Digital perfumery
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CHEMICAL REACTION **BY STEVE HERMAN**

Digital Perfumery

"It may not be a coincidence that the two systems in the universe that most impress us with their open-ended complex design—life and mind—are based on discrete combinatorial systems."
—Steven Pinker, *The Language Instinct*

All through cosmetic science there is complexity

JUST HOW MATHEMATICAL is traditional science? Physics is almost entirely mathematical, chemistry less so, and biology even less. A seminal work of science, Darwin's The Origin of Species, contains not one equation. Mathematics works well in describing the attraction between an electron and a proton, but has nothing to add to a discussion of the evolutionary theory.

Even in physics, mathematics hits a wall. Newton's equation of gravitational attraction is a foundation of classical physics:

$$F = \frac{Gm_1m_2}{r^2}$$

F is the force of attraction, m_1 and m_2 the masses of the two objects, r the distance separating them, and G is a constant.

Now take a look at Figure 1, the Andromeda galaxy M31. M31 has been shaped by gravity into a spectacularly beautiful spiral. Using Newton's equation, try to plug in 100 billion stars and get the pattern of M31. It can't be done, so just how mathematical is physics, the most exact of sciences?

Not a fair example, some may say; the galaxy is a big, complicated system, and that is precisely the point. The physics that physicists have concentrated on are simple systems yielding equations that then can predict the behavior of other simple systems. Complexity does not work well with this model.

FIGURE 1. ANDROMEDA NEBULA M31

Source: NASA

A New Kind of Science (NKS) by Stephen Wolfram[1] shows how complicated patterns can be created by simple rules and relates these patterns to a variety of natural phenomena.

Yet, mathematics works best with continuous systems, while computer programs—for example, those utilizing cellular automata—deal better with discrete systems. Are perfumes, olfactory recognition and brain decoding discrete or continuous? The simple lilac fragrance in Table 1 is clearly discrete. It contains eight chemicals. While the composition will change during evaporation, the composition of the fragrance and the aromatic compounds released to the air will remain discrete proportions of clearly defined chemicals. Make the perfume as complicated as possible, using many more ingredients and natural products of great complexity, and the resultant blend will remain a mixture of precisely

TABLE 1. SIMPLE LILAC FRAGRANCE

The composition of a simple fragrance such as lilac includes eight chemicals.

Phenyl ethyl alcohol	30
Hydroxycitronellal	30
Geraniol	2
Amyl cinnamic aldehyde	4
Benzyl acetate	5
Ionone	3
Eugenol	1
Terpineol	25

The discrete nature of smell is at the heart of attempts to use computers to transmit fragrances.

defined molecules. There is no "pixie dust" to thrust the fragrance compound suddenly into the realm of mystery. Its discrete nature is at the heart of attempts to use computers to transmit fragrances by companies such as DigiScents, which is no longer in business, Trisenx and AromaJet.

The odor receptors are clearly discrete, and the understanding of their structure was revolutionized by the discovery of the receptor genes.[2] They are made of odor-binding proteins that contain pockets serving as receptor cavities. The structure of the molecules, 7-transmembrane G-coupled proteins, is highly complex but hardly magical.[3] The modeling for these proteins through the lipid membranes is achieved through computer programs, the accuracy of which is determined by the algorithms employed. These structures are an obvious example of computer programs being more useful than the direct application of chemistry, precisely because of the degree of complexity.

The odor receptors do not form a one-to-one correspondence with ligands, a fact that is made evident by the ratio of receptors (about 1000) to odors that can be distinguished (about 10,000). The combinatorial patterns are created in balls of nerves in the olfactory bulb called glumeruli.[4] The numerous combinations of patterns formed in the glumeruli have proven difficult to unravel fully via conventional approaches. Once again, the complexity and combinatorial nature of this process makes computer programs the best approach to analysis.

The signal goes to the core of the brain, to several areas of the limbic system, especially the hippocampus and amygdala. Surely, some mystery must arise in the emotional center of our brain. Modern techniques such as PET scans and MRI can track the areas of the brain that are activated by particular stimuli. This process can be understood best using computers because the brain *is* a computer! Connections are established by experience and learning, although some responses probably are hard wired in the womb. The limbic system is not magical simply because it is emotive.

There is a missing step: the complex pattern of the odor molecules as they swirl through the air before a select few find the olfactory receptors. It is here where the computer model is most valuable—even the harshest critics of NKS agree that it is a superior way to study the complex patterns of fluid dynamics and turbulence.

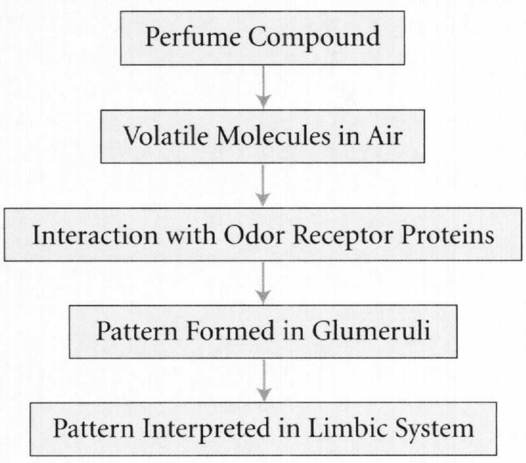
Of course, the programming approach does not eliminate the need for experimentation. One example is a method of locating the odor receptor proteins that respond to specific odors. The work of Stuart Firestein and his colleagues[5,6] at Columbia University illustrates a possible methodology. The establishment of the human genome has allowed data mining of the olfactory genes. The gene for one receptor can be removed from a mouse, producing a "knock out mouse." The mouse will not respond to an odor. The receptor protein can be put back in via an adenovirus—a virus which has the deleted odor receptor gene spliced in. The mouse can then detect the odor, so the exact correspondence of odor to receptor is established. This becomes one data point in olfactory recognition.

A method for studying fragrances and their recognition in the brain is shown by the sequence shown in Figure 2. Structure-function relationships for fragrances have never been satisfactory in the past due to the complexity of the recognition process. This is not the end of the journey but only the beginning. The data to input is still fragmentary, and the algorithm employed by the programming is subject to constant refining as the database expands. The use of computers does not provide the answers, but rather provides a framework for pursuing the ultimate understanding of smell. There is no reason why this method cannot include the possible existence and effects of human pheromones.[7]

NKS devotes Chapter 10 to "Processes of Perception and Analysis." The chapter focuses

FIGURE 2. ORDER RECOGNITION COMPUTATION

A sequence for studying fragrances and their recognition in the brain.



on visual perception, auditory perception and human thinking. Not a word in the basic text of the book is devoted to human olfaction, which is confined to one note on page 1105. The neglect is likely due to the fact that analysis of the odor reception process has been recent and largely confined to specialized literature. The information needed to create the complete model is essentially available but scattered in a multitude of disciplines, from genome data mining to protein modeling to genetic experiments to studies of the amygdala to sociology, psychology and even anthropology. The task is indeed multidisciplinary and daunting!

All through cosmetic science there is complexity. From the formation of emulsions to the interaction of formulations with skin and hair, to the variables that influence the success of products in the marketplace, all are complex systems. The approach proposed in NKS may lead to increasingly refined models illuminating the core concerns of the personal care industry, elevating new formulations and marketing techniques to higher levels than could be achieved by our current methods. GCI

Editor's Note:

This is part two of a two-part series that discusses Stephen Wolfram's book, *A New Kind of Science*. Part 1 appeared in October 2002.

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