[SQUEAKING]

[RUSTLING]

[CLICKING]

JOSH MCDERMOTT: We made it. It's the last lecture of the term. I hope everybody's hanging in there. I know it's a little bit of a hectic time. Today we're going to talk about the sense of smell and the sense of taste, which are fairly related. Scientific terms for that is olfaction and gustation.

So these are really interesting senses. They're kind of an important part of a lot of the things we care a lot about in life, but they're not nearly as well studied, especially in humans, as the other senses that we've been talking about so far. So we'll talk about the sense of smell and the sense of taste.

So the basic idea of smell is that there are odorants that are given off by substances in the world. So the term "odor" refers to the sensation of smell, and it's caused by an odorant. So an odorant is a molecule that produces the sensation of smell. So for a molecule to be smelled, the odorant has to be volatile. So it has to be able to float through the air. It's got to be small. It's got to be hydrophobic, repellent to water.

But not all such molecules can be smelled. So a famous example is carbon monoxide. So most people have carbon monoxide detectors or alarms in the places where they live because it's toxic, but it doesn't produce a smell. So you have to have an alarm that goes off. So we think these kinds of molecules were probably irrelevant when the odorant receptors evolved.

So the sense of smell, it's obviously pretty important to humans in a lot of respects. We use it to evaluate lots of things. For some animal species, it's sometimes their most important sense. So it's well known that animals can track odorant signals over very long distances. This is a really famous picture. I think this is from *National Geographic* from a long time ago, where there's a dog and a bird that was dragged across a field.

And the dog has some lights on its collar. So this is a time-lapse photo. So there's a yellow trace here that shows the path over which the bird was dragged across this field. And then the dog was trained to find animals, like in the context of hunting. And so you can see the track of the dog over time. And so it's following the scent trace back and forth.

So initially, it runs around until it finds some hint of the smell, and then it kind of is able to follow this. And so dogs are really good at this. And you've probably heard about this being done in the context of police work and stuff, and they've been doing this for millennia.

So animals do this a lot. People can do this to some extent. So this is kind of a crazy experiment that was done at UC Berkeley about 15 years ago, where they measured the ability of humans to track scents just using their noses. And so the way that they did this was-- it's inspired, obviously, by that classic photo of the dog, where there was a chemical that was kind of dragged across the field. That's the yellow line.

So I think they used the smell of chocolate or something. And then the person was given the task of following the scent. And so to make sure that they were only using their noses, they were blindfolded. And you can't really see this very clearly, but they're wearing earmuffs. And they're wearing these really thick mittens so they can't really feel anything.

So basically, all that they could do was move or crawl and smell. And then the red trace is the position of the person's body as they're moving over the field. So people are able to do this to some extent. A lot more slowly than dogs.

So the human olfactory apparatus resides in the nose. So the nose has a couple functions. It filters, warms, and humidifies the air that we breathe. So it's part of breathing. But it also contains olfactory receptors. And so the olfactory epithelium is a mucous membrane whose primary function is to detect odorants in the inhaled air.

So this is a face. That's the nose. Here's a cut through the nose that shows the various structures. So you have these cavities in here. You inhale. The air kind comes in, containing odorants. The olfactory epithelium contains receptors. The receptors interact with odorants, and that creates signals that are then sent to the olfactory bulb and then on to the cortex.

All right. So there's three types of cells in the olfactory epithelium. There's supporting cells that provide metabolic and physical support for the olfactory sensory neurons. There are basal cells, which are precursor cells to olfactory sensory neurons. So the olfactory sensory neurons are kind of constantly regenerating themselves. And there's the olfactory sensory neurons themselves. This is the main kind of cell type that does a lot of the work that you think of as smell.

So they're small neurons. They're located beneath a watery mucus layer in the epithelium. And then there are these cilia that kind of stick out that contain receptors. So you breathe in air. The air is wafting around here. It contains molecules. And then the molecules, in some way, are sensed by receptors on the cilia, and that changes the membrane potential in the olfactory sensory neuron. Yeah?

AUDIENCE: Is that what the brain eating amoeba target?

JOSH MCDERMOTT: Is that what, sorry?

AUDIENCE: The brain-eating amoeba.

JOSH MCDERMOTT: A brain-eating amoeba? Sorry, what about the brain-eating amoeba?

AUDIENCE: Are those what target?

JOSH MCDERMOTT: Are those what they target?

AUDIENCE: I don't know if you know.

JOSH MCDERMOTT: I didn't know about that, actually. They're supposed to target the olfactory receptor neurons?

AUDIENCE: I just wondered how they get in the brain.

JOSH MCDERMOTT: I see, I see. Could be. Yeah. I mean, this is-- I mean, these receptor neurons, they are kind of unusual in the sense that they're unprotected. So they're not behind anything. So the hair cells in your ear are kind of inside this bony thing. The photoreceptors are inside the eye. So these things are kind of just out there. So yeah, I guess they're vulnerable.

OK, so we got these cilia. There are these little things, kind of hair-like protrusions. And they contain the receptor sites for the odorant molecules. And the olfactory receptor is the region on the cilia where the odorant molecules bind. And so we'll talk in a second about how we think that works. Takes about seven or eight odor molecules binding to a receptor to initiate an action potential.

So there's a lot of things that are different about the sense of smell compared to the senses that we have talked about so far. One big difference is that smell is slow. So this is a graph that shows an example of that. So here's an experiment where the experimenter had an electrode next to or patch-clamped to this olfactory sensory neuron. Yeah, I guess it's a patch-clamp recording. You spritz odorant around the cilia of the olfactory sensory neuron, and then you measure the change in the membrane potential over time.

So you can see there at time 0, that's when the odorant is spritzed onto the cilia. And then there's a change in the response of the neuron. But the thing to notice here is the x-axis. So that's in seconds. So this change in the response has a time constant of five or six seconds. It's like an fMRI signal, which we think of as incredibly slow relative to neural activity. So smell is slow.

And it's slow, presumably in part because the signal itself is probably very smooth in time. So odorants are there in the air. And you can't just kind of instantly get rid of an odorant. So it's dependent on-- the stimulus is dependent on airflow, and that makes it temporally sluggish. And so that's probably why this is the way that it is.

So we got these olfactory sensory neurons with their receptors. And their axons go through this bony structure, called the cribriform plate. So it's a bone that's got all these holes in it that separates the nose from the brain. And this is the olfactory bulb where those signals project. So the consequence of this, because these receptors are just out there on the other side of this bone, is that you can lose your sense of smell if you get hit hard in the head.

So there's lots of reasons why you should try not to hit your head, but one of them is that if you hit your head in the right way hard enough, that bone, that cribriform plate, kind of gets knocked. And it can slice off the olfactory sensory neurons and can cause anosmia, a profound loss of smell, which also impacts the sense of taste. So as we're going to discuss later, smell is not important just for smell, but also because it combines with the sense of taste to create flavor when you're eating food.

So olfactory sensory neurons, they project to the olfactory bulb. It's about the size of a blueberry. It's just above the nose. It's where olfactory information is first processed. And there are two of them, one in each brain hemisphere corresponding to the left and the right nostrils. And the connections are ipsilateral. So in other words, the left nostril projects to the left olfactory bulb, and the right nostril projects to the right olfactory bulb.

So you've got two nostrils. They project to different bits of the brain. And they get odorant input from different parts of space. So this is showing a velocity field of the air around the nose. And so you can see that the two nostrils are getting most of their input from different regions of space.

So you might wonder, all right, what's that good for? We know that you benefit from having two ears. We've talked about how you benefit from having two eyes. What's the benefit from having two nostrils? Well, one measure of the effect of two nostrils came from this experiment of human scent tracking where, to investigate whether or not people use information from the two nostrils to help localize scents, they got rid of the two nostrils effectively, using what they call a nasal prism.

So a nasal prism is this thing that you stick into your nostrils-- so that goes in one nostril, that goes to the other-- and the input comes from a single aperture as opposed to-- this is the control apparatus where, again, you stick something up your nose. But now, the two nostrils are still getting input from two different regions of space.

And so the question is, well, if you're using the fact that the two nostrils are getting input from slightly different regions of space, that should show up in your ability to do stuff-- in this case, perform this scent tracking task. And that's what the results show. So these are two different measures of how well people could track scents across the grass.

So this one is showing the number of runs that were completed. So I guess sometimes people just gave up. They lost track of the scent or something. So that's the number of runs completed. And this is the control, where you have effectively two nostrils, and this is the nasal prism. So you don't make it through the path as many times.

And then this is how fast you can track scents. So meters per second squared. So the control is going about 24% faster than the people with the nasal prism. OK? All right. It kind of makes sense. Two nostrils. You have some ability to tell where smells are coming from. So that's part of the story.

But just not to take this too seriously. Humans are pretty slow compared to a lot of animals. So if you look at-- so this is showing-- I guess they had people do this over multiple days. And so people do get better at this. But this is the mean velocity in meters per second squared. And so the absolute numbers here are very, very low. So 0.05 meters per second squared. It's very, very, very slow. But you can do it to some extent.

So the olfactory bulb, an important structure in the processing of olfactory sensory information. The olfactory bulb contains these things called glomeruli. So these are these groups of cells that contain the axons of the olfactory sensory neurons of a particular type. And then the mitral cells are these output neurons that are contained within the olfactory bulb.

So you have all of these axons that accumulate in this one place. And then the mitral cell gets input from that. And these are all of a certain type of receptor. And then that goes on to the rest of the brain.

So the olfactory system is unusual relative to other senses in that it's the only one that doesn't go through the thalamus remember. So remember, the thalamus is kind of like this relay. And in vision, you go through the lateral geniculate nucleus. In hearing, you go through the medial geniculate nucleus. But smell doesn't do that. The olfactory bulb projects directly to the cortex.

So normally, we think of primary sensory cortex as this distinct region that's typically-- primary sensory cortex is typically defined as the region-- as the site of the first projections onto the cortex within that sensory system. So we have primary auditory cortex, primary visual cortex, primary somatosensory cortex we just talked about.

So primary olfactory cortex. It's defined in the same way, but it's a little bit different in that it's much less of a unified region. So it's different parts of the brain that we often associate with having different functions. So the amygdala, hippocampal complex, and entorhinal cortex, these are regions that classically are associated with emotion and memory. So there doesn't seem to be a dedicated primary sensory region for olfaction, unlike these other sensory systems, at least in humans.

So a lot is known-- OK, just to step back for a second, we just finished talking about the sense of touch. And so we talked about how, in the sense of touch, a lot of what we know is about the receptors. So half of that lecture was essentially about the different types of receptors and what differentiates them. And the same is true with olfaction.

So there's been a lot of work on understanding how the receptors work. And a lot is actually known about the genetic basis, which is pretty interesting. So Linda Buck and Richard Axel discovered that the genome contains about 1,000 different olfactory receptor genes, each of which codes for a single type of olfactory receptor.

And so what's really interesting is that, essentially, all mammals have pretty much the same set of these 1,000 genes. But not all of the genes are active. Some of them are non-functional what are called pseudogenes. And this varies a lot across species. So you have the same base set of genes that code for the set of possible receptors. But some species only have a small subset of them and others have more.

So in dogs and mice, which are organisms that we associate with having really exceptional senses of smell, there's only about 20% that are pseudogenes. So that would mean about 800 different unique receptor types. Whereas with humans, something like 60% to 70% are pseudogenes. So that leaves us with more like 300 or 400 receptor types. So not nearly as many receptors.

And these vary from person to person. So every person has a different number of these pseudogenes, and this results in individual differences in sensitivity to smells. There are certain smells that are kind of well known to elicit big individual differences in terms of how sensitive people are, cilantro being one that's especially well known.

So let's talk about how the receptors work. So there's been historically two main theories of how these receptors work. One is called shape-pattern theory. This is the current dominant biochemical theory for how receptors transduce odorants. So the idea here is that different scents-- depending on the compatibility of the odorant shape-- so the shape of the molecule and the shape of the receptor-- different scents activate different arrays of olfactory receptors in the olfactory epithelium.

So the various arrays produce specific firing patterns in the olfactory bulb, which determine the scent that we perceive. So this is, again, a very simplistic schematic where we're actually depicting the different odorants with these geometric shapes and the odorant receptors as having different shapes as well. And the idea is that some of the odorant shapes kind of fit into the odorant receptors and would then cause a response.

So here's, again, another kind of schematic of how this would work. So imagine that this is your olfactory epithelium. And you've got all of these different receptor types here. So here's one odorant. And here's another. Two different molecular shapes. And so this one can bind to those two receptors. And so you get this pattern of response in the olfactory epithelium. This one, because it could be oriented in different ways and has more complicated shape, could bind to these four. And so you'd get this pattern of response.

So that's the current kind of way that people think about this, is that based on the molecular shape, there's binding to particular types of receptors. And now there's this other theory that has been popular at various other times during history, which proposes that every perceived smell has a different vibrational frequency, and that molecules that produce the same vibrational frequencies will smell the same, and that there's some mechanism by which the receptor can measure the vibrational frequencies of the molecule.

And so this is something that was proposed a long time ago. 25 years ago, there was a scientist who became newly convinced of the merits of this theory and talked a lot about it, and it got a lot of attention, culminating in this paper here. So this paper is titled, "A psychophysical test of the vibration theory of olfaction." And it's by Andreas Keller and Leslie Vosshall.

Leslie Vosshall is a scientist who-- currently, she does a lot of work on mosquitoes. So she's interested in what makes mosquitoes like want to bite humans. And it's important because they spread malaria and things like that. And what attracts mosquitoes to humans involves the sense of smell. So she's always been interested in olfaction. I'll just read you the abstract.

So it says. "At present, no satisfactory theory exists to explain how a given molecule results in the perception of a particular smell. One theory is that olfactory sensory neurons detect intramolecular vibrations of the odorous molecule. We used psychophysical methods in humans to test this vibration theory of olfaction and found no evidence to support it." So that's the summary.

So then the intro here describes a little bit of the context. So it says, "A book about physiologist Luca Turin"-- who's this person who tried to revive this theory, "reviewed previously in this journal and elsewhere, has generated new interest in the theory that the smell of a molecule is determined by intramolecular vibrations rather than by the molecule's shape. Vibration theory was introduced in the 1930s and was later extended, but no biological mechanism to convert molecular vibrations into neuronal activation was proposed. As a result, the theory has been largely neglected in the research community.

In the 1990s, Turin proposed a transduction mechanism involving inelastic electron tunneling. Whether because of skepticism or scientific conspiracy, as alleged in the book and echoed in most reviews, his predictions have failed to generate empirical tests by other researchers. In the present study, we tested vibration theory's key psychophysical predictions."

So essentially, the predictions are that certain things ought to smell like certain other things based on the molecular vibrations. And that's described here. So it says, "Turin predicts that the smell of a mixture of guaiacol"-- some chemical-- "and benzaldehyde"-- some other chemical-- "has a vanilla character not found in its components because the combined molecular vibrations of benzaldehyde and guaiacol approximate the vibrations of vanillin" which is what smells like vanilla.

"To test this prediction, we asked subjects to rate the vanilla character of benzaldehyde, guaiacol, and a 1 to 1 mixture of both. Subjects were first familiarized with the individual stimuli at two different concentrations under non-blind conditions. In a subsequent test, vanillin at both concentrations was identified with an accuracy of 84%." So people were able to detect vanilla when it was actually there. OK. All right.

So then they were "familiarized with this 13-point rating scale. 1 means no vanilla, and 13 means extremely vanilla." So this is a vanilla rating task. "Subjects rated the vanilla character of the individual components and the two- and three-component mixtures, presented in random order."

OK. All right. So the results are shown here. So the bars here correspond to different odors, which are different combinations of vanillin, benzaldehyde, and guaiacol. And then the y-axis is plotting the vanilla rating from no vanilla to extremely vanilla. And so the vanilla on its own is rated as a 9. Pretty vanilla. OK. That's good. People are doing what they're supposed to do.

These two chemicals on their own get very low ratings of vanilla. That's what's expected, right? And so the key prediction here is that the combination of these two things ought to smell like vanilla. But instead, it's getting a rating of 2. So no evidence that it smells like vanilla. If you add vanilla to any of these mixtures, then people say it smells like vanilla. But without vanilla, they don't say it. OK?

OK. So this was an attempt to test this prediction. And they concluded that there's no evidence that this particular hypothesis is correct. All right. So that kind leaves us with this shape-pattern theory of olfactory receptors.

So another piece of evidence that's relevant to this is stereoisomers. These are molecules that are mirror-image rotations of one another. So they have different shapes, but they contain the same atoms, and thus vibrate at the same frequencies. But they can smell completely different.

So here's an example. These are two molecules. One of them smells like caraway. One of them smells like spearmint. So it's hard to know how you would explain that unless you have some mechanism that's based on shape. All right.

Another important aspect of our olfactory experience is adaptation. So the sense of smell is very responsive to changes. So think about walking into a bakery where they've made fresh bread. And when you walk in, the sense that there's fresh bread is very, very strong. But then, over time, that kind of dissipates.

Or you may know people who you think wear too much perfume. They presumably are not aware that they're wearing tons of perfume because they've adapted over time to the scent. So some adaptation is known to occur at the receptor level. So repeated exposure to an odorant causes the receptor to stop responding to the odorant or to respond less.

And you can measure this psychophysically. So this is kind of a cool experiment where human participants were given an odorant to take home and have in their house. So they lived with this particular odorant for two weeks, just some chemical that has a particular smell. And then periodically, over time, they were brought into the lab. And the experimenters measured their detection thresholds.

So the detection threshold for an odorant is the same as a detection threshold in some other modality. It's the concentration of the chemical that you need to have present for the person to be able to reliably detect it. And so you can measure that using the same kinds of psychophysical procedures that we've talked about repeatedly in this class.

OK. So this is a graph that shows the detection thresholds-- that's on the y-axis-- over time. So these are different test sessions. And they're measuring the detection thresholds for two odorants. One is the one that the people had to live with. So that's the black dots, the adapting odorant. The other one is just a control odorant that they were repeatedly tested on, but that they did not get repeated exposure to apart from the experiment.

And so the B1 and B2, those are baseline measurements. That's just when they brought them into the lab, before they sent them home with the scent. And then A1 and A2 are during the adaptation period, while the odor was in their home for those two weeks. And then the R1 through R4 is the recovery period. So that's when the odor was removed from the home. And they continued to test them, I think, once a week.

OK. So what does this show? Well, if we just look at what happens with the control odorant, you can see that the thresholds decrease over time. So with repeated tests, the detection thresholds drop. So it's like people get better at detecting the scent that they're repeatedly being tested on. So that's just what normally happens if you test somebody a whole bunch of times in a row.

And you can also see that in the baseline test, B1 and B2, the thresholds for the two odors are about the same. So the black and the white dots are pretty close. But then what you can see is that during the adaptation period-- this is when people are getting all this exposure to the adapting odorant-- the thresholds diverge. So the thresholds get substantially worse for the adapting odorant while they're kind of improving for the control odorant.

And then the other thing that's pretty cool is that once you remove the chemical from the person's home, it takes three weeks for the sensitivity to the adapting odor to reach the same level as the control odor. OK. All right. So the consequence of this repeated exposure to something is changing the way that the people smell. And it lasts a while. So this is just a fact about adaptation to odors. It's kind of interesting. Any questions about that?

OK. All right. So where does the adaptation happen? Well, there's evidence that it's happening at multiple stages. This is a graph that tries to get at this by measuring the extent to which adaptation transfers across nostrils. So remember, you've got two nostrils and two olfactory bulbs.

And so in this experiment, the participants were subjected to unilateral adaptation. So there was some odor that was squirted up into one of the nostrils. And what is being measured in the experiment, before and after the adaptation, is ratings of odor magnitude at different odor concentrations. So we expect that as we increase the concentration of the odorant-- so there's more of these molecules in the air-- the odor magnitude is going to go up with some shape.

And so the unadapted curve shows you the magnitude ratings for these odors just when you're not adapted. And then there are two conditions following adaptation. There's ipsilateral. So that means that you test people with the same nostril that has been adapted. So you squirt all this odor up into the left nostril, and then you test them for their odor magnitude on the left nostril. Then you can also test them on the right.

And so what you're supposed to take away from the graph is two things. The first is that both of those graphs, the contralateral and ipsilateral, are below the unadapted. So there's some transfer of adaptation across nostrils. The second is that the ipsilateral is lower than the contralateral. And so the inference from that is that there's some central component to the adaptation, as well as some more peripheral component, at a stage where the two nostrils are separated. Yeah.

AUDIENCE: Is it possible that during the adaptation, the molecules kind of traveled into the other nostril?

JOSH MCDERMOTT: Yeah. So this is one of the reasons why I think these experiments are challenging, is that I think the most likely possibility is that-- so the odorant is squirted into the nostril. But then the person is breathing in and out. And so you exhale, and then you inhale. And so as some consequence of that, there could be some leakage. Yeah.

So it's a little-- I don't know how to fully estimate the extent of that. And that's probably an asterisk surrounding the result. Yeah. Yeah. Yeah. These experiments are hard. Any other questions?

So another thing that really is important with olfaction is hedonics. So some smells are nice, and some smells are not so nice. It's natural to wonder, what is it that makes the smells that are nice nice, and what is it that makes the smells that are not nice, not nice? And in particular, you might wonder whether the hedonic responses that we have are innate or learned. And there's probably components of both.

So infant odor preferences, anecdotally, often seem to be very different from adults. There's also cross-cultural data that support associative learning. There's just all these examples that people know about of foods that, in some cultures, are considered to be delicacies. The example shown here is the Japanese food of natto. This is fermented soybeans that have a very, very strong odor. A lot of Westerners don't like the smell, but somebody who's from Japan, it's something that a lot of them enjoy, whereas a lot of the smell of cheese, which is something in the West that a lot of people enjoy, is considered disgusting by a lot of Japanese eaters.

So there are these differences between cultures that everybody has probably experienced. But there's also some pretty interesting evidence that there's components of the perception of odor pleasantness that are shared across cultures. This is a pretty cool paper that came out fairly recently from the lab of Asifa Majid, who was our colloquium speaker just a few weeks ago. She does a lot of interesting cross-cultural research.

And so what they did in this study is to test 10 different cultures that were quite diverse. Some hunter-gatherers and horticulturalists, as well as some people in the US and other places. And they had them smell a whole bunch of different odorants and then asked them-- and they asked them how pleasant they found the odors.

So this is a picture that kind of shows the places where they ran these experiments. So they did one in Mexico and one in the US and then a bunch of different places that are all kind of hard to get to. And so here are the results. So there were about 10 different odors that participants had to smell. 10 odorants. And in every different culture, there was some number of individuals. Every individual is a column here.

And the color is the ranking of the odor. So they ranked the odorants in order from most pleasant-- that's 1, that's in blue-- to least pleasant. And what you can see just from eyeballing it is vanillin is pretty blue across the board. So that's a smell that people generally like. And as you move up the plot, things kind of shift from being blue to being pretty red.

And so the gestalt that you're supposed to take away from this is that each of the 10 cultures has fairly similar rankings of the pleasantness of these odorants. All right. So there's supposed to be some universal component to the evaluation of odors. And where that comes from and why is debatable, probably because odors provide a signal for things that are toxic or potentially have bacteria that you want to stay away from. But this is some evidence that there's some shared component to pleasantness.

So that's the whirlwind tour of olfaction. Here's a summary of what we talked about olfaction. So the first thing is that there's lots of receptors. And I actually probably should have emphasized this a little bit more, which is that you can think of-- I mean, it's interesting to think about the number of different types of receptors that we have across the senses.

And so, in vision, at least in photopic conditions, you have three cones if you have normal color vision. By comparison, olfaction in humans has got 300 receptor types. Of course, there's no spatial information. Well, minimal, because you have two nostrils. So much less spatial information but many, many more receptor types. So the receptor the space of receptor activation is very, very high dimensional. So that probably really changes the problem of estimating odors and separating odors and things like that. So there's lots of receptors.

We believe that odorants bind to receptors based on molecular shape. The number of receptor types vary across species, again, in kind of the way that you would expect. So the species that we think have really exceptional senses of smell, that are very dependent on senses of smell, have more receptors.

The general structure of the system is that the receptors project to glomeruli in the olfactory bulb, which then projects to the cortex. We talked about how responses are slow. So that's a difference between the olfactory system and the other sensory systems that we've talked about. We have some ability to localize smells based on the fact that we have two nostrils. There are strong effects of adaptation that happen on multiple time scales, including some over weeks. And there are effects of culture that are superimposed on a shared sense of pleasantness.

OK. So gustation, or the sense of taste. All right. So here's the big picture. So when substances enter your mouth, either intentionally or unintentionally, molecules in the substances stimulate receptors in your tongue.

The standard view is that there are four main receptor types that correspond to four basic tastes-- salty, sour, bitter, and sweet. Knowledge of the receptors is still evolving, but again, the study of taste is still primarily centered on the receptors. And activation of these taste receptors couples with olfactory stimulation when you eat to produce flavor.

All right. So taste buds are embedded in papilla. These are bumps on your tongue. Each taste bud contains taste receptor cells. Information is sent to your brain via the cranial nerves. All right. That's the tongue. The tongue. All these nerves go up to your brain. Receptors are all over your tongue. Here's a picture that shows some of those taste buds.

OK. Here's a close up of a taste bud. So that's a taste bud. And there are lots of these receptors in a given taste bud. So you eat. There are molecules in the food. They bind to receptors in the microvilli. So again, things kind of like cilia. Another example of these cells that kind of have something sticking out of them. It's got receptors. So your taste buds, they don't last very long but are constantly replenished.

All right. So a tastant is kind of the analog of an odorant. So it's any stimulus that can be tasted. And we can divide tastants into two large categories. So some are made up of small charged particles, and those generally taste salty or sour. And in these cases, there are small ion channels within the microvilli that allow some types of charged particles to enter, but not others. And when those charged particles enter, it changes the membrane potential, and you have some sense that you've tasted something.

OK. Other tastants are perceived via G protein-coupled receptors, similar to those in the olfactory system, where we think it's a function of the molecular shape binding to the receptor. And these are cases where the molecules taste sweet or bitter. So two broad classes of particles and receptor mechanisms-- salty and sour, where the molecules are small and they're charged and they pass through ion channels, and then sweet or bitter, where the molecules tend to be larger and have complicated shapes that determine their binding to particular receptors.

So we're going to talk about each of these four types of receptors in turn. So salt is made up of two charged particles-- a cation with a positive charge and an anion with a negative charge. So here are some examples. So common table salt is sodium chloride. So sodium is the cation. Chloride is the anion. And the cation is the part that's responsible for the salty taste. So you eat some salt, and the sodium passes through an ion channel. You get enough of this inside the cell there's a change in the membrane potential.

So things that taste sour, by contrast, come from acidic substances. So generally, acidity is proportional to the concentration of hydrogen ions. And so the taste of something sour is produced by hydrogen. So there's two main ways for hydrogen to get inside the receptor cell, which is shown here. So there's ion channels that are selective for hydrogen. They can pass through that. Or they can make their way inside the cell membrane.

Either way, the sour taste is driven by the concentration of hydrogen inside the receptor. So salty and sour. Again, these small charged particles that pass into the receptor cell and change the concentration inside of it.

All right. Bitter. Many substances that taste bitter are poisonous. We often can't really distinguish between the tastes of different bitter compounds, at least not very well. They all just taste bad, at least at first. The kind of current view of bitterness is that we have about 25 different bitter receptors. They each respond to different molecules and different combinations of those molecules.

So the columns here are different receptors. The rows here are different things that taste bitter. And this indicates which of the receptors responds to which of these chemicals. Again, we believe this is a function of the molecular shape and what binds to what.

And so the thought here is that because a lot of the things that are bitter are poisonous, we evolved the ability to detect all these different types of molecules based on their toxicity, but it wasn't really important to be able to distinguish them. You just want to know that you're not supposed to eat it. So spit it out if you taste it.

And of course, in modern times, we leverage the fact that we have these bitter receptors when we cook. A lot of people actually like the taste of bitter. I like bitter things. But historically, that's presumably what they evolved for. All right. So that's bitterness.

We've also got things that are sweet. So things that are sweet typically contain sugar. So there's glucose, which is the main source of energy for most animals. There's also fructose and sucrose, common table sugar, which is a combination of glucose and fructose.

So in contrast to bitterness, we think that there's a relatively small number of receptors that's responsible for all of the perception of sweetness. And different sweeteners stimulate different parts of the receptors. And we think that artificial sweeteners kind of trick us by stimulating the receptor as well, even though they don't actually contain energy in the way that sugars do.

All right. So here's an example of one of these G protein-coupled receptors. So you've got a binding site here. And the sweet molecules kind of fit into the receptors and then initiate a process by which you detect the presence of the molecule.

All right. So like I said, we think that taste is a system for detecting nutrients and antinutrients. We think the sense of bitter probably is useful for signaling poisons. Sour is probably important for detecting acidic solutions that might harm the body. Sweet and salty are important because our bodies need sodium and sugar to survive.

And you can again look at infants to get a little bit of a window into this. So infants' behavior and facial expressions reveal apparently innate preferences for certain kinds of foods or certain kinds of tastes. So you give a baby something sweet, and they make a facial expression indicate indicating a positive response. Give them something sour, they'll purse their lips. Bitter things will tend to cause them to spit things out.

All right. So four main tastes, different kinds of receptors. How many people have heard of the possibility of a fifth taste? Yeah. OK. So this is kind of well known at this point, umami. So monosodium glutamate, or MSG, is a chemical that's often added to Asian food. It kind of got a bad rap, at least in the United States, as far as I can tell, unjustly. It's derived from natural sources and I don't think is actually associated with any health risks.

And it makes things taste savory. So umami is the taste of things that are savory. And we believe that this is a function of glutamate. So glutamate is an important neurotransmitter. It's used throughout the brain. And so the general thinking is that glutamate receptors have been co-opted to augment the sense of taste. And you have foods that are high in glutamate, and that contributes to that sense of taste that you get for certain kinds of savory foods.

So that's the deal with the receptors. The taste pathway is shown here. So the input from the taste receptors is carried up the cranial nerve to part of the thalamus. The thalamus projects to gustatory cortex, which lives in a part of the brain called the insula, which projects to the orbitofrontal cortex.

So the insular cortex is the primary cortical processing area for taste. Again, that's where the taste input kind of first projects. Orbitofrontal cortex is in the frontal lobe, like it sounds. Receives projections from insular cortex, and it's involved in a whole bunch of stuff, including the sense of taste.

And again, in contrast to what is known about other sensory systems in terms of what goes on in the cortex, we know much less, especially in humans, about cortical processing of smell and taste. Just a little bit about the pathways.

So the other thing that's really cool about the sense of smell is its role in flavor. So anytime you eat something, the molecules in the food, they stimulate the taste receptors. But really, you've got maybe four or five types of taste receptors. So four or five dimensions of the response of the tongue, more or less.

But in addition, as you're chewing the food, odorants are emitted by the stuff you're chewing, and they travel through the back of your throat and stimulate the olfactory epithelium. This is called retronasal olfaction. Through the retronasal passage. And so that's a huge component of flavor.

So retronasal olfactory sensation. It refers to the sensation of an odor that is perceived when chewing or swallowing food force an odorant in the mouth up behind the palate into the nose. And so the really interesting thing is that these odor sensations are perceived as originating from the mouth, even though the actual contact of the odorant and the receptor occurs in the nose at the olfactory mucosa.

And so flavor is the combination of what people refer to as true taste-- so sweet, salty, sour, bitter, maybe umami-- and then retronasal olfaction. And if you've ever had a cold and noticed that the food just doesn't quite taste as interesting, you will have seen the role of retronasal olfaction in flavor, which is really significant. So when you have a cold and your nose is stuffed up, you're missing that component. And so the sense of taste gets greatly impoverished.

So you might wonder, what happens when we can't perceive taste but can still smell? So there are, again, patient cases that give some insight into this. So there have been patients where the taste nerves are damaged, but they have normal olfaction. And so in this particular case, the person could smell lasagna, but there was no flavor. So they would eat the lasagna, and it wouldn't taste like anything.

And so you can do something similar in the lab, by anesthetizing the relevant nerves with lidocaine. So this is a branch of the cranial nerve that carries taste information from the anterior tongue. And you retain the ability to smell, but you don't get that sense of flavor.

So somehow or another, the brain processes odors differently depending on whether they're coming from the nose or the mouth, even though it's the same receptors that are being stimulated. So presumably there's some process by which the stimulation of the taste receptors kind of integrates with the input from the olfactory receptors. And that gives you the sense of flavor.

All right. So here's the big picture of gustation. Molecules stimulate receptors in the tongue. The standard view is that there are four receptor types that correspond to four basic tastes-- salty, sour, bitter, and sweet. Remember, with salty and sour, they're driven by small charged molecules that pass through ion channels and change the concentration inside the receptor. Bitter and sweet have receptors that are selective for the molecular shape, so particular kinds of molecules can bind to them.

In the case of bitter, we've got a large set of receptors. We don't really differentiate the responses, at least not very much. In the case of sweet, there's a smaller number of receptors, and different types of sugars can bind to different parts of receptors. And artificial sweeteners can trick our sense of taste by binding to those same receptors.

So the knowledge of the receptors is still evolving. That's kind of what we know right now. And then activation of the taste receptors couples with olfactory stimulation to produce flavor. All right. So that's the whirlwind tour of taste.

So as I said, taste and smell, they're really interesting and important for life. And we don't know nearly as much about them as we should. And they would be fun things, I think, for someone to go make a career in. But there's, at present, not a whole lot of people who study these two modalities. The end.

So this brings us to the conclusion of 9.35. And it's been great having all of you in class. I appreciated all of the questions. And I hope that this inspires you to learn more about perception. And if you're around next year, please drop by and tell me how you're doing. If you're a graduating senior, congratulations. Wish you all the best on your next endeavors. And I'll leave it at that.