

by Mina Bissell, shows that “phenotype can override genotype” (1), irrespective of the number of genetic changes in the tumor cells. The book does not even mention the most spectacular case, Beatrice Mintz’s demonstration that highly malignant mouse teratoma cells can, if placed in an early embryonic environment, be induced to develop all normal tissues of the mouse (2). On the other hand, Weinberg provides a very interesting discussion on epithelial-mesenchymal transition during the development of invasive tumors and the reverse, mesenchymal-epithelial transition in late tumor progression. These transitions, which mimic certain stages of embryonic development, are very relevant for an understanding of interactions between cells and their normal or modified neighbors.

The space and detail Weinberg devotes to general and tumor immunology are somewhat surprising in view of his repeated emphasis of the “state of flux” of that particular field. We still lack a decisive answer to the original question: Does the immune system regard tumor cells as self or as nonself? Most of the observed nonself responses with an indisputable rejection potential have involved virus-transformed cells. The power of such responses can be demonstrated by the ability of immunocompetent T cells to bring even widely disseminated Epstein-Barr virus-driven immunoblastomas in immunodeficient patients to complete regression. Most nonviral tumors never have to face a comparable recognition. Although antibodies are (as the book shows) widely detected against many tumor proteins, this may be the symptom of a response rather than evidence of rejection-mediating effectors. Many ongoing efforts to mobilize tumor inhibitory immune responses may be akin to breaking tolerance to self. This approach is well presented in the book, but the question remains how far tumor inhibitory immune responses can be driven in the face of multifactorial protection against autoimmune reactions. Weinberg does not hesitate to reveal his own ambivalence, while doing justice to the current efforts that dominate the field.

The Biology of Cancer is no doubt the definitive statement on its topic today. But nothing remains definitive for too long in this field. An updated edition will be needed in a few years’ time. By then, the RNA revolution and particularly the role of the regulatory microRNAs that can play both oncogene and tumor suppressor roles (3) will have delivered a vast body of new information. The concept of junk DNA may have

been abandoned altogether. But however revolutionary these developments may be, they will stand on the solid foundation compiled in Weinberg’s monumental book.

References

1. C. M. Nelson, M. J. Bissell, *Semin. Cancer Biol.* **15**, 342 (2005).
2. B. Mintz, K. Illmensee, *Proc. Natl. Acad. Sci. U.S.A.* **72**, 3585 (1975).
3. A. Esquela-Kerscher, F. J. Slack, *Nature Rev. Cancer* **6**, 259 (2006).

10.1126/science.1131416

HISTORY OF SCIENCE

On Smell and Scientific Practice

Miriam Solomon

A delightful book about the science of smell, *The Secret of Scent* takes the reader through a tour of the almost infinite range of human olfactory possibilities. Luca Turin also presents the recent history of theories of smell, culminating with his own frequency theory. Turin possesses an unusually sensitive nose and has the ability to detect and describe, like a wine expert, the character of individual odors and complex scents, natural and synthetic, pleasing and noxious. A perfume guide he wrote (1) became a best seller in France. His perfume reviews (2) contain such colorful lines as “This thing smells like an infant’s breath mixed with his mother’s hair spray.... What

The reviewer is in the Department of Philosophy, Temple University, Philadelphia, PA 19122, USA. E-mail: msolomon@temple.edu

BROWSING

Strategies of Commitment and Other Essays. Thomas C. Schelling. Harvard University Press, Cambridge, MA, 2006. 355 pp. \$39.95, £25.95, €36.90. ISBN 0-674-01929-6.

Schelling shared the 2005 Nobel Prize in Economic Sciences for use of game theory to understand the bases of conflict and cooperation. In this collection of previously published articles and excerpts, he offers informative perspectives on a wide range of topics. Some, such as the nature of commitment and the avoidance of nuclear war, have interested Schelling since early in his career. (A 1960 book review of his helped inspire *Dr. Strangelove*.) Others reflect more recent concerns, including end-of-life controversies, addictions, global warming, and using prices as regulatory instruments to protect the environment. One chapter reprints his 1971 “Dynamic Models of Segregation,” which demonstrated a tipping point in the racial composition of neighborhoods. Several of the essays consider cases in which the usual assumptions of economists (e.g., rational decision-makers) do not hold. Anyone interested in the behaviors of individuals or societies will find many of the pieces thought-provoking; in one, Schelling even argues “that there are free lunches all over just waiting to be discovered or created.”

Rush can do, as all great art does, is create a yearning, then fill it with false memories of an invented past” and “Python ... belongs in a tree shaped diffuser dangling from the rearview mirror of a Moscow taxi.” The success of his perfume guide led to invitations to visit and consult with scent and perfume manufacturers, from which Turin learned much about the process of creation of scent.

In part because of this unusual access to perfumery materials and manufacture, Turin has found the leading theory of smell—that humans detect small volatile molecules by assessing the shape of the molecule or part of the molecule—unsatisfactory. Shape theories were originally proposed by Linus Pauling (3) and R. W. Moncrieff (4) in the 1940s and subsequently developed by John Amoore and others. Turin observes that research on creating new smell molecules is trial and error. Data mining for correlations between molecular shape and smell has not generated useful predictions. Scent manufacturers typically synthesize 1000 new molecules to get one that they can use. Turin observes that, contrary to the predictions of shape theories, molecules very different in shape can sometimes smell the same (e.g., boranes smell sulfurous) and molecules very similar in shape can smell different (e.g., isotopes of the same molecule such as acetophenone and deuterated acetophenone).

Turin has a Ph.D. in biophysics. At the time that he developed his theory of smell, he was a lecturer at University College

The Secret of Scent
Adventures in Perfume
and the Science of Smell

by Luca Turin

Faber and Faber, London,
2006. 217 pp. £12.99. ISBN
0-571-21537-8. Forthcoming
from Ecco, New York. ISBN
0-06-113383-3.

London. His research has ranged from electrophysiology to protein semiconductors and work on solitons. He has always read widely in the fields related to his research. He also has a taste (unusual among researchers) for used science books, which he purchases on his travels and which connect him with both recent history of science and non-Anglophone science.

The author knew of the theories of Malcolm Dyson (5) and Robert Wright (6), which claimed that smell (like sound and color perception) is based on frequency detection. For smell, the frequencies detected and measured are the vibrational frequencies of odorant molecules. Historically, the frequency theory faltered on the observation that enantiomers (mirror images of the same molecule, having the same vibrational spectrum) sometimes smell different and on the lack of a known mechanism for measuring vibrational frequency of molecules. Turin noted, however, that (as mentioned above) shape theories also have substantial contrary observations. He argues for a balanced look at all the evidence, and he considers the ability of each theory to accommodate contrary observations. Building on his earlier work on the electrical conductivity of proteins, Turin proposes that smell receptors are sensitive to particular ranges of vibrational frequency of molecules and use electron tunneling to transmit an electric signal when the appropriate odorant molecule is in the receptor. (This explanation is an interesting application of quantum mechanics to understand a physiological phenomenon.) Genomic sequencing by Linda Buck and her colleagues has identified about 350 different smell receptors in humans (7, 8). Turin does not suggest that each smell receptor responds to a different range of frequency. He thinks it more likely that classes of smell receptors respond to the same ranges of frequency but fit different sizes and shapes of molecule. (In this way, Turin explains the findings about enantiomers, but also complicates his theory with a shape component governing the affinity of odorants for receptors.)

Journalist Chandler Burr's widely read and (mostly) favorably reviewed book (9) has already told the story of the development and reception of Turin's theory. Academic and commercial smell researchers alike have been largely dismissive of Turin's hypothesis. Turin submitted a paper proposing his spectroscopic mechanism for olfactory reception to *Nature*, where it was rejected after a lengthy review process (described in Burr's book). The paper was then



Sensing scents. M. Maumus's advertising poster for the perfume Nelombo (1932).

published in a specialty journal, *Chemical Senses* (10), and Turin subsequently presented a refined version of his theory (11). Skepticism about Turin's theory has been evident in *Nature Neuroscience*, which published a scathing review of Burr's book (12), a short paper reporting three experiments that failed to support the vibration theory (13), and an editorial commenting on that paper and complaining about "the extraordinary—and inappropriate—degree of publicity that the theory has received from uncritical journalists" (14).

Burr saw in the early responses to Turin's theory a "failure of the scientific process," but he has been accused of excessive partiality toward his subject. *The Secret of Scent* is an interesting sequel, and partial corrective, to Burr's account. It is much more a book about science than about scientists, and it is refreshingly non-egotistical. Turin does not describe his own theory until page 160, and he presents the relevant contributions of many scientists from a range of scientific subdisciplines, including organic chemistry, the physics of electron tunneling, and the physiology of insect olfaction. Of particular note is Turin's coverage of findings from Soviet and Russian researchers.

Intended for a general audience, *The Secret of Scent* skillfully presents the necessary concepts from physics and chemistry. For example, Turin explains molecular vibrations by using an analogy with dance: vibrations can be local to parts of the molecule (like head movements in Indian dance) or involve the whole molecule (like 1970s

disco). The book is not a polemic, but rather a straightforward presentation of odor, theories of odor, and the author's theory of odor in particular.

Turin continues to work with his theory, presently in a corporate rather than an academic context. He is currently the chief scientist of Flexitral, a privately held U.S. company that uses his theory to design new scents, seeking molecules that are cheap to synthesize and have favorable toxicological and environmental profiles. Turin claims a success rate of 10% (one in ten syntheses produces a commercially viable molecule), which is two orders of magnitude above the industry average. Perhaps he will persuade the corporate world to take his frequency theory seriously before the academic community does.

As one would expect, Turin wishes his theory had found a more positive reception. Insofar as he assigns blame for its current fate, he faults the process of peer review. Turin believes that in areas requiring a high degree of specialized knowledge, any competent referee will have a conflict of interest. Competition will get in the way of a fair review. Moreover, he thinks that interdisciplinary research is especially vulnerable to deficient review, because it is difficult to find reviewers with the required broad range of expertises.

The Secret of Scent should appeal to anyone curious about smell, whether as a researcher or an intrigued layperson. It also touches on various aspects of science practice and policy, including scientific creativity, the difficulties of interdisciplinary research, the importance of unusual skills, and the consequences of unusual access to data. And Turin's story will also attract those, like myself, interested in scientific controversy.

References and Notes

1. L. Turin, *Parfums: Le Guide* (Hermé, Paris, 1992). A 1994 version is available online (www.flexitral.com/research/Guide1994.pdf).
2. L. Turin, in *The Smell Culture Reader*, J. Drobnick, Ed. (Berg, Oxford, 2006), chap. 23.
3. L. Pauling, *Chem. Eng. News* **24** (10), 1375 (1946).
4. R. W. Montcrieff, *Am. Perfum.* **54**, 453 (1949).
5. M. Dyson, *Chem. Ind.* **57**, 647 (1938).
6. R. H. Wright, *J. Appl. Chem.* **4**, 611 (1954).
7. L. Buck, R. Axel, *Cell* **65**, 175 (1991).
8. B. Malnic, P. A. Godfrey, L. B. Buck, *Proc. Natl. Acad. Sci. U.S.A.* **101**, 2584 (2002).
9. C. Burr, *The Emperor of Scent: A Story of Perfume, Obsession, and the Last Mystery of the Senses* (Heinemann, London, 2003).
10. L. Turin, *Chem. Sens.* **21**, 773 (1996).
11. L. Turin, *J. Theor. Biol.* **216**, 367 (2002).
12. A. Gilbert, *Nature Neurosci.* **6**, 335 (2003).
13. A. Keller, L. B. Vosshall, *Nature Neurosci.* **7**, 337 (2004).
14. "Testing a Radical Theory," *Nature Neurosci.* **7**, 315 (2004).

10.1126/science.1131937