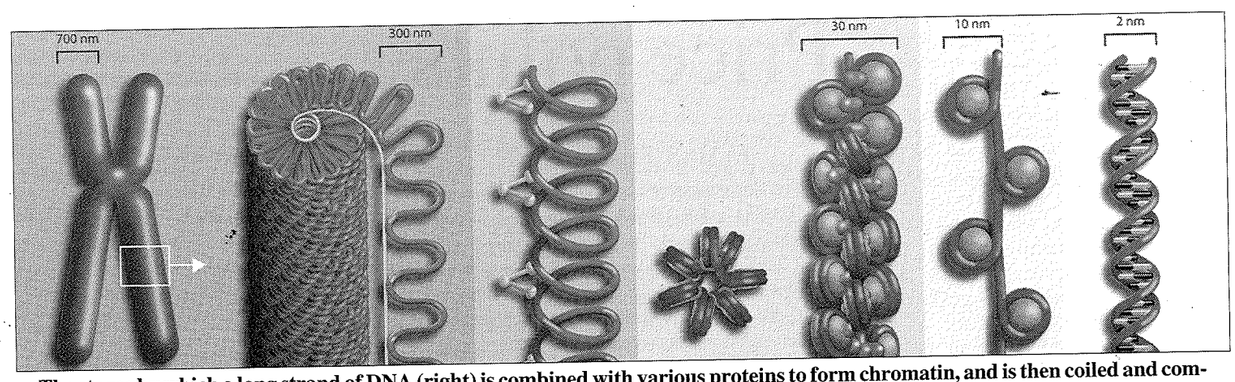
Thin and fat from the start

JONATHAN HODGKIN



The stages by which a long strand of DNA (right) is combined with various proteins to form chromatin, and is then coiled and compacted to form a chromosome (left)

Nessa Carey

THE EPIGENETICS REVOLUTION
How modern biology is rewriting our understanding of genetics, disease and inheritance
339pp. Icon. Paperback, £9.99.
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Life is complicated. Even when great unifying insights arrive in biology, subsequent research always reveals exceptions and qualifications. This book, intended for the general reader, argues that the simplistic view of genes as constant and immutable dictators of function is being supplanted by a more nuanced version, in which gene activity can be modified by environment, history and experience. Epigenetics is the baggy term used to refer to both the experiential effects and their underlying molecular mechanisms. Nessa Carey, in *The Epigenetics Revolution*, provides a clear and very readable survey of current research in epigenetics, which includes work on human obesity, schizophrenia, cloning and stem cells. Even so, epigenetics doesn't really amount to a revolution.

The simple version of genetics proposes that the function of a gene is determined by the base sequence of its DNA. But a gene may also be subjected to modifications in its chemistry, or in its chromosomal environment, which don't change this coding DNA sequence but do affect how efficiently it works. These epigenetic modifications come in two main flavours. First, the DNA itself may be modified by a process called methylation. Second, the DNA in chromosomes is wrapped around special proteins called histones, and the histones may also be altered by methylation or other simple chemical additions. Both kinds of epigenetic change add only a few atoms to the giant DNA or protein molecules, but they can have significant consequences, sometimes resulting in the complete silencing of a gene or even a whole chromosome.

The analogy used by Carey is the difference between the primary text of a drama and what actually happens in its performance as a play. The DNA sequence, in this analogy, is the initial script, and the epigenetic changes are the pencil scribbles that the director and actors make on this script, which determine much of what will happen on stage. But those pencil marks don't get perpetuated very efficiently, and will usually be erased at the end of the play's run. So it is with epigenetic changes: most of the marks get erased during the formation of gametes, the cells that will create the next generation.

This erasure is also essential in order to turn a differentiated cell like a skin cell, which accumulates many epigenetic marks during its development, back into a less differentiated state, such as a stem cell with the potential to multiply and create other cell types. Stem cells have enormous therapeutic potential, and consequently erasure has become an intensely active research area, as well as attracting interest from the pharmaceutical industry.

Epigenetically acquired characteristics generally do not get inherited, and therefore do not have much significance for evolution, but striking exceptions to this rule do occur. One example has been seen in children born to mothers who were pregnant through the Dutch Hunger Winter of 1944: many of those whose mothers were malnourished late in pregnancy were born small and stayed small throughout life, whereas those whose mothers were starved in early pregnancy grew up with a tendency to obesity. Remarkably, there is evidence for similar tendencies in the next generation, the grandchildren of those who were starved. Epigenetic inheritance is also observed in the parental imprinting of a few human genes, which become silenced when inherited from the father for some genes, or the mother for others. But these genes, although important in development, are very much the exception rather than the rule.

The stability and perpetuation of epigenetic changes is critical, so it is important to appreciate that the two kinds of modification differ in their inheritance. DNA methylation patterns can be faithfully copied and transmitted from one cell to both its daughters, but the histone modifications are a different story. It is not known how histone marks can be perpetuated from one cell generation to the next, or how reliably this occurs. Moreover, there is still much argument as to whether histone marks are a cause or merely a consequence of altered gene expression. As Carey also admits, even DNA methylation is not universal among animals, being absent in many invertebrates, although in honey bees it may be responsible for making worker bees so different from their queen bee sisters.

Some scientists feel that the novelty of epigenetics has been exaggerated. The odd fact that tortoiseshell cats are almost always female was noted by Darwin in *The Origin of Species* (1859) and a satisfying explanation (based on epigenetic X chromosome inactivation) was provided by Mary Lyon, fifty years ago. Thus, much of epigenetics is standard fare in molecular biology, and scarcely revolutionary. The more contentious areas of epigenetics are those claiming a strong causative role for histone modification, and here the jury is very much still out, more so than Nessa Carey implies. Nevertheless, she provides an excellent and largely accurate account of a fascinating and fast-moving area of modern biology.

Art in numbers

ALEXANDER MARR

Mark A. Peterson

GALILEO'S MUSE
Renaissance mathematics and the arts
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978 0 674 05972 6

The premiss of *Galileo's Muse* is simple and sensible: that in the Renaissance there developed a mutually beneficial relationship between the mathematical sciences, the humanities and the arts. Galileo, it is argued, exemplifies this trend. A well-rounded courtier, he turned his hand to literary criticism as well as to scientific experimentation, was a connoisseur of the visual arts and a talented mathematician, played the lute and peered at the heavens. Focusing especially on the humanist roots of this broad skill set, Mark A. Peterson takes us on a lively journey through these various domains in a book that is really an overview of Renaissance intellectual and cultural life centred on mathematics, rather than a detailed investigation of Galileo's world. For the latter, read John Heilbron's or David Wootton's brilliant recent biographies of Galileo (reviewed in the *TLS*, December 24, 2010), both of which delve into the social and cultural context in much greater scholarly depth. Since the appearance of Heilbron's book, in particular (published, presumably, too late for Peterson to have taken account of it), it is no longer the case that the significance of Galileo's humanism for his science "remains largely unexplored".

We should take the author at his word when he tells us that he is writing as a generalist, "assembling evidence and synthesizing a narrative that makes sense" of how mathematics and the arts interacted in the period. In some respects *Galileo's Muse* is an updated version of Dan Pedoe's *Geometry and the Liberal Arts* (1976): a useful survey for beginners that ranges widely but is not too diffuse, introduces its mathematics in an accessible fashion, and compels us to comprehend the infamous "two cultures" of the humanities and sciences as genuinely integrated in the period. The book moves briskly from prefatory material setting up Galileo as paragon to the classical legacy in mathematics he inherited, tours the arts of poetry, painting, music and architecture, and concludes with chapters on the changing fortunes of mathematics in the fifteenth and sixteenth centuries. Along the way, we are treated to vignettes depicting such subjects as the geometry of Dante's *Divina Commedia*, the elegant intertwining of painting and mathematics in the work of Piero della Francesca, Johannes Kepler's mathematical music of the spheres, and Alberti's Vitruvian *concinnitas*.

The final chapter argues that Niccolò Aggiunti's *Oratio de mathematicae laudibus* (1627) should in fact be attributed to Galileo. The general thrust of Peterson's argument is that the text of the *Oratio* reads a bit like Galileo and takes up Galilean themes, and that although writing in Latin (when Galileo favoured Tuscan), Aggiunti occasionally undertook Latin translations for his mentor. None of this is terribly surprising when one considers that Aggiunti was a devoted disciple of Galileo, and is not sufficient for a reattribution. Nor is Peterson's somewhat contorted case about the book's dedication to Grand Duke Ferdinand II convincing. The fact that the dedication was signed not by Aggiunti but by Marcantonio Pieralli, on behalf of the University of Pisa (where Aggiunti held the chair of mathematics), is entirely unremarkable, and should surely be viewed as an uncomplicated token of institutional gratitude for Medici support.

This episode betrays Peterson's inexperience in handling and interpreting early modern sources. Ironically, given his distrust of the *Oratio*, he takes other primary sources at face value. For instance, that inveterate hagiographer Vincenzo Viviani (exposed with particular verve by David Wootton) is described as having been motivated by a "sincere attempt to be accurate", while John Aubrey's account of Hobbes's late discovery of mathematics is read uncritically. Such quibbles aside, *Galileo's Muse* is a welcome addition to the growing literature on art and science in the early modern period. As Peterson says of Vasari's *Vite*, despite moments of unreliability, "it is a charming and useful book nonetheless".