What all the buzz is about

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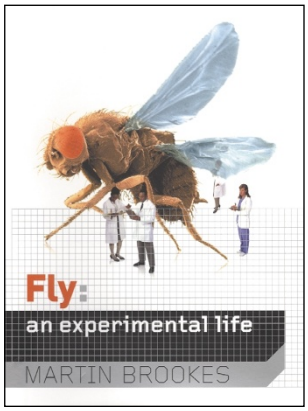
Fly: An experimental life
By Martin Brookes
Weidenfeld & Nicolson
221 pages, £16.99 hardcover,
ISBN 0753813270, 2001

Just over a year ago, I had the pleasure of sitting in a large and drafty hall in Pittsburgh from which one could hear the squeal of freight train wheels as they negotiated a curve just outside the building. Nobody minded, because we were in the presence of an historic (at least for the media) event: the revelation of the complete genome sequence of our favorite fly, *Drosophila melanogaster*. There was star power on the stage and there were television cameras. The event was synchronized with papers in that day's issue of *Science* and a story on the front page of the *New York Times*. We were on CNN. Heady stuff for a small insect. So what is all the fuss about?



When I was an arrogant and idiotic undergraduate 20 years ago, I was convinced that fly research was dead. A few old guys still worked on them—but most of the really interesting questions had been addressed and research would be drawing to a close within the next five years anyway. But something happened in my final year—I met the fly and I woke up just in time.

In his book, Martin Brookes begins at the beginning—with the *really* old fly guys at the turn of the last century. He gives us some amusing anecdotes about Thomas Hunt Morgan and his group. Fortunately for Brookes, all of these people are long dead and can't hire lawyers. The pace is fast and the reading is light. Along the way Brookes teaches us some useful genetics, albeit at a rather superficial level. Don't buy this book in order to learn how to do recombination mapping, or even to learn enough to read the classic papers. What you do get is a little bit of a voyeuristic thrill. At his best, Brookes takes you to the viewpoint of a fly on Morgan's wall.

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Things were happening in the fly field in the late 1970s: the genetics of development were being vigorously pursued. Most famously, Lewis was unraveling the *bithorax* complex and Nüsslein-Volhard and Wieschaus were doing their saturation screens for zygotic segmentation genes. But there was a lot more going on: cell-lineage compartments were discovered, as well as the maternal effect genes that control the patterning of the oocyte and the determination of the major body axes. Brookes deals very superficially with all this. He is really more interested in other areas, such as evolution and behavioral genetics. While his book is a personal perspective, I think these omissions detract from his account.

Also around this time, molecular biology was coming to eukaryotes in general and to the fly in particular. By the early 1980s, the first homeotic genes were cloned and discovered to be a family of transcription factors, and RNA *in situ* hybridization was developed and quickly showed that many of the critical developmental genes are expressed in informative patterns. Another key development was the invention of *Drosophila* transgenesis—based on the P transposon. There followed an explosion of cloning, all manner of developmental genes were isolated, and their mutant phenotypes analyzed and their expression patterns published. It seemed as if every issue of *Nature* was just one page of striped *in situ's* after another. This was all very exciting—but surely this could not last. Everyone was sure that it would all be over within five years.

Then at the end of the 1980's the HOX clusters were found to be conserved in vertebrates and the gold rush to mice seemed to be on. If the fly was really a little mouse, then surely the time had come to move on up to a "higher" organism. Meanwhile, there were some new tricks coming out of the fly. Eye development became very hot and this led rapidly to first elucidation of the ras pathway. Other aspects of nervous system development were explored, and with that whole families of neurogenic genes. Technical developments included new ways to discover genes purely on the basis of their expression patterns (enhancer trapping) and new ways to use yeast tricks in flies (*GAL4* for gene expression and the Flp/FRT system for site-specific recombination). However, mice were off and running—there was a new kid on the block, and it looked a pretty safe bet that flies would be pretty well over within five years or so.

The Berkeley *Drosophila* Genome Project got under way in the 1990s. This included not only the sequencing of the genome but projects (still under way) to characterize all the transcription units, and to obtain expression patterns and insertional mutations for them all. The biotechnology and pharmaceutical industries began to pay attention to the fly as means to ectopically express human disease (and other) genes in the compound eye led to new ways to model human disease—and search for human disease genes. When the genome sequence was published in March 2000, it really seemed like the fly was reaching some enormous crescendo. The number of papers on *Drosophila* (from MedLine searches) is a geometrically rising curve. It now seems that human genes become interesting when someone finds a fly homolog—rather than the other way around. One can project current trends and estimate when the study of *Drosophila* will consume every dollar spent on science worldwide and occupy every page of every journal. At that point the field must surely collapse and that date is, of course, about five years hence.

Martin Brookes perspective is somewhat different to mine. He came to the fly from a previous life in the study of ecology and evolution, and thus he places some emphasis on the contributions that have come to that field from *Drosophila* biology. Brookes has produced an amusing book that should be an easy read for those interested in finding out what all the fuss is about. He nicely connects the "classical" period (i.e., everything pre-cloning) with the astonishing fly-centric world of today. However, the book is not a very clear or comprehensive review of fly biology or technology. That said, it does go down quite smoothly and will help an outside reader understand why so many people are obsessed with flies. I can recommend it to anyone interested in what is going on in genetic science now and how things got this way.

Interestingly, the flyleaf of the book has only two short sentences describing the author, Martin Brookes, the second of which is "*He hates flies.*" I wonder why?