Molecular Drive: the Third Force in evolution

Geneticist Gabriel Dover claims that there is a third force in evolution: 'Molecular Drive' beside natural selection and neutral drift. Molecular drive is operationally distinct from natural selection and neutral drift. According to Dover it explains biological phenomena, such as the 700 copies of a ribosomal RNA gene and the origin of the 173 legs of the centipede, which natural selection and neutral drift alone cannot explain.

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Were Darwin and Mendel both wrong?

Molecular Drive is, according to Dover, an important factor in evolution, because it shapes the genomes and forms of organisms. Therefore Neo-Darwinism is incomplete without Molecular Drive. It is no wonder that the spread of novel genes was ascribed to natural selection, because it was the only known process that could promote the spread of novel genes. Dover doesn't reject the existence of natural selection but points out cases where natural selection clearly fails as a mechanism. Molecular drive is a non-Darwinian mechanism because it is independent of selection. We certainly need *forces* in evolution, since natural selection itself is not a force. It is the passive outcome of other processes. It is not an active process, notwithstanding its name. Natural selection as an explanation is too powerful for its own good. Molecular drive is non-Mendelian because some DNA segments are multiplied disproportional. In Mendelian genetics genes are present in just two copies (one on the maternal and one on the paternal chromosome). One of the components of molecular drive, 'gene conversion' shows a biased transmission in favour of one of the two copies. In Mendelian genetics the two copies (alleles) are transmitted in equal proportions. Furthermore Mendelian genes have fixed positions on the chromosome. One of the components of molecular drive, 'transposition', moves genes from one chromosome to the other ('jumping genes'). Conclusion: depending on how the theories are formulated, one should say either that orthodox-neo-Darwinism and orthodox-Mendelism are 'refuted' and replaced or that both neo-Darwinism and Mendelism are supplemented with additional mechanisms. Dover is clearly non-orthodox in the sense that he rejects the 'gene as the ultimate selfish unit of selection' view of Richard Dawkins, John Maynard Smith, Robert Trivers, William Hamilton, Edward O. Wilson and George C. Williams.

173 pairs of legs

The story of the centipede is one of Dover's most illuminating and intriguing examples. Some centipedes ('hundred-legged') have as much as 173 pairs of legs (a head segment, 173 body segments with 1 pair of legs, and two closing segments without legs), the species with the lowest number has 15 pairs of legs.

Did the centipede arrive at 173 pairs of legs solely by mutation and natural selection? Are 173 pairs of legs an adaptation to a special kind of environment? Are 15 pairs of legs an adaptation to another environment? Have 16 pairs (the first step towards 173!) higher survival value than 15 pairs? Even involving neutral drift requires that one (?) segment at a time spreads through an entire population by accidents of sampling in many generations until 173 pairs are established. Not a very likely possibility. Dover convincingly casts doubt on natural selection and neutral drift as the sole cause. This does not automatically prove his case for Molecular Drive as the correct

explanation. However Dover suggests that properties of *Hox* genes could explain the duplication of identical segments with identical legs.

700 copies of a gene

Mendelian inheritance started with the discovery of heritable variations of a single character. For example Mendel's garden peas with round versus wrinkled seeds. Later these characters turned out to be based upon a mutation in one gene. Eye colour is an example of a genetic variant in one gene. Soon after the introduction of genome sequencing it was discovered (to the surprise of geneticists!) that genes were present in many copies. In humans 700 copies of the ribosomal RNA gene were found (1). All copies are functional. The next surprise was that the copies were identical. This is really a non-Mendelian situation. In Mendelian genetics genes are present in just two copies. Imagine that genes for eye colour or hair colour were present in 700 copies! However this observation and many similar observations can now be found in the textbooks (2) and their *existence* is not doubted. That the copies are useful for producing large amounts of the gene products is not doubted either. What is controversial is the *explanation* of the fact that the copies are still identical. One would expect that different mutations accumulated in all those copies. But this is not observed. Dover rejects the standard explanation that natural selection ('*purifying selection*') is able to keep the 700 copies identical because mutated copies will be compensated for by many intact copies. They are below a threshold. He explains the observation by Molecular Drive: a collection of mechanisms that keeps copies of genes identical. The word Molecular Drive itself is not adopted in the textbooks (5), but the mechanisms behind it are. I still find homogenisation a mysterious mechanism.

Messy Design

The genome is complex, intertwined, ever changing, redundant, contaminated, in short: 'a mess, but it works'. Genomes are ten thousand or a hundred thousand times larger than necessary. ... For example humans have alpha-satellite DNA, that consists of several hundred thousand copies spread in tandem arrays all over our 23 pairs of chromosomes. ... Humans carry enough DNA in each cell nucleus to code for 3 million genes. In reality we need only about 70,000 genes.... Why are all genomes subject to such a bizarre variety of Non-Mendelian mechanisms? ('slippage', 'transposition', 'unequal crossing-over', 'gene conversion', 'homogenisation', 'concerted evolution', 'jumping genes', 'mobile elements'). It is clear that nobody is supervising the evolution of the genome. It is anarchy. It is really time to clean up the mess and enforce rules. Who designed this mess? Who's in charge around here? Is this mess 'the wisdom of the body'? (3). It's really irresponsible to let ignorant DNA molecules build highly complex multicellular conscious beings! Through Dover I realised that mutations not only produce piecemeal fine tuning of existent proteins and enzymes, but that mutations also produce and modify the bodyplan of organisms. That is a huge conceptual leap. A leap that could not be made as long Darwinists knew nothing about the genetic control of bodyplans. As if Darwinists secretly believed that the bodyplan, the basic layout of organisms, could not evolve step by step, but must have been created in one big step (by an intelligent designer!). Dover shows molecular mechanisms that could be responsible for mutations affecting the bodyplan. The new science of developmental genetics shows how the bodyplan is genetically controlled and how mutations produce modifications of the bodyplan. That is the knowledge Darwinists unknowingly (?) were waiting for.

All genes are interacting with one another. One gene can contribute to many different structures and functions, and any given structure is built by many different genes. I was amazed that Dover did not notice that this is a serious problem for evolution driven by random mutations. The critics of evolution would enthusiatically point out that it becomes very difficult to *improve* the whole intertwined mess by random mutations. For the impact of a mutation in a gene would not be restricted to the gene product itself but would influence many other gene products as well. The chance that a random mutation would be beneficial in all those gene products is small.

A marriage of 3

One cannot fail to notice after reading *Dear Mr Darwin*, that Dover is an expert on the molecular structure of the genome (8). However *Dear Mr Darwin* is as much about molecular genetics, as about evolutionary biology as about developmental biology. It is impossible to separate the disciplines here. They are closely intertwined. The *Hox* gene family is a good example: they are genes (*genetics*) and they build an organism (*development*), and modifications of *Hox* genes give rise to different organisms (*evolution*). People have speculated about this synthesis. Dover smoothly integrates evolution, genetics and development. I got the feeling that once we know how 'development' builds a differentiated multicellular organism out of one cell, we

will know how 'evolution' build the millions of organisms we observe now. Since development is controlled by genes, modifications of those genes could show us, what kind of organisms result from genetic modifications (6). Geno-Evo-Devo: that is the future of biology. An exciting future!

DNA fingerprinting

DNA fingerprinting is now one of forensic science's most reliable and potent weapons. I was amazed to find out that the fingerprinting technique is based on variation in the number of copies of a 20 base DNA sequence. The repeat number is so variable that everybody has a unique genetic fingerprint. This was discovered by Alec Jeffreys (7), just as Dover from the University of Leicester. The mechanisms responsible for this variability are unequal crossing-over and slippage. Slippage is the most frequently occurring mechanism of gain and loss of DNA in genomes. It is one of the mechanisms Dover included in 'Molecular Drive'. Thanks to Molecular Drive DNA-fingerprinting is possible.

Dear Mr Dover

Dover uses imaginary letters to Darwin, and replies (!) from Darwin, to convince Darwin of the existence of a third force in evolution. In this way Dover created a lively discussion. At the same time there is a perfect opportunity to teach Darwin the relevant parts of genetics. Although Darwin knew everything of evolution, he knew nothing of Mendelian genetics and molecular genetics. However Dover doesn't really seize the opportunity to explain basic concepts in genetics. The task to explain progress in genetics since Darwin's time is a huge task indeed. Genetics and history-of-genetics textbooks has been written to do just that. Darwin and the reader need to do a lot of homework (2) to catch up with Dover's exposition. So this book is for the advanced (professional?) reader or determined lay reader. However Dover has important things to tell. The book is not a mess like the genome, but it is certainly complex with a lot of intertwined parts. I read it twice from cover to cover. I found subjects like gene conversion and the population genetics aspects of gene conversion insufficiently explained. I wonder if field or lab data exist about the spread of gene conversions (in humans)? Could molecular drive spread mutations faster than traditional population genetics allows for? *Dear Mr Darwin* contains an indispensable glossary. And there are black and white *drawings* (because the book consists of a correspondence?). The science of genetics includes a lot of technicalities and abstract mechanisms. Color illustrations could help (4), but are absent. Dover chose to include all the technical terms. This is in contrast to the style of Enrico Coen in his *The Art of Genes*, who left out virtually all technical terms and almost exclusively works with metaphors. At face value the art of book publishing has not improved since Darwin's time... or is

"Dear Mr Darwin. Letters on the evolution of life and human nature"
by Gabriel Dover
University of California Press
2000, hardback
268 pages.
ISBN: 0-520-22790-5
Contents:

this to give *Dear Mr Darwin* a historical look?

Notes:

1. The genome is some kind of database of sequences. From the viewpoint of information storage in relational databases it is a crazy idea to store hundreds of copies of the same item. Only unique items are stored and duplications are prevented or eliminated, because duplicate items cause a maintenance problem.
2. Dan Grauer and Wen-Hsiung Li(2000) *Fundamentals of Molecular Evolution* have an extensive discussion of 'Concerted evolution' on p304-322, which is a good preparation for reading Dover.
3. According to Kevin Davies ('*Cracking the Genome*'), Francis Collins believes the human genome sequence is "the language of God" (see: From the Publisher at Barnesandnoble.com).
4. see for example the superbly illustrated *Exploring the Biomedical Revolution* of the Howard Hughes Medical Institute or the irresistible *Developmental Biology*, Sixth Edition published by Sinauer Associates.
5. The concept 'molecular drive' is not adopted by Grauer & Li(2000). However it is discussed by Jablonka and Lamb(1995) *Epigenetic Inheritance and Evolution*. Wallace Arthur(200) *The Origin of Animal Body Plans* has 5 references to Dover, but apparently does not see a great role for molecular drive in generating body plans.
6. Walter Gehring(1998) *Master Control Genes in Development and Evolution. The Homeobox Story*. (primarily about developmental genetics, secondary but inevitable about evolution).
7. Matt Ridley(2000) tells the DNA fingerprinting story in a more popular way in: *Genome*, p131-134.
8. Gabriel Dover started publishing in 1980 about "Modes of genome evolution" (with W. Ford Doolittle), Nature Vol 288, p.646. 18/25 Dec 1980

Links:

- Home page of Gabriel Dover. I was unable to find an email adddress of Gabriel Dover.
- Enrico Coen(1999) *The Art of Genes. How organisms make themselves* (my short review at amazon). This book is highly praised by Dover. It has high educational value. The emphasis is, contrary to Dover's book, on development and genetics, not on evolution. See also a review in *Nature* **398**, 302-303 (25 March 1999) by John Maynard Smith.
- E.J. Steele(2000) *'The Evidence for Lamarck'*, QUADRANT March 2000 No. 364 Vol XLIV Number 3 pages 47-56. This is an extremely useful and masterfully written summary of Steele's arguments for the general reader. "Conventional neo-Darwinian population genetics will not handle this one, nor will Gabriel Dover's molecular drive concepts."
- John Alcock reviews **Dear Mr Darwin**: *What Would Darwin Think?* in American Scientist January-February, 2001. (John Alcock is Professor of Biology at Arizona State University). Regrettably Professor Alcock did not evaluate the role of Molecular Drive in evolution, which is the main theme in Dover's book.
-  Letter from Jack Haas at the Feedback page.
- John Waller shows why Dover is wrong when stating: "Mendel's flash of inspiration was to deduce from this that the cells making up each individual pea plant contained **two copies** of each gene..." (p.11). See the review of Fabulous Science. Fact and Fiction in the history of scientific discovery (John Waller).
- Gabby Dover (1999) "Looping the evolutionary loop", *Nature* **399**, 217-218, 20 May 1999. This is a very dismissive and unfair review of John Maynard Smith & Eörs Szathmáry (1999) "The origins of life" (see: review on this site).
- Gabriel Dover (2001) "Anti-Dawkins" as chapter 4 in "Alas poor Darwin", Vintage.

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