

So it should be a virus but is extremely resistant to normal virucidal procedures. Recent approaches claim, after 40 years of struggle, to be getting near the truth, but the whole Scrapie-BSE-CJD-GSS-TME phenomenon has to me a hint of the Turin Shroud about it. I congratulate the encyclopedia team for its inclusion.

The article on bacterial chemotaxis shows the lengths to which *Escherichia coli* has gone to evolve a very sophisticated system for applying random walk theory to climbing up a liquid food gradient. Forty genes contribute to the flagellum, which can be rotated clockwise or anti-clockwise, this extraordinary engine being illustrated on page 90 by a drawing of the large working model that R. M. McNab built in his laboratory at Yale: I saw it working. A number of other genes control the switch-of-rotation mechanism and the transfer of information about any existing gradients. *Klebsiellas* are non-motile bacteria very closely related to *E. coli*, and I wish someone would make the easy checks as to which if any of the *E. coli* chemotaxis genes they possess.

As I hope I have indicated, this encyclopedia is very different from a textbook, and while it would not make a satisfactory replacement for a good textbook in class, it is far better as an easy source of information on molecular biology and covers much more ground. I think it would be of considerable value to many students and research workers – perhaps in the library rather than on the laboratory shelves because it is quite difficult to shut it after one has started browsing. Its only problem is the price.

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*Epigenetic Inheritance and Evolution: The Lamarckian Dimension.* By E. JABLONKA and M. LAMB. Oxford University Press. 1995. x+346 pages ill., index. Hard cover, \$29.50. ISBN 0 19 854062 0.

Young biologists will wonder what the sub-title is about. They may have been taught (or more likely, not) that over a century ago Weismann demolished Lamarck's theory that 'the acquisitions or losses wrought by nature on individuals... are preserved by reproduction', and that over half-a-century ago the Modern Synthesis of natural selection and Mendelism created a coherent, testable theory of evolution, and that Lamarck was finally consigned to oblivion by the central dogma of molecular biology. In the first two chapters of this book they will find that the really ancient belief in pangenesis is not so easily shaken off, and has tempted many distinguished biologists, and some not so distinguished like Lysenko, to explore possible exceptions to the generally accepted neo-Darwinian view. There is no harm in that; but it is a side-alley particularly attractive to those who would

like to improve our inheritance through environmental manipulation, which probably explains why the publisher's blurb commends this text as relevant to 'science and society' issues. Some hope!

Jablonka and Lamb are hooked on Lamarck, who is essentially an historical irrelevance: and they make their case by redefining Lamarckism as: a specific and reproducible change induced by the environment, not necessarily adaptive, involving a transmissible change in hereditary information (my words, not theirs). This is a 'soft' definition (cf. Lamarck above) which opens the door to welcoming anything which apparently contravenes the rules of DNA genetics. Not, let me emphasize, that the authors reject the Modern Synthesis: they accept it (and that relegates what they call epigenetic evolution to a side-show) but they claim it has imposed an ideological strait-jacket on evolution theory. One consequence of this stance is that there is a great deal in this book peripheral to its thesis (a gratuitous sniping at neo-Darwinism, in short). But don't let that put you off: this is otherwise a thorough, academic study of a tenable thesis (by their definition, above) which provides an entry to the relevant literature. I don't agree with the thesis but don't let that put you off, either.

The first issue examined is whether or not gene mutation is random or adaptive, for the latter would make the Lamarckian case. Since it has long been known that different loci have very different mutation rates, the data have to come from selective systems, i.e. from the last bastion of Lamarckism, namely, bacteria. The Luria and Delbrück fluctuation test which demonstrated random mutation is dismissed, and the work of Cairns and others showing that bacteria sometimes respond to selective nutritional environments by adaptive mutations is emphasized. References to papers disputing this 'directed mutation' explanation are quoted, but the arguments in them are not. This gives one the feeling of biased reporting, which tends to taint the book. But what do we mean by 'epigenetic inheritance' in bacteria? What else is there?

'An epigenetic inheritance system... enables a particular functional state or structural element to be transmitted from one cell generation to the next, even when the stimulus which originally induced it is no longer present.' Epigenesis is an embryological concept and should apply only to processes which occur during an individual's development; but the above definition allows the concept to include generational transmission. And for that to work the authors have to invent an *epiallele*, defined as 'one of the heritable chromatin forms of a gene with an unchanged DNA sequence'. So far as I am aware, no-one has isolated such an entity. Its existence can be deduced only from inheritance patterns: single epiallele effects.

Jablonka and Lamb use the dosage compensation of eutherian mammals, i.e. X-chromosome inactivation, as their first example of epigenetic trans-

mission. A curious choice rather too simply explained by them and ignoring the complexity of the molecular mechanisms involved, particularly the presence of an X-inactivation centre and the role of DNA methylation. True, they recognize that DNA methylation 'is the only biochemically well-characterised mechanism of epigenetic inheritance' but they fail to point out that in nearly all animal species, other than vertebrates, the genome appears free of methylation; and that fact makes it difficult to assume that this system plays any part in evolution, other than the one proposed by Bird. His theory is that methylation evolved to suppress the 'noise' caused by transcriptional slippage of relatively inactive genes, which then allowed the untrammelled increase of gene numbers in eucaryotes, especially vertebrates. But this has nothing to do with the postulated epigenetic, generational inheritance.

In most cases, as with X-inactivation, there is no evidence that epigenetic states can survive the hurdle of meiosis. Genomic imprinting (the process through which gene expression depends on the sex of the parent from which it is inherited) is an even more interesting example of epigenesis, *sensu strictu*, and it is carefully and thoroughly described, and again gene inactivation is laid at the door of methylation. Since this description was written the evidence is that methylation is a secondary step following some antecedent events which define the genes to be inactivated. However this may be, imprinting does not survive meiosis; and if it does create epialleles they have no future.

So we come to a rag bag, they themselves say, of putative epigenetic inheritance systems culled (and very usefully, too) from the literature. Restricting ourselves to the metazoa, the type of epigenetic inheritance found is generally put down to 'chromatin marks – methylation', which is hardly convincing. Many years ago, Harold Plough asked me to repeat one of the earliest experiments they quote, namely the induction of inherited changes in *Drosophila* caused by heat shock. Like Plough, I got phenocopies of wing venation but no inheritance, no Dauermodificationen as Jollos claimed for his experiments. One has to ask, therefore, how many of the items in the tabulation have been successfully confirmed? Again, anyone who has made phenocopies will know that Goldschmidt showed that many apparently wild-type strains of *Drosophila* respond differently to the same treatment because they carry isoalleles (mutants which can be distinguished from the wild-type locus only by special tests). These genes must confuse any search for epialleles, as must Hubby and Lewontin's data on the frequency of locus heterozygosity. These complications are not mentioned although they will undermine the conclusions of some of the listed experiments.

The most recent *Drosophila* experiment is a different proposition, and comes from the work of Dorn *et al.* who have identified a transposon whose product

establishes an open chromatin conformation at many chromosomal sites, including on the Y. Since it opens chromatin, the consequences of this activity were tested against position effect variegation. Variegation occurs when a tester locus (here *white eye*) is transposed (positioned) close to heterochromatin which 'spreads' over the locus and inactivates it. This inactivation is a curious, ill-understood event since adjacent cells react differently during development, one switching on and its neighbour switching off to give a variegated phenotype, in this case, red–white patches of eye colour. The expectation, then, was that the transposon product would reduce heterochromatinization and increase the amount of red pigment, and this was found even though the transposon product (in the absence of the transposon) was on the Y chromosome. The surprising result was that the 'progeny' of these modified Y chromosomes continued to be just as effective after 11 generations. Dorn *et al.* reckon this to be an imprinting-like phenomenon where the transposon product is actively involved in the transmission of the altered chromatin conformation between generations. We can only say that the jury is still out on that proposition, and remember that variegation is not usually assumed to be an epigenetic event, that the extensively heterochromatinized Y chromosome is itself peculiar, and this would not be an epiallele.

The organization of chromatin is obviously important as it affects epigenetic inheritance systems, and here this is formulated as the problem of chromatin marking. If I have understood the argument, we are concerned with the alteration of gene expression by the association of (particular?) chromatin proteins with the DNA gene. This is a rather ill-defined sort of mark, and as we have noted, it is generally associated with methylation. Methylation is usually but not always, an inhibitor of transcription which makes it difficult to define what is being looked for. This may not matter at this time since the literature on chromosome organization, which is very carefully surveyed in the text, is still in an elementary state, peppered with 'possibles', 'perhapses' and other qualifications. It is useful, then, to see that there is a real gap in our knowledge of gene regulation during development. But that is not an argument for concluding that epigenes exist, though the authors tend so to imply.

It is easy to imagine how epigenes might contribute to evolution. First, a changed 'chromatin mark' might result in a physiological, adaptive improvement of development, and such somatic selection could lead to a conventional selective advantage for its carriers. Of course, any alteration of a chromatin protein will depend on a DNA mutation, which is what would be selected for, at a second remove. Assuming that such chromatin-modified expression variants do occur, they would add to the complement of inherited variability and be subject to the already worked-out rules of

quantitative genetics. This is also explored, but with a bias towards 'directed epigenetic changes', and their possible role in microevolution. We are again in the world of speculation, and nowhere do we find a suggested experiment which would bring us back to earth.

One problem with this book is that it contains so much carefully garnered information (there is an excellent bibliography); but that is also why I would recommend it to final-year and graduate students. Where else will they find an up-to-date discussion of, say, Bell's views on the evolution of sex, meiosis and the emergence of multicellularity, or of Haldane's rule, or of Goldschmidt's hopeful monster, and of a whole variety of topics which tend to have disappeared from today's textbooks? But the difficulty of steering a student through all the facts and hypotheses remains.

I suggest three guide posts: where an epigenetic inheritance system (EIS) is referred to, check if this concerns events happening during development (if not, take it with a pinch of salt); and ask if the phenomenon described is real (not a hypothetical 'possible', which should be ignored, even though all things are possible in biology); and if there is any reason to discard the conventional DNA-genetics explanation. It is surprising, surely, that there is no reference throughout this book to the successes of conventional molecular biology in describing the development of *Drosophila*. That shows my bias, of course; and also that of the authors.

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