The search for particulate units of inheritance

In pursuit of the gene: from Darwin to DNA
James Schwartz
Reviewed by AMITABH JOSHI*

Offspring tend to resemble parents, but not exactly: this is the fundamental observable that any science of heredity would need to explain. At a finer resolution, often offspring are intermediate between parents for a particular trait, whereas at other times they resemble one or the other parent closely. At a populational level, offspring of parents with extreme phenotypes, relative to the population mean, tend to be less extreme, on average, than their parents. All these observations, on a variety of species ranging from plants to humans, were in the purview of biologists trying to discover ‘laws’ of heredity in the mid-nineteenth century. The studies beginning with these observations eventually led, about a century later, to the identification of DNA as the genetic material and to the elucidation of its double-helical structure so crucial to its functioning as the material basis of heredity. What is interesting—and often ignored today amidst the mass of factual information pertaining to how genes are expressed and regulated in any given context, and how they give rise to phenotypes—is that more or less all the basic principles governing the transmission of genetic information from parents to offspring had been elucidated before anybody even knew for sure what the genetic material was. The studies that led to this understanding involved interesting and varied personalities, inspired hypotheses and guesses, numerous controversies and many masterpieces of inference and deduction that are largely unmatched in biology. It is these studies, described with a focus on the personalities and professional lives of people who carried them out, that are the main subject of the book ‘In pursuit of the gene’ by James Schwartz. To this end, Schwartz draws upon not only published work of both scientists and historians of science, but also on the correspondence of the principal actors, some of it not hitherto tapped by historians of biology.

Schwarz’s book is particularly welcome at this time of renewed interest in various philosophical issues in genetics and evolution, especially questions about the nature and definition of the concepts of ‘genes’ and ‘characters’, the nature of evolutionary explanations, and the whole philosophical structure of the genetics-centric neo-Darwinian synthesis (e.g. Beurton et al. 2000; Wagner 2001; Hallgrimsson and Hall 2005). Debate and discussion on these issues is immensely benefited by a clear historical perspective on how, and in what context, the concepts of genes and characters originated and evolved, and how a line of inquiry, focussed primarily on the problem of heredity and variation, at various times intertwined with and diverged from the studies of fossils, embryos and extant natural populations (e.g. Creath and Maienschein 2000; Amundson 2005). Indeed, though heredity had been of interest to humans for a long time, the early attempts to formulate clear principles of hereditary transmission of traits were all made within a broader framework of evolutionary theories trying to explain the diversity, relatedness and adaptedness of species (Rose 2000). It is, thus, fitting that Schwarz starts his story of the search for the units of heredity with the publication 140 years ago of Darwin’s ‘provisional hypothesis of pangenesis’ in the second volume of his book ‘The variation of animals and plants under domestication’ (Darwin 1868).

Darwin was trying to conjure up a mechanism of heredity that would, unlike blending inheritance, tend to maintain genetic variation in populations such that selection could then act upon it. This led him to posit that there were hereditary particles in the body, originating from all tissues, that got affected by the environments faced by the organism during its lifetime; in positing the inheritance of acquired characters, Darwin was thus a Lamarckian. In the first three chapters, Schwartz shows us how Galton, Darwin’s cousin, incorporated his notion of particulate units of inheritance to explain the normal distribution of various traits, while avoiding the

Keywords. heredity; genetics; mutation; evolution; chromosomes; history of biology; Galton; de Vries; Bateson; Muller; Drosophila.
Lamarckian aspect of the theory of pangenesis. These three chapters explore the development of ‘biometrical’ thinking on heredity, catalyzed by Galton’s development of the ideas of regression and correlation, and provided a firmer statistical foundation by Pearson. The association of Weldon, a close friend and later implacable scientific adversary of Bateson, with this programme brought to the biometrical cause a grounding in empirical data. These chapters, together with the next four, essentially provide a history of the ‘biometrician-Mendelian’ debate, with particular emphasis on the role played by the views of de Vries (one of the discovers of Mendel’s laws) on the evolutionary role of large saltationary changes on the hardening of Bateson’s views on the primary role of discontinuous variants in evolution.

These first seven chapters chart the course of how early speculations on the mechanisms and ‘laws’ of inheritance eventually came to fruition with the establishment of Mendel’s laws as well accepted principles governing the transmission of hereditary characters. It is also clear from the discussion of the ‘biometrician-Mendelian’ debate that evolutionary thinking was closely intertwined with the early thinking on genetics. Indeed, the debate was as much about tempo and mode in evolution as it was about the nature of hereditary variation. One omission that I found slightly jarring is that there is no mention of the elegant resolution of the ‘biometrician-Mendelian’ debate by Fisher (1918), a discussion that would have logically concluded the detailed exposition of the debate itself.

The most important and satisfying aspect of this part of the book to me was the detailed discussion of how de Vries’ views on heredity and evolution developed. When I had first encountered a brief description of the Mutation Theory of de Vries as a student of genetics, it had never entirely made sense. Upon reading Schwarz’s account, I was left with a much better understanding of what de Vries was trying to achieve with this theory, and why. I was also struck by how modern some of his speculations were: de Vries proposed, based on the observation that most plant cells were totipotent, that all genetic material was present in the nucleus of each cell, and went on to write “We can say: the instructions in the nucleus, the realization takes place in the protoplasm!”

The second half of the book traces the crystallization of modern genetics, from the realization that the Mendelian behaviour of the units of heredity are probably on the chromosomes is well detailed, and again gives far more insight into how these ideas developed than the cursory accounts in most textbooks. The telling of the events in Morgan’s fly-room is done in a fairly Muller-centric manner by Schwarz, thus providing a counterpoint to the canonical version of Sturtevant (2001). While Muller’s preascence and contributions to the growth of genetics are not disputed, I think that Schwarz has perhaps gone slightly overboard in championing Muller’s cause, especially when he tries to link Muller’s elucidation of the genetic underpinnings of the ‘truncate’ phenotype to quantitative genetics. There is a wealth of information on Muller’s work in this part of the book, including his stint in the USSR when Lysenkoism was beginning to gather steam. The descriptions of Muller’s work on the ‘truncate’ and ‘beaded’ phenotypes, the latter leading to the notion of balanced lethals, are particularly lucid and would convey even to a nonexpert some of the beauty of the experimental design and inference that permeates this work, and indeed much of classical genetics. Muller’s X-ray work on mutations is also well described. Indeed, one of the strengths of this book lies in the manner in which Schwarz has been able to describe some of the key discoveries in genetics such that the elegance of the thinking that went into those experiments would be accessible even to a nontechnical reader.

Another point that this book illustrates well is that the sociological aspects of science are quite similar across different eras. Personalities and prejudices play a major role in science, whether or not we like to accept it. Some of the disagreements, ego problems and conflicts described in this book still have a resonance today. At the same time, it is heartening to see examples of people changing their firmly-held views in the face of new data, to the extent of reversing them. All in all, the book is an excellent read, accessible even to the nontechnical reader, and is to be strongly recommended to all persons interested in how we came to understand the mysteries of heredity. It would also be a very useful adjunct to a basic course in genetics, or indeed to a course in the history and sociology of science. Even practicing geneticists would undoubtedly find the book of considerable interest and would, like me, learn a few new things about the development of our subject. Schwartz is to be commended for a fine book: it is more than worth the price.

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Book review


Received 26 November 2008; accepted 26 November 2008
Published on the Web: 1 December 2008

Erratum

Haldane and the first estimates of the human mutation rate

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J. Genet. 83, 231–233

Page 1, right column, para 1, line 6 from bottom, ‘three times’ should read ‘one third’.