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 onco- 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

BROWSING


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.”
London. His research has ranged from electro- 
physiology 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 re- 
searchers) 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. His- 
 torically, 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 fre- 
quency 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 evi- 
dence, and he considers the ability of each 
theory to accommodate contrary observa- 
tions. Building on his earlier work on 
the electrical conductivity of proteins, Turin 
proposes that smell receptors are sensitive 
to particular ranges of vibrational fre- 
quency of molecules and use electron tun- 
eling to transmit an electric signal when 
the appropriate odorant molecule is in the 
receptor. (This explanation is an interesting 
application of quantum mechanics to under- 
stand a physiological phenomenon.) Geno- 
mic sequencing by Linda Buck and her col- 
leagues has identified about 350 different 
smell receptors in humans (7, 8). Turin does 
not suggest that each smell receptor re- 
sponds to a different range of frequency. He 
thinks it more likely that classes of smell 
receptors respond to the same ranges of fre- 
quency but fit different sizes and shapes of 
molecule. (In this way, Turin explains the 
findings about enantiomers, but also compli- 
cates his theory with a shape component gov- 
erning 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 develop- 
ment and reception of Turin’s theory. Aca- 
demic and commercial smell researchers 
ally have been largely dismissive of Turin’s 
theory. Turin submitted a paper pro- 
posing his spectroscopic mechanism for olfactory reception to Nature, where it was 
rejected after a lengthy review process (de- 
scribed in Burr’s book). The paper was then

published in a specialty journal, Chemical 
Senses (10), and Turin subsequently pre- 
 sented a refined version of his theory (11). 
Skepticism about Turin’s theory has been 
evident in Nature Neuroscience, which pub- 
blished 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 extraor- 
dinary—and inappropriate—degree of pub- 
licity 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 partial- 
ty 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 neces- 
sary 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 mole- 
cule (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, the- 
ories 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 ac- 
ademic context. He is currently the chief 
scientist of Flextral, 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 com- 
unity 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 com- 
petent referee will have a conflict of interest. 
Competition will get in the way of a fair 
review. Moreover, he thinks that interdisci- 
plinary research is especially vulnerable to 
deficient review, because it is difficult to 
find reviewers with the required broad range 
of expertise.

The Secret of Scent should appeal to any- 
one 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 conse- 
quences of unusual access to data. And 
Turin’s story will also attract those, like 
myself, interested in scientific controversy.

References and Notes
2. A. Gilbert, Senses (10), and Turin subsequently pre- 
Yes, generic Viagra is available in the U.S. The original patent for Viagra was set to expire in 2020; however, Pfizer entered into an agreement to allow Teva Pharmaceuticals to launch the generic. In 2020, other generic manufacturers will be able to enter the market with generic Viagra. Pfizer is also offering its own generic that ditches the blue color (it’s white) and half of the $65-a-pill retail price. Generic Viagra has been available in Canada since 2012. In Europe, Viagra became available generically in 2013. The lower dose form of Revatio (sildenafil) became available generically in t