DNA is life's blueprint? No, master controller of the cell

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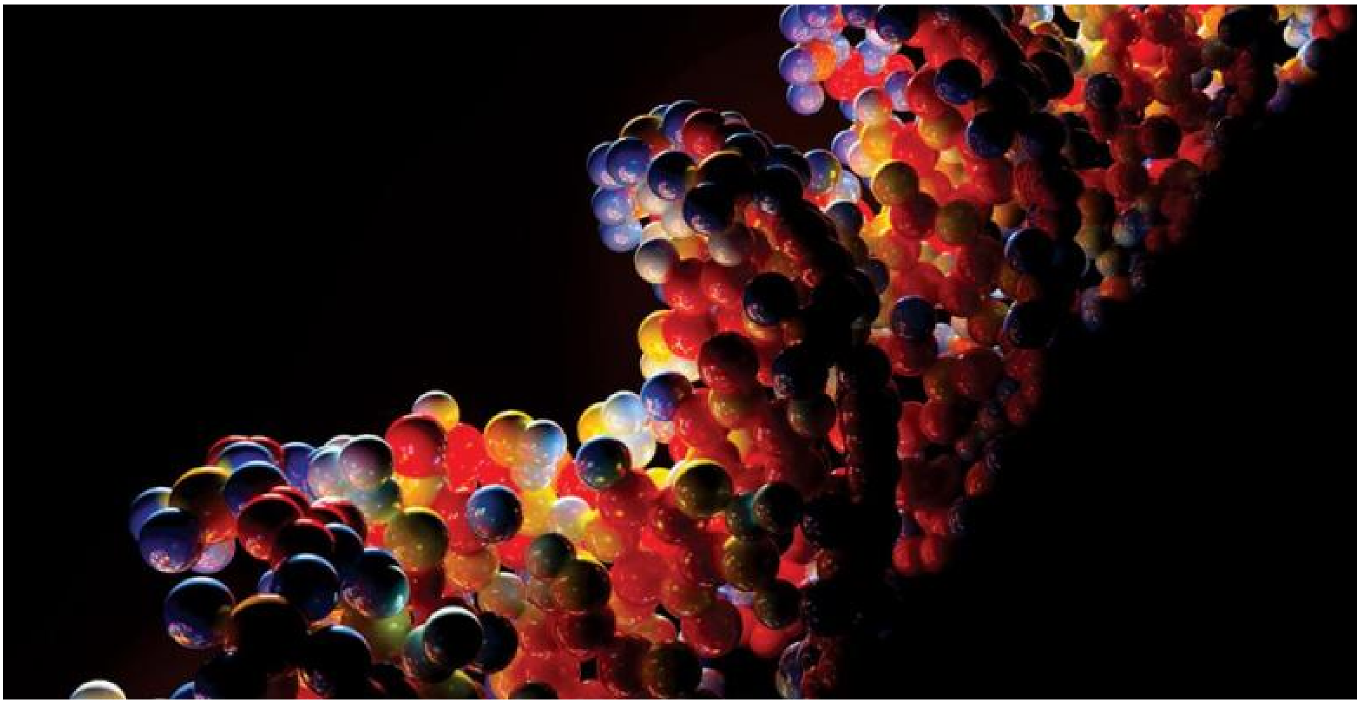

Now two new books about the genome show the limitation of that metaphor for something so intricate, complex, multilayered and dynamic. Both underscore the risks of taking metaphors too literally, not just in undermining popular understanding of science, but also in trammelling scientific enquiry. They are for anyone interested in how new discoveries and controversies will transform our understanding of biology and of ourselves.

John Parrington is an associate professor in molecular and cellular pharmacology at the University of Oxford. In *The Deeper Genome*, he provides an elegant, accessible account of the profound and unexpected complexities of the human genome, and shows how many ideas developed in the 20th century are being overturned.

Take DNA. It's no simple linear code, but an intricately wound, 3D structure that coils and uncoils as its genes are read and spliced in myriad ways. Forget genes as discrete, protein-coding "beads on a string": only a tiny fraction of the genome codes for proteins, and anyway, no one knows exactly what a gene is any more.

A key driver of this new view is ENCODE, the Encyclopedia of DNA Elements, which is an ambitious international project to identify the functional parts of the human genome. In 2012, it revealed not only that the protein-coding elements of DNA can overlap, but that the 98 per cent of the genome that used to be labelled inactive "junk" is nothing of the sort. Some of it regulates gene activity, some churns out an array of different kinds of RNA molecules (RNAs for short), some tiny, some large, many of whose functions are hotly debated. Parrington quotes ENCODE scientist Ewan Birney as saying at the time, "It's a jungle in there. It's full of things doing stuff." And that is one of the most apt genome metaphors I've ever read.

Recent insights into what some of this "stuff" is reveal problems with another classic idea: that DNA is the master controller of the cell, with information flowing in one direction from it, via RNA, to proteins. Some of ENCODE's mystery RNAs control gene activity, others make changes that the cell remembers and passes on when it divides, and which can even be passed down generations. The RNAs may be one way the environment alters the behaviour of genes without changing their DNA sequences, a phenomenon known as epigenetics.

Growing evidence of the extent of epigenetic influence on the genome has led some researchers to argue that much of medical research, and indeed mainstream evolutionary theory, places too much importance on genes in determining an organism's characteristics. They think the environment plays a much bigger role in their emergence as an organism develops.

This developmental view of the genome is a key theme in *The Developing Genome* by David Moore. He is a professor of psychology at Pitzer College, Claremont, California, with an interest in cognition in infants, and behavioural epigenetics – the study of how epigenetics shapes individual cognition, behaviour and mental health. This includes the famous studies by researchers Michael Meaney and Moshe Szyf, which showed that baby rats that are licked and groomed by their mothers grow up to be less sensitive to stress, and that this correlates with changes to the pup's neurobiology and the epigenetic alterations associated with certain genes.

Behavioural epigenetics is a controversial field, with critics arguing that many of its findings are little more than correlation and conjecture. Moore is suitably sceptical without shying away from the more contentious areas, such as research suggesting that being abused as a child can cause long-term epigenetic changes in the brain. Some researchers speculate that this could be a mechanism by which the cycle of violence transmits down generations.

But just as genes are not destiny, neither is epigenetics. Like Parrington, Moore warns against oversimplification. Epigenetic determinism is just as unhelpful as the deterministic gene-as-blueprint idea. "Do not assume you are trapped by your biology," he says.

That genetics is complicated isn't news, but Parrington and Moore underline the limitations and the power of trying to understand its complexity by reducing it to simpler divisions. For example, the molecular and computing technologies spawned by such attempts are now giving researchers the potential to work out how to integrate it all to form a greater whole. Time, surely, to rip up the old metaphors and create some new ones.

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