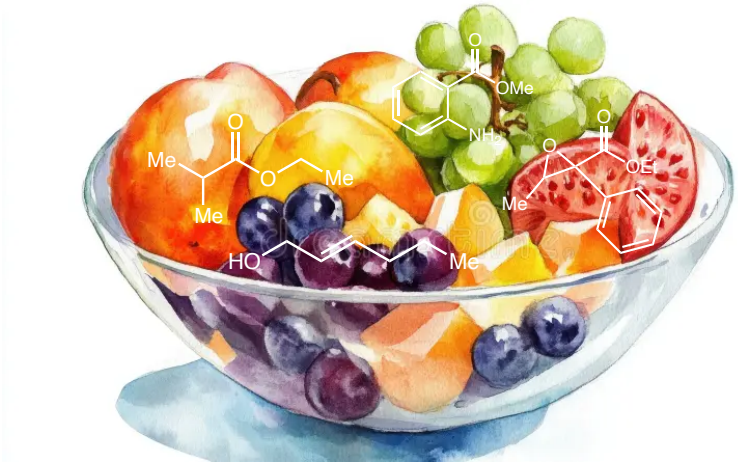
Food Additives:
Flavorings and Sweeteners



Eva Lin

Literature Talk

May 9th, 2025

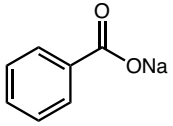
What are food additives?

Food additives as defined by the FDA:

A food additive is defined in Section 201(s) of the FD&C Act **as any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristic of any food.**

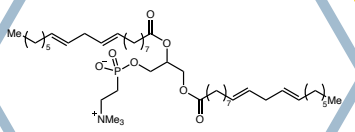
Categories of food additives

Preservatives



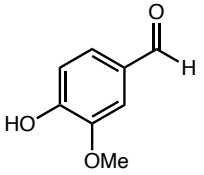
Benzoates

Emulsifiers + Stabilizers



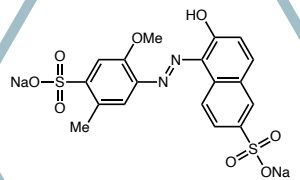
Lecithin

Flavoring agents



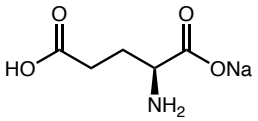
Vanilin

Colorants



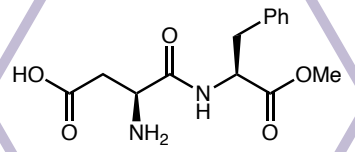
Red 40

Flavor Enhancers



MSG

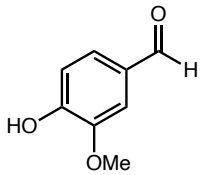
Sweeteners



Aspartame

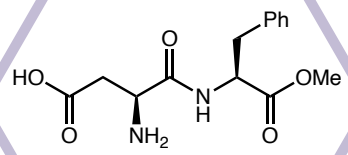
Categories of food additives

Flavoring agents



Vanilin

Sweeteners



Aspartame

Outline of Talk

What is flavor?

Flavorings

Sweeteners

Health Concerns

Outline of Talk

What is flavor?

Flavorings

Sweeteners

Health Concerns

The basic senses

Sight

Hearing

Touch

Smell

Taste

The basic senses

Chemical senses

Triggered by direct interactions with specific molecules

Smell

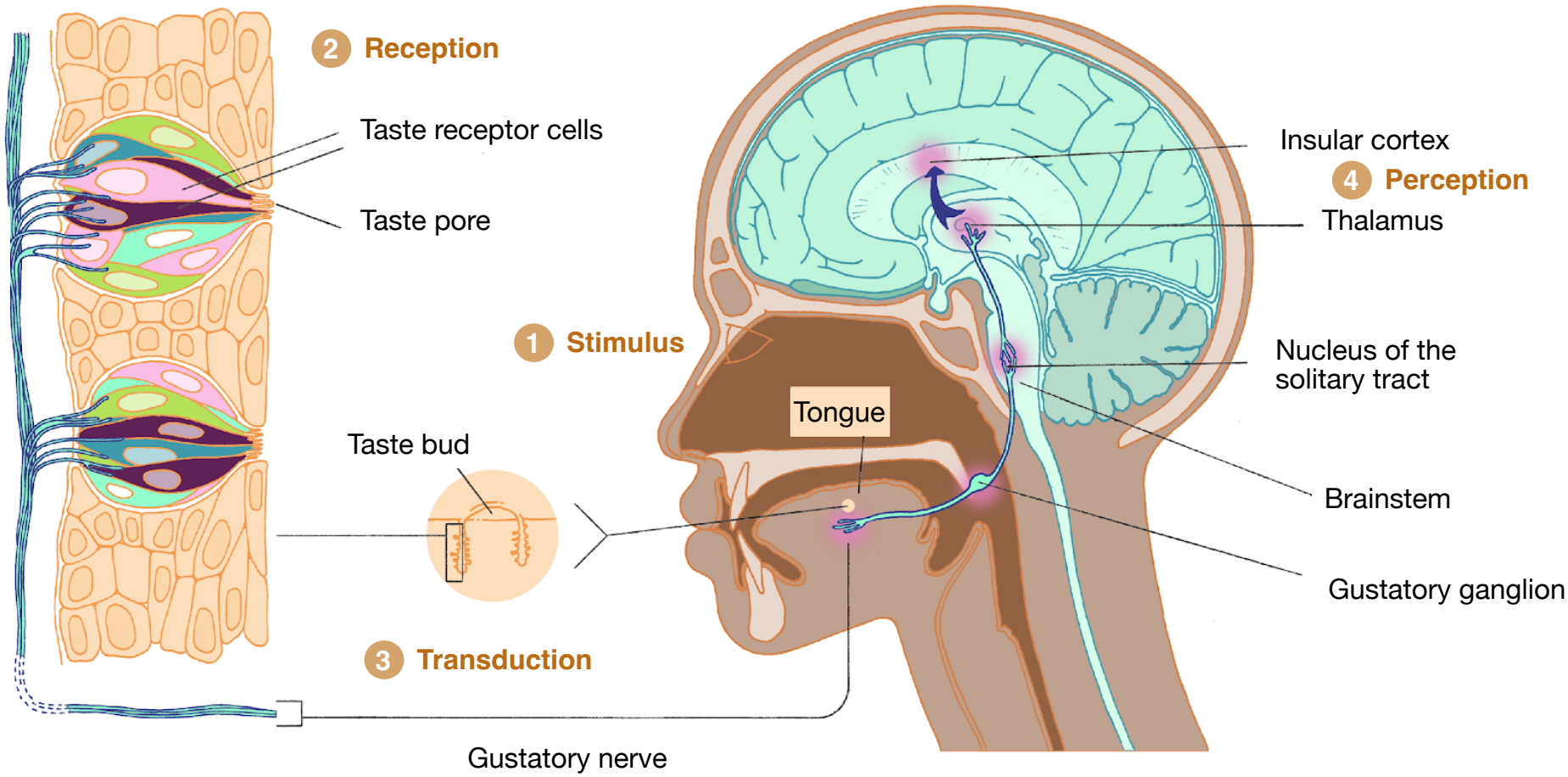
Organ: Nose (olfactory epithelium in the nasal cavity)
Stimuli: Volatile molecules

Taste

Organ: Tongue and parts of the oral cavity (taste buds on papillae)
Stimuli: Dissolved chemicals in food and beverages

The sense of taste

The **gustatory system** is the sensory system responsible for detecting and processing taste

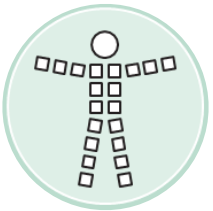


Gravina, S. A.; Yep, G. L.; Khan, M. **2013**, *33* (3), 217–222.

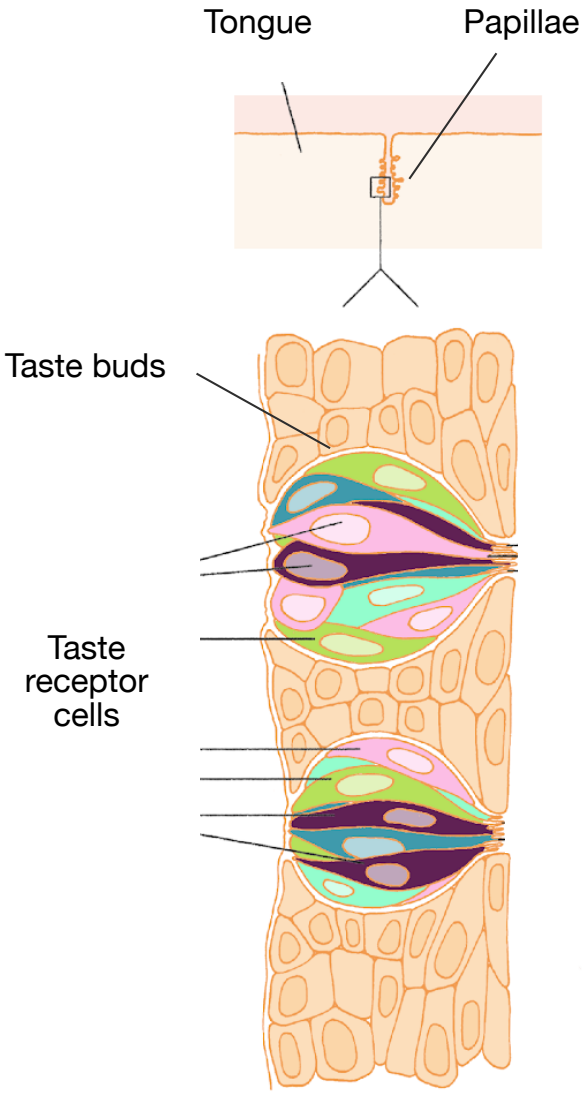
The basic tastes and their functions

Flavor = Taste + Smell

- **Taste** (gustation): sour, sweet, bitter, salty, umami
- **Smell** (olfaction): detects volatile compounds in the nose

Sweet	Umami	Sour	Bitter	Salty
				
Ensures intake of carbohydrates for energy	Ensures intake of proteins for energy	Prevents intake of toxic substances	Prevents intake of toxic substances	Maintain electrolyte balance

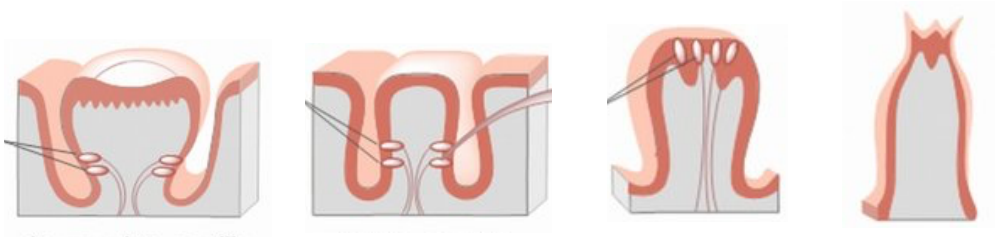
Taste buds



Papillae

Visible bumps located on the surface of the tongue

Four major types of papillae
Different number and functions



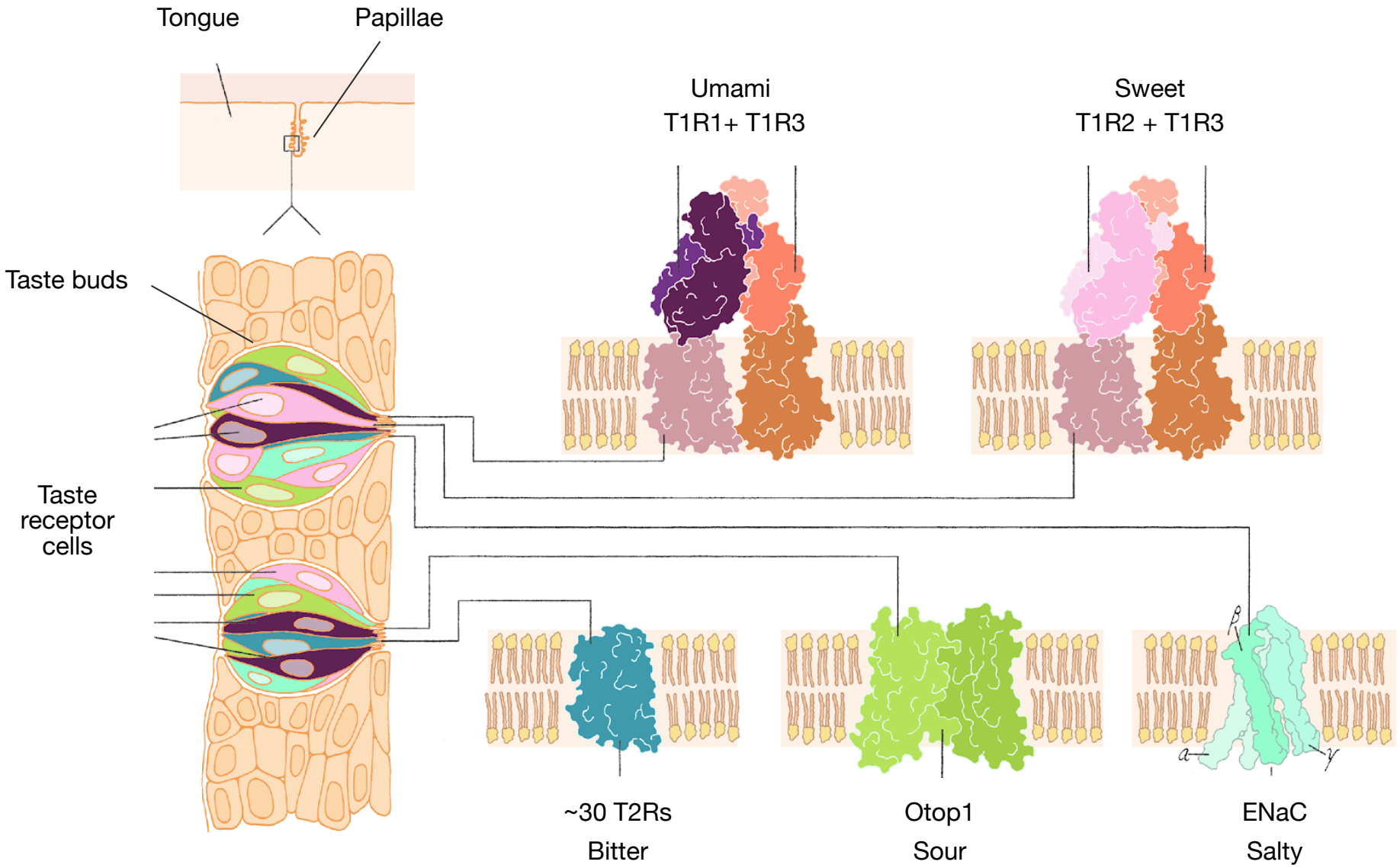
Circumvallate Foliate Fungiform Filiform

Up to 10,000 taste buds
Each contain 50-100 taste receptor cells (TRCs)

3 main types of TRCs: Type I, II, and III transduction mechanism to identify a taste

Ahmad, R.; Dalziel, J. E. *Front. Pharmacol.* **2020**, *11*, 587664., Luo, L. *Principles of Neurobiology*; Garland Science, 2015

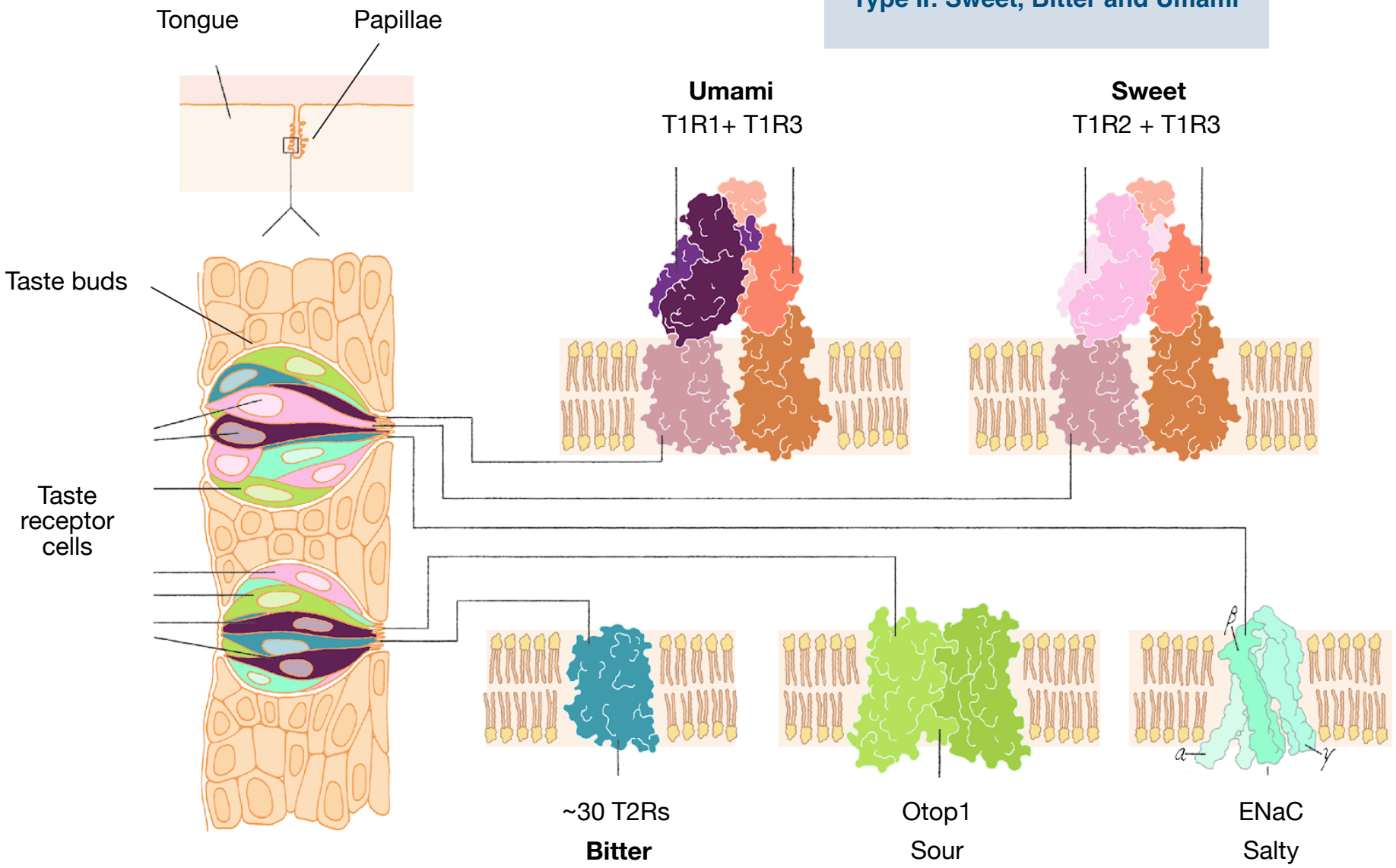
Taste receptor cells



Ahmad, R.; Dalziel, J. E. *Front. Pharmacol.* **2020**, *11*, 587664., Luo, L. *Principles of Neurobiology*; Garland Science, 2015

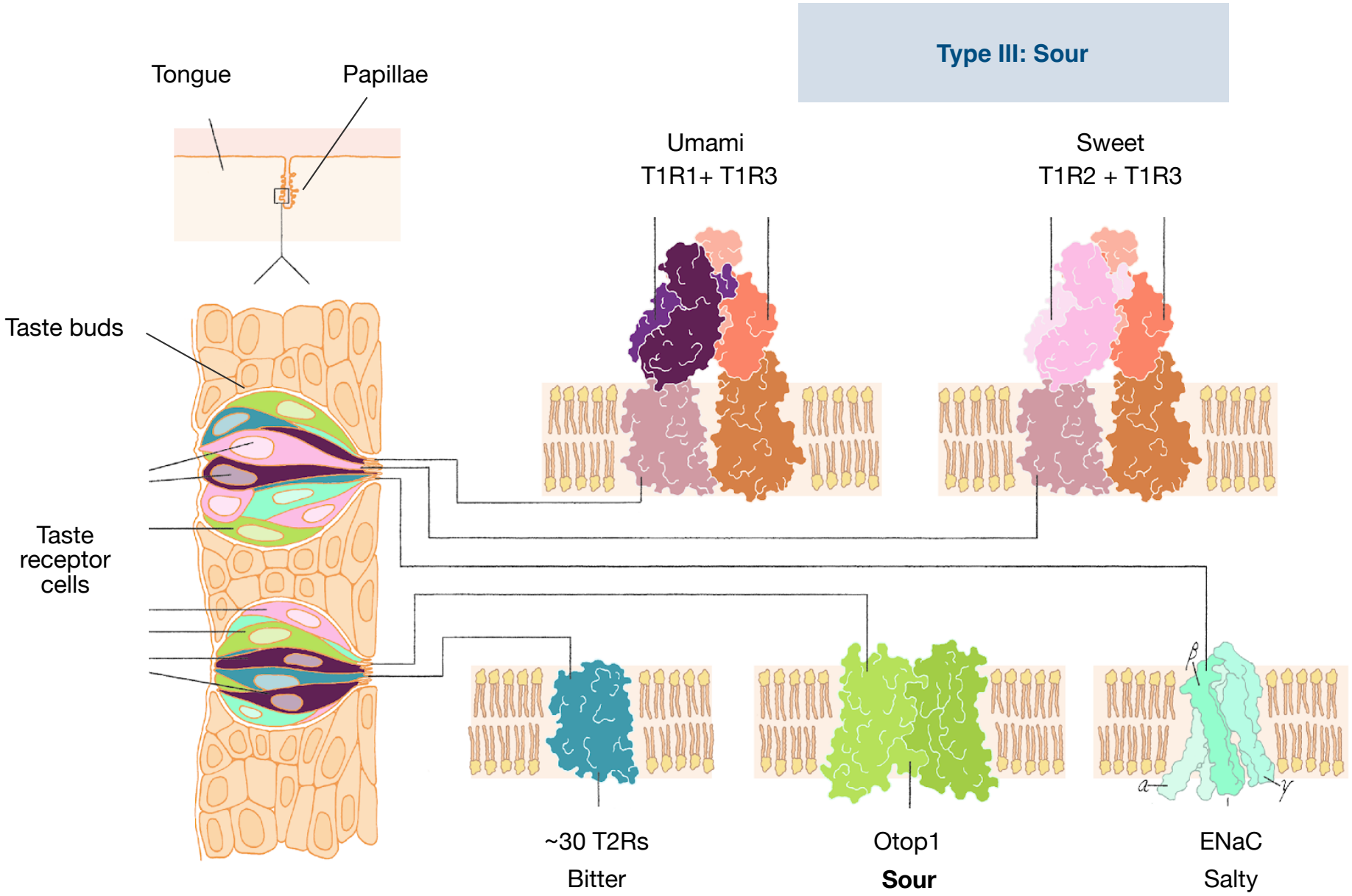
Taste receptor cells

Type II: Sweet, Bitter and Umami



Ahmad, R.; Dalziel, J. E. *Front. Pharmacol.* **2020**, *11*, 587664., Luo, L. *Principles of Neurobiology*; Garland Science, 2015

Taste receptor cells



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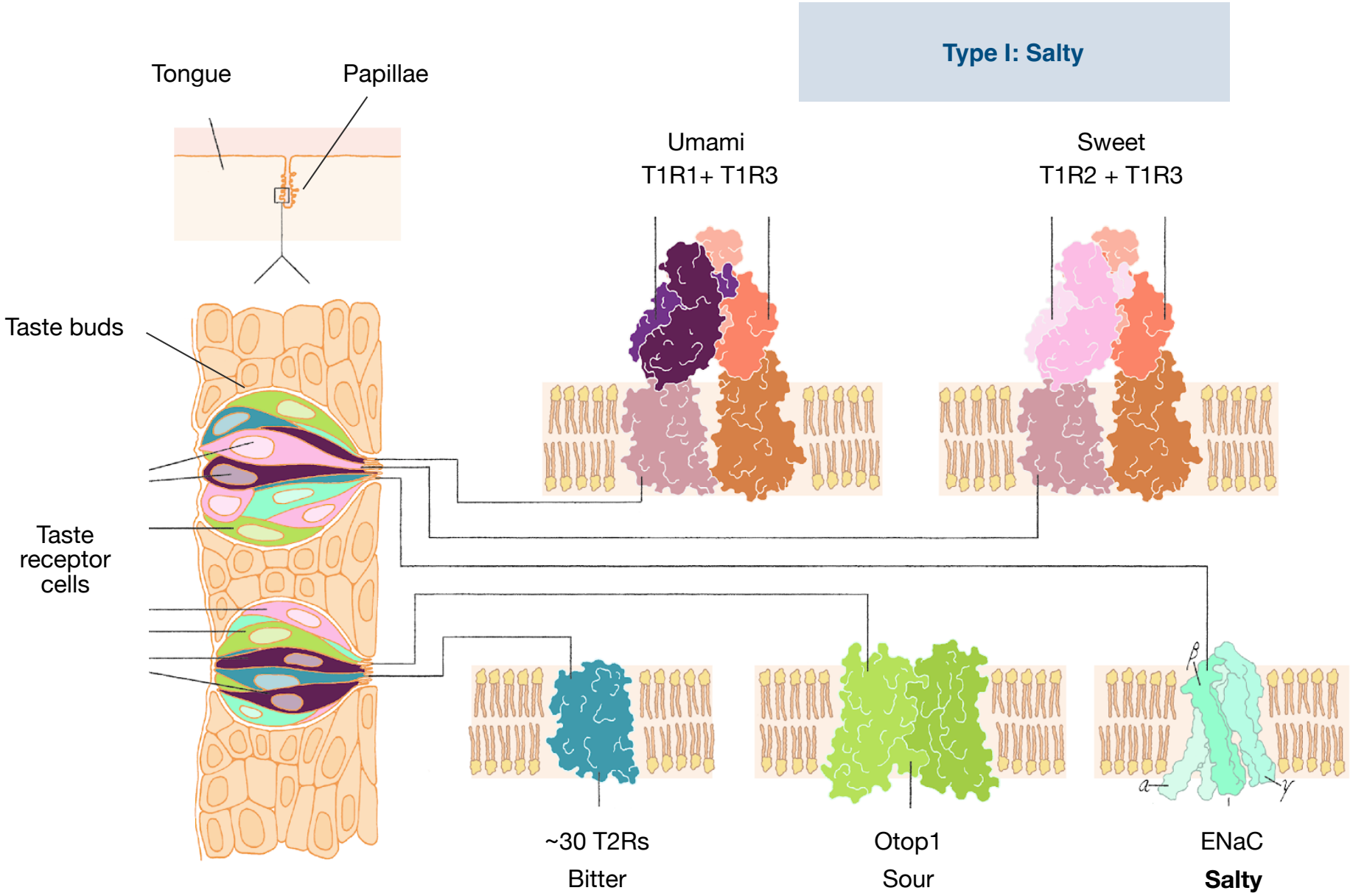
Taste receptor cells



Ahmad, R.; Dalziel, J. E. *Front. Pharmacol.* **2020**, *11*, 587664., Luo, L. *Principles of Neurobiology*; Garland Science, 2015

Outline of Talk

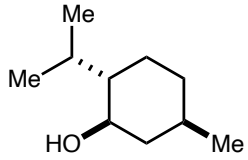
What is flavor?

Flavorings

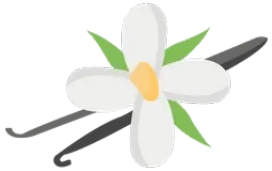
Sweeteners

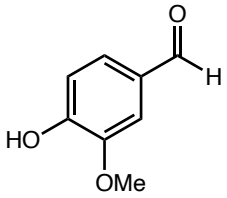
Health Concerns

Common chemicals that flavor foods

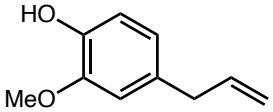


Menthol

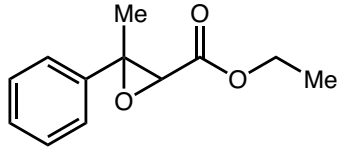




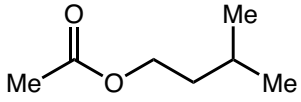
Vanillin



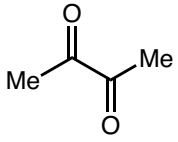
Eugenol



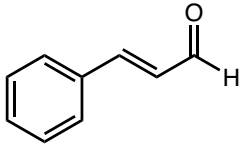
“Strawberry aldehyde”



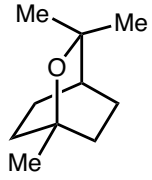
Isoamyl acetate



Diacetyl



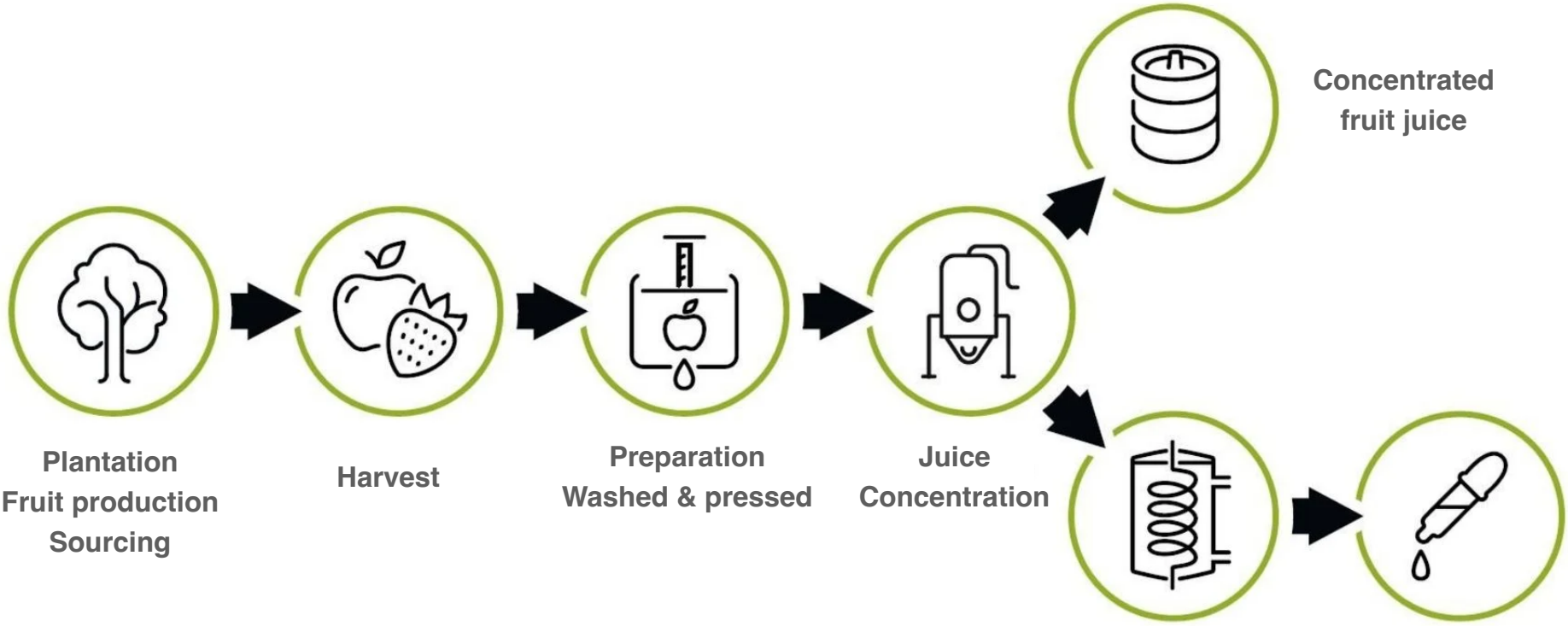
Cinnamaldehyde



Eucalyptol

Differences between artificial, natural, and other added flavors

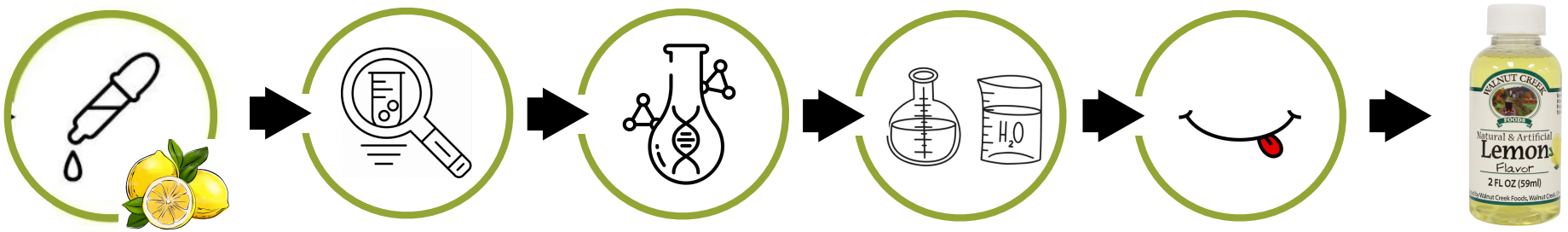
Sources of natural flavors- From the named fruit (FTNF) flavors



Ohloff, G.; Flament, I.; Pickenhagen, W. *Food Reviews International* **1985**, *1* (1), 99–148.

Differences between artificial, natural, and other added flavors

Development of artificial flavors



Natural flavors **Chemical analysis**

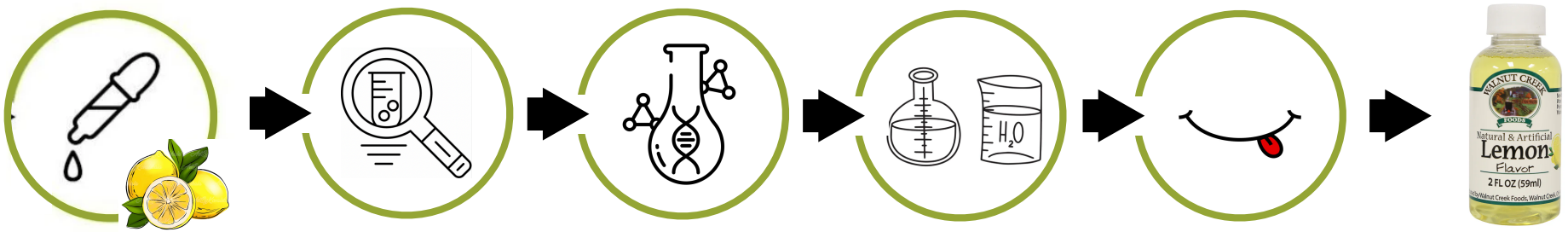
- GC-MS (volatile compounds)
- GC-O (identify key aroma compounds)

Hojjati, M.; Barzegar, H.; *Nutr Food Sci Res* **2017**, *4* (4), 15–24, Shukla, P.; Akshay S; Ashok S.; *MOJ Biorg Org Chem* **2017**, *1* (3)

Differences between artificial, natural, and other added flavors

Development of artificial flavors

- Natural lemon contains over 100 volatile compounds, but not all of them contribute equally to its aroma or taste.
- Around 10–20 key aroma-active molecules account for most of what we *perceive* as “lemon.”



Natural flavors | **Chemical analysis** | **Identification & synthesis of key compounds**

Hojjati, M.; Barzegar, H.; *Nutr Food Sci Res* **2017**, *4* (4), 15–24, Shukla, P.; Akshay S; Ashok S.; *MOJ Biorg Org Chem* **2017**, *1* (3)

Differences between artificial, natural, and other added flavors

Development of artificial flavors

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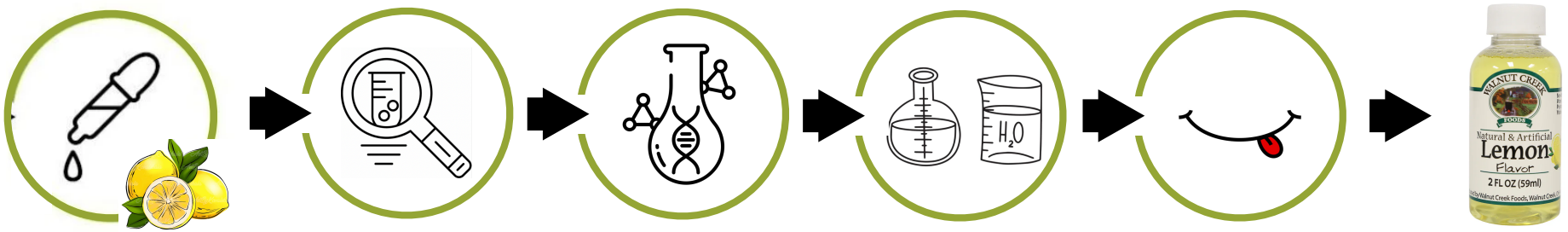
- Around 10–20 key aroma-active molecules account for most of what we *perceive* as “lemon.”

Formulation is largely a trial-and-error method of chemical analysis done in a lab.

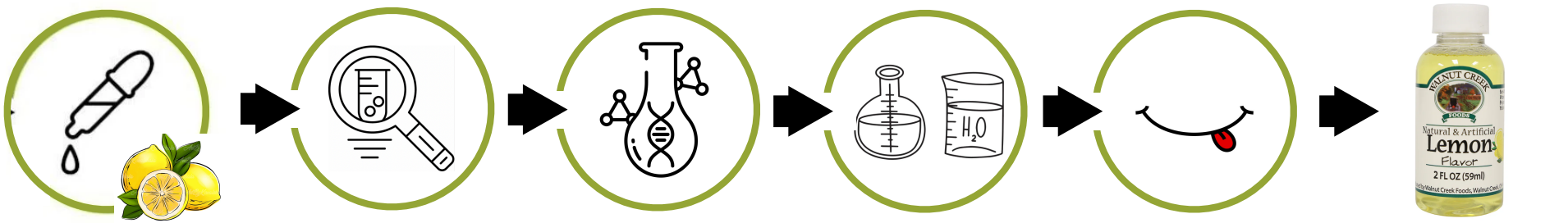


Natural flavors → **Chemical analysis** → **Identification & synthesis of key compounds** → **Formulation**

Hojjati, M.; Barzegar, H.; *Nutr Food Sci Res* **2017**, *4* (4), 15–24, Shukla, P.; Akshay S; Ashok S.; *MOJ Biorg Org Chem* **2017**, *1* (3)

Differences between artificial, natural, and other added flavors

Development of artificial flavors

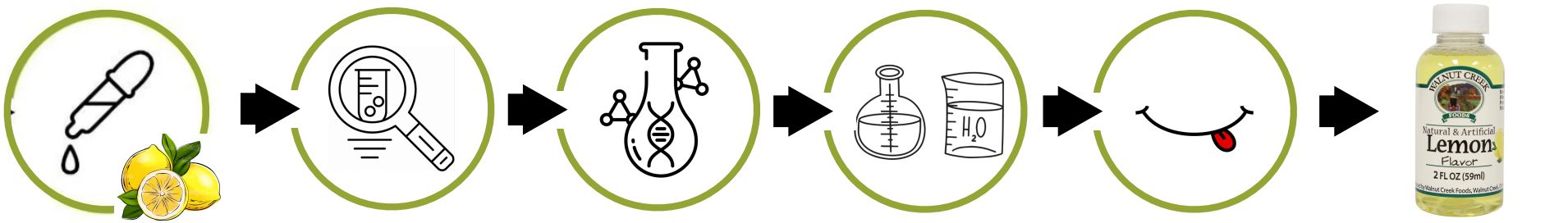


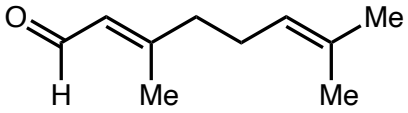
Hojjati, M.; Barzegar, H.; *Nutr Food Sci Res* **2017**, *4* (4), 15–24, Shukla, P.; Akshay S; Ashok S.; *MOJ Biorg Org Chem* **2017**, *1* (3)

Differences between artificial, natural, and other added flavors

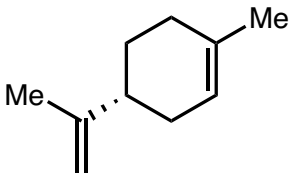
Development of artificial flavors

A convincing artificial lemon flavor can be recreated with 5–10 compounds

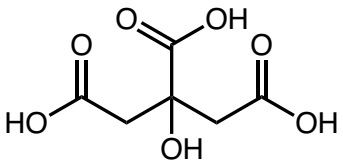




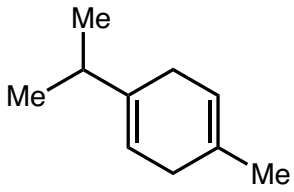
Citral
Strong lemon scent



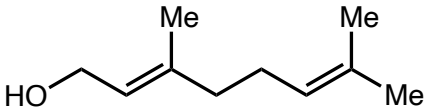
Limonene
Citrusy scent



Citric acid
Sour taste



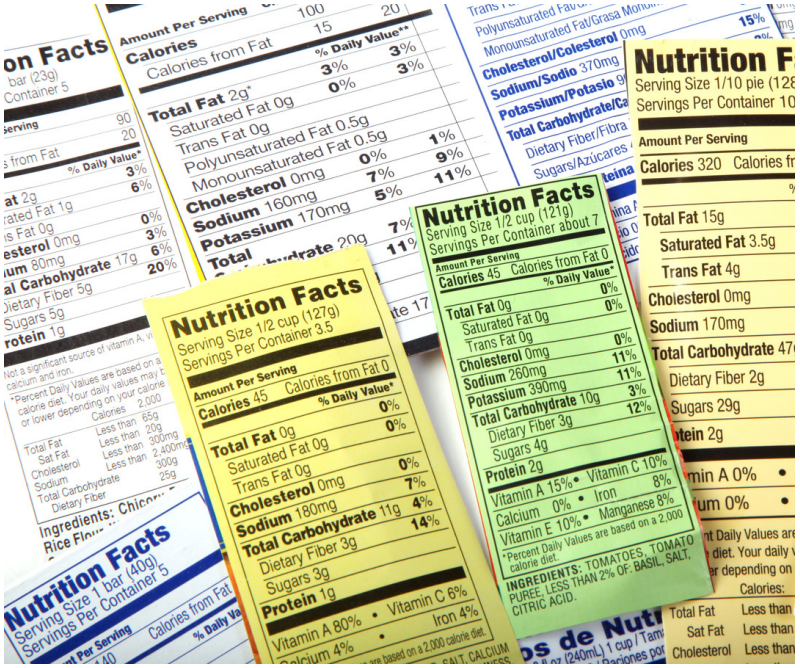
γ-Terpinene
Herbal notes



Geraniol
Floral, citrusy

Hojjati, M.; Barzegar, H.; *Nutr Food Sci Res* **2017**, *4* (4), 15–24, Shukla, P.; Akshay S; Ashok S.; *MOJ Biorg Org Chem* **2017**, *1* (3)

Understanding flavor labeling



The FDA does not require flavor companies to disclose the individual ingredients of their flavors as long as they've been deemed Generally Recognized As Safe **(GRAS)**.

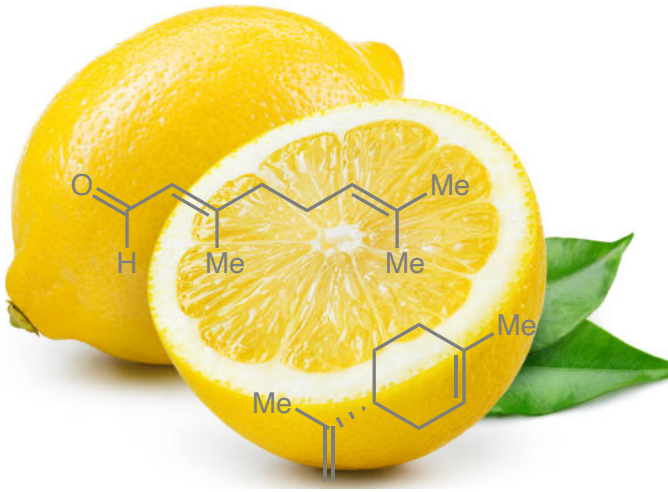
a single flavor can contain 50 to 100 compounds

label to simply disclose whether artificial and/or natural flavors have been used in the product.

21 CFR Part 101.22

Understanding flavor labeling

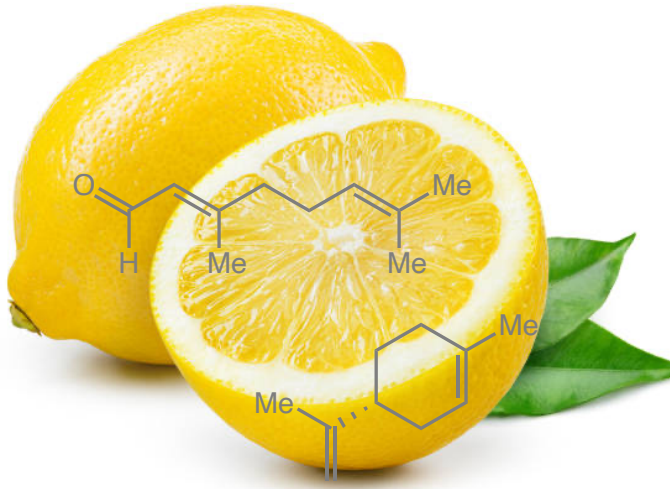
Natural flavor type	*Example*	*Relative cost*
1 Natural lemon flavor FTNF • FTNF stands for “from the named fruit” • All flavor ingredients directly from a lemon	🍋	**$$$+**



21 CFR Part 101.22

Understanding flavor labeling

Natural flavor type	*Example*	*Relative cost*
1 Natural lemon flavor FTNF • FTNF stands for “from the named fruit” • All flavor ingredients directly from a lemon	🍋	**$$$+**
2 Natural lemon flavor WONF • WONF stands for “with only natural flavors” • Contains any amount of a flavor ingredient from lemon (ex. Citric acid) + flavors from other natural sources	🍋 🍊 🌿	**$$$**



21 CFR Part 101.22

Understanding flavor labeling

Natural flavor type	*Example*	*Relative cost*
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2 Natural lemon flavor WONF • WONF stands for “with only natural flavors” • Contains any amount of a flavor ingredient from lemon (ex. Citric acid) + flavors from other natural sources		**$$$**
3 Natural-type flavor for lemon • All flavor ingredients from natural sources, but not necessarily derived from a lemon • ex. citral extracted from lemongrass		**$$**

21 CFR Part 101.22

Understanding flavor labeling

Flavor type	***Example***	***Relative cost***
1 Artificial vanilla flavor • Made from synthetic ingredients, often petrochemicals • Often contain other additives (preservatives, colorants)		**<$**

Understanding flavor labeling

Flavor type	*Example*	*Relative cost*
1 **Artificial vanilla flavor** • Made from synthetic ingredients, often petrochemicals • Often contain other additives (preservatives, colorants)		**<$**

Madagascar vanilla pods (~2% vanillin)

Dried, cured, and extracted for the production of vanilla extract

USD 600/kg

Synthetic vanillin

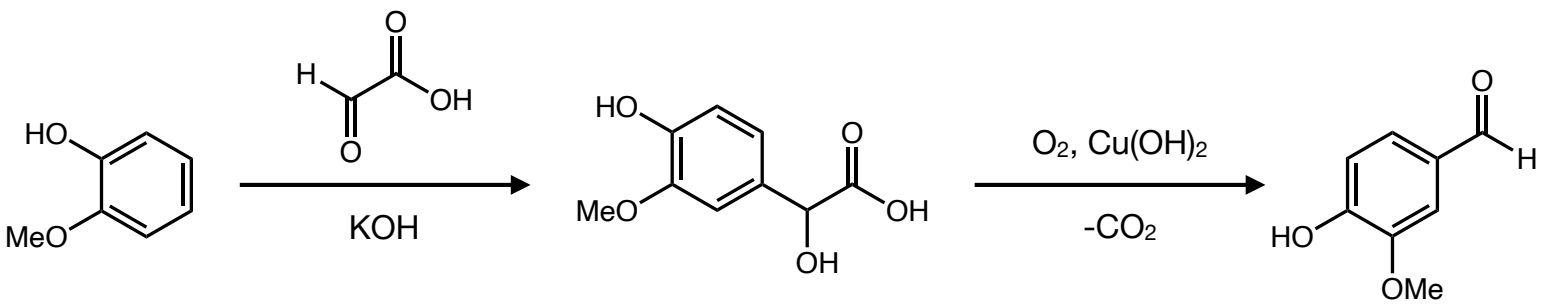
"nature-identical" flavoring

USD 10-22/kg

21 CFR Part 101.22

Synthetic vanillin

Riedel process: accounts for 85% of total production of synthetic vanillin



guaiacol

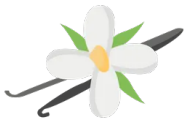
(Petrochemical)

vanillylmandelic acid

vanillin

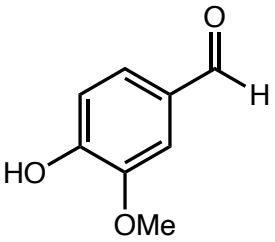
D'Arrigo, P.; Rossato, L. A. M.; Strini, A.; Serra, S. *Molecules* **2024**, *29* (2), 442.

Understanding flavor labeling

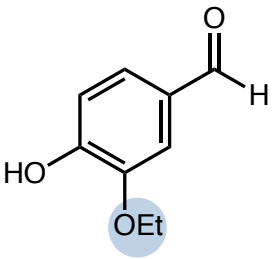
Flavor type	***Example***	***Relative cost***
1 Artificial vanilla flavor • Made from synthetic ingredients, often petrochemicals • Often contain other additives (preservatives, colorants)		**<$**
2 Natural and artificial vanilla flavor • Flavor ingredients contain any amount from natural vanilla source and other unnatural sources	 	**$**

Modifications to nature-identical compounds

Non-nature identical flavor:
Artificial flavors that are not based on a natural compound



Vanillin



Ethyl vanillin

3–4× stronger *than natural vanillin*

Ethyl vanillin vs. vanillin:

- Ethyl vanillin has **a higher LogP** (~1.6) than vanillin (~1.2)
- Enhanced binding to hydrophobic pockets in olfactory receptors
- Ethyl vanillin has a lower odor threshold, requiring smaller amounts to achieve the same sensory effect as vanillin

It delivers a more intense, longer-lasting vanilla aroma, making it especially valuable in flavor formulations.

Shukla, P.; Akshay S; Ashok S.; *MOJ Biorg Org Chem* **2017**, *1* (3), Zhang, H.; Zhang, K.; Yu, M.; Guo, J.; Xu, S.; Wang, Y. *Journal of Molecular Liquids* **2022**, *365*, 120059.

The evolution of food flavor analysis

Ji, H.; Pu, D.; Yan, W.; Zhang, Q.; Zuo, M.; Zhang, Y. *Trends in Food Science & Technology* **2023**, *138*, 738–751.

The evolution of food flavor analysis

Human evaluation and empirical methods to assess appearance, aroma, flavor, texture, sound etc.

Ji, H.; Pu, D.; Yan, W.; Zhang, Q.; Zuo, M.; Zhang, Y. *Trends in Food Science & Technology* **2023**, *138*, 738–751.

The evolution of food flavor analysis

Chromatographic techniques such as GC, LC, IMS, FIDs, and TCDs emerging as the predominant methods.

Ji, H.; Pu, D.; Yan, W.; Zhang, Q.; Zuo, M.; Zhang, Y. *Trends in Food Science & Technology* **2023**, *138*, 738–751.

The evolution of food flavor analysis

GC–MS, GC-O, and Odor Activity Values (OAV). These methods not only qualified and quantified flavors but also provided molecular-level descriptions.

Ji, H.; Pu, D.; Yan, W.; Zhang, Q.; Zuo, M.; Zhang, Y. *Trends in Food Science & Technology* **2023**, *138*, 738–751.

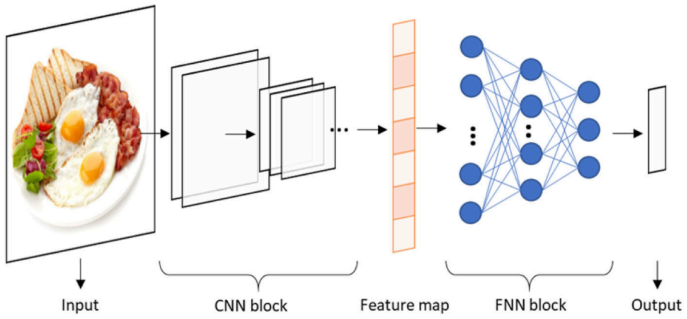
The evolution of food flavor analysis

“Flavor Engineering 4.0 era”
ML models to predict and regulate, and develop flavors.

Ji, H.; Pu, D.; Yan, W.; Zhang, Q.; Zuo, M.; Zhang, Y. *Trends in Food Science & Technology* **2023**, *138*, 738–751.

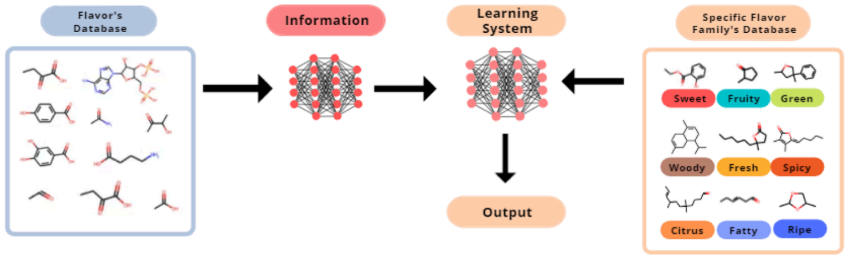
Examples of artificial intelligence in flavor engineering

Deep Learning



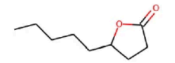
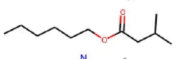
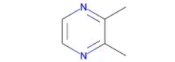
food recognition, calorie estimation, quality detection

Scientific Machine Learning (SciML)



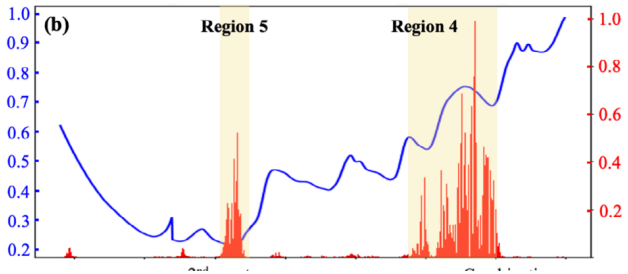
molecular design for flavor-based product development

Quantitative Structure-Odour Relationship (QSOR) model + ML

Molecular structure	Odor descriptors
	Buttery; Coconut; Creamy; Oily; Sweet.
	Apple; Fruity; Green; Sweet.
	Cocoa; Coffee; Nut; Potato; Roasted.
...	...

predict wine aroma

Deep Learning + Machine Learning

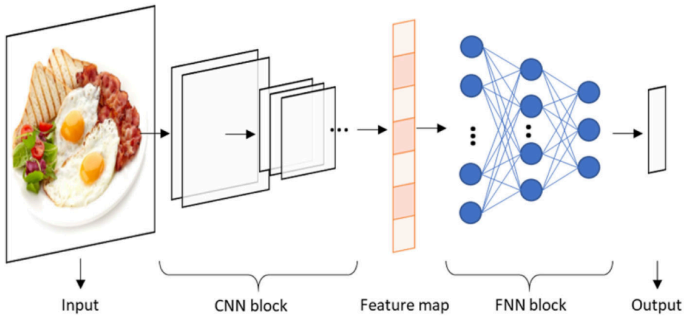


predict the flavors of specialty coffee

Queiroz, L. P.; Nogueira, I. B. R.; Ribeiro, A. M. *Food Research International* **2024**, *196*, 115100.

Examples of artificial intelligence in flavor engineering

Deep Learning



food recognition, calorie estimation, quality detection

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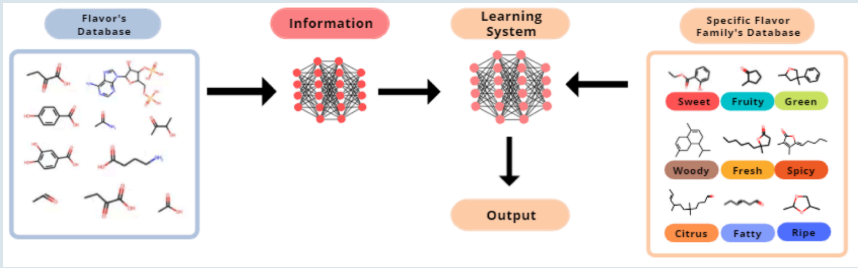

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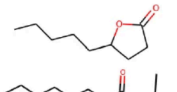
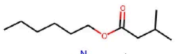
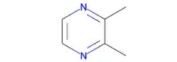
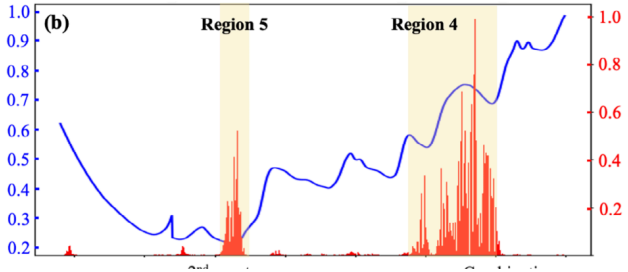
Molecular structure	Odor descriptors
	Buttery; Coconut; Creamy; Oily; Sweet.
	Apple; Fruity; Green; Sweet.
	Cocoa; Coffee; Nut; Potato; Roasted.
...	...

predict wine aroma

Deep Learning + Machine Learning



predict the flavors of specialty coffee

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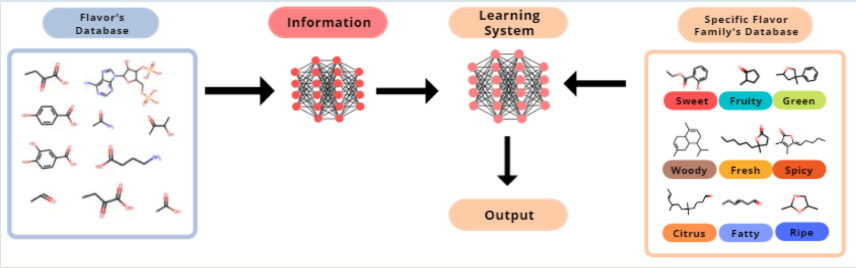
Examples of artificial intelligence in flavor engineering

Scientific Machine Learning (SciML)



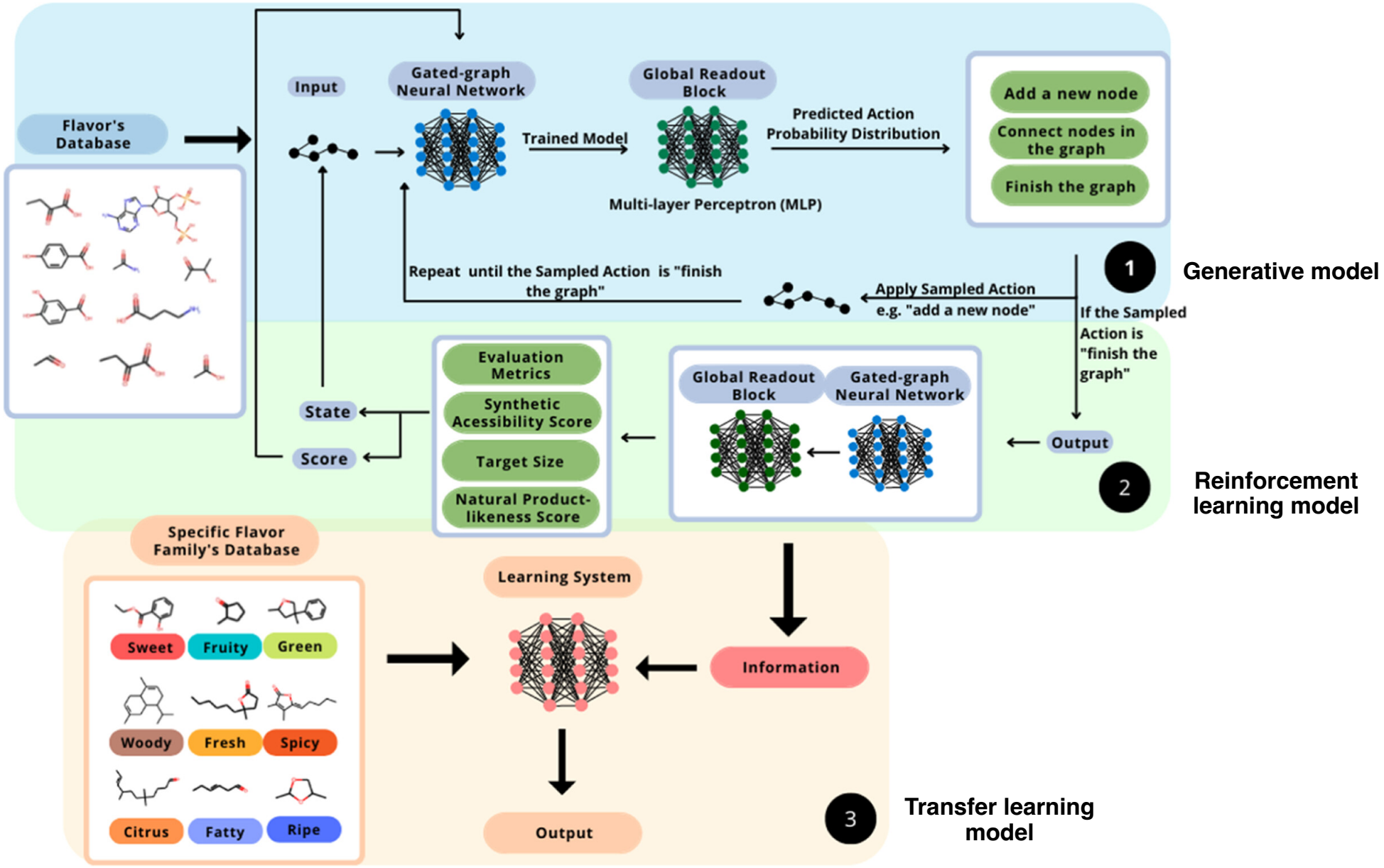
molecular design for flavor-based product development

Idelfonso B. R. Nogueira
Associate Professor
Department of Chemical Engineering
Norwegian University of Science and Technology

AiP$_2$S$_2$ – *Artificial Intelligence-powered Products, Processes, Scales, and Systems*

Queiroz, L. P.; Nogueira, I. B. R.; Ribeiro, A. M. *Food Research International* **2024**, *196*, 115100.

SciML molecular design for flavor development

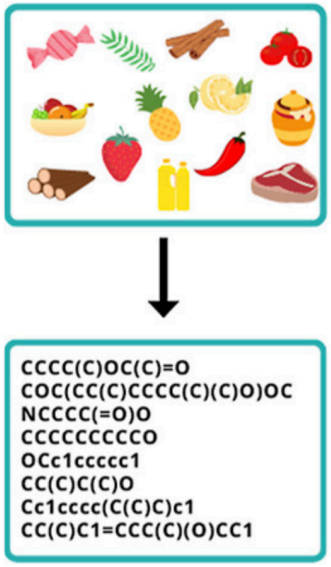


Queiroz, L. P.; Rebello, C. M.; Costa, E. A.; Santana, V. V.; Rodrigues, B. C. L.; Rodrigues, A. E.; Ribeiro, A. M.; Nogueira, I. B. R. *Ind. Eng. Chem. Res.* **2023**, *62* (23), 9062–9076.

Database Curation

Layers 1 & 2: Generative + Reinforcement Learning

General database

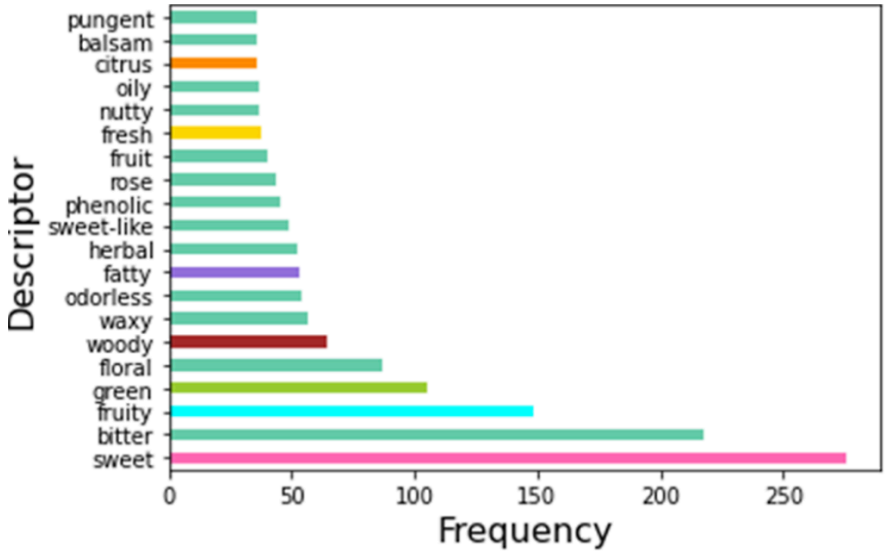


Contains **3,613 molecules** from FlavorDB

Each molecule entry includes:

- PubChem ID
- Chemical name
- **Flavor descriptors**
- **Canonical SMILES**

Top 20 most frequent flavor descriptors



Total of **417** different flavor descriptors

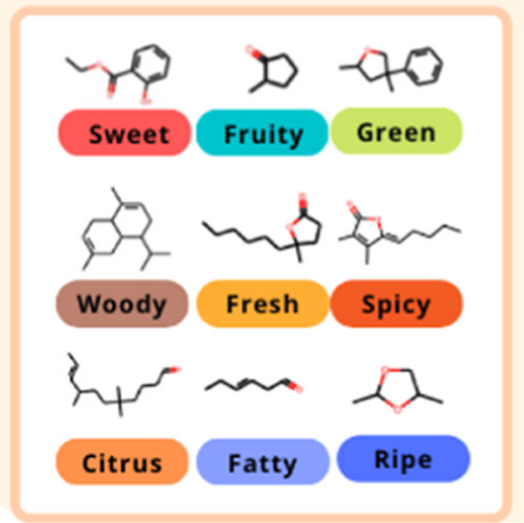
- model learns general structure–property relationships
- design realistic molecules with desirable sensory properties

Queiroz, L. P.; Rebello, C. M.; Costa, E. A.; Santana, V. V.; Rodrigues, B. C. L.; Rodrigues, A. E.; Ribeiro, A. M.; Nogueira, I. B. R. *Ind. Eng. Chem. Res.* **2023**, *62* (23), 9062–9076.

Database Curation

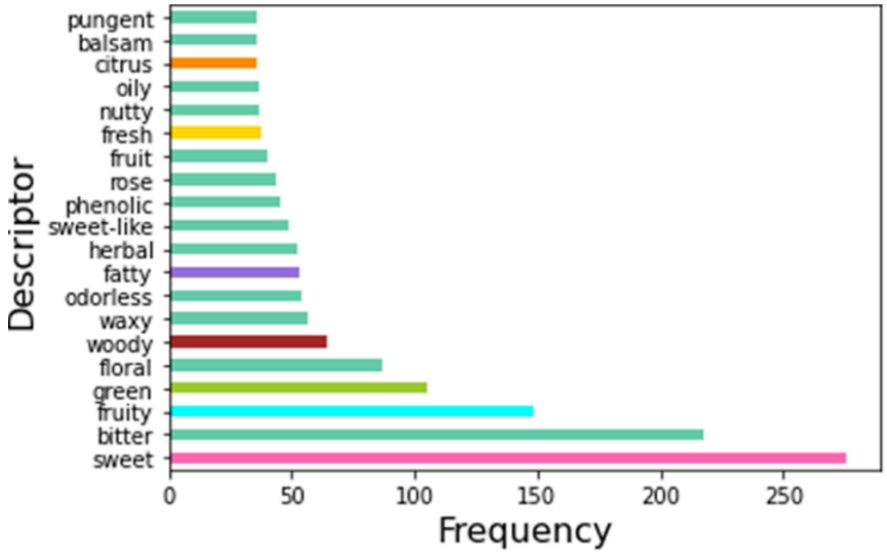
Layers 3: Transfer Learning

9 flavor family subdatabases



- Extracted from general database
- Flavor-specific dataset used for transfer learning had around **100 molecules each**
- Model is able to generate molecules that are tailored to a particular sensory profile — rather than broadly flavor-active.

Top 20 most frequent flavor descriptors



7 of the 9 target families are among the top 20 most common descriptors

spicy and ripe are underrepresented

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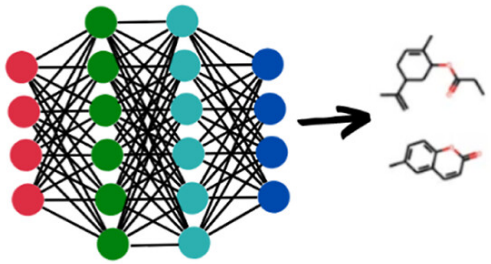
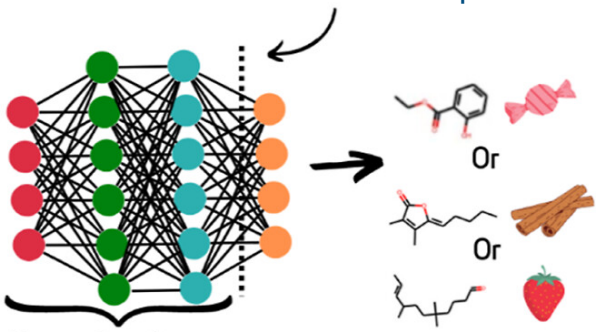
Transfer learning

Original “pre-trained” network
Trained for generating
molecules of flavors



Transfer Learning

Only train the new final layer on a
small dataset to generate
molecules with specific flavors



Parameters frozen

Evaluation metrics to assess quality of generated molecules

- Synthetic accessibility **(SA) score < 3**
- Natural product-likeness **(NP) score > 0**

Summary of results

- For all 9 flavor descriptors, over 50% of generated molecules met at least one of the two target metrics
- In 6 out of 9 descriptors, over 50% of the molecules met both criteria simultaneously
- Fruity had the highest percentage of optimal molecules, indicating strong model performance
- Spicy had the lowest, reflecting greater molecular complexity and scarce training data

Queiroz, L. P.; Rebello, C. M.; Costa, E. A.; Santana, V. V.; Rodrigues, B. C. L.; Rodrigues, A. E.; Ribeiro, A. M.; Nogueira, I. B. R. *Ind. Eng. Chem. Res.* **2023**, *62* (23), 9062–9076.

Generated Molecule Assessment Results for the Fruity, Sweet, and Spicy Descriptors

flavor descriptor	categories	number of molecules	percentage of molecules (%)
fruity	valid molecules	93	94.90
	invalid molecules	4	4.08
	existing	91	92.86
	nonexisting	2	2.04
	used in the flavor industry	87	88.78
	used in the flavor industry as fruity	76	77.55
	not yet used in the flavor industry	5	5.10
Sweet	valid molecules	97	98.98
	invalid molecules	2	2.04
	existing	96	97.96
	nonexisting	1	1.02
	used in the flavor industry	91	92.86
	used in the flavor industry as sweet	70	71.43
	not yet used in the flavor industry	5	5.10
spicy	valid molecules	96	97.96
	invalid molecules	3	3.06
	existing	92	93.88
	non-existing	3	3.06
	used in the flavor industry	82	83.67
	used in the flavor industry as spicy	70	71.43
	not yet used in the flavor industry	11	11.22

High performance

Medium performance

Low performance

Summary of results

Queiroz, L. P.; Rebello, C. M.; Costa, E. A.; Santana, V. V.; Rodrigues, B. C. L.; Rodrigues, A. E.; Ribeiro, A. M.; Nogueira, I. B. R. *Ind. Eng. Chem. Res.* **2023**, *62* (23), 9062–9076.

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Queiroz, L. P.; Rebello, C. M.; Costa, E. A.; Santana, V. V.; Rodrigues, B. C. L.; Rodrigues, A. E.; Ribeiro, A. M.; Nogueira, I. B. R. *Ind. Eng. Chem. Res.* **2023**, *62* (23), 9062–9076.

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deep transfer learning can be utilized to obtain molecules for flavor-based products without requiring new synthesis.

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Outline of Talk

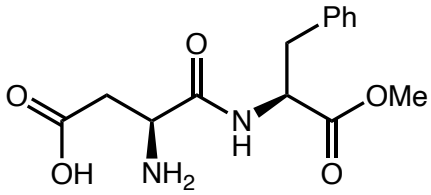
What is flavor?

Flavorings

Sweeteners

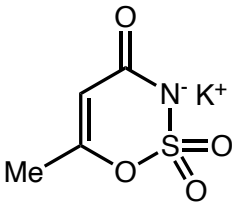
Health Concerns

FDA approved artificial sweeteners



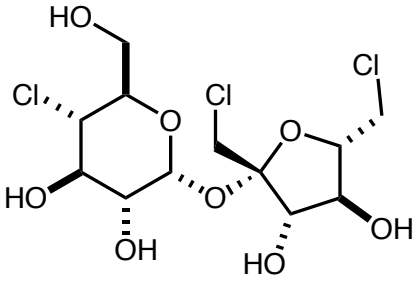
Aspartame

Approval in 1981



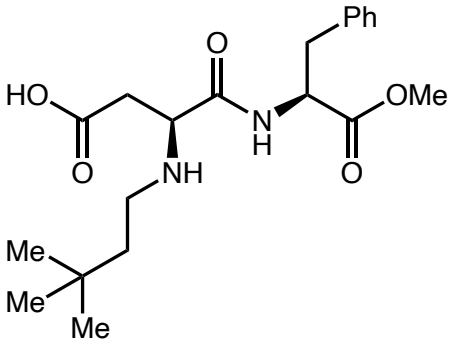
Acesulfame potassium (Ace-K)

Approval in 1988



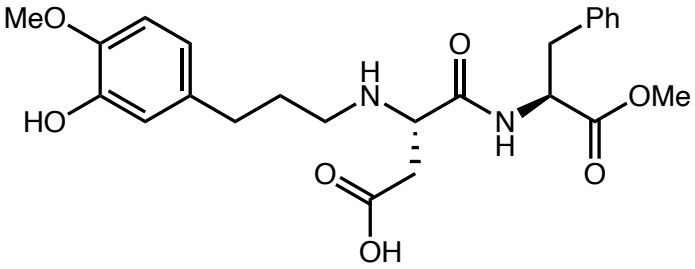
Sucralose

Approval in 1988



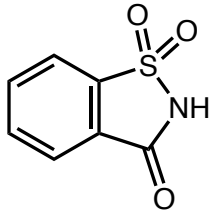
Neotame

Approval in 2002



Advantame

Approval in 2014



Saccharin

Approval in 1879

FDA approved artificial sweeteners

Aspartame

Approval in 1981

Acesulfame potassium (Ace-K)

Approval in 1988

Sucralose

Approval in 1988

Neotame

Approval in 2002

Advantame

Approval in 2014

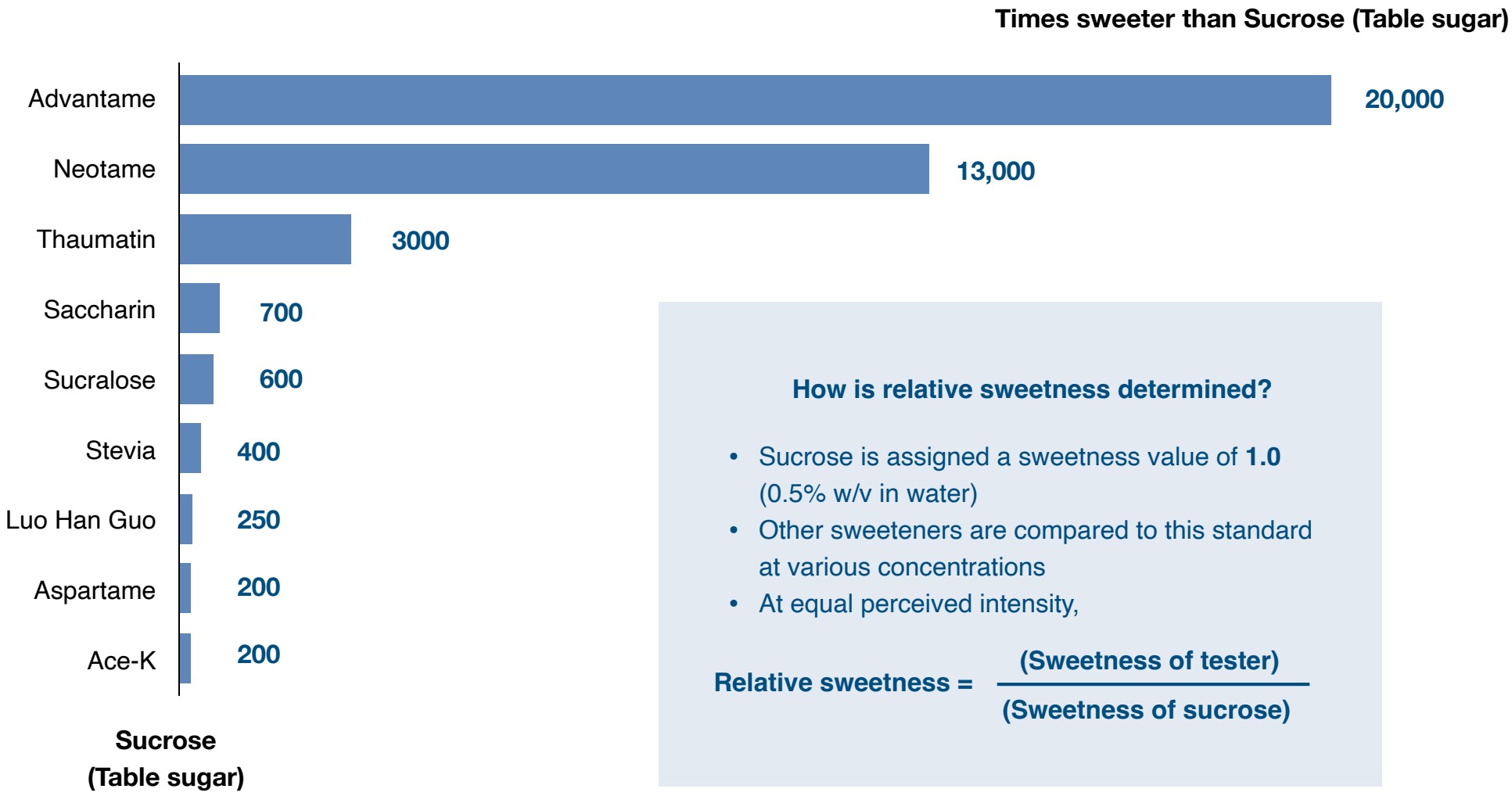
Saccharin

Approval in 1879

High-intensity sweeteners

High affinity binding to T1R2 + T1R3 sweet taste receptors and prolonged activation.

Sweetness intensity of sweeteners compared to table sugar



How is relative sweetness determined?

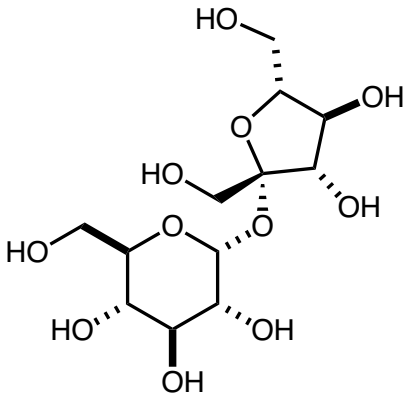
- Sucrose is assigned a sweetness value of **1.0** (0.5% w/v in water)
- Other sweeteners are compared to this standard at various concentrations
- At equal perceived intensity,

$$\textbf{Relative sweetness} = \frac{\textbf{(Sweetness of tester)}}{\textbf{(Sweetness of sucrose)}}$$

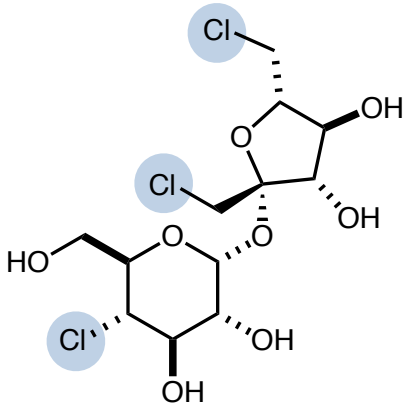
U.S. Food and Drug Administration website **2025**; Chattopadhyay, S.; Raychaudhuri, U.; Chakraborty, R. *J Food Sci Technol* **2014**, *51* (4), 611–621.

Sucrose vs. Sucralose

The Famous Miscommunication, 1976



Sucrose



Sucralose

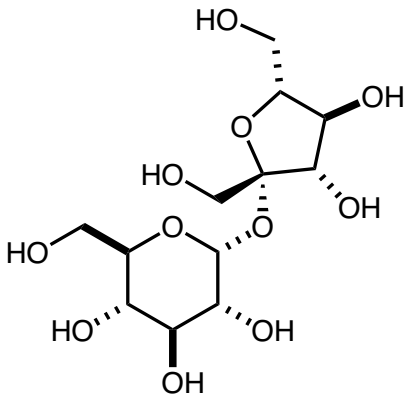
"My work at QEC was aimed at chemical modifications of sucrose for possible applications in the industry…We were particularly interested in chlorosucroses. During discussions…**Les Hough suggested me to test a sample of tetrachlorinated sucrose "Serendipitose"** which, perhaps he wanted to send to Tate & Lyle plc. **I thought I needed to taste it! My thinking was not unusual because we were also interested in knowing if one could enhance the natural sweetness of sucrose by playing around with its structure.**"

— Dr. Shashikant Phadnis, then graduate student in Hough lab

Dr. Leslie Hough

Fraser-Reid, B. *London – Hough, Khan and Pfadnis Get Together. In From Sugar to Splenda: A Personal and Scientific Journey of a Carbohydrate Chemist and Expert Witness;* Springer, **2012**.

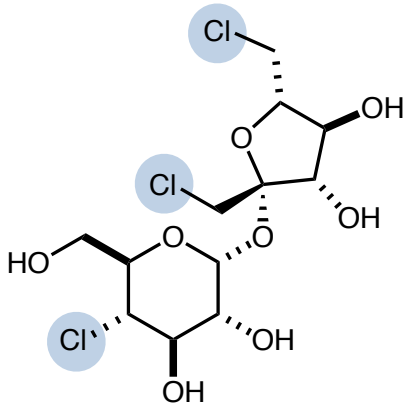
Sucrose vs. Sucralose



Sucrose

Sweetness = 1

- Rapidly metabolized (4 cal/g)
- Relatively week binding to T1R2/T1R3
- Moderately heat-stable



Sucralose

Sweetness = 600

- Not metabolized (0 cal/g)
- Stronger binding to T1R2/T1R3
- Very Heat-stable (good for baking)

Minimal structural change leading to dramatic difference in **sweetness and bioavailability**

Hao, S.; Guthrie, B.; Kim, S.-K.; Balanda, S.; Kubicek, J.; Murtaza, B.; Khan, N. A.; Khakbaz, P.; Su, J.; Goddard, W. A. *Commun Chem* **2024**, *7* (1), 236.

FDA approved artificial sweeteners

Aspartame

Acesulfame potassium (Ace-K)

Sucralose

Neotame

Advantame

Saccharin

The FDA establishes an **Acceptable Daily Intake (ADI)** for each approved sweetener, indicating the maximum amount considered safe to consume each day over a lifetime

Acceptable Daily Intake for each approved sweetener

Aspartame

50 mg/kg bw/d

Acesulfame potassium (Ace-K)

15 mg/kg bw/d

Sucralose

5 mg/kg bw/d

Neotame

0.3 mg/kg bw/d

Advantame

33 mg/kg bw/d

Saccharin

15 mg/kg bw/d

The FDA establishes an **Acceptable Daily Intake (ADI)** for each approved sweetener, indicating the maximum amount considered safe to consume each day over a lifetime

U.S. Food and Drug Administration website **2025**

mg/kg bw/d = milligram per kilogram body weight per day

*Number of sweetener packets to consume to reach ADI**

Aspartame

50 mg/kg bw/d

75 packets

Acesulfame potassium (Ace-K)

15 mg/kg bw/d

23 packets

Sucralose

5 mg/kg bw/d

23 packets

Neotame

0.3 mg/kg bw/d

23 packets

Advantame

33 mg/kg bw/d

4920 packets

Saccharin

15 mg/kg bw/d

45 packets

*Based on a 60 kg person

U.S. Food and Drug Administration website **2025**

mg/kg bw/d = milligram per kilogram body weight per day

Sweeteners used in top selling soft drinks

In beverage formulation, sweeteners are chosen strategically to optimize:

- **Taste profile:** blends improve realism and reduce off-notes
- **Caloric content:** zero or near-zero
- **Functional stability** in shelf-stable, carbonated, and flavored environments

Sweeteners used in top selling soft drinks

Aspartame

Aspartame

Aspartame + Ace-K

Aspartame + Ace-K

Stevia + Erythritol

Sucralose + Ace-K

Aspartame + Ace-K

Sucralose + Ace-K + Erythritol

Why mix sweeteners?

Aspartame

Aspartame

Clean, sugar-like taste

Aspartame + Ace-K

Aspartame + Ace-K

Ace-K adds early sweetness,
aspartame masks aftertaste

Stevia + Erythritol

“Natural” marketing,
mild sweetness

Sucralose + Ace-K

Long-lasting sweetness,
Improves aftertaste

Aspartame + Ace-K

Sucralose + Ace-K + Erythritol

Long-lasting sweetness,
Erythritol adds mouthfeel

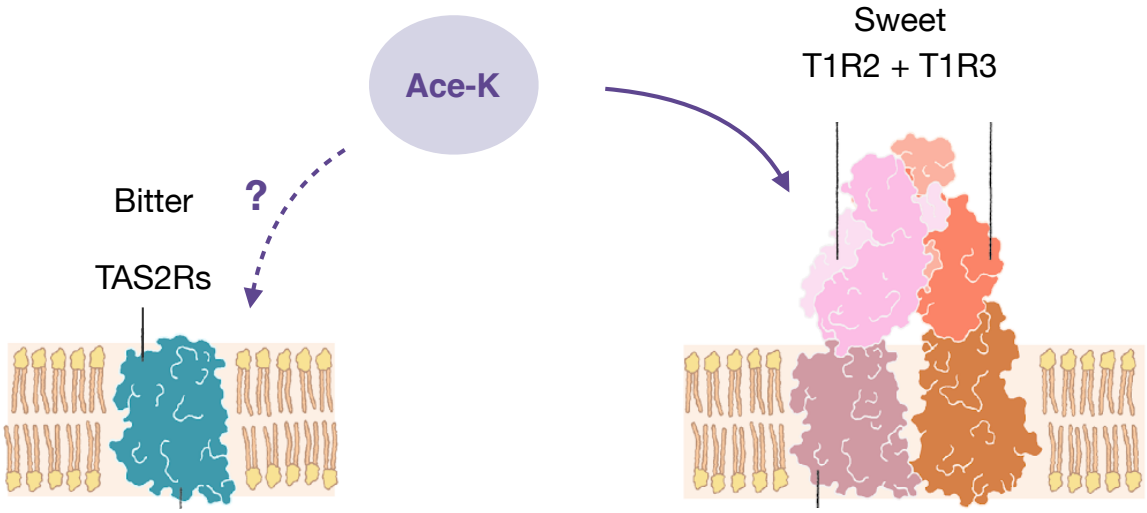
Why do artificial sweeteners taste bitter to some people?

Blending sweeteners

Aspartame + Ace-K

Sucralose + Ace-K

- Sweetener mixtures **mask bitterness** and round out flavor
- Some artificial sweeteners (ex. Ace-K, Saccharin) activate **both sweet and bitter receptors**

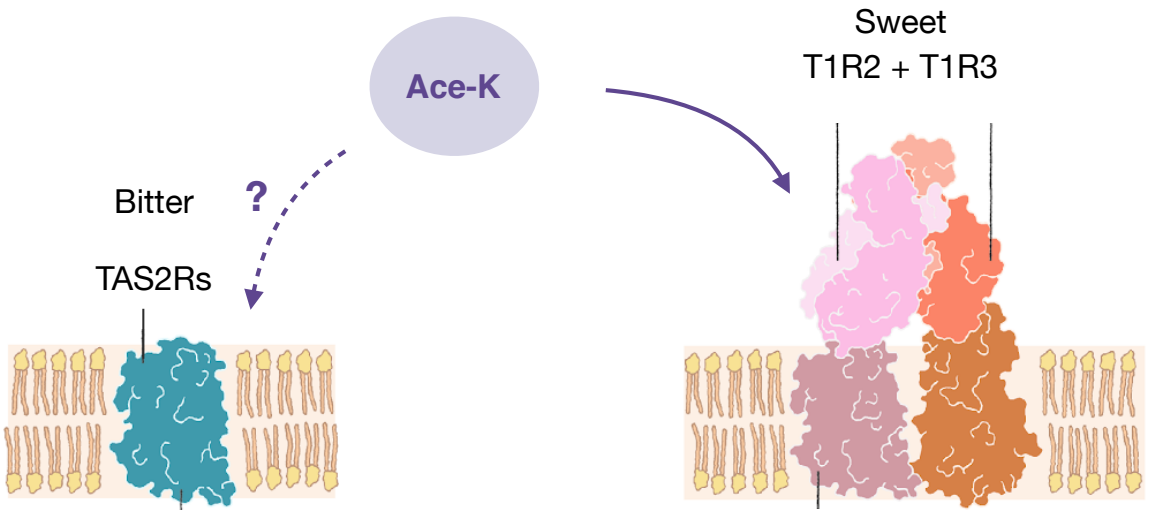


Allen, A. L.; McGeary, J. E.; Knopik, V. S.; Hayes, J. E. *Chemical Senses* **2013**, *38* (5), 379–389.

Why do artificial sweeteners taste bitter to some people?

Case study: Genetic Basis for Bitterness Perception of Acesulfame Potassium

- Why do **some people perceive Ace-K as bitter** while others do not?
- Do **genetic polymorphisms in bitter taste receptors (TAS2Rs)** explain this variability?



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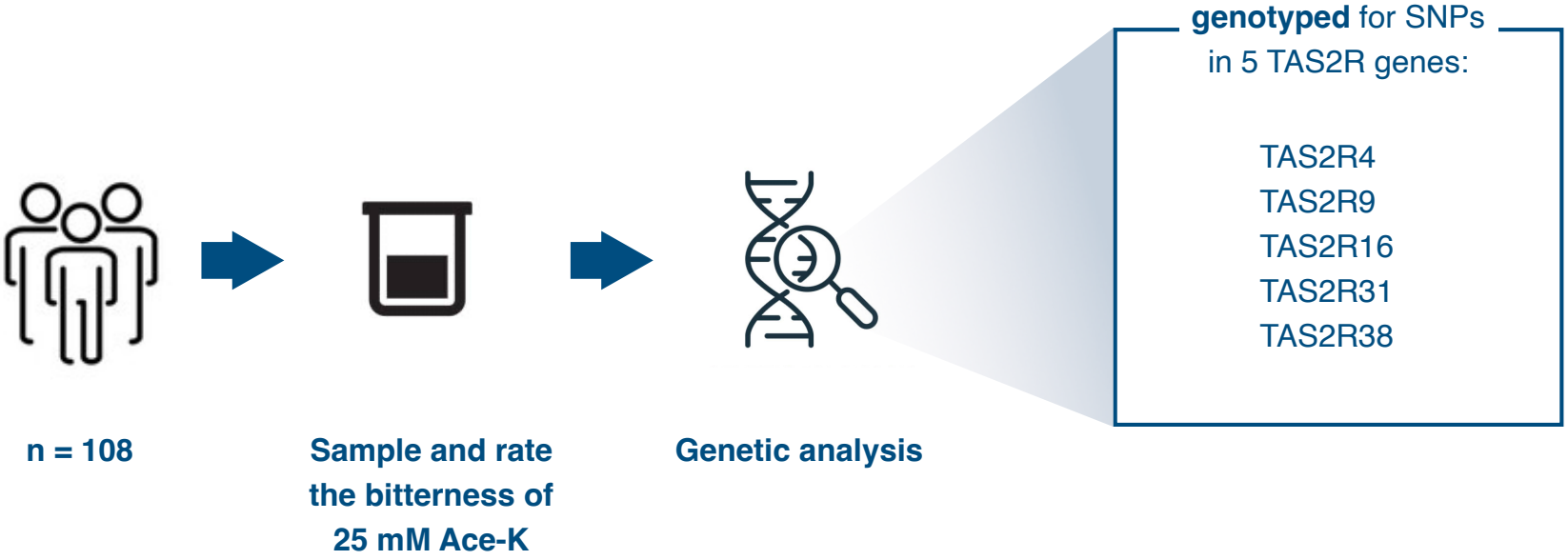

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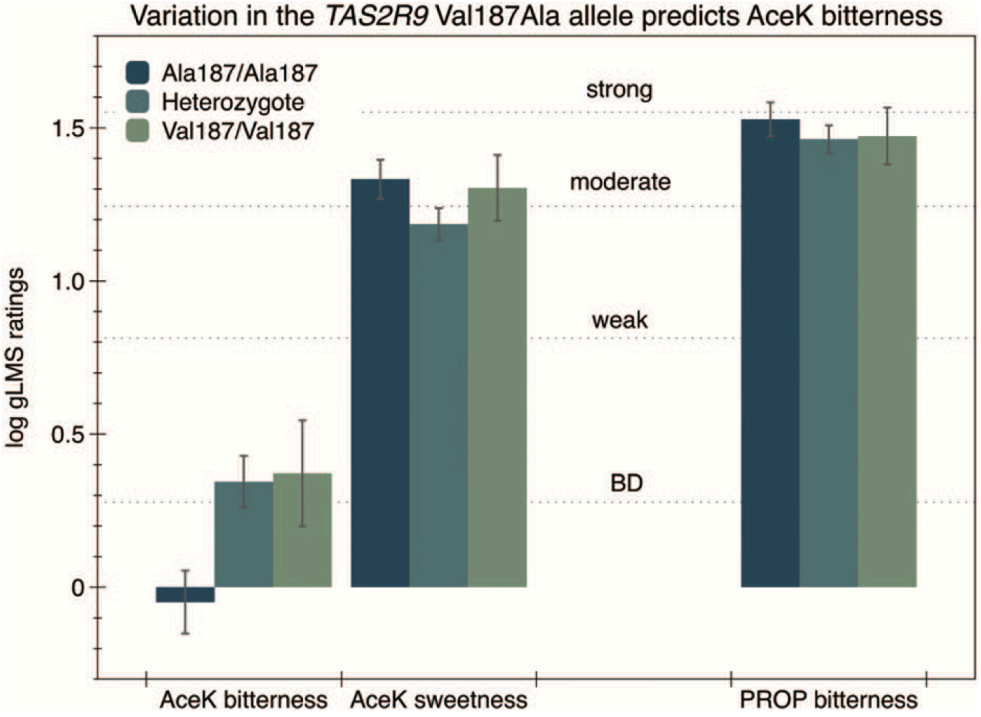

- Previous studies showed T2R9 responds to bitter drugs (ofloxacin, procainamide, pirenzepine) and varies by Val187Ala SNP.
- Ala187/Ala187 was associated with reduced bitterness perception of Ace-K.
- Heterozygotes and Val187/Val187 individuals showed similar and higher bitterness ratings
- **Suggests a dominant effect of the Val allele.**
- **SNP explained 7.0% of variance in Ace-K bitterness**
- **No effect observed on Ace-K sweetness or PROP bitterness.**

Allen, A. L.; McGeary, J. E.; Knopik, V. S.; Hayes, J. E. *Chemical Senses* **2013**, *38* (5), 379–389.

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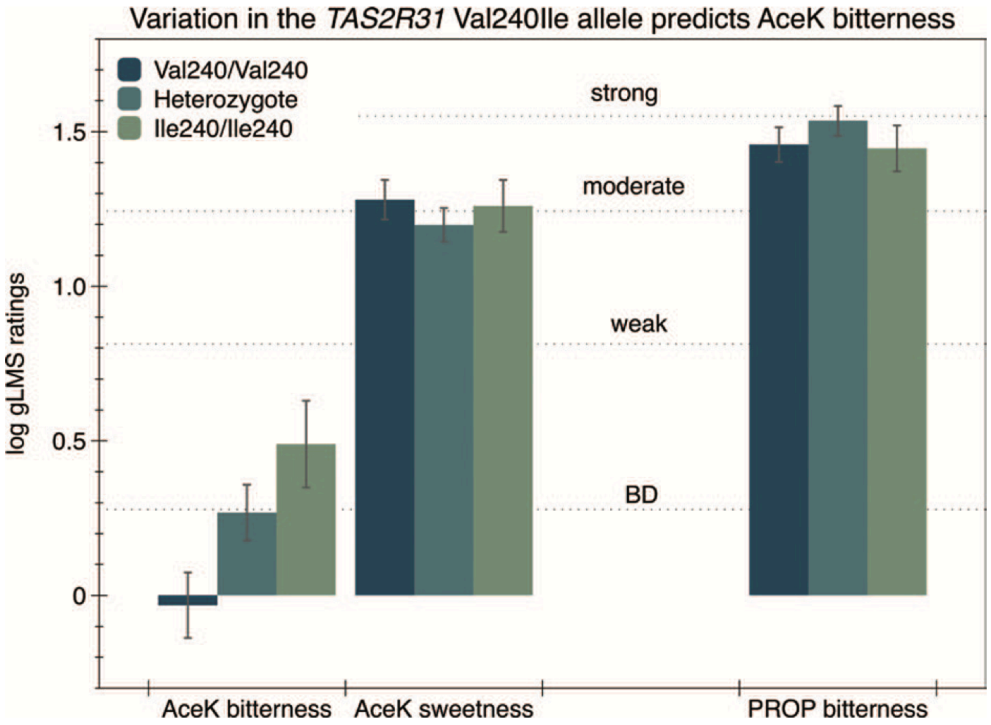
Case study: Genetic Basis for Bitterness Perception of Acesulfame Potassium

- The Ile240 allele likely contributes to heightened activation of the bitter taste receptor by Ace-K.
- The SNP explained 8.7% of the variance in Ace-K bitterness
- **No effect observed on Ace-K sweetness or PROP bitterness.**



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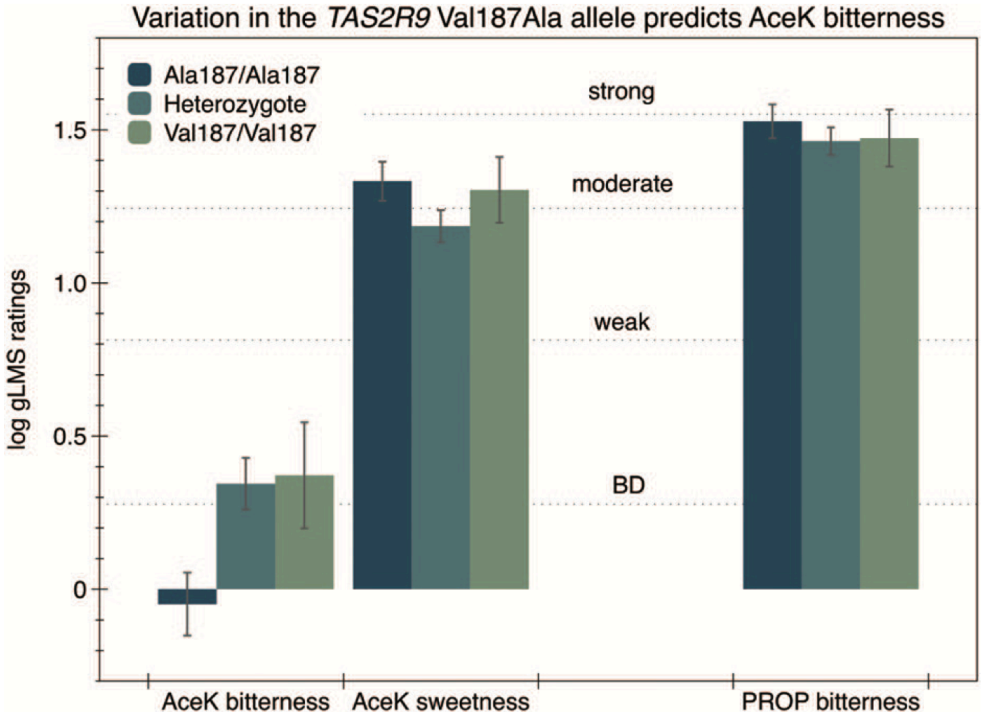

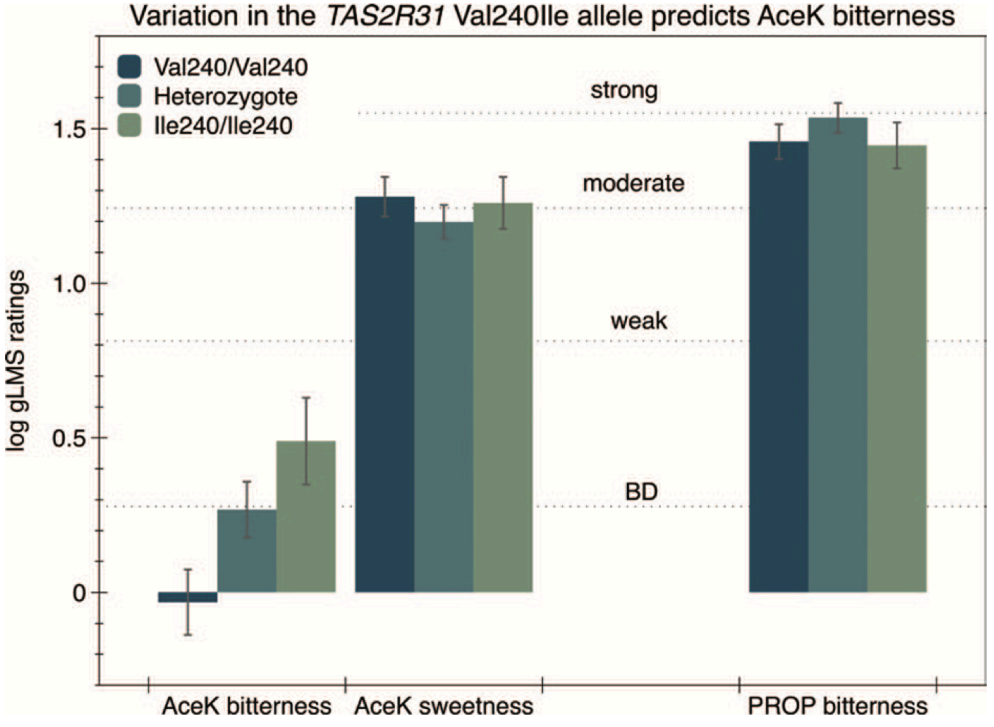

- **TAS2R31 and TAS2R9 SNPs** significantly associated with bitterness perception.
- A model including SNPs from both explained **13.4% of variation** in perceived bitterness.
- TAS2R4, TAS2R38, and TAS2R16 showed **no significant effect**.

Allen, A. L.; McGeary, J. E.; Knopik, V. S.; Hayes, J. E. *Chemical Senses* **2013**, *38* (5), 379–389.

Why do artificial sweeteners taste bitter to some people?

Follow up case study: Genetic Basis for Bitterness Perception of Stevia

Stevia

South American plant
Natural zero-calorie sweetener

n = 122

Sample and rate the bitterness of:

- 219 mM sucrose (control)
- 20 mM gentiobiose (control)
- 6.8 mM aspartame
- 1.65 mM RebA
- 1 mM RebD

Genetic analysis

TAS2R4
TAS2R9
TAS2R31
TAS2R38

Allen, A. L.; McGeary, J. E.; Hayes, J. E. *Chem. Percept.* **2013**, *6* (3), 109–117.

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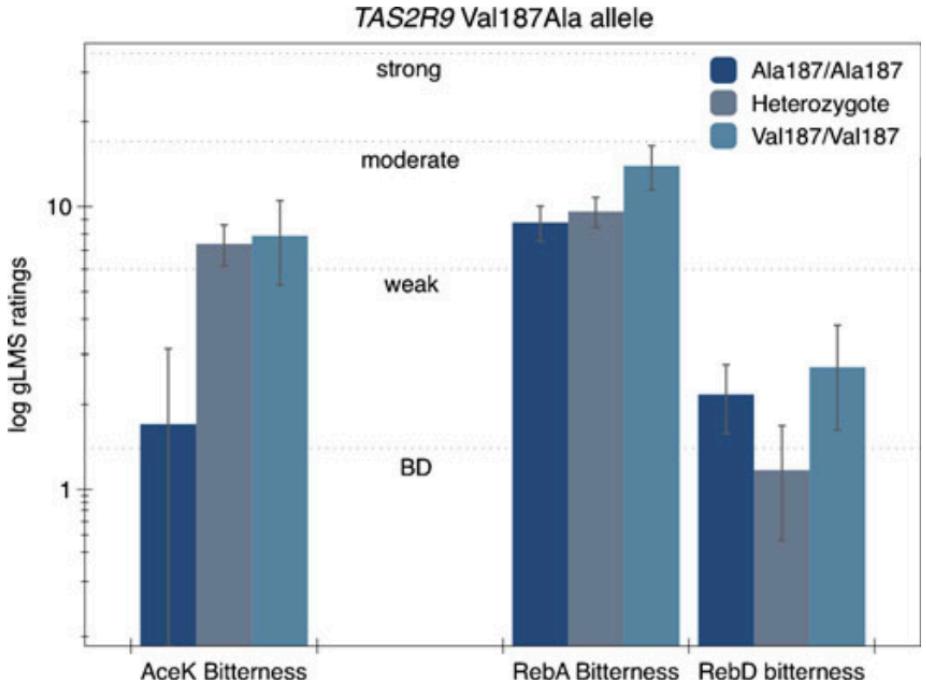

- The bitterness of AceK was significantly different across genotype
- No effect of genotype was observed for RebA or RebD

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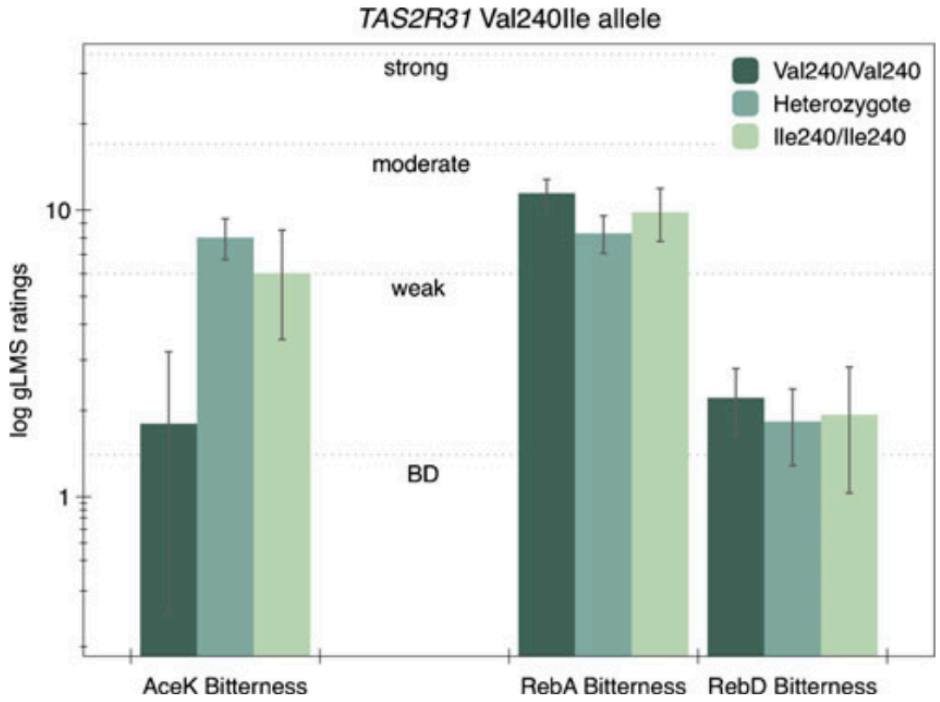

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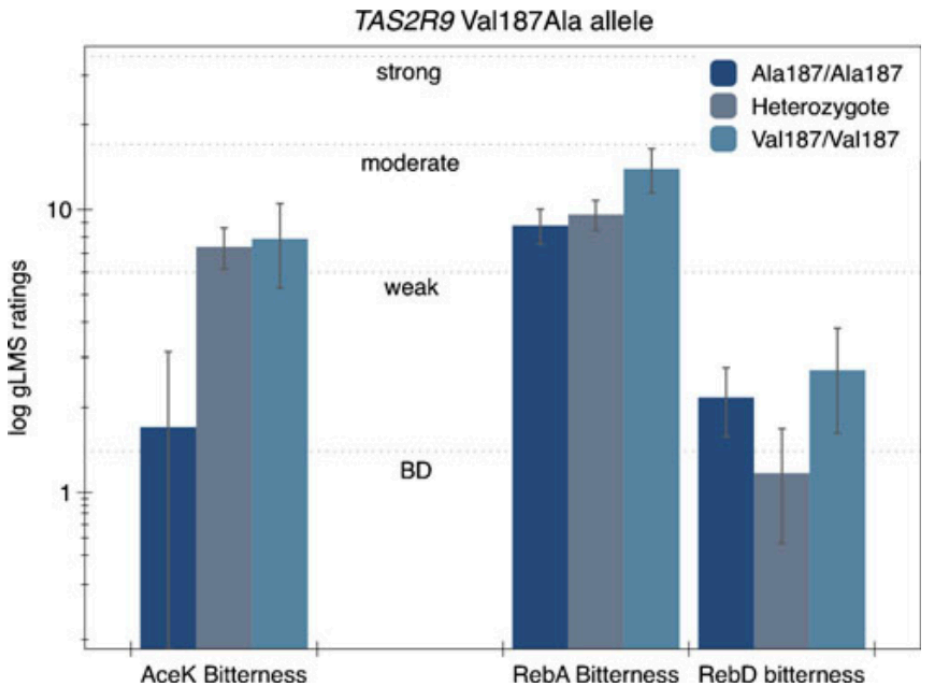

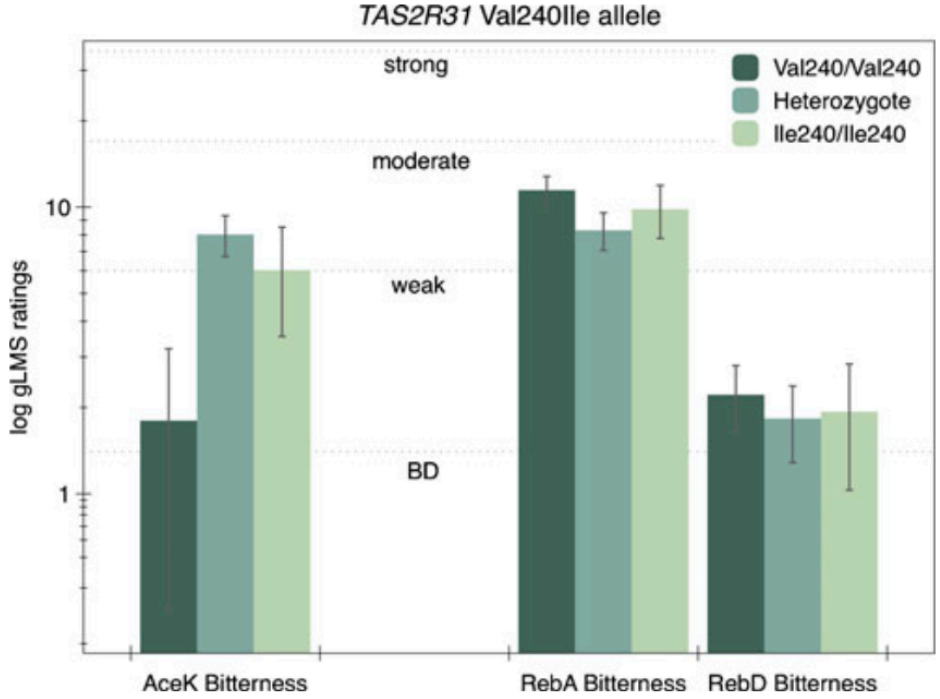

- Of the stevia extracts, the participants considered **RebD to be much less bitter than RebA.**
- RebA and RebD bitterness **did not covary** with AceK bitterness.
- Variation in the TAS2R9 and TAS2R31 genes **did not predict** RebA and RebD bitterness.

Allen, A. L.; McGeary, J. E.; Hayes, J. E. *Chem. Percept.* **2013**, *6* (3), 109–117.

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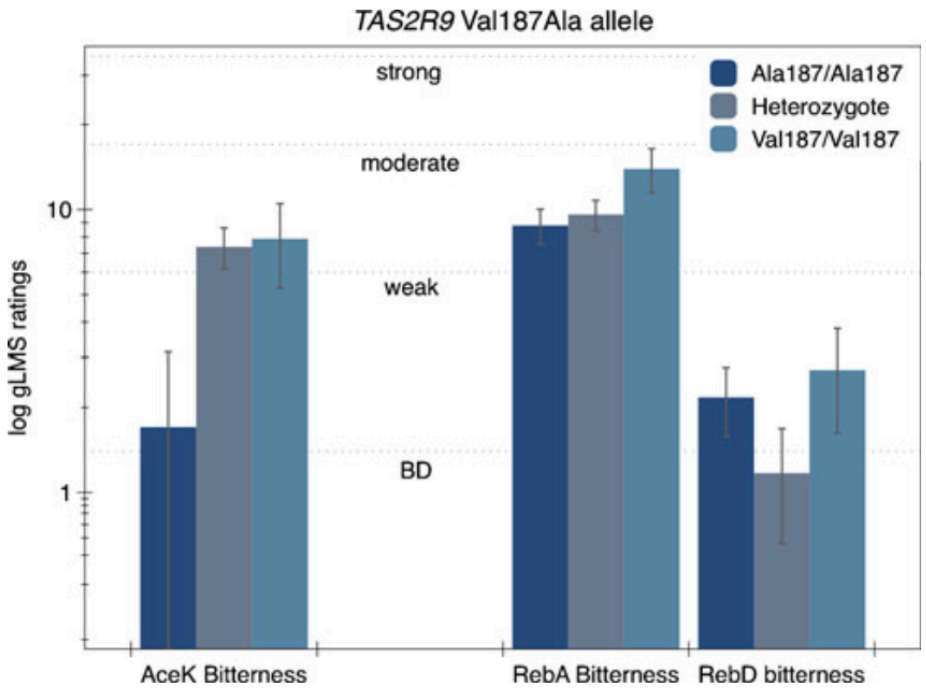

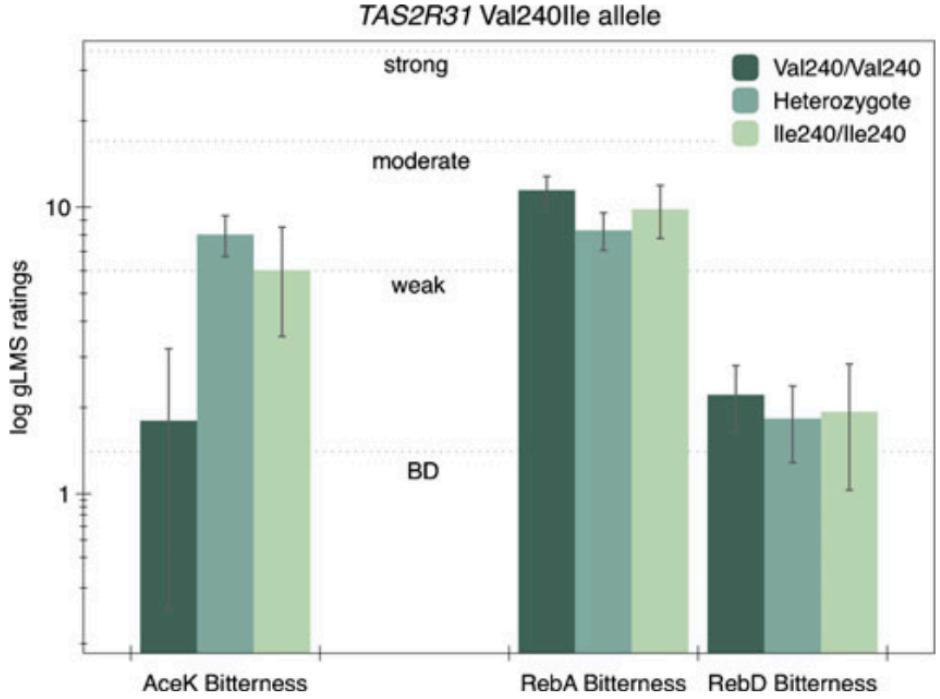

Bitterness is not a simple monolithic trait that is high or low in an individual.

Allen, A. L.; McGeary, J. E.; Hayes, J. E. *Chem. Percept.* **2013**, *6* (3), 109–117.

Outline of Talk

What is flavor?

Flavorings

Sweeteners

Health Concerns

Health concerns for artificial flavorings and sweeteners

Artificial flavorings

1. May cause allergic reactions

Some allergens may be present in tiny amounts, if not “big 9”, might go undeclared.

2. May affect gut health

May affect composition of gut microbiota

3. May increase risk of cancer

FDA banned 7 synthetic flavorings in 2018 after studies linked them to cancer in animals.

4. May increase risk of cardiovascular diseases

Flavorings in e-cigs found to impair endothelial function

Artificial sweeteners

Skypala, I. J. *Front Immunol* **2019**, *10*, 673., Pang, M. D.; Goossens, G. H.; et al. *Front Nutr* **2021**, *7*, 598340., Aguayo-Guerrero, J. A.; Méndez-García, L. A.; et al. *Life (Basel)* **2024**, *14* (3), 323., Kanny, G.; Hatahet, R.; Moneret-Vautrin, D. A.; et al. *Allerg Immunol (Paris)* **1994**, *26* (6), 204–206, 209–210., Fetterman, J. L.; Weisbrod, R. M.; et al. *ATVB* **2018**, *38* (7), 1607–1615.

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Artificial sweeteners

1. May not help with weight control

Artificial sweeteners don’t fully mimic the reward or hormonal effects of sugar.

2. May lead to temptation to eat more

Potential overeating to “make up” for the missing calorie signal

3. May overstimulate your sugar receptors

May alter your perception of sweetness

4. May be highly addictive

May reinforce sweet cravings and habitual intake

Skypala, I. J. *Front Immunol* **2019**, *10*, 673., Pang, M. D.; Goossens, G. H.; et al. *Front Nutr* **2021**, *7*, 598340., Aguayo-Guerrero, J. A.; Méndez-García, L. A.; et al. *Life (Basel)* **2024**, *14* (3), 323., Kanny, G.; Hatahet, R.; Moneret-Vautrin, D. A.; et al. *Allerg Immunol (Paris)* **1994**, *26* (6), 204–206, 209–210., Fetterman, J. L.; Weisbrod, R. M.; et al. *ATVB* **2018**, *38* (7), 1607–1615.

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Artificial sweeteners

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3. May overstimulate your sugar receptors
4. May be highly addictive

Overall, there's a lack of research into how these chemicals might interact when consumed over decades. Realistically, it would be incredibly challenging to cut out these foods from your diet entirely.

Reducing how much ultra-processed food you eat is a very good idea.

Questions?

the main attributes of flavor are the following: sweet, sour, bitter, s
recognized fifth one ‘umami’ ("oo-mommy" or savory/pleasant), fo