

Preface

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WHEN A MAP IS A MAP?

"That's another thing we've learned from your Nation", said Mein Herr, "map-making. But we've carried it much further than you. What do you consider the largest map that would be really useful?"

"About six inches to the mile."

"Only six inches" exclaimed Mein Herr. "We very soon got to six yards to the mile. Then we tried a hundred yards to the mile. And then came the grandest idea of all! We actually made a map of the country, on the scale of a mile to the mile!"

"Have you used it much?" I enquired.

"It has never been spread out, yet," said Mein Herr: "the farmers objected: they said it would cover the whole country, and shut out the sunlight! So we now use the country itself, as its own map, and I assure you it does nearly as well.

Lewis Carroll (1893) Sylvie and Bruno Concluded

The aim of the Preface is to show that "Falconer's book" (Falconer (1960, 1981, 1989); Falconer and Mackay (1996))

- has been a very good (text)book,
- it needs to be replaced with a new (text)book, and
- the new book should follow the successful tradition of Falconer's book.

Do we need a new book on quantitative genetics (QG)?

There is no doubt that Falconer's book (*Introduction to Quantitative Genetics*) has been a very successful and influential textbook. About 60 years after its first edition, [Falconer \(1960\)](#), and almost 25 years after its fourth and last edition, [Falconer and Mackay \(1996\)](#), it is still being referred to in its traditional fields (quantitative genetics, animal and plant

breeding), and many other fields, such as evolutionary genetics, genetic epidemiology, and behavioral genetics.

However, 25 years is a long time, especially, in a very active field of research such as QG (e.g. compare [Lynch and Walsh \(1998\)](#) and [Walsh and Lynch \(2018\)](#)). The theory of QG has been pushed forward partly because scientists from many "*non-traditional*" fields have brought their questions to QG, and partly because of the momentum created by the massive amounts of new data that quantitative geneticists need to analyze.

Unfortunately, the monumental work by [Lynch and Walsh \(1998\)](#) and [Walsh and Lynch \(2018\)](#) are too "*voluminous*" to be used in an introductory course as a textbook. It was the lack of a good modern textbook that spurred us to undertake the task of writing a replacement for [Falconer and Mackay \(1996\)](#). The first step in this endeavor is to find out why Falconer's book has been so successful, and how it can be updated.

Success factors of Falconer's book

Falconer's *Introduction to Quantitative Genetics* owes its success to a number of inter-related principles that permeated all four editions of the book.

Model simplicity/complexity

Falconer kept the model complexity to a minimum with a view of making his book "*useful to as wide a range of readers as possible, particularly biologists who, . . . , have no more than ordinary mathematical ability*". Thus, the book could be used as an introductory textbook for advanced undergraduate and early postgraduate courses. Further, professionals from other fields could easily learn the basics of QG. By analogy to the text cited from Lewis Carroll, Falconer kept the balance between simplicity/complexity at an informative and usable level.

Shallow/deep discussions

Falconer's book started each subject from an intuitive conceptual definition, and an associated simple equation reflecting the core of that conceptual definition. Therefore, it was easy to grasp a subject before reaching the diverse operational definitions that might exist for the subject. The distinction between conceptual and operational definitions can be exemplified by the two concepts of heritability and inbreeding for each of which there are several, more or less, equivalent equations. Falconer's book also avoided the formal derivation of many equations with mathematical rigor, and tried to simplify the equations as much as possible.

Staying true (or not) to QG

Utilization of QG in other fields often requires knowledge in some neighboring fields. As an example, the use of QG in animal and plant breeding requires help from statistical theory (e.g. in the fields of estimation and prediction theories). Falconer, successfully resisted the temptations to venture out in such fields. Keeping the balance between QG and neighboring fields helped the reader to have the opportunity to acquire a grasp of core of QG, while other sources could fill the gaps for application.

Number of subjects

Falconer's book, despite its relatively small size (378 pages of main text, including end of chapter problems, in the 4th edition) has a wide coverage of core QG subjects, and also application areas. There parts of the QG theory that are missing from Falconer's book (see the next section). However, it could be argued that the balance between too few or too many has been crucial, and inclusion of some of the missing parts was in contrast to other success factors, and indeed might have been excluded on purpose.

Diversity of examples and references

Another success factor for Falconer's book is the use of examples from many different species and settings. Experimental (laboratory) animals and plants, as well as field data are used throughout the book. Even data from a specific animal species, commonly known as "*human*", has been extensively used in the book. Irrespective of the reader's background, Falconer's book provides a balance among the usage of examples from, and references to, many species and areas of research.

Updated/outdated

Ironically, different editions of Falconer's book could be considered as both very updated, and at the same time rather outdated at the time of their publication. The reason is (was) a general tendency to use the original publications on many subjects rather than using the latest research. This had ensured that the sources (literature cited), in the majority of cases, had successfully passed the test of time. The use of old references was balanced by using the latest experimental results, and the latest theoretical developments in the core subjects of QG.

What is missing from Falconer's book?

Given the long time that has passed since the last edition of Falconer's book ([Falconer and Mackay \(1996\)](#)), the passage of time has made its presence more pronounced. It also important to bear in mind that the structure of Falconer's book, even for the last edition, is much influenced by the decisions made prior to the first edition (the date at the end of Preface of the 1st edition is December 1958).

An important question for a new book on QG is whether the balance point chosen by Falconer (and later by Falconer and Mackay) for each of the above mentioned success factors are the right point for today's needs? If the right balance is not established, then the new book will be "*out of joint*". The effects of passage of time can be categorized, at least, under four headings.

Scientific advances of the last 25 years

The obvious effect of the last 25 years is that QG, and all of its neighboring branches of science, including molecular genetics, population genetics, and statistical genetics have made tremendous amount of theoretical and experimental advances. The most relevant advances need to be outlined in a new body of QG theory.

Technical advances in molecular genetics

Scientific advances in the field of molecular genetics have brought about many technical advances that provide massive amounts of data useful for QG studies. It has been shown repeatedly in the past (e.g. [Kuhn \(1996\)](#), and [Cohen \(1985\)](#)) that technological advances are one of the prerequisites of advances in scientific theories.

Technical advances in statistical genetics

Apart from scientific advances in the field of statistical genetics, there are Information Technology tools that are now available to students of QG that were not available to anyone in the "*old days*". These include both hardware (e.g. desktop and laptop computers, and powerful local, regional, and national server networks), and software (e.g. general statistical and special statistical genetics computer programs). These kinds of tools facilitate numerical analysis of large amounts of data with all sorts of statistical methods and models. The technical advancements in this area have a profound impact on the choice of balance between opposing options in the success factors mentioned above. Many things that were complicated before, might be considered relatively easy now.

Technical advances in book writing

Modern techniques of book writing provide a plethora of tools for typesetting, use of color, inclusion of footnotes and sidenotes, and many other visually enhancing areas. The use of such tools is thought after because of the assumption that they add pedagogical values to a book. Probably the most important development is that nowadays books can be used "*electronically*". Thus, cross-referencing in text, to specific elements of the book (equations, figures, cited literature, and so on) has become essential.

Main references

These are the books that have been used extensively in writing of this book. The list will be assembled when writing the book has finished.

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To be written later.

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Bibliography

Citations in alphabetical order.

Alberts, B., A. Johnson, J. Lewis, D. Morgan, M. Raff, K. Roberts, and P. Walter (2015). *Molecular biology of the cell*. Sixth edition. New York, NY: Garland Science, Taylor and Francis Group. 1465 pp. (cited on page 5).

Bagheri, H. C. and G. P. Wagner (2004). Evolution of Dominance in Metabolic Pathways. *Genetics* **168**: 1713–1735. doi: [10.1534/genetics.104.028696](https://doi.org/10.1534/genetics.104.028696) (cited on page 11).

Bateson, W. (1901). Problems of heredity as a subject for horticultural investigations. *Journal of the Royal Horticultural Society* **25**: 54–61. doi: [10.1017/CBO9780511693946](https://doi.org/10.1017/CBO9780511693946) (cited on page 4).

Bolormaa, S., J. E. Pryce, B. J. Hayes, and M. E. Goddard (2010). Multivariate analysis of a genome-wide association study in dairy cattle. *Journal of Dairy Science* **93**: 3818–3833. doi: [10.3168/jds.2009-2980](https://doi.org/10.3168/jds.2009-2980) (cited on page 13).

Bolormaa, S., J. E. Pryce, A. Reverter, Y. Zhang, W. Barendse, K. Kemper, B. Tier, K. Savin, B. J. Hayes, and M. E. Goddard (2014). A Multi-Trait, Meta-analysis for Detecting Pleiotropic Polymorphisms for Stature, Fatness and Reproduction in Beef Cattle. *PLoS Genetics* **10**: ed. by J. Flint, e1004198. doi: [10.1371/journal.pgen.1004198](https://doi.org/10.1371/journal.pgen.1004198) (cited on page 13).

Bromham, L. (2016). What is a gene for? *Biology & Philosophy* **31**: 103–123. doi: [10.1007/s10539-014-9472-9](https://doi.org/10.1007/s10539-014-9472-9) (cited on page 12).

Bulmer, M. G. (2003). *Francis Galton: pioneer of heredity and biometry*. Baltimore: Johns Hopkins University Press. 357 pp. (cited on page 17).

Bünger, L., U. Renne, G. Dietl, and S. Kuhla (1998). Long-term selection for protein amount over 70 generations in mice. *Genetical Research* **72**: 93–109. doi: [10.1017/S0016672398003401](https://doi.org/10.1017/S0016672398003401) (cited on pages 13, 14).

Casella, G. and R. L. Berger (2002). *Statistical inference*. 2nd Ed. Duxbury. 686 pp. (cited on page 6).

Castle, W. E. (1905). The Mutation Theory of Organic Evolution, from the Standpoint of Animal Breeding. *Science* **21**: 521–525. doi: [10.1126/science.21.536.521](https://doi.org/10.1126/science.21.536.521) (cited on page 19).

Chang, C.-W., W.-C. Cheng, C.-R. Chen, W.-. Shu, M.-L. Tsai, C.-L. Huang, and I. C. Hsu (2011). Identification of Human Housekeeping Genes and Tissue-Selective Genes by Microarray Meta-Analysis. *PLOS ONE* **6**: e22859. doi: [10.1371/journal.pone.0022859](https://doi.org/10.1371/journal.pone.0022859) (cited on page 11).

Cohen, I. B. (1985). *Revolution in science*. 1st Ed. Harvard University Press. 746 pp. (cited on page viii).

Collas, P., T. M. Liyakat Ali, A. Brunet, and T. Germier (2019). Finding Friends in the Crowd: Three-Dimensional Cliques of Topological Genomic Domains. *Frontiers in Genetics* **10**: 602. doi: [10.3389/fgene.2019.00602](https://doi.org/10.3389/fgene.2019.00602) (cited on page 5).

Crow, J. F. and M. Kimura (2009). *An introduction to population genetics theory*. OCLC: 1027901624. Jodhpur; New Jersey: Scientific Publisher (India) ; The Blackburn Press (cited on pages 7, 13, 16).

Darwin, C. R. (1859). *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*. John Murray, London. 502 pp. (cited on pages 15, 16, 18, 19).

Dean, A. M., D. E. Dykhuizen, and D. L. Hartl (1986). Fitness as a function of β -galactosidase activity in *Escherichia coli*. *Genetical Research* **48**: 1–8. doi: [10.1017/S0016672300024587](https://doi.org/10.1017/S0016672300024587) (cited on page 11).

Dudley, J. W. (2007). From Means to QTL: The Illinois Long-Term Selection Experiment as a Case Study in Quantitative Genetics. *Crop Science* **47**: (Supplement_3), S–20. doi: [10.2135/cropsci2007.04.0003IPBS](https://doi.org/10.2135/cropsci2007.04.0003IPBS) (cited on page 13).

Dudley, J. W. and R. J. Lambert (2010). '100 Generations of Selection for Oil and Protein in Corn'. *Plant Breeding Reviews*. Oxford, UK: John Wiley & Sons, Inc., pp. 79–110. doi: [10.1002/9780470650240.ch5](https://doi.org/10.1002/9780470650240.ch5) (cited on page 14).

Dunnington, E. A., C. F. Honaker, M. L. McGilliard, and P. B. Siegel (2013). Phenotypic responses of chickens to long-term, bidirectional selection for juvenile body weight: A Historical perspective. *Poultry Science* **92**: 1724–1734. doi: [10.3382/ps.2013-03069](https://doi.org/10.3382/ps.2013-03069) (cited on page 13).

Dykhuizen, D. E., A. M. Dean, and D. L. Hartl (1987). Metabolic Flux and Fitness. *Genetics* **115**: 25–31 (cited on page 11).

East, E. M. (1910). A Mendelian Interpretation of Variation that is Apparently Continuous. *The American Naturalist* **44**: 65–82 (cited on page 19).

Eisenberg, E. and E. Y. Levanon (2013). Human housekeeping genes, revisited. *Trends in Genetics* **29**: 569–574. doi: [10.1016/j.tig.2013.05.010](https://doi.org/10.1016/j.tig.2013.05.010) (cited on page 11).

Eldredge, N. and S. J. Gould (1972). 'Punctuated equilibria: an alternative to phyletic gradualism'. *Models in paleobiology*. Cooper and Co., San Francisco, pp. 82–115 (cited on page 19).

Ewens, W. J. (2004). *Mathematical population genetics. 1: Theoretical introduction*. 2. ed. Interdisciplinary applied mathematics Mathematical biology. New York, NY: Springer. 417 pp. (cited on page 7).

Falconer, D. S. (1960). *Introduction to Quantitative Genetics*. 1st edition (cited on page v).

Falconer, D. S. and T. F. C. Mackay (1996). *Introduction to Quantitative Genetics*. 4th ed. Longman Group Ltd. 480 pp. (cited on pages v, vi, viii).

Fisher, R. A. (1918). The correlation between relatives on the supposition of Mendelian inheritance. *Transactions of the Royal Society of Edinburgh* **525**: 399–433 (cited on pages 4, 10, 20, 23, 26).

Galton, F. (1865). Hereditary talent and character. *Macmillan's Magazine* **12**: 157–166, 318–327 (cited on page 18).

Galton, F. (1877). Typical laws of heredity, 492–533 (cited on page 18).

Galton, F. (1886). Regression towards mediocrity in hereditary stature. *Journal of the Anthropological Institute of Great Britain and Ireland* **15**: 246–263 (cited on pages 4, 19).

Galton, F. (1889). *Natural inheritance*. Macmillan, London (cited on page 19).

Geiger, T., A. Wehner, C. Schaab, J. Cox, and M. Mann (2012). Comparative Proteomic Analysis of Eleven Common Cell Lines Reveals Ubiquitous but Varying Expression of Most Proteins. *Molecular & Cellular Proteomics : MCP* **11**: doi: [10.1074/mcp.M111.014050](https://doi.org/10.1074/mcp.M111.014050) (cited on page 11).

Gould, S. J. (2002). *The structure of evolutionary theory*. Cambridge, Mass: Belknap Press of Harvard University Press. 1433 pp. (cited on page 19).

Griffiths, A. J., S. R. Wessler, J. Carroll, and J. Doebley (2015). *Introduction to genetic analysis*. 11th Ed. W. H. Freeman & Company (cited on pages 5, 15).

Haldane, J. B. S. (1924). A mathematical theory of natural and artificial selection. Part I. (cited on pages 23, 24).

Haldane, J. B. S. (1932). *The causes of evolution*. Longmans, Green and Co. 235 pp. (cited on page 23).

Hamilton, M. B. (2009). *Population genetics*. OCLC: ocn259716125. Chichester, UK ; Hoboken, NJ: Wiley-Blackwell. 407 pp. (cited on page 7).

Hartl, D. L. and A. G. Clark (2007). *Principles of population genetics*. 4th Ed. Sinauer Associates (cited on page 7).

Hartl, D. L., D. E. Dykhuizen, and A. M. Dean (1985). Limits of Adaptation: The Evolution of Selective Neutrality. *Genetics* **111**: 655–674 (cited on page 11).

Hill, W. G. (2005). A Century of Corn Selection. *Science* **307**: 683–685 (cited on page 14).

Hill, W. G. (1984a). *Quantitative Genetics: Explanation and analysis of continuous variation*. Van Nostrand Reinhold. 376 pp. (cited on page 21).

Hill, W. G. (1984b). *Quantitative genetics: Selection*. Van Nostrand Reinhold. 426 pp. (cited on page 21).

Hofmeyr, J.-H. S. and A. Cornish-Bowden (1991). Quantitative assessment of regulation in metabolic systems. *European Journal of Biochemistry* **200**: 223–236. doi: [10.1111/j.1432-1033.1991.tb21071.x](https://doi.org/10.1111/j.1432-1033.1991.tb21071.x) (cited on page 11).

Hogg, R. V., J. W. McKean, and A. T. Craig (2019). *Introduction to mathematical statistics*. Eighth edition. Boston: Pearson. 746 pp. (cited on page 6).

Holt, M., T. Meuwissen, and O. Vangen (2005). Long-term responses, changes in genetic variances and inbreeding depression from 122 generations of selection on increased litter size in mice. *Journal of Animal Breeding and Genetics* **122**: 199–209. doi: [10.1111/j.1439-0388.2005.00526.x](https://doi.org/10.1111/j.1439-0388.2005.00526.x) (cited on page 13).

Houle, D., D. K. Hoffmaster, S. Assimacopoulos, and B. Charlesworth (1992). The genomic mutation rate for fitness in *Drosophila*. *Nature* **359**: 58–60. doi: [10.1038/359058a0](https://doi.org/10.1038/359058a0) (cited on page 13).

Hubby, J. L. and R. C. Lewontin (1966). A Molecular Approach to the Study of Genic Heterozygosity in Natural Populations. I. the Number of Alleles at Different Loci in *Drosophila Pseudoobscura*. *Genetics* **54**: 577–594 (cited on page 11).

Hull, D. L. (1988). *Science as a process: an evolutionary account of the social and conceptual development of science*. Paperback ed., [Nachdr.] Science and its conceptual foundations. OCLC: 837696311. Chicago: University of Chicago Press. 586 pp. (cited on page 15).

Jensen, J. D., B. A. Payseur, W. Stephan, C. F. Aquadro, M. Lynch, D. Charlesworth, and B. Charlesworth (2019). The importance of the Neutral Theory in 1968 and 50 years on: A response to Kern and Hahn 2018: COMMENTARY. *Evolution* **73**: 111–114. doi: [10.1111/evo.13650](https://doi.org/10.1111/evo.13650) (cited on page 18).

Jiang, J., L. Ma, D. Prakapenka, P. M. VanRaden, J. B. Cole, and Y. Da (2019). A Large-Scale Genome-Wide Association Study in U.S. Holstein Cattle. *Frontiers in Genetics* **10**: 412. doi: [10.3389/fgene.2019.00412](https://doi.org/10.3389/fgene.2019.00412) (cited on page 13).

Johansson, A. M., M. E. Pettersson, P. B. Siegel, and Ö. Carlberg (2010). Genome-Wide Effects of Long-Term Divergent Selection. *PLoS Genetics* **6**: ed. by B. Walsh, e1001188. doi: [10.1371/journal.pgen.1001188](https://doi.org/10.1371/journal.pgen.1001188) (cited on page 14).

Kacser, H. (1989). 'Quantitative variation and the control analysis of enzyme systems.' *Hill W. G., and T.F.C. Mackay (1989) Evolution and Animal Breeding: Reviews on Molecular and Quantitative Approaches in Honour of Alan Robertson*. C.A.B. International, Wallingford, UK, pp. 219–226 (cited on page 11).

Kacser, H. and J. A. Burns (1979). Molecular Democracy: Who Shares the Controls? *Biochemical Society Transactions* **7**: 1149–1160. doi: [10.1042/bst0071149](https://doi.org/10.1042/bst0071149) (cited on page 11).

Kacser, H. and J. A. Burns (1981). The Molecular Basis of Dominance. *Genetics* **97**: 639–666 (cited on pages 5, 11).

Keel, B. N., D. J. Nonneman, A. K. Lindholm-Perry, W. T. Oliver, and G. A. Rohrer (2019). A Survey of Copy Number Variation in the Porcine Genome Detected From Whole-Genome Sequence. *Frontiers in Genetics* **10**: 737. doi: [10.3389/fgene.2019.00737](https://doi.org/10.3389/fgene.2019.00737) (cited on page 5).

Keightley, P. D. and W. G. Hill (1992). Quantitative Genetic Variation in Body Size of Mice From New Mutations. *Genetics* **131**: 693–700 (cited on page 13).

Kempthorne, O. (1976). 'Status of quantitative genetics'. *Proceedings of the International Conference on Quantitative Genetics*. Iowa State University Press, pp. 719–760 (cited on page 4).

Kern, A. D. and M. W. Hahn (2018). The Neutral Theory in Light of Natural Selection. *Molecular Biology and Evolution* **35**: ed. by S. Kumar, 1366–1371. doi: [10.1093/molbev/msy092](https://doi.org/10.1093/molbev/msy092) (cited on page 18).

Kimura, M. (1968). Evolutionary Rate at the Molecular Level. *Nature* **217**: 624–626. doi: [10.1038/217624a0](https://doi.org/10.1038/217624a0) (cited on pages 11, 17).

Kuhn, T. S. (1996). *The structure of scientific revolutions*. 3rd Ed. Chicago, IL: University of Chicago Press. 212 pp. (cited on page viii).

Larsen, R. J. and M. L. Marx (2017). *An Introduction to Mathematical Statistics and Its Applications* (cited on page 6).

Laurie, C. C., S. D. Chasalow, J. R. LeDeaux, R. McCarroll, D. Bush, B. Hauge, C. Lai, D. Clark, T. R. Rocheford, and J. W. Dudley (2004). The Genetic Architecture of Response to Long-Term Artificial Selection for Oil Concentration in the Maize Kernel. *Genetics* **168**: 2141–2155. doi: [10.1534/genetics.104.029686](https://doi.org/10.1534/genetics.104.029686) (cited on page 14).

Lehmann, E. L. and G. Casella (1998). *Theory of point estimation*. 2nd Ed. Springer texts in statistics. New York: Springer. 589 pp. (cited on page 6).

Lehninger, A. L., D. L. Nelson, and M. M. Cox (2013). *Lehninger principles of biochemistry*. 6th ed. OCLC: ocn820352899. New York: W.H. Freeman. 1119 pp. (cited on page 5).

Lewontin, R. C. and J. L. Hubby (1966). A Molecular Approach to the Study of Genic Heterozygosity in Natural Populations. II. Amount of Variation and Degree of Heterozygosity in Natural Populations of *Drosophila Pseudoobscura*. *Genetics* **54**: 595–609 (cited on page 11).

Liu, Y., X. Chang, J. Glessner, H. Qu, L. Tian, D. Li, K. Nguyen, P. M. A. Sleiman, and H. Hakonarson (2019). Association of Rare Recurrent Copy Number Variants With Congenital Heart Defects Based on Next-Generation Sequencing Data From Family Trios. *Frontiers in Genetics* **10**: 819. doi: [10.3389/fgene.2019.00819](https://doi.org/10.3389/fgene.2019.00819) (cited on page 5).

Liu, Y. and X. Li (2014). Has Darwin's Pangenesis Been Rediscovered? *BioScience* **64**: 1037–1041. doi: [10.1093/biosci/biu151](https://doi.org/10.1093/biosci/biu151) (cited on page 17).

Lynch, M. and B. Walsh (1998). *Genetics and analysis of quantitative traits*. Sunderland, Mass: Sinauer. 980 pp. (cited on pages vi, 25).

Mackay, T. F. C., J. D. Fry, R. F. Lyman, and S. V. Nuzhdin (1994). Polygenic mutation in *Drosophila melanogaster*: estimates from response to selection of inbred strains. *Genetics* **136**: 937–951 (cited on page 13).

Magdeldin, S., S. Enany, Y. Yoshida, B. Xu, Y. Zhang, Z. Zureena, I. Lokamani, E. Yaoita, and T. Yamamoto (2014). Basics and recent advances of two dimensional- polyacrylamide gel electrophoresis. *Clinical proteomics* **11**: 16. doi: [10.1186/1559-0275-11-16](https://doi.org/10.1186/1559-0275-11-16) (cited on page 11).

Maindonald, J. and W. J. Braun (2010). *Data Analysis and Graphics Using R - an Example-Based Approach*. 3rd Ed. Cambridge University Press (cited on page 6).

Malthus, T. (1798). *An Essay on the Principle of Population*. J. Johnson. 125 pp. (cited on pages 16, 17).

Marouli, E. et al. (2017). Rare and low-frequency coding variants alter human adult height. *Nature* **542**: 186–190. doi: [10.1038/nature21039](https://doi.org/10.1038/nature21039) (cited on page 12).

Mayr, E. (1977). Darwin and Natural Selection: How Darwin may have discovered his highly unconventional theory. *American Scientist* **65**: 321–327 (cited on pages 15, 16).

Mayr, E. (1982). *The growth of biological thought: diversity, evolution, and inheritance*. Cambridge, Mass.: Harvard Univ. Pr. 974 pp. (cited on page 21).

Mayr, E. (1988). *Toward a new philosophy of biology: Observations of an evolutionist*. Harvard University Press. 564 pp. (cited on page 15).

Meaburn, K. J. and T. Misteli (2019). Assessment of the Utility of Gene Positioning Biomarkers in the Stratification of Prostate Cancers. *Frontiers in Genetics* **10**: 1029. doi: [10.3389/fgene.2019.01029](https://doi.org/10.3389/fgene.2019.01029) (cited on page 5).

Mendel, G. (1866). Versuche über Pflanzenhybriden. *Verhandlungen des naturforschenden Vereines in Brünn*, 3–47 (cited on pages 4, 19).

Moose, S. P., J. W. Dudley, and T. R. Rocheford (2004). Maize selection passes the century mark: a unique resource for 21st century genomics. *Trends in Plant Science* **9**: 358–364. doi: [10.1016/j.tplants.2004.05.005](https://doi.org/10.1016/j.tplants.2004.05.005) (cited on page 14).

Mrode, R. A. (2013). *Linear models for the prediction of animal breeding values*. 3rd ed. Boston, MA: CABI (cited on pages 6, 26).

Nielsen, R. and M. Slatkin (2013). *An Introduction to Population Genetics: Theory and Applications*. Oxford, New York: Oxford University Press. 287 pp. (cited on page 7).

O'Farrell, P. H. (1975). High Resolution Two-Dimensional Electrophoresis of Proteins. *The Journal of biological chemistry* **250**: 4007–4021 (cited on page 11).

Pearson, K. (1904a). Report on Certain Enteric Fever Inoculation Statistics. *BMJ* **2**: 1243–1246. doi: [10.1136/bmj.2.2288.1243](https://doi.org/10.1136/bmj.2.2288.1243) (cited on pages 19, 26).

Pearson, K. (1904b). III . Mathematical contributions to the theory of evolution. XII. On a generalised Theory of alternative Inheritance, with special reference to Mendel's laws. *Philosophical Transactions of the Royal Society of London. Series A, Containing Papers of a Mathematical or Physical Character* **203**: 53–86. doi: [10.1098/rsta.1904.0015](https://doi.org/10.1098/rsta.1904.0015) (cited on page 19).

Perason, K. and A. Lee (1903). On the Laws of Inheritance in Man: I. Inheritance of Physical Characters. *Biometrika* **2**: 357–462 (cited on page 19).

Pierce, B. A. (2012). *Genetics: A conceptual approach*. 4th ed. New York: W.H. Freeman. 1 p. (cited on page 5).

Portin, P. and A. Wilkins (2017). The Evolving Definition of the Term "Gene". *Genetics* **205**: 1353–1364. doi: [10.1534/genetics.116.196956](https://doi.org/10.1534/genetics.116.196956) (cited on page 12).

Price, G. R. (1970). Selection and covariance. *Nature* **227**: 520–521 (cited on page 7).

Robertson, A. (1966). A mathematical model of the culling process in dairy cattle. *Animal Science* **8**: 95–108. doi: [10.1017/S0003356100037752](https://doi.org/10.1017/S0003356100037752) (cited on page 7).

Rogers, S. O. (2017). *Integrated Molecular Evolution* (cited on page 12).

Rowley, M. J. and V. G. Corces (2018). Organizational principles of 3D genome architecture. *Nature Reviews Genetics* **19**: 789–800. doi: [10.1038/s41576-018-0060-8](https://doi.org/10.1038/s41576-018-0060-8) (cited on page 5).

Ruse, M. (2014). 'Gould, Stephen Jay'. *eLS. John Wiley & Sons, Ltd: Chichester*. American Cancer Society, pp. 1–10. doi: [10.1002/9780470015902.a0025067](https://doi.org/10.1002/9780470015902.a0025067) (cited on page 19).

Sanders, M. F. and J. L. Bowman (2015). *Genetic Analysis - An Integrated Approach*. OCLC: 915123587 (cited on pages 5, 15).

Santiago, E., J. Albornoz, A. Dominguez, M. A. Torot, and C. Lopez-Fanjul (1992). The Distribution of Spontaneous Mutationson Quantitative Traits and Fitness in *Drosophila melanogaster*. *Genetics* **132**: 771–781 (cited on page 13).

Savage, J. E. *et al.* (2018). Genome-wide association meta-analysis in 269,867 individuals identifies new genetic and functional links to intelligence. *Nature Genetics* **50**: 912–919. doi: [10.1038/s41588-018-0152-6](https://doi.org/10.1038/s41588-018-0152-6) (cited on page 12).

Schaeffer, L. R. (2019). *Animal models*. L. R. Schaeffer. 381 pp. (cited on pages 6, 26).

Shannon, W. D., M. A. Watson, A. Perry, and K. Rich (2002). Mantel statistics to correlate gene expression levels from microarrays with clinical covariates. *Genetic Epidemiology* **23**: 87–96. doi: [10.1002/gepi.1115](https://doi.org/10.1002/gepi.1115) (cited on page 12).

Sorensen, D. and D. Gianola (2002). *Likelihood, Bayesian and MCMC methods in quantitative genetics*. Statistics for biology and health. New York: Springer-Verlag. 740 pp. (cited on pages 6, 26).

Strachan, T., J. Goodship, and P. F. Chinnery (2015). *Genetics and genomics in medicine*. New York: Garland Science/Taylor & Francis Group. 526 pp. (cited on page 5).

Terman, L. M. (1917). The Intelligence Quotient of Francis Galton in Childhood. *The American Journal of Psychology* **28**: 209–215 (cited on page 18).

Tymoczko, J. L., J. M. Berg, and L. Stryer (2015). *Biochemistry, a short course*. Third edition. New York: W.H. Freeman & Company, a Macmillan Education imprint. 900 pp. (cited on page 5).

Uhlén, M., L. Fagerberg, B. Hallström, C. Lindskog, P. Oksvold, A. Mardinoglu, Å. Sivertsson, C. Kampf, E. Sjöstedt, A. Asplund, I. Olsson, K. Edlund, E. Lundberg, S. Navani, C. A.-K. Szigyarto, J. Odeberg, D. Djureinovic, J. O. Takanen, S. Hober, T. Alm, P.-H. Edqvist, H. Berling, H. Tegel, J. Mulder, . Rockberg, P. Nilsson, J. M. Schwenk, M. Hamsten, K. v. Feilitzen, M. Forsberg, L. Persson, F. Johansson, M. Zwahlen, G. v. Heijne, J. Nielsen, and F. Pontén (2015). Tissue-based map of the human proteome. *Science* **347**: doi: [10.1126/science.1260419](https://doi.org/10.1126/science.1260419) (cited on page 11).

Visscher, P. M., N. R. Wray, Q. Zhang, P. Sklar, M. I. McCarthy, M. A. Brown, and J. Yang (2017). 10 Years of GWAS Discovery: Biology, Function, and Translation. *The American Journal of Human Genetics* **101**: 5–22. doi: [10.1016/j.ajhg.2017.06.005](https://doi.org/10.1016/j.ajhg.2017.06.005) (cited on page 12).

Wackerly, D. D., W. Mendenhall III, and R. L. Scheaffer (2008). *Mathematical Statistics*. 8th Ed. Brooks/Cole, Cengage Learning. 946 pp. (cited on page 6).

Walsh, B. and M. Lynch (2018). *Evolution and selection of quantitative traits*. New York, NY: Oxford University Press. 1459 pp. (cited on pages vi, 7, 25).

Watson, M. A., A. Perry, V. Budhjara, C. Hicks, W. D. Shannon, and K. M. Rich (2001). Gene Expression Profiling with Oligonucleotide Microarrays Distinguishes World Health Organization Grade of Oligodendrogiomas. *Cancer Research* **61**: 1825–1829 (cited on page 12).

Wilhelm, M., J. Schlegl, H. Hahne, A. M. Gholami, M. Lieberenz, M. M. Savitski, E. Ziegler, L. Butzmann, S. Gessulat, H. Marx, T. Mathieson, S. Lemeer, K. Schnatbaum, U. Reimer, H. Wenschuh, M. Mollenhauer, J. Slotta-Huspenina, J.-H. Boese, M. Bantscheff, A. Gerstmair, F. Faerber, and B. Kuster (2014). Mass-spectrometry-based draft of the human proteome. *Nature* **509**: 582–587. doi: [10.1038/nature13319](https://doi.org/10.1038/nature13319) (cited on page 11).

Wood, A. R. *et al.* (2014). Defining the role of common variation in the genomic and biological architecture of adult human height. *Nature Genetics* **46**: 1173–1186. doi: [10.1038/ng.3097](https://doi.org/10.1038/ng.3097) (cited on page 12).

Wright, S. (1921a). Systems of mating: I-V. *Genetics* **6**: 111–178 (cited on pages 10, 23, 24).

Wright, S. (1921b). Systems of mating. I. The biometric relations between parent and offspring. *Genetics* **6**: 111–123 (cited on page 10).

Wright, S. (1921c). Systems of mating. II. The effects of inbreeding on the genetic composition of a population. *Genetics* **6**: 124–143 (cited on page 10).

Wright, S. (1921d). Systems of mating. III. Assortative mating based on somatic resemblance. *Genetics* **6**: 144–161 (cited on page 10).

Wright, S. (1921e). Systems of mating. IV. The effects of selection. *Genetics* **6**: 162–166 (cited on page 10).

Wright, S. (1921f). Systems of mating. V. General considerations. *Genetics* **6**: 167–178 (cited on page 10).

Yoo, B. H. (1980). Long-term selection for a quantitative character in large replicate populations of *Drosophila melanogaster*: 1. Response to selection. *Genetical Research* **35**: 1–17. doi: [10.1017/S0016672300013896](https://doi.org/10.1017/S0016672300013896) (cited on page 13).

Yule, G. U. (1902). MENDEL'S LAWS AND THEIR PROBABLE RELATIONS TO INTRA-RACIAL HEREDITY. *New Phytologist* **1**: 222–238. doi: [10.1111/j.1469-8137.1902.tb07336.x](https://doi.org/10.1111/j.1469-8137.1902.tb07336.x) (cited on pages 19, 26).

Yule, G. U. (1906). 'On the theory of inheritance of quantitative compound characters on the basis of Mendel's laws – a preliminary note.' Report of the Third International Conference 1906 on Genetics : hybridisation (the cross-breeding of genera or species), the cross-breeding of varieties, and general plant-breeding. London: Royal Horticultural Society (cited on page 26).

Yule, G. U. (1907). On the Theory of Inheritance of Quantitatively Compound Characters on the Basis of Mendel's Laws. *Biometrika* **5**: 481–482. doi: [10.2307/2331701](https://doi.org/10.2307/2331701) (cited on page 19).

Zhang, Y., D. Li, and B. Sun (2015). Do Housekeeping Genes Exist? *PLOS ONE* **10**: e0123691. doi: [10.1371/journal.pone.0123691](https://doi.org/10.1371/journal.pone.0123691) (cited on page 11).

Zheng, H. and W. Xie (2019). The role of 3D genome organization in development and cell differentiation. *Nature Reviews Molecular Cell Biology* **20**: 535–550. doi: [10.1038/s41580-019-0132-4](https://doi.org/10.1038/s41580-019-0132-4) (cited on page 5).

Zhu, J., F. He, S. Song, J. Wang, and J. Yu (2008). How many human genes can be defined as housekeeping with current expression data? *BMC Genomics* **9**: 172. doi: [10.1186/1471-2164-9-172](https://doi.org/10.1186/1471-2164-9-172) (cited on page 11).