Good vibrations
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 BY STEVE HERMAN

Good Vibrations

Luca Turin may possess the keys to this secret kingdom of smells, the last human sense to be unraveled by modern science.

> **"Luca Turin is a scientific Mozart beset by Salieris in lab coats."**
> **—*Liesl Schillinger***

THE SCIENCE of olfaction has been revolutionized over the past dozen years. What remains a mystery, however, is the exact way smells trigger these proteins, beginning the cascade of events culminating in the odor decoding deep in the brain. Luca Turin may possess the keys to this secret kingdom of smells, the last human sense to be unraveled by modern science. One would assume that the world—at least the fragrance world—would have beaten a path to his door. The reality has been quite different, and Luca Turin—like a modern John the Baptist—has been a voice crying in the wilderness.

The tale of the development of the vibrational theory, and its reception by the fragrance industry and scientific community, is recounted in a new book. *The Emperor of Scent* by Chandler Burr is essential reading for anyone interested in theories of smell, the workings of the major perfume companies or the politics of scientific publication.

Relationship Building

A ligand is an atom or molecule that is recognized by a receptor. Structure-odor theories are necessary to explain why a molecule has a certain odor and to predict new molecules to match defined odor profiles. A successful QSOR (Quantitative Structure-Odor Relationship) would be worth untold millions to the major fragrance companies. New molecules would power new perfumes and revolutionize the industry. What is it about an odorant ligand that gives it its characteristic smell? Why are some smells orders of magnitude more powerful than others?

For the past few decades, the answer has been shape. The fancy name for this view is the "stereochemical theory of odor." Its greatest proponent was British scientist John Amoore, and every company involved in creating new odor molecules has been using the shape theory. Unfortunately, the methods employed, computer modeling and trial-and-error synthesis—made to appear technical by being described as "combinatorial chemistry,"—have proven costly and inefficient.

The vibrational theory goes back to Dyson in 1938 and was revived by Wright in 1982, but their work lacked the detailed mechanism proposed by Turin. The basic assumption of the modern theory is that the nose is a spectroscope operating by inelastic electron tunneling. First, it is useful to notice just how sensitive the nose can be to chemical structures: SH, CN, NOH can be easily discerned and triple bonds can be smelled. John Amoore, the champion of the stereochemical theory, was drawn to study olfaction by observing chemists easily identifying chemicals with a quick sniff when a wet analysis would take many hours. Whereas it is very difficult to see how a shape-based mechanism could infallibly tell SH from, say OH, a spectroscope finds this easy: they have different vibrations.

But a spectroscope must plug into a source of power. For the olfactory receptor, this power comes from NADPH (nicotinamide adenine dinucleotide phosphate), a roaming biochemical battery used for many functions in the body. Turin's early work, unrelated to olfaction, revealed that proteins could conduct current. A unique quality of molecules is needed for identification, and

LUCA TURIN

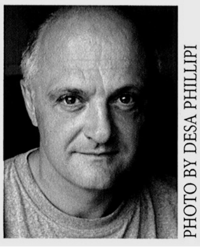


PHOTO BY DESA PHILLIPI

Pure science, academia and industry do not always live together in harmony.

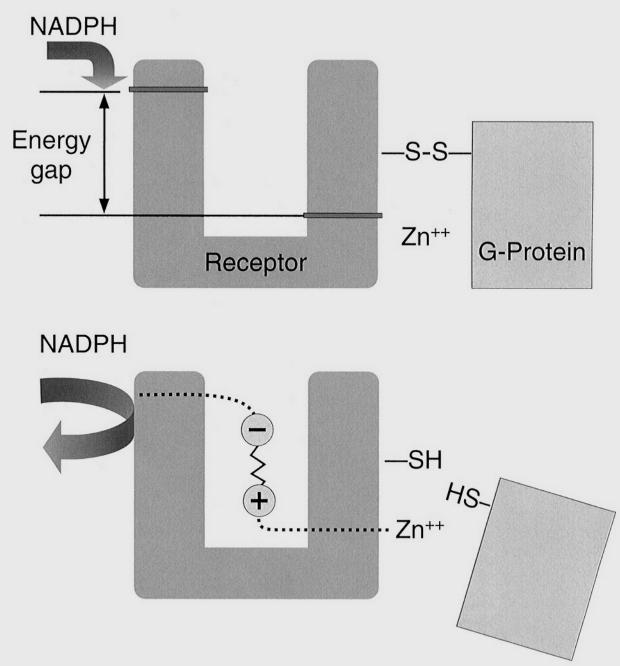
the vibrational properties are a good possibility. Turin found research on inelastic electron tunneling that could, rather remarkably, be engineered in an odor receptor.

The essence of the reception process (see Figure 1) is similar to turning a light switch on and off. The receptor site has an energy gap: the switch is off. When the correct odor molecule enters the receptor, it brings vibrations matching both sides of the receptor. Fed electrons by NADPH, electrons tunnel from the high to the lower energy levels: the switch is on. The current goes to a zinc-binding site in the protein, which reduces an S-S bond, and the G Protein starts a signal cascade terminating in the odor decoding areas of the brain.

So, how easy was it for Turin to publish his work, or to convince the researchers at the major fragrance suppliers? In short: it was not. The battle between research investment and intellectual property competing with the needs of confirming a theory are placed in focus. Turin's theory has, thus far, been denied the necessary resources to sate the appetite of his algorithm.

Pure science, academia and industry do not always live together in harmony. Luca Turin has left his position at the University College London to have free rein to commercialize his discoveries as CTO for a startup company called Flexitral. Someday everyone may know, as the readers of *The Emperor of Scent* do, that

FIGURE 1. TRANSDUCTION MECHANISM



Luca Turin has contributed vital insights into the sense of smell. While the final chapters of his story are unwritten, they are surely destined to profoundly influence the future history of fragrance. ■ **GCI**

Author's Note: Luca Turin has been unfailingly generous with papers, e-mails and phone calls over the years, making this column a genuine pleasure to write. All of Luca Turin's papers are available as PDF files at *www.flexitral.com.*

Steve Herman is vice president, new technology development, at AFF International. He has more than 30 years of experience in the industry, primarily in fragrance application. He serves as an adjunct professor in the FDU Masters in Cosmetic Science program and has been active in numerous capacities with the SCC.