

indifferent as he zips through the ways that we are altering the climate and the planet's ecosystems. A little more passion would have been welcome. After all, these days the evolutionary blackbird is beginning to look more like a canary in a coal mine. ■

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## Metabolic gardening

### **Wandering in the Gardens of the Mind: Peter Mitchell and the Making of Glynn**

by John Prebble and Bruce Weber  
*Oxford University Press: 2003. 344 pp.*  
\$65, £45.50

**E. C. Slater**

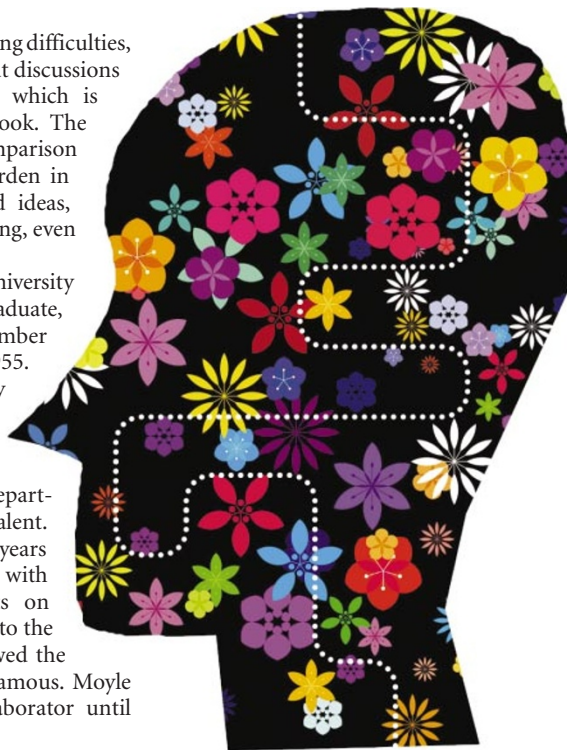
Peter Mitchell was an outstanding theoretical biologist who had what Leslie Orgel has characterized as a counterintuitive idea that led to a fundamental shift in the way that biochemists viewed energy metabolism. The story of the gradual replacement of the chemical hypothesis of energy transduction, which involved a non-phosphorylated high-energy intermediate (not a phosphate compound, as stated in this book), with the chemiosmotic theory has become, for historians of science, a classic example of how a paradigm shift occurs.

In this biography, the story is related again, primarily from Mitchell's viewpoint.

Because of ill-health and hearing difficulties, Mitchell preferred to carry out discussions by lengthy correspondence, which is extensively quoted in this book. The title refers to Mitchell's comparison of the human mind to a garden in which are planted facts and ideas, which one keeps on rearranging, even when asleep.

Mitchell worked in the University of Cambridge as an undergraduate, research student and staff member for 16 years from 1939 to 1955. He did not have a particularly distinguished academic record, nor does he seem to have been completely at home in the biochemistry department, despite its wealth of talent. However, in his last few years there he published, together with Jennifer Moyle, experiments on the transport of phosphate into the bacterial cell that foreshadowed the work for which he became famous. Moyle remained his scientific collaborator until her retirement in 1983.

There are some errors in the description of the Cambridge environment concerning the Molteno Institute of Parasitology and Biology, headed by David Keilin, where Mitchell is described as having found "shelter" (possibly in late 1945 to early 1946). E. F. Hartree was not a member of the technical staff, as stated in this book, but a PhD from the University of London and co-author of most of Keilin's classic papers for over 20 years. I am described as an "occasional post-doctoral researcher" in the institute, which



is surprising, considering that I worked there from late 1946 to 1955, during which time I published the chemical hypothesis of oxidative phosphorylation in *Nature* in 1953. It is the overthrow of this hypothesis by Mitchell that is a major theme of this book.

In 1955, Mitchell moved to the University of Edinburgh, where he developed the first version of the chemiosmotic theory, which was published in *Nature* in 1961. Illness soon caused him to move to Cornwall, where he converted a derelict manor house called Glynn House into a private laboratory as "a quiet haven for untrammelled scientific work and thought", as he wrote to me in 1964. The story of Glynn is the second strand in this biography. In 1966, Mitchell published, in what became known as 'The Grey Book', a modified version of the chemiosmotic theory in which he introduced the concept of proton motive force and 'loops' in the electron-transfer chain.

It took about ten years for the chemiosmotic theory to be generally accepted, and in 1978 Mitchell received the Nobel Prize in Chemistry. Mitchell was so confident that oxidative phosphorylation was solved that in 1976 he resolved to cease biochemical research and move into a new field, perhaps economics. The following year the decision was reversed when he considered that his theory was again under attack. It is worth noting that when the chemiosmotic theory became the new paradigm, Mitchell was just as resistant to attacks on parts of the theory as the supporters of the old paradigm had been.

The first assault came from Mårten

## History in the making

It was one of the most momentous moments in the history of science, but even those people involved didn't know for sure just what its impact would be. *50 Years of DNA*, published by Palgrave Macmillan this month, tells the story of how the structure of DNA was discovered, and describes its subsequent impact on science, medicine and culture.

The book includes facsimiles of the landmark paper by James Watson and Francis Crick (pictured far left), along with those by Maurice Wilkins and Rosalind Franklin (pictured centre) and their colleagues that first appeared in *Nature* on 25 April 1953.

Introductory chapters take the reader on a journey from the early days of molecular biology through to the sequencing of the human genome, incorporating interviews with some of the key players. The book concludes with a collection of essays by prominent experts giving



their views on the history and significance of Watson and Crick's discovery, along with their predictions of what genetics might achieve in the next 50 years. Edited by Julie Clayton and Carina Dennis, both former editors at *Nature*, the book celebrates the triumph of the DNA double helix.

Wikström's experiments showing proton pumping by cytochrome oxidase, published early in 1977. But it was not until 1985 that Mitchell was prepared to accept the evidence presented by Wikström and others, and then only when he had thought up a mechanism (since shown to be incorrect) to accommodate it. In Mitchell's garden of the mind, ideas seem to have deeper roots than facts.

The second attack concerned the chemical mechanism of ATP synthesis. Mitchell's postulate (from which he never wavered) that protons are directly involved in the esterification of ADP by phosphate was challenged by Paul Boyer, Harvey Penefsky and my group, who believed that ATP synthesis is brought about by a conformational change in the ATPase such that ATP, already formed spontaneously on the enzyme, is released. This view led to the Nobel Prize in 1997 for Boyer and John Walker.

Have we reached the end of the story? Not quite. The postulate of a non-phosphorylated high-energy intermediate in the chemical hypothesis is correct; its nature is not. The postulate of the chemiosmotic hypothesis that this intermediate is an electrochemical proton gradient is correct; the way in which it was thought to synthesize ATP is not. The binding-change mechanism of ATP synthesis proposed by Boyer is probably correct; but will the rotary mechanism depicted in the textbooks survive challenges?

I recommend this biography as a scholarly account of the life of one of the giants of late-twentieth-century biochemistry who was also a fascinating, if enigmatic, human being. His amiable character, his eccentricities and his health and emotional problems are fully described. But I still do not think that I really understand the workings of his mind.

Like Tom Blundell, writing in the foreword to this book, I find it quite extraordinary that Mitchell refused to permit Bob Williams to publish their correspondence from before the publication of Mitchell's first paper on the chemiosmotic theory, concerning the possible role of protons in ATP synthesis. The reason given for Mitchell's 1977 reversal of the decision to cease biochemical research — namely that he believed “there was a strong movement among the antagonists of the general chemiosmotic theory... to take advantage of our withdrawal and press new, ill-founded research claims, the effect of which was to undermine the consensus of opinion which we had been working on to promote” — I find even more extraordinary.

But perhaps it is not possible for a mere biochemist to analyse the mind of a genius. ■  
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## Science in culture

# Art after DNA

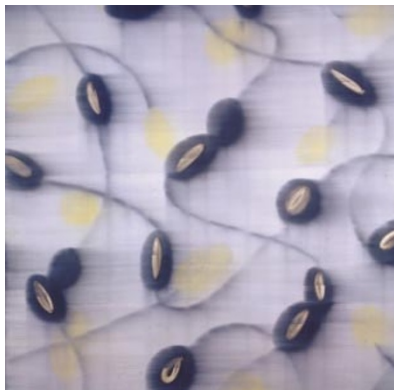
The double helix has inspired scientists and artists alike.

Lynn Gamwell

No sooner had James Watson and Francis Crick published their seminal paper on DNA in 1953 than artists began depicting the double helix as a cultural icon. Salvador Dalí painted swarms of spiralling DNA molecules in his paintings from the late 1950s, such as *Butterfly Landscape (The Great Masturbator in a Surrealist Landscape with DNA)*, 1957–58), and decades later sculptor Tom Otterness forged a bronze double helix joined by tiny stick figures (*DNA Chain*, 1986). Some artists responded to some of the troubling issues surrounding DNA, such as cloning and stem-cell research. Alexis Rockman, for example, painted a colourful landscape populated with genetically modified plants and animals to warn viewers that the future may contain mutated monsters (*The Farm*, 2000).

Although art about science icons and applied science is interesting, it does not focus on the pure science of DNA. That topic is addressed by artists who express wonder at the highly complex, ever-changing organic processes that are the physical mechanism for the force of life. One example is the British painter Mark Francis, whose *Source* (1992) is a wall-size depiction of sperm cells presented not with clinical accuracy but out of focus, as if seen through a veil. Inspired by microscopy, Francis uses a vocabulary of curved, flat shapes that he inherited from nineteenth-century art nouveau designers — who, in turn, first copied the shapes from stained, transparent slices of tissue prepared between glass plates for viewing with a light microscope. Francis uses a modern electron microscope for his source images, but his forms retain the flat, free-form appearance associated with a century of biomorphic abstract art. In a nod to recent methods of charting complex genomic data, Francis paints the sperm cells hovering above a grid.

In the 50 years since Watson and Crick cracked the structure of DNA, biologists and bioinformaticists, have painstakingly mapped and sequenced the genomes of various species: the fruitfly, the mouse



Sex cells: the view of sperm in *Source* by Mark Francis was inspired largely by microscopy.



Genetic screen: Benjamin Fry's *Valence* uses the BLAST algorithm to create moving patterns.



*DNA 2* by Susan Rankaitis is both a stand-alone artwork and a backdrop to the dance of life.

and, in 2001, the human. The computing technology developed for this effort inspired a new generation of video artists, such as Benjamin Fry, a programmer at the Massachusetts Institute of Technology's Media Laboratory, to create visualizations of complex biological data. In *Valence* (2000), Fry has used the BLAST algorithm — a tool for searching through genomes — to produce ever-changing patterns that move rhythmically across a video screen.

The curved free-standing panel *DNA 2*, which measures over 5 metres across, is the result of a collaboration between visual artist Susan Rankaitis, molecular biologist Robert Sinsheimer and choreographer John Pennington. Inspired by the Human Genome Project and tutored by Sinsheimer, Rankaitis combined pictures of DNA with text by the biologist to create her chromosome-shaped collage. It can be viewed alone or used as a backdrop for Pennington, who, attired in coils of pulsing fibre-optic cable, spins across a stage. By projecting flickering light onto her giant chromosome, Rankaitis makes her layered images and text join the dance of life.

Charles Darwin was confident that there was a physical mechanism underlying natural selection, but never found it. Today's artists understand the central role of DNA in this mechanism. It inspires them by embodying Darwin's core idea: that nature is a web of dynamic forces with no predetermined purpose or meaning. Works by artists such as Francis, Fry and Rankaitis resonate with this concept of life, and with the complex, abstract processes that go on silently, systematically and invisibly within the double helix. Lynn Gamwell is director of the Art Museum at the State University of New York, and author of *Exploring the Invisible: Art, Science and the Spiritual* (Princeton University Press, 2002).