BOOKS & ARTS

Defining moments

What are the major principles that controlled the origin of life?

Singularities: Landmarks on the Pathways of Life
by Christian de Duve
Cambridge University Press: 2006. 274 pp.
£30, $48

David Penny

Christian de Duve seeks to understand the mechanisms underlying the major changes that occur during the origin and history of living systems — the singularities. These include the origin of the protometabolism, membranes, protein, DNA and the prokaryote–eukaryote divide. He wants to know whether such transitions are necessary, almost inevitable, or very unlikely (even though they happened anyway). Are there alternatives that were essentially as good, or potentially better? Were the choices externally or internally imposed? And so on.

Singularities — the latest book to be tagged as de Duve's last — is in the tradition of *The Major Transitions in Evolution* by John Maynard Smith and Eörs Szathmáry (W. H. Freeman, 1995), which covered the aforementioned transitions but focused more on later stages, such as meiosis, multicellularity and language. Most of de Duve's book, in contrast, centres on the origin and nature of life, although he does go on a thoughtful scamper from the last universal common ancestor, the origin of eukaryotes, and multicellularity, before reaching the arrival of humans. Most of the book, then, is the great quest for the origin of life, next to which Frodo and Sam's journey into Mordor to destroy the Ring pales into a simple tourist trip.

De Duve poses a very important question: what are the fundamental issues that have to be 'solved' to get life as we know it? In evolutionary biology over the past few decades, we have mainly heard the 'contingency' message, which emphasizes the stochastic nature of evolution and focuses on the details. As we have heard countless times, if we rerun the tape of life again we will get something a bit different, and so on. Certainly, we are unlikely to get a horse-like creature with serine at position 23 of a β-haemoglobin, and a human-like animal with alanine at the equivalent position. But focusing only on contingency misses the more fundamental questions of major principles to which life might be conforming, and whether some general outcomes are predictable. This is the approach taken by de Duve.


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Tougher than Mordor — the quest to understand the large changes that led to the development of life.

As an example, consider Jeremy Knowles' view that an enzyme has catalytic perfection if it is limited by the rate of diffusion of a small substrate molecule onto the enzyme; no change to the properties of the enzyme can speed up the rate of the reaction. Because archaea, bacteria and eukaryotes can each have an equivalent enzyme that is 'perfect', but with very different protein sequences, there must be millions of different sequences that will carry out the reaction at the maximal speed. Now isn't this a much more fundamental and interesting conclusion than just that the sequences differ?

We can either concentrate on the principles, or we can focus on the details. Yes, the details will differ if the tape of life is rerun, but will we get the same basic metabolism and energy sources? Would we start again with RNA? Will we get proteins as the primary catalysts? Will there be a mix of primary producers, herbivores, carnivores and saprophytes, as well as small bacterial-like cells and larger-celled predators? Why do we not have endothermic plants? These are the big, interesting questions. De Duve focuses on these principles, refusing to be sidetracked by contingencies.

The view that de Duve argues is far more darwinian than many have used over the past few decades. Charles Darwin learned from the early statistical interpretations of Adolphe Quetelet that we could make firm predictions about random events if we had really large numbers. Even a rare event will be effectively certain to occur if there are millions of trials over millions of years. From this, you might gather that I like de Duve's contemplative approach. Yes, contingency and the stochastic nature of evolution are very important, but there is much more besides.

De Duve's general approach is fine, then, but how about the specifics? He favours a weak version of the RNA world in which most RNA catalysts are relatively short and are assisted by short (non-coded) peptides combined with other compounds that he calls multimers. It is unfortunate that we don't expect to find much evidence for such relics in modern metabolism — in contrast to cofactors (such as NADH and FAD), which are generally interpreted as relics of catalytic RNA from the RNA world. If there were such multimers, the amino-acid parts at least could be incorporated directly into the protein backbone of modern proteins, and therefore not be recognized as relics.

What are the next experiments? Are the chemical reactions that support life easier or harder at a pressure of hundreds or thousands of atmospheres? Are dilute or high concentrations advantageous? All life now occurs at high concentrations, restricted by membranes.

The biologists' top-down approach is making good progress in simplifying living systems to their basics. However, chemists seem to be having a harder time with their bottom-up approach.

The mathematics of Elchanan Mossel and Mike Steel argue that autocatalytic cycles, given relatively simple assumptions, are expected to occur in simple non-living systems. Experiments with *in vitro* RNA evolution are able to test many trillions of sequences simultaneously. Could chemists carry out trillions of reactions simultaneously? Perhaps the new approach of evolving proteins in oil droplets (*Nature* **440,** 156–157; 2006) could be adapted?

Most of us, most of the time, are solving simpler problems in biology. But we should always be alert to the great problems, such as understanding the processes leading to the origin of life. Given past experience, such great questions will be solved — not by chance but by the prepared mind. This book is a start to preparing that mind. ■

David Penny is at the Allan Wilson Center for Molecular Ecology and Evolution, Massey University, PO Box 11-222, Palmerston North, New Zealand.

Secret giants

Colossus: The Secrets of Bletchley Park's Codebreaking Computers
edited by B. Jack Copeland
Oxford University Press: 2006. 462 pp. £18.99

Jon Agar

"I find it hard to remember in any detail, after keeping the secret for so long — I tried to blot out of my mind everything that happened at BP, for fear that I might talk in my sleep or under an anaesthetic," recalled Catherine Caughey, an operator of the Colossus, the wartime electronic cryptanalysis machine. The intense secrecy around Britain's codebreaking operations of the Second World War was only partially lifted in 1975. Brian Randell, investigating the gap in the life story of Alan Turing between the breathtaking response to Hilbert's decidability question in the 1930s and the construction of the first electronic stored-program computers in the late 1940s, was allowed to see a clutch of Colossus photographs. For another decade those grainy images, accompanied by terse texts, were the only historical trace of one of the most remarkable machines of the twentieth century.

Only in the 1990s did details emerge. Requests filed under the US Freedom of Information Act prised technical details, compiled by visiting liaison officers, from the American archives. Meanwhile, in Britain, veterans of Bletchley Park finally felt able to speak openly. No longer would they fear, like Caughey, that a trip to the dentist might result in a charge under the Official Secrets Act. Copeland's valuable collection brings together both technical commentary and personal narratives in an engaging book that will be essential reading for historians of twentieth-century technology and warfare. However, it is also clear that the secrecy of codebreaking did not merely conceal history, but shape it.

The Nazi state used many encryption machines. The Enigma, a cipher machine sold commercially in the 1930s, is now the most famous, a fame shared by Turing, the man most associated with cracking it. But the higher echelons of Nazi Germany used a more sophisticated machine, the Lorenz SZ40, which was faster, entirely automatic (using Baudot–Murray teleprinter codes), and presumed invulnerable to attack. Eavesdropping stations across Britain recorded radio signals encrypted by the Lorenz SZ40. This stream of data, nicknamed Tunny, was channelled to Bletchley Park. Cracking Tunny was critical to allied success on D-Day: by reading decrypts it was known that Hitler expected only a feint at the Normandy beaches, while the delayed counterattack commands from the Führer to his generals could be read that day in London.

Bletchley Park struggled with Tunny. Two mathematical breakthroughs, by John Tiltman and William Tutte, gave the slenderest of wedges into decryption. But the essence of the problem was speed: only the freshest intelligence would save the most men and matériel. A creaking electromechanical machine, the Heath Robinson, helped in 1943. Fortunately, Tommy Flowers, a skilled Post Office engineer, was shown the problem. His proposal, a fully electronic cryptanalytical machine, met with scepticism even from senior codebreakers. But Flowers, with his team at the Post Office research station at Dollis Hill in North London, built it anyway. Flowers triumphantly presented the Colossus to Bletchley Park in January 1944 (not, as had previously been recorded, in December 1943).

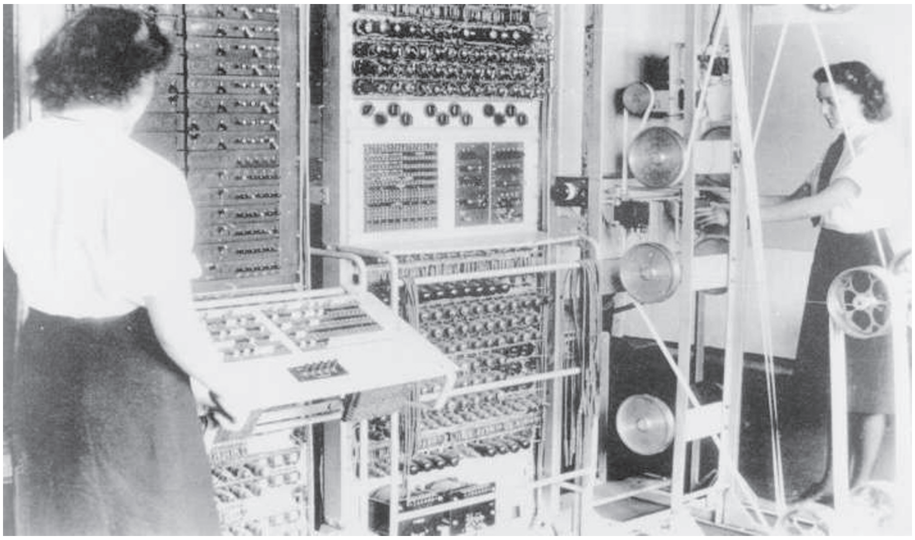
"I don't think they really understood what I was saying — I am sure they didn't," Flowers recalled, "because when the first machine was constructed and working, they were taken aback. They just couldn't believe it! … I don't think they understood very clearly what I was proposing until they actually had the machine."

On 5 February 1944, Copeland writes, the "computer attacked its first message". Flowers wrote of the epochal event in his diary: "Colossus did its first job. Car broke down on way home".

But later he grew bitter: "When, after the war ended, I was told that the secret of Colossus was to be kept indefinitely, I was naturally disappointed. I was in no doubt, once it was a proven success, that Colossus was a historic breakthrough, and that publication would have made my name in scientific and engineering circles — a conviction confirmed by the reception accorded to ENIAC … I had to endure all the acclaim given to that enterprise without being able to disclose that I had anticipated it."

The team that worked on ENIAC, a high-speed electronic calculator in operation by 1945, conceived of stored programs. Neither ENIAC nor the Colossus was a computer, and it warps history to label them thus. But the key concept of the computer was publicized within months of the war's end. The British and US scientists who built the first electronic stored-program computers benefited from this openness. The Colossi, in contrast, were broken up, apart from two which ended up at the UK government's GCHQ listening centre at Cheltenham, and, for all intents and purposes, never appeared in the public world. Only one of these countries has sustained a thriving computer industry. ■

Jon Agar is in the Department of History and Philosophy of Science, University of Cambridge, Cambridge CB2 3RH, UK.



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Cracking invention: the code-breaking Colossus helped Allied commanders intercept Hitler's messages.