

ACKNOWLEDGMENTS

The authors would like to acknowledge S. Kühner for providing the data for **Figure 1** and Á. Gonçalves for comments on parts of the manuscript. This work was partly supported by the European Union Framework Programme 6 grant 'TAMAHUD' (LSHC-CT-2007-037472).

COMPETING INTERESTS STATEMENT

The authors declare no competing financial interests.

Published online at <http://www.nature.com/naturemethods/>.

Reprints and permissions information is available online at <http://npg.nature.com/reprintsandpermissions/>.

1. Michal, G. *Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology* (Wiley, New York, 1998).
 2. Nishizuka, Y. The role of protein kinase C in cell surface signal transduction and tumour promotion. *Nature* **308**, 693–698 (1984).
 3. Levine, M. & Davidson, E.H. Gene regulatory networks for development. *Proc. Natl. Acad. Sci. USA* **102**, 4936–4942 (2005).
 4. Bader, G.D., Cary, M.P. & Sander, C. Pathguide: a pathway resource list. *Nucleic Acids Res.* **34** Database issue, D504–D506 (2006).
 5. Saraiya, P., North, C. & Duca, K. Visualizing biological pathways: requirements analysis, systems evaluation, and research agenda. *Inf. Vis.* **4**, 191–205 (2005).
- This paper represents one of the first attempts to critically evaluate the requirements for visualization software used in biology.**
6. Suderman, M. & Hallett, M. Tools for visually exploring biological networks. *Bioinformatics* **23**, 2651–2659 (2007).
 7. Pavlopoulos, G.A.G., Wegener, A.L.A. & Schneider, R.R. A survey of visualization tools for biological network analysis. *BioData Min.* **1**, 12 (2008).
 8. Charbonnier, S., Gallego, O. & Gavin, A.C. The social network of a cell: recent advances in interactome mapping. *Biotechnol. Annu. Rev.* **14**, 1–28 (2008).
 9. Yu, H. *et al.* High-quality binary protein interaction map of the yeast interactome network. *Science* **322**, 104–110 (2008).
 10. Gavin, A.C. *et al.* Proteome survey reveals modularity of the yeast cell machinery. *Nature* **440**, 631–636 (2006).
 11. Mathivanan, S. *et al.* An evaluation of human protein-protein interaction data in the public domain. *BMC Bioinformatics* **7** (suppl. 5), S19 (2006).
 12. Ma'ayan, A. Network integration and graph analysis in mammalian molecular systems biology. *IET Syst. Biol.* **2**, 206–221 (2008).
 13. Salwinski, L. *et al.* The Database of Interacting Proteins: 2004 update. *Nucleic Acids Res.* **32** (database issue), D449–D451 (2004).
 14. Prasad, T.S., Kandasamy, K. & Pandey, A. Human Protein Reference Database and Human Proteinpedia as discovery tools for systems biology. *Methods Mol. Biol.* **577**, 67–79 (2009).
 15. Aranda, B. *et al.* The IntAct molecular interaction database in 2010. *Nucleic Acids Res.* **38** (database issue), D525–D531 (2010).
 16. von Mering, C. *et al.* Comparative assessment of large-scale data sets of protein-protein interactions. *Nature* **417**, 399–403 (2002).
 17. Fruchterman, T.M.J. & Reingold, E.M. Graph drawing by force-directed placement. *Software Pract. Exper.* **21**, 1129–1164 (1991).
 18. Bader, G.D. & Hogue, C.W. An automated method for finding molecular complexes in large protein interaction networks. *BMC Bioinformatics* **4**, 2 (2003).
 19. Kühner, S. *et al.* Proteome organization in a genome-reduced bacterium. *Science* **326**, 1235–1240 (2009).
 20. Shannon, P. *et al.* Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Res.* **13**, 2498–2504 (2003).
- This paper describes the core Cytoscape software, which has become one of the most popular tools to visualize and analyze biological networks. This is partly due to the modular design of the software that allows developers to create plug-ins to address virtually any network analysis problem.**
21. Junker, B.H., Klukas, C. & Schreiber, F. VANTED: a system for advanced data analysis and visualization in the context of biological networks. *BMC Bioinformatics* **7**, 109 (2006).
 22. Hu, Z. *et al.* VisANT 3.5: multi-scale network visualization, analysis and inference based on the gene ontology. *Nucleic Acids Res.* **37** (web server issue), W115–W121 (2009).
 23. McGuffin, M.J. & Jurisica, I. Interaction techniques for selecting and manipulating subgraphs in network visualizations. *IEEE Trans. Vis. Comput. Graph.* **15**, 937–944 (2009).
 24. Prinz, S. *et al.* Control of yeast filamentous-form growth by modules in an integrated molecular network. *Genome Res.* **14**, 380–390 (2004).
 25. Hu, Z. *et al.* Towards zoomable multidimensional maps of the cell. *Nat. Biotechnol.* **25**, 547–554 (2007).

26. Barsky, A., Munzner, T., Gardy, J. & Kincaid, R. Cerebral: visualizing multiple experimental conditions on a graph with biological context. *IEEE Trans. Vis. Comput. Graph.* **14**, 1253–1260 (2008).
27. Genc, B. and Dogrusoz, U. A layout algorithm for signaling pathways. *Inf. Sci.* **176**, 135–149 (2006).
28. de Lichtenberg, U., Jensen, L.J., Brunak, S. & Bork, P. Dynamic complex formation during the yeast cell cycle. *Science* **307**, 724–727 (2005).
29. Kanehisa, M. *et al.* KEGG for linking genomes to life and the environment. *Nucleic Acids Res.* **36** (database issue), D480–D484 (2008).
30. Matthews, L. *et al.* Reactome knowledgebase of human biological pathways and processes. *Nucleic Acids Res.* **37** (database issue), D619–D622 (2009).
31. Kuhn, M. *et al.* STITCH 2: an interaction network database for small molecules and proteins. *Nucleic Acids Res.* **38** (database issue), D552–D556 (2010).
32. Quackenbush, J. Computational analysis of microarray data. *Nat. Rev. Genet.* **2**, 418–427 (2001).
33. Wang, Z., Gerstein, M. & Snyder, M. RNA-Seq: a revolutionary tool for transcriptomics. *Nat. Rev. Genet.* **10**, 57–63 (2009).
34. Bantscheff, M., Schirle, M., Sweetman, G., Rick, J. & Kuster, B. Quantitative mass spectrometry in proteomics: a critical review. *Anal. Bioanal. Chem.* **389**, 1017–1031 (2007).
35. Gstaiger, M. & Aebersold, R. Applying mass spectrometry-based proteomics to genetics, genomics and network biology. *Nat. Rev. Genet.* **10**, 617–627 (2009).
36. Westenberg, M.A., van Hijum, S.A.F.T., Kuipers, O.P. & Roerdink, J.B.T.M. Visualizing genome expression and regulatory network dynamics in genomic and metabolic context. *Comput. Graph. Forum* **27**, 887–894 (2008).
37. Freeman, T.C. *et al.* Construction, visualisation, and clustering of transcription networks from microarray expression data. *PLoS Comput. Biol.* **3**, e206 (2007).
38. Saraiya, P., Lee, P. & North, C. in *IEEE Symp. Information Visualization (InfoVis 2005)* 225–232 (2005).
39. Tufte, E.R. *The Visual Display of Quantitative Information* 2nd edn. (Graphics Press, Cheshire, Connecticut, USA, 2001).
40. Salomonis, N. *et al.* GenMAPP 2: new features and resources for pathway analysis. *BMC Bioinformatics* **8**, 217 (2007).
41. Neuweger, H. *et al.* Visualizing post genomics data-sets on customized pathway maps by ProMeTra – aeration-dependent gene expression and metabolism of *Corynebacterium glutamicum* as an example. *BMC Syst. Biol.* **3**, 82 (2009).
42. Kincaid, R., Kuchinsky, A. & Creech, M. VistaClara: an expression browser plug-in for Cytoscape. *Bioinformatics* **24**, 2112–2114 (2008).
43. Lee, H.K., Hsu, A.K., Sajdak, J., Qin, J. & Pavlidis, P. Coexpression analysis of human genes across many microarray data sets. *Genome Res.* **14**, 1085–1094 (2004).
44. Dunn, W.B. & Ellis, D.I. Metabolomics: current analytical platforms and methodologies. *TrAC Trends Anal. Chem.* **24**, 285–294 (2005).
45. Scholz, M. & Fiehn, O. Setup X – a public study design database for metabolomic projects. *Pac. Symp. Biocomput.* 169–180, doi:10.1142/9789812772435_0017 (2007).
46. Thimm, O. *et al.* MAPMAN: a user-driven tool to display genomics data sets onto diagrams of metabolic pathways and other biological processes. *Plant J.* **37**, 914–939 (2004).
47. Paley, S.M. & Karp, P.D. The Pathway Tools cellular overview diagram and omics viewer. *Nucleic Acids Res.* **34**, 3771–3778 (2006).
48. Tokimatsu, T. *et al.* KaPPA-view: a web-based analysis tool for integration of transcript and metabolite data on plant metabolic pathway maps. *Plant Physiol.* **138**, 1289–1300 (2005).
49. Mlecnik, B. *et al.* PathwayExplorer: web service for visualizing high-throughput expression data on biological pathways. *Nucleic Acids Res.* **33** (web server issue), W633–W637 (2005).
50. Caspi, R. *et al.* The MetaCyc database of metabolic pathways and enzymes and the BioCyc collection of pathway/genome databases. *Nucleic Acids Res.* **36** (database issue), D623–D631 (2008).
51. Funahashi, A. *et al.* CellDesigner 3.5: a versatile modeling tool for biochemical networks. *Proc. IEEE* **96**, 1254–1265 (2008).
52. Sauro, H.M. *et al.* Next generation simulation tools: the Systems Biology Workbench and BioSPICE integration. *OMICS* **7**, 355–372 (2003).
53. Demir, E. *et al.* PATIKA: an integrated visual environment for collaborative construction and analysis of cellular pathways. *Bioinformatics* **18**, 996–1003 (2002).
54. Schreiber, F., Dwyer, T., Marriott, K. & Wybrow, M. A generic algorithm for layout of biological networks. *BMC Bioinformatics* **10**, 375 (2009).
55. Thomas, J.J. & Cook, K.A. *Illuminating the Path: The Research and Development Agenda for Visual Analytics*. (National Visual Analytics Center & IEEE, Richland, Washington, USA, 2005).

56. Saraiya, P., North, C. & Duca, K. An Insight-based methodology for evaluating bioinformatics visualizations. *IEEE Trans. Vis. Comput. Graph.* **11**, 443–456 (2005).
57. Dwyer, T., Koren, Y. & Marriott, K. IPSEP-COLA: an incremental procedure for separation constraint layout of graphs. *IEEE Trans. Vis. Comput. Graph.* **12**, 821–828 (2006).
58. Dwyer, T. *et al.* Exploration of networks using overview+detail with constraint-based cooperative layout. *IEEE Trans. Vis. Comput. Graph.* **14**, 1293–1300 (2008).
59. Viégas, F.B., Wattenberg, M., van Ham, F., Kriss, J. & McKeon, M. ManyEyes: a site for visualization at internet scale. *IEEE Trans. Vis. Comput. Graph.* **13**, 1121–1128 (2007).
60. Heer, J., Viégas, F.B. & Wattenberg, M. Voyagers and voyeurs: supporting asynchronous collaborative information visualization. in *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems (CHI'07)* 1029–1038 (ACM, New York, 2007).
61. Heer, J. & Agrawala, M. Design considerations for collaborative visual analytics. *Inf. Vis.* **7**, 49–62 (2008).
62. Pico, A.R. *et al.* WikiPathways: pathway editing for the people. *PLoS Biol.* **6**, e184 (2008).
63. Pavlopoulos, G.A. *et al.* Arena3D: visualization of biological networks in 3D. *BMC Syst. Biol.* **2**, 104 (2008).
64. Ball, R. & North, C. Realizing embodied interaction for visual analytics through large displays. *Comput. Graph.* **31**, 380–400 (2007).
65. Berman, H., Henrick, K. & Nakamura, H. Announcing the worldwide Protein Data Bank. *Nat. Struct. Biol.* **10**, 980 (2003).
66. Hermjakob, H. *et al.* The HUPPO PSI's molecular interaction format—a community standard for the representation of protein interaction data. *Nat. Biotechnol.* **22**, 177–183 (2004).
67. Hucka, M. *et al.* The systems biology markup language (SBML): a medium for representation and exchange of biochemical network models. *Bioinformatics* **19**, 524–531 (2003).
68. Lloyd, C.M., Halstead, M.D. & Nielsen, P.F. CellML: its future, present and past. *Prog. Biophys. Mol. Biol.* **85**, 433–450 (2004).
69. Le Novère, N. *et al.* The Systems Biology Graphical Notation. *Nat. Biotechnol.* **27**, 735–741 (2009).
- This publication marks the first serious attempt to create a community standard for a graphical notation to represent networks in systems biology.**
70. Walter, T. *et al.* Visualization of image data from cells to organisms. *Nat. Methods* **7**, S26–S40 (2010).
71. O'Donoghue, S.I. *et al.* Visualization of macromolecular structures. *Nat. Methods* **7**, S42–S55 (2010).
72. Nielsen, C.B., Cantor, M., Dubchak, I., Gordon, D. & Wang, T. Visualizing genomes: techniques and challenges. *Nat. Methods* **7**, S5–S15 (2010).
73. Procter, J.B. *et al.* Visualization of multiple alignments, phylogenies and gene family evolution. *Nat. Methods* **7**, S16–S25 (2010).
74. Burrage, K., Hood, L. & Ragan, M.A. Advanced computing for systems biology. *Brief. Bioinform.* **7**, 390–398 (2006).
75. Awad, I.A., Rees, C.A., Hernandez-Boussard, T., Ball, C.A. & Sherlock, G. Caryoscope: an open source Java application for viewing microarray data in a genomic context. *BMC Bioinformatics* **5**, 151 (2004).
76. Lau, C. *et al.* Exploration and visualization of gene expression with neuroanatomy in the adult mouse brain. *BMC Bioinformatics* **9**, 153 (2008).
77. Weber, G.H. *et al.* Visual exploration of three-dimensional gene expression using physical views and linked abstract views. *IEEE/ACM Trans. Comput. Biol. Bioinform.* **6**, 296–309 (2009).
78. Barsky, A., Gardy, J.L., Hancock, R.E. & Munzner, T. Cerebral: a Cytoscape plugin for layout of and interaction with biological networks using subcellular localization annotation. *Bioinformatics* **23**, 1040–1042 (2007).
79. Mookherjee, N. *et al.* Modulation of the TLR-mediated inflammatory response by the endogenous human host defense peptide LL-37. *J. Immunol.* **176**, 2455–2464 (2006).
80. Spellman, P.T. *et al.* Comprehensive identification of cell cycle-regulated genes of the yeast *Saccharomyces cerevisiae* by microarray hybridization. *Mol. Biol. Cell* **9**, 3273–3297 (1998).
81. Kuntzer, J. *et al.* BNDB – the Biochemical Network Database. *BMC Bioinformatics* **8**, 367 (2007).
82. Baitaluk, M., Sedova, M., Ray, A. & Gupta, A. BiologicalNetworks: visualization and analysis tool for systems biology. *Nucleic Acids Res.* **34** (web server issue), W466–W471 (2006).
83. Cline, M.S. *et al.* Integration of biological networks and gene expression data using Cytoscape. *Nat. Protoc.* **2**, 2366–2382 (2007).
84. Hooper, S.D. & Bork, P. Medusa: a simple tool for interaction graph analysis. *Bioinformatics* **21**, 4432–4433 (2005).
85. Kao, H.L. & Gunsalus, K.C. Browsing multidimensional molecular networks with the generic network browser (N-Browse). *Curr. Protoc. Bioinformatics* **9**, 9.11.1–9.11.21 (2008).
86. Brown, K.R. *et al.* NAViGATOR: Network Analysis, Visualization and Graphing Toronto. *Bioinformatics* **25**, 3327–3329 (2009).
87. Kohler, J. *et al.* Graph-based analysis and visualization of experimental results with ONDEX. *Bioinformatics* **22**, 1383–1390 (2006).
88. Breitkreutz, B.J., Stark, C. & Tyers, M. Osprey: a network visualization system. *Genome Biol.* **4**, R22 (2003).
89. Batagelj, V. & Mrvar, A. Pajek – Program for large network analysis. *Connections* **21**, 47–57 (1998).
90. Forman, J.J., Clemons, P.A., Schreiber, S.L. & Haggarty, S.J. SpectralNET—an application for spectral graph analysis and visualization. *BMC Bioinformatics* **6**, 260 (2005).
91. Auber, D. A huge graph visualization framework. in *Graph Drawing Software* (eds. Mutzel, P. & Jünger, M.) 105–126 (Springer, Heidelberg, Germany, 2004).
92. Zinovyev, A., Viara, E., Calzone, L. & Barillot, E. BiNoM: a Cytoscape plugin for manipulating and analyzing biological networks. *Bioinformatics* **24**, 876–877 (2008).
93. Huttenhower, C., Mehmood, S.O. & Troyanskaya, O.G. Graphlet: interactive exploration of large, dense graphs. *BMC Bioinformatics* **10**, 417 (2009).
94. Longabaugh, W.J., Davidson, E.H. & Bolouri, H. Visualization, documentation, analysis, and communication of large-scale gene regulatory networks. *Biochim. Biophys. Acta* **1789**, 363–374 (2009).
95. Streit, M., Lex, A., Kalkusch, M., Zatloukal, K. & Schmalstieg, D. Caleydo: connecting pathways and gene expression. *Bioinformatics* **25**, 2760–2761 (2009).
96. Okuda, S. *et al.* KEGG atlas mapping for global analysis of metabolic pathways. *Nucleic Acids Res.* **36** (web server issue), W423–W426 (2008).
97. van Iersel, M.P. *et al.* Presenting and exploring biological pathways with PathVisio. *BMC Bioinformatics* **9**, 399 (2008).
98. Holford, M., Li, N., Nadkarni, P. & Zhao, H. VitaPad: visualization tools for the analysis of pathway data. *Bioinformatics* **21**, 1596–1602 (2005).
99. Chung, H. J., Kim, M., Park, C. H., Kim, J., and Kim, J. H. ArrayXPath: mapping and visualizing microarray gene-expression data with integrated biological pathway resources using scalable vector graphics. *Nucleic Acids Res.* **32** (web server issue), W460–W464 (2004).
100. Weniger, M., Engelmann, J.C. & Schultz, J. Genome Expression Pathway Analysis Tool—analysis and visualization of microarray gene expression data under genomic, proteomic and metabolic context. *BMC Bioinformatics* **8**, 179 (2007).
101. Letunic, I., Yamada, T., Kanehisa, M. & Bork, P. iPath: interactive exploration of biochemical pathways and networks. *Trends Biochem. Sci.* **33**, 101–103 (2008).
102. Karp, P.D., Paley, S. & Romero, P. The Pathway Tools software. *Bioinformatics* **18** (suppl. 1), S225–S232 (2002).
103. Dogrusoz, U. *et al.* PATIKAweb: a Web interface for analyzing biological pathways through advanced querying and visualization. *Bioinformatics* **22**, 374–375 (2006).
104. Santamaria, R., Theron, R. & Quintales, L. BicOverlapper: a tool for bicluster visualization. *Bioinformatics* **24**, 1212–1213 (2008).
105. Goncalves, J.P., Madeira, S.C. & Oliveira, A.L. BIGGESTS: integrated environment for biclustering analysis of time series gene expression data. *BMC Res Notes* **2**, 124 (2009).
106. Shamir, R. *et al.* EXPANDER—an integrative program suite for microarray data analysis. *BMC Bioinformatics* **6**, 232 (2005).
107. Sturn, A., Quackenbush, J. & Trajanoski, Z. Genesis: cluster analysis of microarray data. *Bioinformatics* **18**, 207–208 (2002).
108. Hibbs, M.A., Dirksen, N.C., Li, K. & Troyanskaya, O.G. Visualization methods for statistical analysis of microarray clusters. *BMC Bioinformatics* **6**, 115 (2005).
109. Seo, J. & Shneiderman, B. Interactively exploring hierarchical clustering results. *Computer* **35**, 80–86 (2002).
110. Saldanha, A.J. Java Treeview—extensible visualization of microarray data. *Bioinformatics* **20**, 3246–3248 (2004).
111. Dietzsch, J., Gehlenborg, N. & Nieselt, K. Mayday – a microarray data analysis workbench. *Bioinformatics* **22**, 1010–1012 (2006).
112. Gehlenborg, N., Dietzsch, J. & Nieselt, K. A framework for visualization of microarray data and integrated meta-information. *Inf. Vis.* **4**, 164–175 (2005).
113. Saeed, A.I. *et al.* TM4: a free, open-source system for microarray data management and analysis. *Biotechniques* **34**, 374–378 (2003).
- One of the first and still one of the most commonly used applications for the management, analysis and visualization of microarray data.**
114. Hochheiser, H., Baehrecke, E.H., Mount, S.M. & Shneiderman, B. Dynamic querying for pattern identification in microarray and genomic data. *Proc. IEEE Multimedia and Expo Int. Conf.* **3**, 453–456 (2003).



115. Kapushesky, M. *et al.* Expression Profiler: next generation—an online platform for analysis of microarray data. *Nucleic Acids Res.* **32** (web server issue), W465–W470 (2004).
116. Reich, M. *et al.* GenePattern 2.0. *Nat. Genet.* **38**, 500–501 (2006).
117. Quackenbush, J. Microarray data normalization and transformation. *Nat. Genet.* **32** (suppl.), 496–501 (2002).
118. Brettschneider, J., Collin, F., Bolstad, B.M. & Speed, T.P. Quality assessment for short oligonucleotide microarray data. *Technometrics* **50**, 241–264 (2008).
119. Kauffmann, A., Gentleman, R. & Huber, W. ArrayQualityMetrics—a bioconductor package for quality assessment of microarray data. *Bioinformatics* **25**, 415–416 (2009).
120. Morgan, M. *et al.* ShortRead: a bioconductor package for input, quality assessment and exploration of high-throughput sequence data. *Bioinformatics* **25**, 2607–2608 (2009).
121. Robinson, M.D., McCarthy, D.J. & Smyth, G.K. edgeR: a Bioconductor package for differential expression analysis of digital gene expression data. *Bioinformatics* **26**, 139–140 (2010).
122. Smyth, G.K., Yang, Y.H. & Speed, T. Statistical issues in cDNA microarray data analysis. *Methods Mol. Biol.* **224**, 111–136 (2003).
123. Nesvizhskii, A.I., Vitek, O. & Aebersold, R. Analysis and validation of proteomic data generated by tandem mass spectrometry. *Nat. Methods* **4**, 787–797 (2007).
124. Perkins, D.N., Pappin, D.J., Creasy, D.M. & Cottrell, J.S. Probability-based protein identification by searching sequence databases using mass spectrometry data. *Electrophoresis* **20**, 3551–3567 (1999).
125. Li, X.J. *et al.* A tool to visualize and evaluate data obtained by liquid chromatography-electrospray ionization-mass spectrometry. *Anal. Chem.* **76**, 3856–3860 (2004).
126. Sturm, M. & Kohlbacher, O. TOPPView: an open-source viewer for mass spectrometry data. *J. Proteome Res.* **8**, 3760–3763 (2009).
127. Kopka, J. Current challenges and developments in GC-MS based metabolite profiling technology. *J. Biotechnol.* **124**, 312–322 (2006).
128. Broeckling, C.D. *et al.* Metabolic profiling of *Medicago truncatula* cell cultures reveals the effects of biotic and abiotic elicitors on metabolism. *J. Exp. Bot.* **56**, 323–336 (2005).
129. Beckonert, O. *et al.* Metabolic profiling, metabolomic and metabonomic procedures for NMR spectroscopy of urine, plasma, serum and tissue extracts. *Nat. Protoc.* **2**, 2692–2703 (2007).
130. Lindon, J.C. & Nicholson, J.K. Spectroscopic and statistical techniques for information recovery in metabonomics and metabolomics. *Annu. Rev. Anal. Chem.* **1**, 45–69 (2008).
131. Xia, J., Bjorndahl, T.C., Tang, P. & Wishart, D.S. MetaboMiner—semi-automated identification of metabolites from 2D NMR spectra of complex biofluids. *BMC Bioinformatics* **9**, 507 (2008).
132. Hotelling, H. Analysis of complex statistical variables into principal components. *J. Educ. Psychol.* **24**, 417–441 (1933).
133. Kruskal, J. Multidimensional scaling by optimizing goodness of fit to a nonmetric hypothesis. *Psychometrika* **29**, 1–26 (1964).
134. Venna, J. & Kaski, S. Comparison of visualization methods for an atlas of gene expression data sets. *Inf. Vis.* **6**, 139–154 (2007).
135. Inselberg, A. The plane with parallel coordinates. *Vis. Comput.* **1**, 69–91 (1985).
136. Eisen, M.B., Spellman, P.T., Brown, P.O. & Botstein, D. Cluster analysis and display of genome-wide expression patterns. *Proc. Natl. Acad. Sci. USA* **95**, 14863–14868 (1998).
- Milestone publication that introduced the heat map visualization to the field of transcriptomics and has been cited several thousand times.**
137. Wilkinson, L. & Friendly, M. The history of the cluster heat map. *Am. Stat.* **63**, 179–184 (2009).
138. Weinstein, J.N. Biochemistry. a postgenomic visual icon. *Science* **319**, 1772–1773 (2008).



