Understanding cancer

The Biology of Cancer
by Robert A. Weinberg
Garland Science: 2006. 796 pp.
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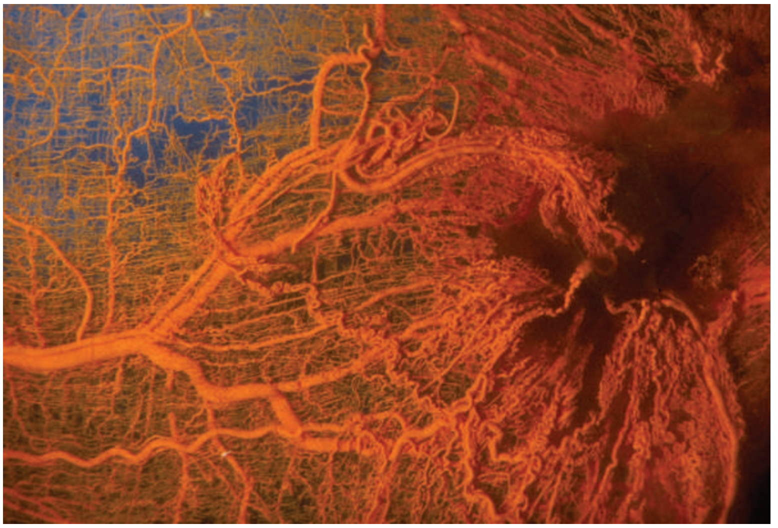
Chris Boshoff

Every cancer researcher knows 'The hallmarks of cancer', an iconic review by Douglas Hanahan and Robert Weinberg (*Cell* **100,** 57–70; 2000) that outlined the principles of tumour development: self-sufficiency in growth signals, insensitivity to antigrowth signals, evading apoptosis, limitless replicative potential, induction of angiogenesis, invasion and metastasis. In *The Biology of Cancer*, Weinberg has expanded these hallmarks into an alluring text. He takes us on a journey from the pioneering days of Gregor Mendel and Peyton Rous, to the latest insights in understanding how tumours become resistant to targeted therapy.



Taking over: a transplanted sarcoma (on the right) has developed an unruly vascular system.

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The book comes laden with expectations, mainly a result of Weinberg's reputation as a cancer biologist and a teacher. The author has borne the weight. Each chapter unfolds as a fascinating tale, from the historical perspective, through key experiments, to interpretation and future challenges. A striking example is the section on the inhibition of pancreatic cancer and medulloblastoma growth (through targeting of the signalling protein Hedgehog), which starts with the story of sheep flocks grazing on corn lily. Their offspring developed malformations including cyclopia, which led to the isolation of cyclopamine and the eventual discovery of mutations in the *patched* and *sonic hedgehog* genes, and new analogues of cyclopamine that inhibit these. The tumour's microenvironment (including the interactions between the seed and the soil) is discussed in detail and becomes an independent hallmark of cancer, along with immunoediting, the crosstalk between tumour niche and host immunity. Weinberg's own laboratory linked the master regulators of certain processes of development (Slug and Twist) to cancer metastases. The insight obtained from processes involved in mammalian development is a recurring theme throughout the book.

In a book of this scope, some readers will inevitably feel disappointed. For example, those studying the bioenergetics of tumour cells will not find a reference to Otto Warburg or discussions about alterations in glycolytic pathways and mitochondrial respiration during tumorigenesis. Epigenetic changes in cancer are covered cursorily, and the book only touches on certain emerging fields such as the role of microRNAs in tumour development, diagnosis and classification, and the mechanisms by which autophagy (a vacuolar process of cytoplasmic degradation) contributes to oncogenesis. These are merely observations, not an indictment.

To get a good idea of the magnitude of this book, the reader must look beyond the imagery and illustrations, and read the numerous vignettes highlighted throughout the text, as well as the supplementary sidebars provided on the accompanying CD-ROM. Here Weinberg demonstrates the breadth of his understanding and insight, and discusses the problems still facing us. For example, if micrometastases are attracted to an environment where they can flourish, why are recurrences of renal cancer not centred on the other kidney? How do we overcome the elevated interstitial pressure inside tumours, which has bedevilled attempts to deliver therapeutics effectively? Furthermore, despite the promise of mechanism-based therapeutics and pharmacogenetics, the best predictor of survival after treatment of lung cancer with an anti-EGFR inhibitor is still smoking status.

There is no comparable text in cancer biology and no single book that is so current and informative. Weinberg was ably assisted by an artist, Nigel Orme, in translating complex concepts into imaginative illustrations.

I would recommend the hardback copy: my soft-bound version came apart after one week of bed-time reading.

Although the book's stated intention is "to stimulate a new breed of cancer researchers", there is much here even for scholars to learn or be reminded of. Most molecular- and cell-biology students are familiar with *Molecular Biology of the Cell*, edited by Bruce Alberts and colleagues, now in its fourth edition (Garland Science, 2002). In a similar way, I hope that professionals and students in all spheres of cancer research will get to know *The Biology of Cancer*. ■

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Detecting hidden objects

Seeing Spatial Form
by Michael R. M. Jenkin & Laurence R. Harris
Oxford University Press: 2005. 449 pp.
£38.99

Manfred Fahle

Seeing Spatial Form covers an apparently eclectic mix of topics in visual perception, from 'pictorial relief' and 'vision in flying' to 'neuronal damage' and 'dopamine receptors'. In the introduction, the editors, Michael Jenkin and Laurence Harris, relate these and other seemingly disparate themes to the general topic of 'spatial form' — the detection of (often hidden) shapes in the visual world. In my view, detecting objects' shapes in the enormous complexity of retinal signals is one of the most elaborate feats achieved by the human brain. One excellent example of this feat is the detection of camouflaged items, which is proving a tough problem for artificial intelligence.

The book does not provide a systematic treatment of the perception of spatial form in vision, so how did the editors decide what to include? They were guided by three principles: the choice of first-rate contributors; the adoption of a systems-analytical and model-driven approach; and the desire to select topics close to David Martin Regan's heart. This is because the book is a *Festschrift* in honour of Regan's 68th birthday. So, instead of an integrated, textbook-like coverage of the perception of spatial form, the book provides rather specialized, mostly very well written, chapters that are more or less closely related to the topic, by some of the most prominent people in the field.

The individual chapters provide excellent reviews on state-of-the-art research in a wide range of topics, all related to Regan's interests. And wide they are, at a time when many researchers devote their life to a single topic, or even to a single technique. Regan is more of a Renaissance man, not only being interested in and using psychophysical methods, both in normal observers and patients suffering from different deficits of visual perception, but also sum-potential recordings, 'active' vision with eye movements, functional magnetic resonance imaging, neuropharmacology and developmental methods. Accordingly, the book covers a wide range of topics, and a wide range of methods for studying them.

It is not possible to mention all these topics in a short review. Suffice it to say that Regan's friends and colleagues produced an excellent *Festschrift*, with well structured, well formulated and well argued synopses on many facets of visual perception, not just spatial form. Even a reader seasoned in vision research will find not just new pieces of knowledge, but plenty of new insights — this, in my opinion, makes it an ideal book to choose for those times when you're stranded on a desert island. It will tell you about all those topics in vision research that you always wanted to discover but did not have the time to read about.

Let me give you four examples. You probably know, or would have guessed, that attention plays an important role in programming saccades, or rapid eye movements. But were you aware that planning and executing them 'costs' cognitive resources, and that a batsman cannot follow an approaching ball with his eyes but needs to estimate its time of arrival with an accuracy better than one-hundredth of a second? Second, it turns out that the processing of motion-defined form may be defective in patients even though simple motion detection is intact. Third, although retinal images are flat and the detection of surfaces represents an early stage of visual computation, perception is always inherently three-dimensional, even in the pictorial space of photographs. Finally, great progress has been made in understanding the neural basis of 'form vision'. For example, three-dimensional shape can be perceived from as few as two frames of a motion sequence.

If, once you have read the book, you want to know even more, no problem: there are selected references after each chapter, and a CD-ROM with additional material to keep you busy for quite a while. ■

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SCIENCE IN CULTURE

Reaching for the stars

The beauty of a rocket engine designed by Valentin Glushko lies in its functionality.

Martin Kemp

How and when does a utilitarian piece of technology become an object of beauty? This question was triggered by an early rocket engine designed by Valentin Petrovich Glushko (1908–89) that is on display in the Museum of Space Exploration and Rocket Technology in St Petersburg.

Glushko's 'Rocket Motor 50' (shown here), elegantly sectioned to disclose the chamber where paraffin and nitric acid mixed, sits gleaming on a white plinth in a museum case. It was invented for a rocket conceived by Mikhail Tikhonravov, a visionary advocate of space travel. To eyes attuned to the aesthetic delights of high-tech objects by generations of twentieth-century artists, such as Russian sculptor Naum Gabo, this is a beautiful object.

Glushko, born in the Ukrainian city of Odessa, pioneered electric and liquid propulsion systems at the Gas Dynamics Laboratory, which then occupied the site of the present museum on Peter the Great's fortified island of Zayatchy. In 1935 he published his book *Rockets, their Construction and Utilization*.

Although imprisoned during a Stalinist purge, Glushko returned to become the leading engine designer for the Soviet missile and space programme. A falling-out with rocket designer Sergei Korolev, over the right propellants for the ill-fated Moon programme, left him sidelined again, but after Korolev's death he returned to head the space bureau.

It seems that Glushko's engine designs

M. KEMP

were concerned solely with function. So is there even the slightest justification for seeing his rocket engines as anything other than obsolete relics of a great technological adventure?

There seem to be two reasons why our fascination with such relics goes beyond historical curiosity. The first is largely superficial: there is an undeniable romantic attraction to old technologies, once modern but now quaint. The crowds at shows of veteran cars or early aeroplanes testify to the emotional pull of antique machinery. An early electron microscope in a science museum exudes an air of nostalgic quaintness, even for spectators who know little of the history of such devices. Such items have acquired a 'period style' that speaks eloquently of their eras.

The Glushko engine, however, has little period style, so the second factor must predominate. This is what I call the aesthetic of ineffable rightness. Supreme designs in technology and the applied arts often exude an intense air of inevitability. Once invented, we can see that the design presents an optimal solution that transcends the idiosyncrasies of its human designer. In relation to function and materials, we can intuit that the solution presented is the right one.

The form of Glushko's engine is dictated by technical parameters, such as the angles and bends of the pipes that feed fuel to the central cylinder. They were not designed to look good — but they do.

At a time when the United States is contemplating manned expeditions to Mars, those motivations that lie outside the strict scientific imperatives again come to the fore. The aesthetics of space flight — the beauty of the technology, whether sleek or quirky — are important if the programmes are to garner public support.

Was Glushko himself solely driven by scientific and technological imperatives? My guess, looking at his Rocket Motor 50, is that he was deeply engaged with the visual 'rightness' of his invention as an integral component in his quest for functionality.

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