

# The Monell Connection

Fall 1996  
*The Monell Connection...*  
from the Monell Chemical  
Senses Center, a nonprofit  
scientific institute devoted to  
research on taste, smell,  
and chemosensory irritation.

## Tales of Taste

Information about  
the sense of taste  
continues to  
accumulate —  
questions are  
answered and  
others are raised.

The sense of taste doesn't get the attention it deserves. Yet taste has much to tell us.

For many creatures, taste provides critical information about the environment, particularly about the safety, palatability, and appropriateness of what to eat and drink.

However, humans rely much more heavily on visual and auditory information than do most other species, and taste is regarded by some as a minor sense. Indeed, while people certainly enjoy the pleasures of food and drink, what is often labelled "taste" is really a complex mix of factors that includes taste, as well as olfaction, texture, and temperature.

In part because taste is still not well understood, most people don't realize how many questions remain to be answered about this so-called "secondary sense." But for research scientists who study sensory systems, learning more about how taste works is a major focus — and a significant challenge.

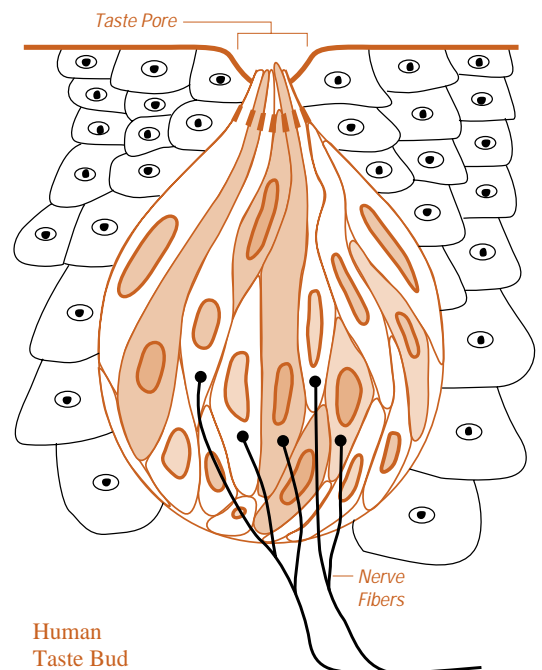
*A world without taste is a diminished world. Most patients with taste disorders report decreased enjoyment of food and many significantly alter their eating patterns, sometimes affecting nutritional status.*

A pervasive question for taste research is how molecules corresponding to the basic taste qualities of sweet, sour, salty, bitter — and a possible fifth taste sensation described as savory, or umami — become electrical messages that send the brain information about what substance is in the mouth.

*It is commonly believed that there are regional specificities on the tongue, with the front being sensitive to sweet and salty, the sides to sour, and the back to bitter. In actuality, although certain regions are better at perceiving specific tastes than others, each taste quality can be sensed on any region of the tongue where taste buds are found.*

This process of taste transduction starts on the tongue. In humans, the tongue contains around 5000 taste buds, but the number of buds can vary considerably from one person

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Human  
Taste Bud



## New Human Testing Labs Now in Use

even in the library. Studies using foods and flavors were conducted right next door to studies employing radioactive tracers and animals. Occasionally, olfactory studies would be disrupted by the stench from nearby chemistry laboratories.

With the strengthening and expansion of the nutrition program in the early 1980s, four small test rooms were constructed for human work. However, even these were located amidst animal and biochemical test areas, with obvious attendant problems.

By the early 1990s, it was clear that Monell needed to expand and isolate its human testing facilities. Fortunately, half of the third floor was still undeveloped — not that it wasn't being used. It contained storage space for old data, equipment people couldn't bear to throw out, empty boxes (for some reason these are very difficult to get people at Monell to discard), and crowded desk space for graduate students and postdocs.

I won't go through all our steps in planning and designing the new facility. Members of the Board of Directors, the International Advisory Council, and the Nutrition Advisory Council were a constant source of advice and encouragement. Many people at Monell worked to complete the project on time and within budget. Several provided service far beyond the call of duty — they took on the difficult task of lessening the gaps between what our scientists wanted, the budget permitted, and the architects envisioned.

Some of our goals for the new facility included: tripling the amount of space available for human testing, making the space flexible in order to meet the needs of both current and future scientists, and ensuring that human testing was carried out in a dedicated and centralized area.

We also wanted to be able to increase the relevance of our research in relation to the

interests of sponsors. To achieve this, we included new facilities such as environmental chambers to permit long-term studies of exposure to volatiles under very controlled conditions, a research kitchen so that we could more readily use real foods as stimuli, and a group testing room for studies that more closely parallel those of our corporate sponsors.

At the same time, of course, we had to raise the money. The Monell Foundation, our long-term benefactor, was very generous. They pledged about half the money, providing we could raise the other half. Many of our corporate sponsors, along with a local foundation, provided the necessary funds. To all, we are deeply grateful for their vision and willingness to participate in this important project during very difficult financial times.

I cannot resist a little nostalgia. When I first came to Monell in 1971 the Center had just moved into its current 60,000 square-foot building. However, Monell itself actually occupied less than half the space. The rest was rented out to various agencies and even, for awhile, to the architect Buckminster Fuller, whom we would occasionally see in the elevator with a suitcase in one hand and a geodesic dome in the other. During the next 25 years, Monell gradually took over the rest of the building.

Now, with completion of our human testing laboratories, we occupy the entire building. Last year we retired the mortgage and thus own the building free and clear. The newest space is highly-functional — as well as bright, cheerful, and comfortable. In conjunction with the facility at Jefferson, Monell scientists are now able to conduct a much wider range of exciting studies on human chemosensation.

Drinking champagne and proposing toasts are not the usual routine at Monell. But neither is the chance to celebrate the opening of long-awaited new laboratory space. On May 2nd, as part of the annual Executive Meeting and Dinner, we formally dedicated the Human Chemosensory Research Laboratories, and since then the space has been in full and productive use.

We are deeply grateful to those who, with both intellectual and financial contributions, have shown confidence in the current and future scientists who will utilize the new facility. And most of all, we are grateful for their encouragement of Monell's continuing search for the knowledge that will come because of the existence of these laboratories. ■

Although human sensory studies have been conducted at Monell almost since the Center's creation, our human research has accelerated in the last decade.

This has been driven by at least two factors. First, increased government interest in clinical issues relevant to the chemical senses has encouraged studies of human chemosensory perception. Certainly, establishment in 1986 of the NIH-funded Monell/Jefferson Chemosensory Clinical Research Center gave significant momentum to human sensory work.

The second major push has come from Monell's corporate sponsors. Many expressed strong interest in combining our expertise in biochemistry and in cellular and molecular biology with studies of the sensory biology and psychology of the organism that is of ultimate interest to most of us: humans.

Before the mid-1980s, human testing at Monell was carried out all over the place — in multipurpose laboratories, closets, and

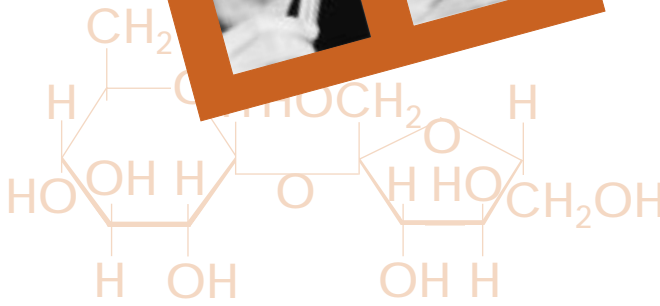
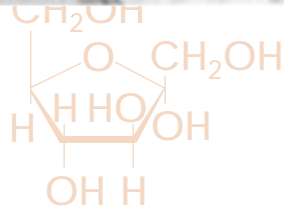
# The Search

## for Sweet

## Genes



Alexander Bachmanov  
D.V.M., Ph.D.



Obstacles involving time, distance, political history and mail delivery complicated Dr. Alexander Bachmanov's arrival at Monell. But his eagerness and persistence, heightened by the enthusiasm of scientists who were looking forward to working with him, finally overcame the barriers.

The journey from the Pavlov Institute in St. Petersburg to Philadelphia took more than three years. Although Bachmanov's scientific goal — to study genetic aspects of taste preferences — had been present for a long time, his vision was tempered by the need to juggle practical realities of working as a scientist in his native country.

Now that he is here, doing what his colleagues describe as "one of the neatest pieces of research going on at Monell right now," it all seems quite logical. After graduating from high school, he didn't pursue a childhood interest in plant biology because the school he needed to attend was too far away. Fortunately, the Veterinary Institute was nearby. Bachmanov reasoned that veterinary studies could provide a useful bridge connecting his interest in plants with an increasing

curiosity about eating behavior "because most of the animals were eating plants."

Bachmanov especially wanted to learn more about food intake, and specifically about taste preferences. "I've always wondered why animals choose the foods they eat," he explains. He pursued this question even though no one at the Veterinary Institute shared his interest. After receiving the veterinary degree, he obtained funds to work toward a Ph.D. with colleagues at the Pavlov Institute of Physiology, where he studied behavior and physiology related to salt appetite in a strain of rats with genetically-transmitted hypertension.

In the course of his studies, he came upon literature about experiments at Monell on mechanisms of salt taste and salt appetite. "It was just the kind of work I'd been dreaming about," he says.

That was in 1990 — a hard time for scientists in Russia. Bachmanov notes that science is expensive, and there was not suf-

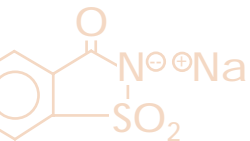
ficient funding to do the basic research that intrigued him. "Life changed so much in my country," he reports. "People didn't know what was going to happen, and if I wanted to keep on doing research on taste it seemed a good idea to look for a position abroad."

He made initial inquiries to Monell. Although there was great mutual interest — two scientists from Monell managed to visit the Pavlov Institute and talk with Bachmanov — no funding was available to support his work.

Bachmanov decided to accept a fellowship at Cambridge University. But at the same time he was arranging the move to England, Monell's director, Dr. Gary K. Beauchamp, finally was able to obtain the necessary funds for Bachmanov to come to Philadelphia. Beauchamp immediately sent a letter offering a position.

"It amazes me the way time and space intercross," muses Bachmanov. Because of slow mail between the U.S. and Russia, the letter didn't reach him for six months. He, of course, was "still very interested."

After a year at Cambridge, he arrived at Monell early in 1994 and, working with Beauchamp and Dr. Michael Tordoff, started studies on the genetic basis of salt preference. "As often occurs in science," he notes, "our findings related to sweet taste happened by chance" when he and his colleagues noticed that the two strains of inbred mice they were using to study salt preference also exhibited striking differences in preference for sweet solutions.



*Within an inbred strain, all mice are genetically identical. When two different inbred strains are crossed, resulting in the first filial or  $F_1$  generation, 50% of the genes of each offspring are identical to those of one parental strain and 50% are identical to the other. When the  $F_1$  animals are subsequently mated, unlinked genes from the two inbred strains are randomly mixed in the resulting  $F_2$  generation.*

Bachmanov and his colleagues, along with Dr. Danielle Reed and Dr. R. Arlen Price from the University of Pennsylvania, crossed the two inbred mouse strains and measured taste preferences of the  $F_2$  generation. They then analyzed fragments of DNA samples from each of the animals to determine which of the original parental strains contributed the DNA, and found two genes that influenced the level of sucrose preference.

This work, as much of what is done at Monell, is highly collaborative and multidisciplinary. Bachmanov and his colleagues at Monell and Penn recruited Dr. Yuzo Ninomiya, from Asahi University in Japan, to join the project. Dr. Ninomiya, one of the world's experts in taste physiology, working with a Monell post-doctoral fellow, Dr. Masahi Inoue, found that each of the two genes was related to a different component of the electrophysiological response of taste nerves to sucrose.

Based on findings that the two genes influence both a behavioral and an electrophysiological response to sucrose, Bachmanov speculates that one gene might code for a sweet taste receptor and the other might be related to intracellular events involved in sweet taste transduction.

The eventual goal is to clone the genes involved in detecting and responding to sweet-tasting substances. "I'm pretty sure," he says, "that this is significant work," citing its clinical and commercial possibilities, in addition to the great scientific value.

The studies have led to another line of research for Bachmanov and his colleagues. They have shown that in the mouse, preference for sweet taste is genetically linked to

preference for alcohol. Because alcohol flavor has a sweet taste component, it is possible that liking for sweet taste may be one of the factors that influences alcohol consumption.

Mostly, however, Bachmanov appreciates having the opportunity to be at "the best place I've ever worked in my life." He describes Monell as "an unusual intersection of academic science, clinical studies, and

industry." This fits well with his interests because "at some stage I told myself that although it's very exciting to satisfy my own curiosity about ingestive behavior, there has to be some usefulness to it. Sometimes a scientist might move away from what's important to people, but Monell is real life. Scientists here hold on to an awareness of what's actually needed." ■

### Tales of Taste continued from page 1



to the next. Chickens, by comparison, are believed to have only about 24 taste buds and catfish have close to 300,000.

*Because most of their taste buds lie along the surface of the body, catfish are able to taste food just by swimming in water. Hence, they are often called "swimming tongues." The large number of accessible taste buds makes the catfish a powerful model system for scientists studying taste.*

Taste buds on the tongue are located in small nipple-like structures known as papillae — bumps or ridges that can be seen with the naked eye. Interestingly, a sizable number of taste buds are located in areas other than the tongue, such as on the roof of the mouth and down the throat. Unlike taste buds on the tongue, these buds are not located in papillae, but are situated within the outermost layer of tissue lining the mouth and throat.

On the tongue, there are three types of papillae that contain taste buds: fungiform, shaped like little mushrooms, are at the tip and sides; foliate are folds along the sides of the rear portion of the tongue; and on the back are the circumvallate papillae, shaped like a flat hill surrounded by a valley. Human papillae can have from one to fifteen taste buds, with each taste bud containing forty to sixty taste cells, arranged in segments like an orange.

It used to be thought that each papilla was responsive to only a single taste quality, but it is now known that a human taste papilla responds to more than one quality. Since each papilla can contain many taste buds, the logical next question is whether a

single bud — or a single cell — responds to just one taste quality. Animal studies suggest that some taste buds respond to multiple stimuli, but that individual cells within the bud may respond to just one taste quality. However, for humans the question remains unanswered.

Earlier research on taste was directed primarily toward identifying common characteristics of molecules that act as stimuli for the different basic taste properties. Now, because of advances in technology, it is also possible to describe the biochemical events that take place inside a taste cell after a tastant molecule joins with a receptor on the cell's surface.

For each of the basic taste qualities, both the way in which the tastant molecule interacts with its receptor and the subsequent biochemical changes inside the cell appear to be different. To make it even more complex, within any given taste quality these processes also might differ. For example, there may be separate transduction mechanisms for different bitter-tasting compounds. Whatever the mechanism, all taste cells release neurotransmitter to signal the presence of a taste stimulus. The neurotransmitter is then detected by a sensory nerve that communicates with the brain.

Although we know more about taste than we did ten years ago, there is still much that is not known. Many questions address the relationship between taste physiology and psychology. For example, certain individuals are more sensitive than others to sweet and bitter compounds. Is this related to the wide variation in number of taste buds? How is information about taste processed in the brain? What is the role of genetics in determining factors such as number of taste buds and sensitivity to different taste qualities? How do various medications affect taste transduction? What is the influence of aging on the taste system, and how does it impact on food choice in the elderly? These and many other questions are tales yet to be told by the tongue. ■

# Q&A

## Why does anticipation of food make your mouth water?

When your mouth waters or your stomach grumbles in expectation of food, you are experiencing what is known as a *cephalic phase reflex*. This is a physiological response that occurs when one is exposed to a food-related sensory stimulus.

The taste of food, as well as its smell and visual appeal, sends a message to the brain signalling that food is available in the environment. The brain then initiates a series of physiological reflexes: release of saliva, gastric acid, pancreatic enzymes, and insulin — all of which prepare the body for incoming nutrients and therefore are believed to optimize digestion and absorption of food. Research has shown that when cephalic phase reflexes do not occur — for example, when food is put directly into the stomach — there is reduced utilization of nutrients.

It follows that populations with impaired cephalic phase reflexes, such as the obese or diabetics, might not metabolize nutrients to the same extent as healthy individuals.

Thus, the smell, taste, and appearance of food do more than contribute to flavor and pleasure. These sensory components also stimulate reflexes that are required if we are to receive maximum nutritional benefits from the food we eat.

## Why is chocolate candy so well-liked?

While eating chocolate candy, you enjoy sweet taste combined with the mouthfeel of fat, two highly pleasurable sensations. These attributes of sweetness and fat, along with aroma, play a major part in liking for chocolate candy.

One theory about food palatability is that people like complex flavors in which mouthfeel changes over time. When chocolate candy is in the mouth it changes

from solid form to a smooth paste, gradually releasing the flavor. This is because cocoa butter melts at body temperature.

Aroma is another factor in the chocolate flavor experience. The aroma of chocolate is enjoyed in foods such as milk, cake, and ice cream.

Chocolate is cited in many surveys as the most frequently craved food. This has been attributed to chocolate's pharmacological properties — for example, it is a mild stimulant. However, recent scientific studies show that chocolate's pharmacology plays no role in craving for chocolate.

## Why do many odors seem to fade so quickly?

It is a common experience to be disappointed because newly-purchased air fresheners or recently-applied perfumes seem to lose their fragrance quickly.

Has the odor really disappeared? Probably not. The perceived intensity of many odors declines over time because we process the odor differently after smelling it for awhile. The change that causes an odor to smell weaker with continued exposure is known as *odor adaptation*.

Olfactory receptors respond to chemical molecules in the air and send odor information to be processed in the brain. Odors appear to fade with repeated exposure because these receptors respond less when they are being continuously bombarded by the same chemical. Additionally, parts of the brain that deal with attention and memory might contribute to a decline in perceived intensity when an odor is experienced repeatedly, particularly within the same context.

In certain situations, adaptation to an odor occurs very quickly — often after just a few sniffs. In other situations, adaptation occurs more slowly, and occasionally it doesn't take place at all.

Nevertheless, some level of adaptation is a common reaction to continuous or repeated odor exposure, and represents the normal response of the olfactory system. ■

**Contributors:** Pamela Dalton, Ph.D.; Marcia Levin Pelchat, Ph.D.; Karen Teff, Ph.D.

**Growing  
Model  
Olfactory  
Cells**

Studies on human olfactory neurons have been hampered because these cells are difficult to obtain. As a possible alternative, Dr. Gomez and colleagues examined characteristics of cells derived from olfactory neuroblastoma (ONB), a rare malignancy of the olfactory mucosa that may originate from the same tissues that produce olfactory neurons.

ONB cells were maintained in the presence or absence of growth factors known to affect growth and development of olfactory tissue. The scientists used changes in intracellular calcium, which occur when functional olfactory neurons are exposed to specific odorants, to assess responsiveness of ONB cells to odorants. Odor responsiveness was induced in cells treated with a growth factor, while untreated cells did not respond to odorants. The calcium responses of treated ONB cells were similar to those found in olfactory receptor neurons.

Subsequent experiments using specific blockers of second messenger pathways indicated that mechanisms of odor transduction — the process by which information about odorant molecules is converted to electrical signals in neurons — in the treated ONB cells may be similar to those used by normal human olfactory neurons.

The results suggest that ONB cells do originate from olfactory tissue and may therefore be a useful model to study normal and abnormal cell biology of human olfactory neurons.

**Induction of differentiation of human olfactory neuroblastoma cells into odorant-responsive cells.**

G. Gomez, D. Restrepo, N. Rawson, L.D. Lowry (Thomas Jefferson University), W.M. Keane (Thomas Jefferson University) and J.L. Rothstein (Thomas Jefferson University). *Neuroscience*, 1996, 74, 567-577.

**Low Dietary  
Protein and  
High Salt  
Intake**

Several studies suggest a relationship between dietary protein levels and salt intake. To confirm this relationship and investigate its physiological basis, Dr. Okiyama and his collaborators fed diets with varying protein contents to rats and measured intake of a concentrated salt solution. Animals given low-protein diets consumed much greater amounts of salt compared to rats receiving adequate dietary protein.

Additional studies found that the elevated salt intake could not be explained by decreased sodium in the blood or by differences of body sodium balance. Levels of hormones known to affect salt intake were normal in rats fed the low-protein diets. Altered intakes of other components of the diet — such as fat, carbohydrate, or minerals —

incidental to its lowered protein content also were excluded as a cause of the high salt intake.

The authors conclude that the results cannot be accounted for by any of the major hypotheses that attempt to explain why rats ingest salt. They suggest that a novel physiological mechanism is responsible for the high salt intake of rats fed a diet low in protein. Future studies will attempt to identify and characterize this mechanism.

**Increased NaCl intake of rats fed low-protein diet.**

Atsushi Okiyama (Ajinomoto Company), Kunio Torii (Torii Nutrient-Stasis Project), and Michael G. Tordoff. *American Journal of Physiology*, 1996, 270, R1189-R1196.