

BOOKS & ARTS

Biological programming

The digital nature of molecules such as DNA means they can be used in computers.

Genesis Machines: The New Science of Biocomputing

by Martyn Amos

Atlantic Books: 2006. 320 pp. £18.99

Christoph Adami

When visiting the Santa Fe Institute in autumn 1994, I was chatting with Chris Langton when Stuart Kauffman came running down the hall waving a manuscript and shouting unprintables. When we cornered him, he was slapping his forehead mumbling: "I could have done this, if I had only thought of it!" It turns out that 'this' was the first example of a DNA-based computation, carried out by Leonard Adleman of the University of Southern California, launching the field of DNA computation (*Science* **266**, 1021–1024; 1994). Martyn Amos's book *Genesis Machines* looks back on the 12 years since this event, and speculates about the future of the increasingly intertwined fields of biology and computer science.

The computational feat reported in Adleman's seminal article was innocuous enough: examine a graph of seven nodes, and determine whether a one-way path exists that connects all the nodes once and only once (an example of the hamiltonian path problem). But the importance of this work did not lie in the sophistication of the problem, but in the fact that it showed that strands of DNA, mixed together in a vial, could be controlled such that their biochemistry could be viewed as a computation. And this is perhaps the central message that Amos tries to convey in his book: all physical systems can be viewed as performing computations; it is down to the skill of the investigator to make them perform useful ones.

Since 1994, DNA computation has advanced considerably, and programmable computers have been developed using DNA molecules only and with no moving parts. But for the reader to appreciate the story of how vials of DNA molecules could be coaxed to do something nature never intended, Amos has to reach far beyond the basic biochemistry of DNA, to the origins of computer science and complexity theory. Indeed, DNA computation was not the brainchild of biologists, but computer scientists who became fascinated by the 'digital' nature of DNA and its role in information processing. The roots go back to luminaries such as John von Neumann and Alan Turing, and Amos goes to considerable lengths to expose these foundations.



Programmable computers have been developed that use DNA.

Perhaps one of the weaknesses of this book is a result of the unavoidable interdisciplinary nature of its subject. For the lay reader for whom this book is written, the concepts of Turing universality, the complexity of 'P versus NP', and the biochemistry of DNA are likely to be difficult subjects, and Amos's introductions include biographical sketches of their main protagonists. As a result, more than 100 pages go by before Adleman's pioneering experiment can be described in detail, and even then it is interrupted by a narrative of the trials, tribulations and ultimately triumph of Kary Mullis and his discovery of the polymerase chain reaction.

Nevertheless, the central discoveries in this rapidly evolving field are covered, and the inevitable critics of this endeavour are not overlooked. Amos does a good job of injecting

some sobriety into the narrative, lest the reader believes that home computers running on DNA are just around the corner. Indeed, he points out right from the beginning that DNA computation is unlikely to replace its silicon-based forerunner, but rather be confined to special problems. What these will be is not at all clear, because the initial excitement about DNA's ability to tackle problems in the most difficult category, such as factoring a number into its prime components, quickly waned when it became clear that thousands of litres of DNA would be necessary to solve problems that are now just beyond the reach of conventional computers. But Amos insists that DNA computation is interesting in its own right because of the lessons it teaches us about computation in biology. The last two chapters are therefore devoted to endeavours only indirectly related to the quest for a DNA-based computer, namely DNA self-assembly and synthetic biology.

As Amos explains, the stability of DNA and its digital nature can be used to create — or should we say program — structures on a nanometre scale, a feat that is exceedingly difficult to achieve using non-biological material.

Inspired by the pioneering work of crystallographer Ned Seeman at New York University, Erik Winfree and Paul Rothemund of the California Institute of Technology set out to show that DNA can be programmed to fold into arbitrary structures whose intricacy can only be revealed by atomic force microscopy.

Synthetic biology, on the other hand, concerns the creation of biological systems from scratch or from components that had other functions. Behind it lies the concept that we do not need to understand every single detail of a complex system in order to be satisfied with what we know. After all, very few people understand down to the level of the electronics the workings of my laptop computer. But this does not worry me because I know that someone knows how to make it, so there is sufficient knowledge to create another one just

like it. The same can be said for biomolecular systems: we may never be able to comprehend every molecular interaction within a cell, but if we can build a system that behaves just like its natural counterpart, then perhaps we should be satisfied with that.

Amos's account of the different paths to synthetic biology covers most of the recent advances that have made the headlines. These range from pieces of DNA called 'biobricks' and the 'repressilator' to a way of coaxing yeast to produce the precursor for a malaria drug — a feat for which Jay Keasling, a biochemical engineer at the University of California, Berkeley, won *Discover* magazine's first 'scientist of the year' award.

But I have to take Amos to task for presenting the work of James Shapiro, a microbiologist at the University of Chicago, as if his investigations of the mechanisms of evolution somehow contradict darwinian evolution. Shapiro, who

studies the many ways in which organisms can actively restructure their genetic material, believes that such processes should be more widely incorporated into evolutionary thinking. Although Darwin could not possibly have anticipated such processes, they follow the general darwinian paradigm and do not, in my opinion, necessitate a 'third way' somewhere between creationism and what Shapiro calls 'neo-darwinian orthodoxy'.

But apart from this quibble, this is an enjoyable book that could perhaps have profited from more illustrations to convey some of the computational and experimental methods. I recommend it to anyone interested in computation writ large who is not afraid to cross disciplinary boundaries that once seemed impassable. ■

Christoph Adami is at the Keck Graduate Institute of Applied Life Sciences, Claremont, California 91711, USA.

Mammals on the move

The Beginning of the Age of Mammals by Kenneth D. Rose

Johns Hopkins University Press: 2006.
428 pp. \$150

Zofia Kielan-Jaworowska

Just looking at *The Beginning of the Age of Mammals* by Kenneth Rose, with its Henri Rousseau-style jacket picture, catapults the reader right into enchanted Early Eocene life. The book is a scholarly treatment of an important period in the evolution of mammals. Mammals originated some 225 million years ago, and for about 160 million years they were small nocturnal creatures living in the shadow of the dinosaurs. Most of them would have been size of a shrew or rat, with only a few being as big as a fox. When the dinosaurs died out at the end of the Cretaceous, 65 million years ago, mammals changed lifestyle and started to increase their size, with many entering niches abandoned by the extinct giants. This was the age of mammals.

Kenneth Rose's book *The Beginning of the Age of Mammals* is devoted to this explosion of mammals, particularly their evolution during the first half of the Cenozoic period. Rose highlights in particular the development of placental mammals in the Palaeocene and Eocene (between 65 million and 33 million years ago).

One of the charms of this book is the abundance of figures, with many attractive reconstructions of Eocene mammals. Some of these have been made possible by the unusual preservation of complete mammalian skeletons from the Middle Eocene in Messel, Germany. Rose had an opportunity to collaborate with German colleagues when describing some of these mammals. As well as line drawings and

black-and-white photographs, there are eight full-page colour plates with photographs of the best-preserved fossils and reconstructions.

Although the bulk of the book is devoted to this mammalian explosion, Rose starts at the beginning of the mammals' tale. Two introductory chapters are followed by four on the origin of mammals and their early evolution in the Mesozoic.

The author no doubt faced a problem when dividing the rest of the book into chapters. Details about the roots of many groups are hazy, and the earliest representatives of most

orders are unknown, so it would be impossible to restrict the contents of chapters to strictly monophyletic units. Nowadays, taxonomists have to deal with two different taxonomies: a traditional one, based on morphology, and a modern one, based on molecular analysis. Each chapter begins with an introduction describing our changing views on the relationships of the animals to be discussed. These introductions show the perspective and knowledge that Rose uses when examining the data. When available, he provides two alternative cladograms showing the relationships among the studied forms, one based on morphology, the other on molecular studies. His preference is decidedly morphological, as is evident from his attitude to the clade Afrotheria.

The notion of Afrotheria arose around 1990, based on DNA analyses demonstrating that six living orders of African placental mammals form a monophyletic clade. Although Rose often mentions the Afrotheria, he states: "No morphological evidence supporting Afrotheria has been found." However, the Cretaceous representatives of modern mammalian orders are unknown, and the lack of an early fossil record for most groups may be responsible for any morphological gaps between them. Among the groups assigned to Afrotheria, Rose, on the basis of morphology, accepts the monophyly of Hyracoidea, Elephantidea and Sirenia. But, against the molecular evidence, he assigns Tenrecidae and Chrysochloridae not to Afrosoricida but to Insectivora; Macroscelidea to the relatives of the Anagalida; and finally Tubulidentata (not described because of a lack of fossils) to the archaic Ungulata.

Each chapter contains a systematic table using linnaean taxa and a hierarchy of systematic units following Malcolm McKenna and



Fossil skeletons of Middle Eocene mammals such as *Kopidodon* have been found in Messel, Germany.

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