña, J Bjrkegren, and J Tegnér. Growing Bayesian network models of gene networks from seed genes. *Bioinformatics*, 21 Suppl 2:ii224–ii229, Sep 2005.
- [101] Bruno-Edouard Perrin, Liva Ralaivola, Aurelien Mazurie, Samuele Bottani, Jacques Mallet, and Florence d’Alche Buc. Gene networks inference using dynamic Bayesian networks. *Bioinformatics*, 19(90002):138ii–148, 2003.
- [102] Fabio Piano, Aaron J Schetter, Diane G Morton, Kristin C Gunsalus, Valerie Reinke, Stuart K Kim, and Kenneth J Kempfues. Gene clustering based on RNAi phenotypes of ovary-enriched genes in *C. elegans*. *Curr Biol*, 12(22):1959–64, Nov 2002.
- [103] Iosifina Pournara and Lorenz Wernisch. Reconstruction of gene networks using Bayesian learning and manipulation experiments. *Bioinformatics*, 20(17):2934–2942, 2004.
- [104] Claudia Rangel, John Angus, Zoubin Ghahramani, Maria Lioumi, Elizabeth Sotheran, Alessia Gaiba, David L. Wild, and Francesco Falciani. Modeling T-cell activation using gene expression profiling and state-space models. *Bioinformatics*, 20(9):1361–1372, 2004.
- [105] Claudia Rangel, David L. Wild, Francesco Falciani, Zoubin Ghahramani, and Alessia Gaiba. Modeling biological responses using gene expression profiling and linear dynamical systems. In *Proceedings of the 2nd International Conference on Systems Biology*, pages 248–256, Madison, WI, 2001. Omnipress.
- [106] Jonathan M Raser and Erin K O’Shea. Control of stochasticity in eukaryotic gene expression. *Science*, 304(5678):1811–4, Jun 2004.
- [107] John Jeremy Rice, Yuhai Tu, and Gustavo Stolovitzky. Reconstructing biological networks using conditional correlation analysis. *Bioinformatics*, 10 2004.
- [108] Robert W. Robinson. Counting labeled acyclic digraphs. In F. Harary, editor, *New Directions in the Theory of Graphs*, pages 239–273. Academic Press, New York, 1973.
- [109] Simon Rogers and Mark Girolami. A Bayesian regression approach to the inference of regulatory networks from gene expression data. *Bioinformatics*, May 2005.

- [110] Nitzan Rosenfeld, Jonathan W Young, Uri Alon, Peter S Swain, and Michael B Elowitz. Gene regulation at the single-cell level. *Science*, 307(5717):1962–5, Mar 2005.
- [111] Julien Royet, Jean-Marc Reichhart, and Jules A Hoffmann. Sensing and signaling during infection in *Drosophila*. *Curr Opin Immunol*, 17(1):11–7, Feb 2005.
- [112] J. Rung, T. Schlitt, A. Brazma, K. Freivalds, and J. Vilo. Building and analysing genome-wide gene disruption networks. *Bioinformatics*, 18(90002):202S–210, 2002.
- [113] Ravi Sachidanandam. RNAi as a bioinformatics consumer. *Brief Bioinform*, 6(2):146–62, Jun 2005.
- [114] Karen Sachs, Omar Perez, Dana Pe’er, Douglas A Lauffenburger, and Garry P Nolan. Causal protein-signaling networks derived from multiparameter single-cell data. *Science*, 308(5721):523–9, Apr 2005.
- [115] Juliane Schäfer and Korbinian Strimmer. An empirical Bayes approach to inferring large-scale gene association networks. *Bioinformatics*, 21(6):754–64, Mar 2005.
- [116] Bernhard Schölkopf and Alexander J. Smola. *Learning with kernels*. The MIT Press, Cambridge, MA, 2002.
- [117] Gideon Schwarz. Estimating the dimension of a model. *Annals of Statistics*, 6(2):461–464, Mar 1978.
- [118] Eran Segal, Nir Friedman, Naftali Kaminski, Aviv Regev, and Daphne Koller. From signatures to models: understanding cancer using microarrays. *Nat Genet*, 37 Suppl:S38–45, Jun 2005.
- [119] Eran Segal, Dana Pe’er, Aviv Regev, Daphne Koller, and Nir Friedman. Learning module networks. *Journal of Machine Learning Research*, 6(Apr):557–588, 2005.
- [120] Eran Segal, Michael Shapira, Aviv Regev, Dana Pe’er, David Botstein, Daphne Koller, and Nir Friedman. Module networks: identifying regulatory modules and their condition-specific regulators from gene expression data. *Nature Genetics*, 34(2):166–176, 2003.
- [121] Shai S. Shen-Orr, Ron Milo, Shmoolik Mangan, and Uri Alon. Network motifs in the transcriptional regulation network of *Escherichia coli*. *Nature Genetics*, 31(1):64 – 68, April 2002. doi:10.1038/ng881.
- [122] Jose Silva, Kenneth Chang, Gregory J Hannon, and Fabiola V Rivas. RNA-interference-based functional genomics in mammalian cells: reverse genetics coming of age. *Oncogene*, 23(51):8401–9, Nov 2004.

-
- [123] I Simon, J Barnett, N Hannett, CT Harbison, NJ Rinaldi, TL Volkert, JJ Wyrick, J Zeitlinger, DK Gifford, TS Jaakkola, and RA Young. Serial regulation of transcriptional regulators in the yeast cell cycle. *Cell*, 106(6):697–708, Sep 2001.
- [124] Peter W. F. Smith and Joe Whittaker. Edge exclusion tests for graphical Gaussian models. In Michael Jordan, editor, *Learning in Graphical Models*, pages 555 – 574. MIT Press, 1999.
- [125] V. Anne Smith, Erich D. Jarvis, and Alexander J. Hartemink. Evaluating functional network inference using simulations of complex biological systems. *Bioinformatics*, 18(90001):216S–224, 2002.
- [126] PT Spellman, G Sherlock, MQ Zhang, VR Iyer, K Anders, MB Eisen, PO Brown, D Botstein, and B Futcher. Comprehensive identification of cell cycle-regulated genes of the yeast *Saccharomyces cerevisiae* by microarray hybridization. *Mol Biol Cell*, 9(12):3273–97, Dec 1998.
- [127] Peter Spirtes, Clark Glymour, and Richard Scheines. *Causation, Prediction, and Search*. MIT Press, Cambridge, MA, second edition, 2000.
- [128] Harald Steck and Tommi Jaakkola. On the dirichlet prior and Bayesian regularization. In *Advances in Neural Information Processing Systems 15*, Cambridge, MA, 2002. MIT Press.
- [129] Harald Steck and Tommi Jaakkola. (Semi-)predictive discretization during model selection. Technical Report AI Memo AIM-2003-002, MIT, 2003.
- [130] Harald Steck and Tommi S. Jaakkola. Unsupervised active learning in large domains. In *Proceedings of the Eighteenth Annual Conference on Uncertainty in Artificial Intelligence*, 2002.
- [131] Harald Steck and Tommi S. Jaakkola. Bias-corrected bootstrap and model uncertainty. In Sebastian Thrun, Lawrence Saul, and Bernhard Schölkopf, editors, *Advances in Neural Information Processing Systems 16*. MIT Press, Cambridge, MA, 2004.
- [132] Korbinian Strimmer and Arndt von Haeseler. Quartet Puzzling: A Quartet Maximum-Likelihood Method for Reconstructing Tree Topologies. *Mol Biol Evol*, 13(7):964–969, 1996.
- [133] Joshua M Stuart, Eran Segal, Daphne Koller, and Stuart K Kim. A gene-coexpression network for global discovery of conserved genetic modules. *Science*, 302(5643):249–55, Oct 2003.
- [134] Yoshinori Tamada, SunYong Kim, Hideo Bannai, Seiya Imoto, Kousuke Tashiro, Satoru Kuhara, and Satoru Miyano. Estimating gene networks from gene expression data by combining Bayesian network model with promoter element detection. *Bioinformatics*, 19(90002):227ii–236, 2003.

- [135] Jesper Tegner, M K Stephen Yeung, Jeff Hasty, and James J Collins. Reverse engineering gene networks: integrating genetic perturbations with dynamical modeling. *Proc Natl Acad Sci U S A*, 100(10):5944–9, May 2003.
- [136] Jin Tian and Judea Pearl. Causal discovery from changes. In Jack S. Breese and Daphne Koller, editors, *Proceedings of the 17th Conference in Uncertainty in Artificial Intelligence*, pages 512–521, Seattle, Washington, USA, 2001. Morgan Kaufmann. Part 1 of a two-part paper.
- [137] Jin Tian and Judea Pearl. Causal discovery from changes: a Bayesian approach. In Jack S. Breese and Daphne Koller, editors, *Proceedings of the 17th Conference in Uncertainty in Artificial Intelligence*, pages 512–521, Seattle, Washington, USA, 2001. Morgan Kaufmann. Part 2 of a two-part paper.
- [138] Simon Tong and Daphne Koller. Active Learning for Structure in Bayesian Networks. In *Proceedings of the Seventeenth International Joint Conference on Artificial Intelligence (IJCAI)*, Seattle, Washington, August 2001.
- [139] Thomas S. Verma and Judea Pearl. Equivalence and synthesis of causal models. In P. B. Bonissone, M. Henrion, L. N. Kanal, and J. F. Lemmer, editors, *Proc. Sixth Conf. on Uncertainty in Artificial Intelligence*, pages 255–268. North-Holland, Amsterdam, 1990.
- [140] Andreas Wagner. How to reconstruct a large genetic network from n gene perturbations in fewer than n^2 easy steps. *Bioinformatics*, 17(12):1183–1197, 2001.
- [141] Andreas Wagner. Estimating Coarse Gene Network Structure from Large-Scale Gene Perturbation Data. *Genome Res.*, 12(2):309–315, 2002.
- [142] Andreas Wagner. Reconstructing pathways in large genetic networks from genetic perturbations. *Journal of Computational Biology*, 11(1):53–60, 2004.
- [143] Wei Wang and Gregory F. Cooper. An bayesian method for biological pathway discovery from high-throughput experimental data. In *Proc. 3rd International IEEE Computer Society Computational Systems Bioinformatics Conference (CSB 2004)*, pages 645–646, Stanford, CA, USA, 2004. IEEE Computer Society.
- [144] Anja Wille and Peter Bühlmann. Tri-graph: a novel graphical model with application to genetic regulatory networks. Technical report, Seminar for Statistics, ETH Zurich, 2004.
- [145] Anja Wille, Philip Zimmermann, Eva Vranová, Andreas Fürholz, Oliver Laule, Stefan Bleuler, Lars Hennig, Amela Prelic, Peter von Rohr, Lothar Thiele, Eckart Zitzler, Wilhelm Gruissem, and Peter Bühlmann. Sparse graphical Gaussian modeling of the isoprenoid gene network in *Arabidopsis thaliana*. *Genome Biol*, 5(11):R92, 2004.

-
- [146] Frank C. Wimberly, Thomas Heiman, Joseph Ramsey, and Clark Glymour. Experiments on the accuracy of algorithms for inferring the structure of genetic regulatory networks from microarray expression levels. In *Proc. IJCAI 2003 Bioinformatics Workshop*, 2003.
- [147] Cecily J. Wolfe, Isaac S. Kohane, and Atul J. Butte. Systematic survey reveals general applicability of "guilt-by-association" within gene coexpression networks. *BMC Bioinformatics 2005*, 6:227, 2005.
- [148] Y. Yamanishi, J.-P. Vert, and M. Kanehisa. Protein network inference from multiple genomic data: a supervised approach. *Bioinformatics*, 20(suppl.1):i363–370, 2004.
- [149] Chen-Hsiang Yeang, Trey Ideker, and Tommi Jaakkola. Physical network models. *Journal of Computational Biology*, 11(2):243 – 262, 2004.
- [150] Chen-Hsiang Yeang, H Craig Mak, Scott McCuine, Christopher Workman, Tommi Jaakkola, and Trey Ideker. Validation and refinement of gene-regulatory pathways on a network of physical interactions. *Genome Biology*, 6(R62), 2005.
- [151] Stephen Yeung, Jesper Tegnér, and James J Collins. Reverse engineering gene networks using singular value decomposition and robust regression. *Proc Natl Acad Sci U S A*, 99(9):6163–8, Apr 2002.
- [152] C. Yoo and G. F. Cooper. An evaluation of a system that recommends microarray experiments to perform to discover gene-regulation pathways. *Journal Artificial Intelligence in Medicine*, 31(2):169–182, 2004.
- [153] Changwon Yoo, Vesteynn Thorsson, and Gregory F. Cooper. Discovery of causal relationships in a generegulation pathway from a mixture of experimental and observational DNA microarray data. In *Proceedings of Pacific Symposium on Biocomputing 7:498-509*, 2002.
- [154] Jing Yu, V. Anne Smith, Paul P. Wang, Alexander J. Hartemink, and Erich D. Jarvis. Advances to Bayesian network inference for generating causal networks from observational biological data. *Bioinformatics*, Jul 2004.
- [155] Daniel E. Zak, Francis J. Doyle, Gregory E. Gonye, and James S. Schwaber. Simulation studies for the identification of genetic networks from cDNA array and regulatory activity data. In *Proceedings of the Second International Conference on Systems Biology*, pages 231–238, 2001.
- [156] Daniel E. Zak, Gregory E. Gonye, James S. Schwaber, and Francis J. Doyle. Importance of Input Perturbations and Stochastic Gene Expression in the Reverse Engineering of Genetic Regulatory Networks: Insights From an Identifiability Analysis of an In Silico Network. *Genome Res.*, 13(11):2396–2405, 2003.
- [157] Min Zou and Suzanne D. Conzen. A new dynamic Bayesian network (DBN) approach for identifying gene regulatory networks from time course microarray data. *Bioinformatics*, 21(1):71–79, 2005.

Notation and Definitions

Here I list often used abbreviations and notations for quick reference. The notation in chapter 3 complies to Steffen Lauritzens book [72], the statistical standard reference on graphical models.

Chapter 1

DNA.....	Deoxyribonucleic acid
RNA.....	Ribonucleic acid
mRNA.....	messenger RNA
RNAi.....	RNA interference

Chapter 2

V	set of graph vertices representing network components
p	number of pathway components, $p = V $.
$T = (V, \mathcal{E})$	network topology on vertices V and edge set \mathcal{E}
D	special case: T is a directed acyclic graph
X, x	a random variable and its realization
\mathbf{X}, \mathbf{x}	a set or vector of random variables and its realization
M	data matrix $M = \{\mathbf{x}^1, \dots, \mathbf{x}^N\}$
N	sample size
$P(X = x) \equiv p(x)$..	if no confusion can arise
$X \perp Y$	X and Y are independent random variables
$X \perp Y \mid Z$	X and Y are independent given Z
$\Sigma, \hat{\Sigma}$	covariance matrix and its estimator
K	precision matrix, inverse covariance matrix, $K = \Sigma^{-1}$
$\theta_{v pa(v)}$	the parameters of random variable X_v given the values of its parents $\mathbf{X}_{pa(v)}$ in the Bayesian network DAG
$\alpha_{i_\delta \mathbf{i}_{pa(\delta)}}$	Dirichlet parameters for a discrete node $\delta \in V$ with parent state $\mathbf{i}_{pa(\delta)}$ in a Bayesian network.
DAG.....	directed acyclic graph
GGM.....	Gaussian graphical model
DBN.....	dynamic Bayesian network
LPD.....	local probability distribution

Chapter 3

$do(X_v = x'_v)$	do-operator: X_v is fixed to state x'_v
$d(x)$	Dirac-function, point mass at $x = 0$
Δ	the set of discrete vertices
Γ	the set of Gaussian vertices
$\mathbf{X} = (\mathbf{I}, \mathbf{Y})$	the set of variables splits into discrete ones (\mathbf{I}) and continuous ones (\mathbf{Y}).
I_δ, i_δ	a discrete random variable ($\delta \in \Delta$) and its realization
Y_γ, y_γ	a Gaussian random variable ($\gamma \in \Gamma$) and its realization
$\mathcal{I}_\delta, \mathcal{I}_{pa(\delta)}$	the state space of I_δ and its parents $\mathbf{I}_{pa(\delta)}$
$\mathcal{P}(\theta, w, t)$	pushing operator applied to parameters θ with strength w towards target state t
$\theta_{\delta \mathbf{i}_{pa(\delta)}}$	parameters of discrete variable I_δ
$\theta_{\gamma \mathbf{i}_{pa(\gamma)}}$	parameters of Gaussian variable Y_γ depending on the values $\mathbf{i}_{pa(\gamma)}$ of discrete parents

Chapter 4

$V = \mathbf{E} \cup \mathbf{S}$	vertices correspond to signaling genes (S-genes) and reporter genes (E-genes)
E_i	reporter genes ($i = 1, \dots, m$)
S_j	signaling genes ($j = 1, \dots, p$)
E_{ik}, e_{ik}	binomial random variable corresponding to the state of E_i in experiment k and its realization
C_{ik}	continuous expression states
T	pathway topology on S-genes
T'	extended topology including S-genes and E-genes
Φ	silencing scheme
α	probability to observe a false positive effect
β	probability to observe a false negative effect
$\theta_i = j$	position parameter: S_j is the parent of E_i in T'
η_i	probability to observe an effect at E_i
η_{is}	probability to observe an effect at E_i given parent state s
M_i^s	data of E_i when parent was in state s
n_{ise}	number of observations $e_{ik} = e$ when parent state is s