GENETICS

The book of life

P Copland

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It has recently been suggested that the practice of bioethics in the area of biology and genetics has been hampered by the lack of an accurate and appropriate metaphor. Beginning with previous metaphors that have compared the genome with a static blueprint or "book of life", I develop a dynamic metaphor that is compatible with our present understanding of the role of genetics in biology. The resulting metaphor is not only an accurate representation of current biology but of particular use to bioethicists and non-biologists in general.

n his editorial, "The double helix 50 years on: models, metaphors, and reductionism", R E Ashcroft argues that there is an increasing divide between biologists' understanding of the role of genetics and that of non-biologists and bioethicists in particular.1 This division is identified as being partly a result of the symbolic power of the double helix and the simplicity of the metaphor of DNA as a metonym for life itself. Attempts to close this divide have been hindered in part by the lack of a suitable alternative metaphor. What is required is a metaphor for bioethicists and other nonbiologists to use that captures the salient points regarding what biologists now know about life and the process of development. In recent times the metaphor used most often has been that of the "book of life" written in the coded sequence of our DNA, a blueprint for every individual, the story of our lives there for all to read in our genome.² ³ Every individual's life thus becomes like the reading of a book that was written in its entirety at the time of their own conception. It is such a metaphor that underlies bioethicists' concerns about the genetic uniqueness and identity of future human clones whose lives may have already been lived.⁴ This metaphor is widely regarded to have outlived its usefulness in biology but has not been replaced outside of biology by a new metaphor that illuminates our current understanding of the processes of biology and specifically the role of genetics.5 The metaphor of life as a book seems to capture something useful and the metaphor itself considerably predates its association with DNA or even genetics. Any new metaphor must to a certain extent incorporate the previous metaphor and explain how our understanding has progressed. To this end I will attempt to update the book of life metaphor to fit with our current understanding of biology.

DNA, genes, and the genome can be effectively represented as a specific sequence of letters and in this respect are much like a book. The mistake was in thinking that the genome was itself the book of life. It is not. The genome is, however, indispensable and is, I suggest, better thought of as the dictionary to the language of life (or at least a very important part of it). Genes are usually thought of as continuous sequences of letters (ATCG—the four bases that make up DNA: adenosine, thymine, cytosine, and guanine) and as such would seem most similar to words. The process of gene expression then becomes like the writing of that word into the book of life. Genes are not expressed as though they are

being read directly from the genome in the order they are found there. If they were we would indeed be able to simply read the book of life as produced by the Human Genome Project. Biologists now suspect that it is the sequence of gene expression that is crucial and that to a great extent this has no connection with the ordering of genes within the genome. The book of life that defines the biological life of every individual organism is thus not already written in our genes but is written by the expression of those genes. How far then can we take the analogy of genes as words in the dictionary of the language of the book of life?

We should begin by noting that a universal gene concept is not going to be sufficient and that genes naturally fall into various groups according to their importance to the individual organism or life in general. Some genes-for example, are more or less crucial to life itself. Many of these necessary genes are often thought of as "housekeeping genes", which are required to produce the basic components of life, such as metabolic enzymes. Generally speaking these genes are found in all living organisms and often diverge modestly from species to species. These genes perhaps play the role that very common words such as "a", "and", and "the" play in language. They provide the underlying structure of the language or organism and provide the foundation for higher levels of complexity and meaning. It is difficult to say much at all without them: indeed, without them, the book (life) never gets off the ground. On the other hand some more specialised genes seem to be more like specific nouns. We can tell a good story even if we do not have certain nouns but there are some things that are very hard to say. This seems to be similar to genetic conditions where there is an individual (a book of life) who is affected by what we would call a genetic disorder. In very many cases the loss of specific genes seems to have very little effect on the individual at all and it would seem that in these cases other genes (words) are used in their place without noticeably altering the story that is told or the individual that is produced. The biological function of genes can thus be usefully compared to words and the expression of genes as the writing of those words into the book of life that is the organism.

Complicating this understanding of genes as words is the evidence that some genes act as transcription factors, whose function is to induce the expression of a range of other genes. It would seem that we might interpret the actions of these transcription factors with regards to our metaphor in two ways. Firstly, we could view them as similar to rules of composition or grammar that place limits on how words (genes) are used (expressed) or ordered. Rules of grammar are after all necessary in order to form meaningful sentences but do not limit what is meant by those sentences. Secondly, we may accept that these programmed sequences of gene expression constitute a programmed sequence of words, what we would perhaps call a sentence. It may be that a great deal of gene expression is controlled by such globally (genome wide) acting transcription factor genes and that many of the sentences and indeed paragraphs that are written into the book of life by gene expression are predetermined by these

transcription factors. This would perhaps explain why-for example, a human book of life always takes the form that it does and is different from a primate book of life even though both books may share up to 99.4% of their vocabularies (genes).6 Nevertheless, predetermined sentences and paragraphs only find their true meaning in the context of the greater work that is the book of life of an individual organism.

Some gene expression may be internally directed but biologists now realise that a great deal of gene expression is induced by interactions between cells and in response to the immediate physicochemical environment of the cell.^{7 8} Life is never static and the book of life is always being written. Like a book, life is a linear process that builds and develops as time passes. Indeed, if anything, it is the process of development that is the author of the book of life that is an individual organism. The book of life is effectively written by our lives, with past interactions influencing responses to future stimuli. What is written into the book of life thus finds its meaning in the context of the greater story. Many words derive much of their meaning from the social or narrative context in which they are used. Similarly biologists have begun to realise that the key to understanding how life works is to analyse both spatial and temporal patterns of gene expression.9 Studying individual genes is often as useful as studying individual words: we may learn a lot about them and know what they do or are for, but they only have meaning when they can be placed into the context of a process or sentence or paragraph. What the Human Genome Project seems to have given us then is the dictionary of human life. By comparing this dictionary with that of other species we may find the genes or words that are specific to humans or we may just find that it is not the genes or words themselves that make us human but the way they are used and the context they are in.10 Reading the dictionary is not a good way to try and understand a language and will tell us almost nothing about what has been written in that language, but without words there can be no language at all.

Different metaphors are useful and informative in different discourses. Reductionist metaphors and models have been particularly useful in science because they are naturally compatible with the reductionist methodology that has historically dominated the practice of science. The metaphor outlined above is a metaphor that is intended to be compatible with the practice of bioethics. This metaphor for example, usefully illuminates some bioethicists' intuitions that the genome is necessary to being human but not on its own sufficient to be a human individual. Similarly, the gradualist position in bioethics regarding becoming human finds a suitable foundation in placing the early embryo in a progressively developing narrative context.10

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Correspondence to: P Copland, Bioethics Research Centre, University of Otago, PO Box 913, Dunedin, New Zealand; paul_c@sanger.otago.ac.nz

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REFERENCES

- Ashcroft RE. The double helix 50 years on: models, metaphors, and reductionism. J Med Ethics 2003;29:63-4.
- 2 Kay L. Who wrote the book of life: a history of the genetic code. Stanford: tanford University Press, 2000.
- 3 **Keller E**. Refiguring life: metaphors of twentieth century biology. New York: Columbia University Press, 1995.
- 4 Gogarty B. What exactly is an exact copy? And why it matters when trying to
- ban human reproductive cloning in Australia. *J Med Ethics* 2003;**29**:84–9.

 5 **Moss L**. *What genes can't do*. Cambridge, MA: MIT Press, 2003.

 6 **Wildman D**, Uddin M, Liu G, *et al*. Implications of natural selection in shaping
- 99.4% non-synonymous DNA identity between humans and chimpanzees: enlarging génus Homo. PNAS 2003;100:7181-8.
- 7 Altman G, Horan R, Martin I, et al. Cell differentiation by mechanical stress. FASEB 2002:16:270-2.
- 8 **Bjorklund LM**, Sanchez-Pernaute R, Chung S, *et al.* From the cover: embryonic stem cells develop into functional dopaminergic neurons after transplantation in a Parkinson rat model. *PNAS* 2002;**99**:2344–9.
- 9 Phillips R, Ernst R, Brunk B, et al. The genetic program of hematopoietic stem cells. Science 2000;288:1635-40.
- 10 Copland P, Gillett G. The bioethical structure of a human being. J Appl Phil 2003;20:123-33.