Biology and Philosophy (2005) 20:401–407
DOI 10.1007/s10539-004-0191-5


# If the genome isn't a God-like ghost in the machine, then what is it?

M. BLUTE
*Department of Sociology, University of Toronto, 3359 Mississauga Road North, Mississauga, Toronto, Canada L5L 1C6 (e-mail: marion.blute@utoronto.ca)*

Received 20 August 2003; accepted in revised form 22 April 2004

**Key words:** Cellular brain, Cellular government, Function of the genome, Gene concepts, Genetic information, Molecular machines, Origin of eukaryotic cell, Selfish gene

**Abstract.** Implicit God-like and ghost-in-the-machine metaphors underlie much current thinking about genomes. Although many criticisms of such views exist, none have succeeded in substituting a different, widely accepted view. Viewing the genome with its protein packaging as a brain gets rid of Gods and ghosts while plausibly integrating machine and information-based views. While the 'wetware' of brains and genomes are very different, many fundamental principles of how they function are similar. Eukaryotic cells are compound entities in which case the nuclear genome might best be thought of more as a government than simply as a brain.

## Gods and ghosts

Some implicit metaphors tend to characterize thinking about genomes. Genomes tend to be thought of as God-like – that which existed from the beginning and for which all else exists. The 'for which all else exists' was most famously made explicit in Dawkins (1976) distinction between genes as replicators and the rest of the cell or organism as their vehicle. It is not uncommon for that to be mistakenly understood to imply 'that which existed from the beginning' although we know on biochemical grounds that is not the case. DNA is a complex molecule whose nucleotides (deoxyribonucleotides) are synthesized by reduction of those found in RNA (ribonucleotides). Experimental work on the origin of life tends to generate amino acids, the constituents of proteins, much more readily than nucleotides. These inconvenient facts are often skirted by assuming that DNA is the lineal descendant, current model or something of whatever the hypothesized first replicators were. Since 1953, when both the Watson–Crick model of DNA's structure and the Miller–Urey origin-of-life-experiments were published, progress in understanding the molecular biology of extant organisms has been immeasurably greater than that in understanding the early history of life (Shapiro 2003). Whatever may have been the case in the past, to the best of our knowledge currently, apart from cultural things, the only things capable of replication and evolution by natural selection are cells, things made of cells, and parasites of cells. Even shorn of the mistaken 'that which existed from the beginning' inference,

Dawkins formulation still leaves us with 'that for which all else exists,' the genome as the owner of the rest of the cell or organism which is its property.

Second, genomes tend to be thought of rather like 'ghosts in the machine' – all knowing, all powerful inner 'agents' of the cell or organism. After Ryle (1949) and Koestler (1967), although somewhat counter to the latter's intention, psychologists often characterize theories which explain behavior by explicit or implicit reference to an inner agent as ghost-in-the-machine theories. This view of DNA as the 'master' molecule is ubiquitous in all branches of genetics whatever the level (molecular, cell/organismic or populational) and whatever the process of interest (transmission, evolution, development or physiology) in this 'age of the genome.'

These sometimes explicit, sometimes implicit metaphors have been criticized of course. In what follows I take for granted the accuracy of most of these. There are multiple levels of selection. DNA is a small proportion by dry weight of what a cell or organism inherits; inheritance is at least as much epigenetic as genetic. Development is at least as much responsible for what evolves as evolution is for what develops. Organisms construct their environments at least as much as environments do organisms. At the same time however it is fair to suggest that none of the critics have succeeded in substituting a different, widely accepted view. If not owner and master, god and ghost, then what?

## Machines and information

Some molecular biologists are fond of viewing the cell as a collection of machines – replication, transcription and translation machines for example (e.g. Lodish et al. 2000). However, viewing other parts of the cell as machines while ignoring the genome leaves the god-like ghost intact. What kind of machine is the genome? Most biologists view DNA as containing encoded information. This view has been criticized in whole or in part (e.g. Sarkar 1996, 2000; Godfrey-Smith 2000a, b) but has also been ably defended in whole or in part (e.g. Maynard Smith 1998, 2000a, b; Godfrey-Smith 2000a, b). Rather than an unnecessary metaphor, it strikes one a straight-forward factual statement about the role of DNA in the life of the cell, distinguishing it from that of phospholipids in membranes in maintaining structural integrity or from that of many proteins in catalyzing chemical reactions for example. (The role of RNA is much more multifaceted – as the genome of RNA viruses and as mRNA in cells it can carry information, as ribozymes and the RNA component of ribosomes it can catalyze chemical reactions, and as miRNA it can control gene expression!). At the same time however, the 'information' view seems incomplete, too static, too passive, too much like Ryle's (1949) knowledge 'that' rather than knowledge 'how'. Particularly if we expand our view beyond DNA (which never comes naked, including in prokaryotes) to include the proteins it is complexed with, and perhaps even to the entire nucleoid in prokaryotes and the nucleus in eukaryotes, genomes are not simply texts.

Rather they, like other organelles, are molecular machines which play a dynamic role in the life of the cell. It seems obvious that their role is that of a brain. Cells have genomes not because the latter were there first or because they own the rest of the cell. Rather, they have them for the same reason that so many of our gadgets have chips these days and that vertebrates have brains. Replete as they are with 'if statements', genomes enable cells to flexibly vary and change their behavior according to conditions such that the latter are able to engage in activities orders of magnitude in complexity greater than would be possible without them. They are, as a first approximation, like brains, 'mind machines'.

## Brains and genomes

Obviously the 'wetware' of brains and genomes are very different but despite that, many fundamental principles of how they function are similar. Information is stored digitally in both cases. In brains, neurons either fire or they do not and packets of neurotransmitters are either released or they are not. In genomes, codons are discrete. The advantages of digital over analogue systems of storing and utilizing information are well known (Dawkins 1995: ch. 1). Both function hierarchically i.e. neurons fire or burst, causing others to do similarly, which cause others to do similarly – just as the transcription products of genes can control the expression of other genes which can control the expression of other genes. Both often involve not a one to one but a many to one and one to many process. In brains, many dendrites converge on a single neuron and the single axon of a neuron may branch influencing many other neurons – phenomena sometimes called convergence and divergence (Nicholls et al. 2001: 9). In genomes, many transcription factors can influence the expression of a single gene and the transcription products of a single gene can act as a transcription factor influencing the expression of many other genes – phenomena sometimes called signal integration and combinatorial control (Watson et al. 2003: ch. 17). Because of this, in both processes there are networks as well as hierarchies. Control can be both positive and negative in both cases (excitation and inhibition in brains, activation and repression in genomes). In both there are larger scale and longer term structures and modifications. Brains include long range circuits as well as local hierarchies and networks. In the nucleosomes of eukaryotes, the modification of histone tails, and on an even larger scale, nucleosome remodeling complexes, make whole regions of the genome more or less functional (Watson et al. 2003: ch. 18). Most fundamentally both neurons and genes with their associated 'packaging' (e.g. glial cells, various proteins including histones) perceive, calculate/think (as you will), and act. [For an overview of three studies revealing how regulatory sequences in genomes calculate cell fate by deciphering a combinatorial code see Ghazi and VijayRaghavan (2000).] Both brains and genomes function flexibly and neither is passive. Brains have endogenously active pacemakers

and coupled groups; from birth and even before, brains are active. Genomes too come poised to act, with maternally produced transcription factors and other influences ready to go.

The purpose of this discussion is conceptual rather than theoretical in the narrow sense. The argument has been that viewing the genome with its protein packaging as a brain gets rid of Gods and ghosts while plausibly integrating machine and information-based views. While some might wish to argue that it is not true on various grounds, the more common reaction is likely to be that it is not new, that we have known it all along. The fact is that, neural and not just information-based concepts have been in use for some time in describing cell interactions, which are widely viewed as communicative in nature. For example, receptors bind ligands, transferring signals across the plasma membrane. Inside the cell receptors pass signals on to other molecules, a process which often eventually ends with a change in the gene-expression program of the cell. Students of cell interactions are concerned with how the accuracy of information flow is maintained and with signal integration by 'crosstalk' (Downward 2001). Despite the fact that the purpose here is conceptual rather than theoretical, it is easy to envisage there being a theoretical payoff to being more explicit about genomes as brains.

Consider the 'gene' problem for example. It is well known that genetic units of structure, function, replication and recombination do not coincide with one another. Units of structure include base pairs, nucleosomes, 30-nm fibres, loops, and chromosomes. Units of function include codons, the traditional molecular 'gene' of a DNA sequence coding for a single strand of a protein molecule as well as many, many potential others e.g. with introns counted in or out, *cis* and even *trans* acting regulatory sequences in or out, sequences coding for other strands of the same protein in or out, sequences coding for other enzymes functioning in the same pathway in or out, and ultimately even whole hierarchies and networks serving some particular ecological, sexual or social function. Units of replication are replicons and chromosomes. Units of recombination can be sequences of a length 'short enough to be different and long enough to make a difference' as the popular version of Williams (1966) definition has it in crossing over, and are chromosomes in independent assortment. (While none of these lists correspond to any another, chromosomes appear often enough to make one suspect that they will turn out to be present in the only list where they are now absent, as a unit of function.) This lack of precise correspondence and consequent multiple 'gene' concepts has been the source of endless angst in the history of biology.

This would all be less perplexing were we to understand genomes as the brains of cells. There too there is a long history of discussion of the only partial correspondence between structure and function – the so-called 'localization' problem. In both cases, we have wonderful examples of a precise correlation – e.g. homeotic genes with their colinear correspondence between the order of the genes along the chromosome and their patterns of expression across the anterior–posterior axis in developing embryos in genomes and the ordered

representation of the body surface on the primary sensory cortex and on the primary motor cortex in brains. At the same time we also have lots of examples of the lack of such a precise correlation. The reason is the same for both – evolution. Both genomes and brains carry a 'burden' of history as Williams (1997) put it. As a consequence, natural selection builds little from scratch but instead 'tinkers' (Monad 1972; Gould 1980). Whatever the origin of introns, even if you could, why start from scratch when it is often so much more economical to gerrymander – paste together a bit of this from here and a bit of that from there. To be sure, it may be more precisely accurate to talk about 'DNA sequences and associated proteins for' rather than 'genes for' functions in most cases. However, cultural evolution, including in science, also has its own burden of history. As in any text, in scientific texts much of the meaning is context-dependent such that, in context, we do not normally have great difficulty in making sense of the many homonymous uses of the 'gene' concept.

## Governments of compound cells

It is unclear whether any cells are simple rather than compound. For example, Maynard Smith and Szathmary (1995) imagine that chromosomes arose from what were originally independently replicating molecules. Cells typically have multiple chromosomes. Surprisingly, this is true of prokaryotes as well as eukaryotes (Downie and Young 2001 and references). It was once thought the prokaryotic genome was a single circular molecule, sometimes accompanied by a few small episomes and/or plasmids. It now turns out that this was an artifact of the experimental focus on *Escherichia coli*. In many other prokaryotes, DNA molecules come in a graded series of sizes. Rather shockingly, this obtains in the absence of a mitotic apparatus to ensure a fair division. However, we may eventually find that some membrane-associated mechanism assures an equitable division on either side of the septum. Eukaryotes too have multiple chromosomes, but ones whose division is coordinated by a mitotic apparatus. However because of the role played by symbiosis in their evolution, they have multiple brains on another level – the genomes/nucleoids of those organelles of independent prokaryotic origin and subsequent proliferation (mitochondria in animals, mitochondria and chloroplasts in plants). The problem of coordinated division has been at least partially solved in multicellular animals and plants in a different way. Mitochondria are almost exclusively inherited through females.

However, compound cells have a problem of coordination, not just of division, but of all activity. The situation can be not unlike that of some primitive nervous systems with a series of ganglia, none of which have taken on a central coordinating role by evolving into a brain proper, and which can result in coordination problems. As the kinds of eukaryotic protists supposedly never having possessed mitochondria shrink to the vanishing point (Williams et al. 2002; Roger and Silberman 2002; Henze and Martin 2003; Tovar et al.

2003), it is becoming obvious that the latter were likely present from the beginning of the former. Is the eukaryotic cytoplasm then something that, in the first instance, colonies of proto-mitochondria built around themselves with their own secretions, not unlike the 'slime' of the gliding bacteria and slime molds? The difference would be that unlike the latter, mitochondria have reached the pinnacle of social evolution in having abandoned an independent phase in their life cycles and evolved an external membrane and mechanism of reproduction (if not exact replication) for the colony. If so, then the nuclear genome and associated mitotic apparatus in eukaryotes (karyomastigont in some protists, Chapman et al. 2000; Dolan et al. 2002), whatever their endogenous or exogenous origin, might best be thought of more as a government than simply as a brain. Like the governments of all federations, part of this government's power stems from having appropriated many of the functions of lower level actors (the transfer of much mitochondrial DNA to the nucleus).

## Conclusion

True to the naturalistic spirit, if not the letter of Dawkins (1976) world-view, I say up with brains and governments and down with Gods and ghosts.

## References

Chapman M.J., Dolan M.F. and Margulis L. 2000. 'Centrioles, kinetosomes: form, function, and evolution'. The Quarterly Review of Biology 75: 409–429.

Dawkins R. 1976. The Selfish Gene. Oxford University Press, Oxford.

Dawkins R. 1995. River Out of Eden: A Darwinian View of Life. HarperCollins Publishers, Inc., London.

Dolan M.F., Melnitsky H., Margulis L. and Kolnicki R. 2002. 'Motility proteins and the origin of the nucleus'. The Anatomical Record 268: 290–301.

Downie J.A. and Young P.W. 2001. 'The ABC of symbiosis'. Nature 412: 597–598.

Downward J. 2001. 'The ins and outs of signalling'. Nature 411: 759–762.

Ghazi A. and VijayRaghavan K. 2000. 'Control by combinatorial codes'. Nature 408: 419–420.

Godfrey-Smith P. 2000a. 'On the theoretical role of ''Genetic Coding'''. Philosophy of Science 67: 26–44.

Godfrey-Smith P. 2000b. 'Information, arbitrariness, and selection: comments on Maynard Smith'. Philosophy of Science 67: 202–207.

Gould S.J. 1980. The Panda's Thumb: More Reflections in Natural History. Norton, New York.

Henze K. and Martin W. 2003. 'Essence of mitochondria'. Nature 426: 127–128.

Koestler A. 1967. The Ghost in the Machine. Hutchinson, London.

Lodish H., Berk A., Zipursky S.L., Matsudaira P., Baltimore D. and Darnell J. 2000. Molecular Cell Biology. W.H. Freeman and Company, New York.

Maynard Smith J. 1998. Shaping Life: Genes, Embryos and Evolution. Weidenfeld & Nicolson, The Orion Publishing Group Ltd., London.

Maynard Smith J. 2000a. 'The concept of information in biology'. Philosophy of Science 67: 177–201.

Maynard Smith J. 2000b. 'Reply to commentaries'. Philosophy of Science 67: 214–218.

Maynard Smith J. and Szathmary E. 1995. The Major Transitions in Evolution. W.H. Freeman and Company Limited, Oxford.

Monad J. 1972. Chance and Necessity: An Essay on the Natural Philosophy of Modern Biology. Vintage, New York.

Nicholls J.G., Martin A.R., Wallace B.G. and Fuchs P.A. 2001. From Neuron to Brain. 4th edn. Sinauer Associates, Inc., Sunderland, MA.

Roger A.J. and Silberman J.D. 2002. 'Mitochondria in hiding'. Nature 418: 827–829.

Ryle G. 1949. The Concept of Mind. Hutchinson, London.

Sarkar S. 1996. 'Biological information: a skeptical look at some central dogmas of molecular biology'. In: Sarkar S. (ed.), The Philosophy and History of Molecular Biology: New Perspectives. Kluwer Academic Publishers, Dordrecht, pp. 187–231.

Sarkar S. 2000. 'Information in genetics and developmental biology: comments on Maynard Smith'. Philosophy of Science 67: 208–213.

Shapiro R. 2003. 'Review of life's origin: the beginnings of biological evolution'. The Quarterly Review of Biology 78: 360.

Tovar J., Leon-Avila G., Sanchez L.B., Sutak R., Tachezy J., van der Glezen M., Hernandez M.M. and Lucocq J.M. 2003. 'Mitochondrial remnant organelles of giardia function in iron–sulphur protein maturation'. Nature 426: 172–176.

Watson J.D., Baker T.A., Bell S.P., Gann A., Levine M. and Losick R. 2003. Molecular Biology of the Gene. 5th edn. Benjamin Cummings, San Francisco.

Williams B.A.P., Hirt R.P., Lucocq J.M. and Embley T.M. 2002. 'A mitochondrial remnant in the microsporidian *Trachipleistophora hominis*'. Nature 418: 865–869.

Williams G.C. 1966. Adaptation and Natural Selection. Princeton University Press, Princeton.

Williams G.C. 1997. The Pony Fish's Glow and Other Clues to Plan and Purpose in Nature. Basic Books, New York.