A Palette of Flavors for Indulging Your Senses

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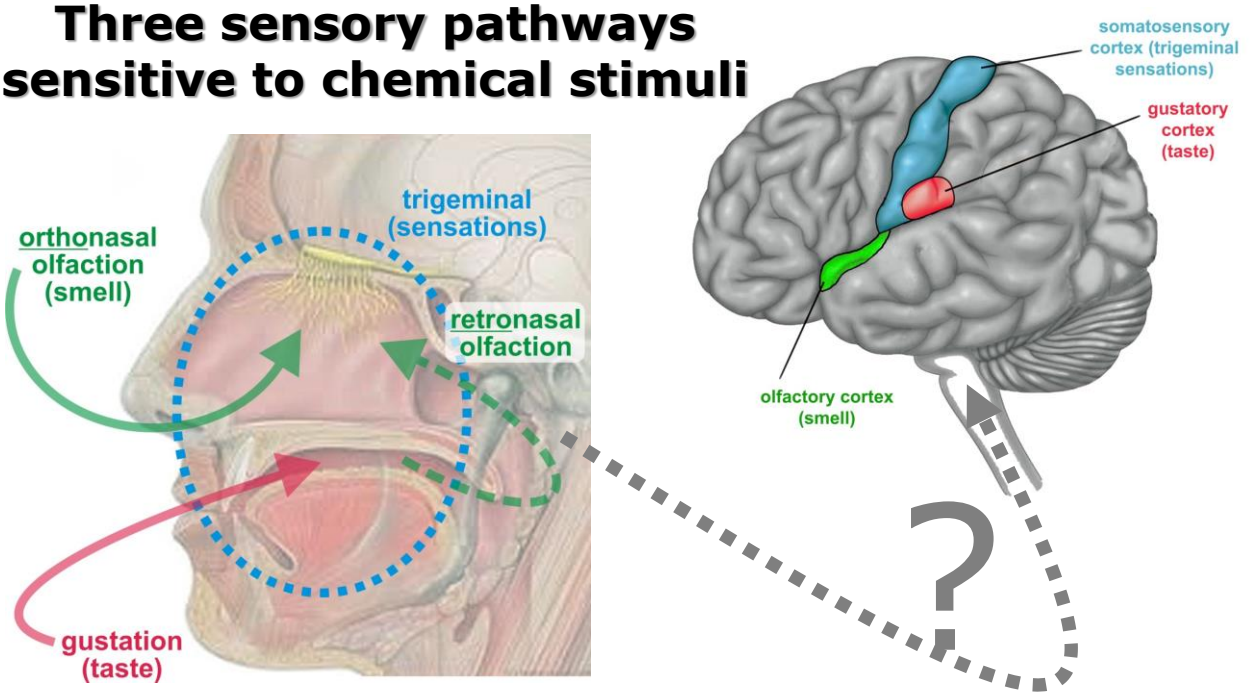
Flavor = Taste + Odor

~80% contribution to flavor perception

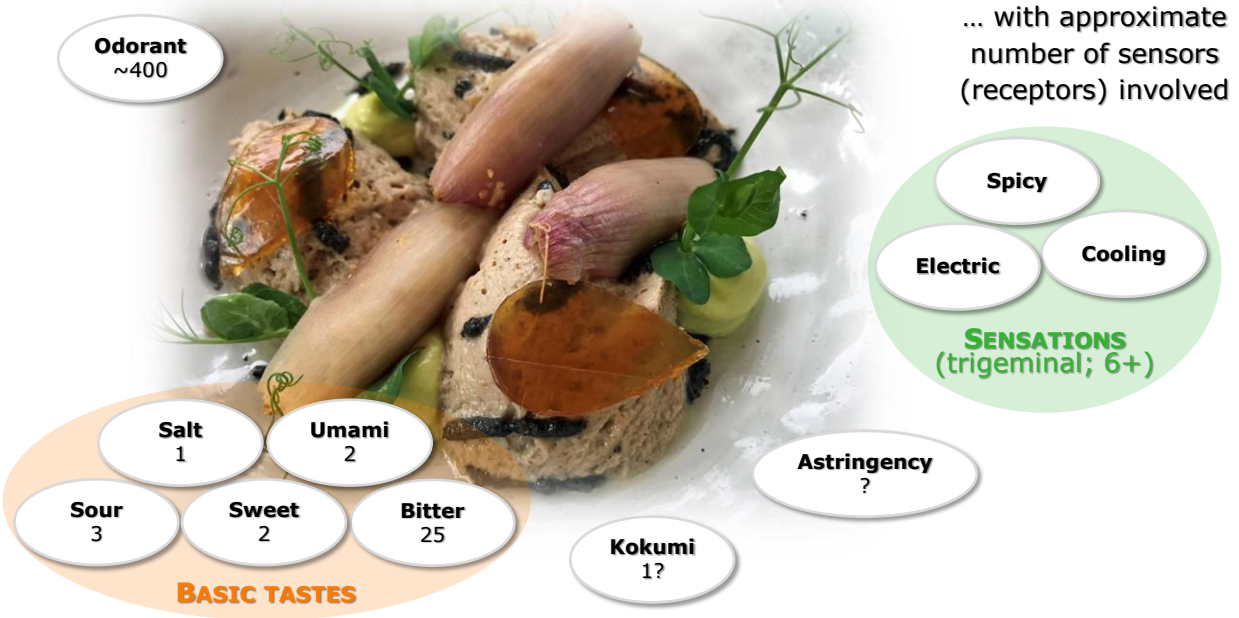
~20% contribution to flavor perception

Flavor = Taste + Odor + "Sensations"

Three sensory pathways sensitive to chemical stimuli

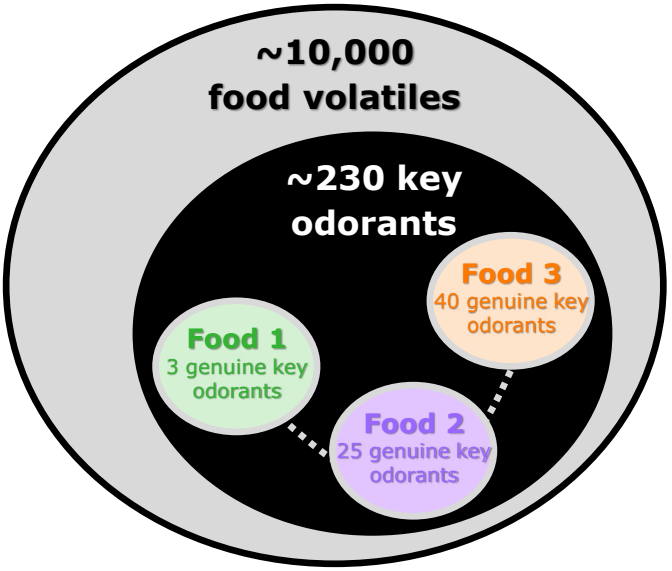


Various flavor modalities ...



... with approximate number of sensors (receptors) involved

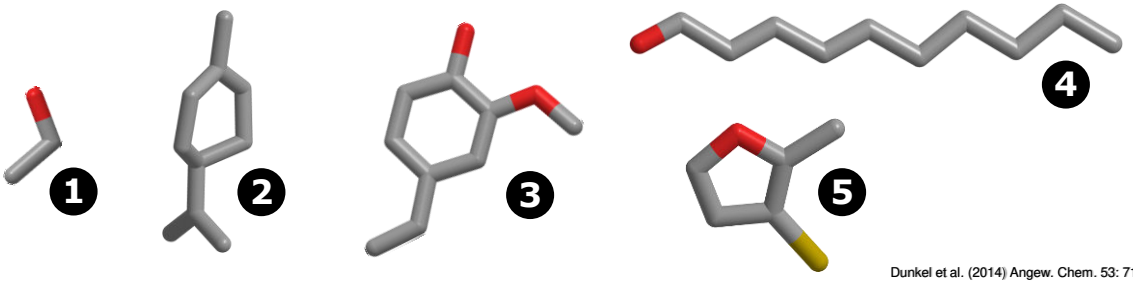
Only relatively few food odorants matter



Dunkel et al. (2014) Angew. Chem. 53: 7124-7143.

Some key food odorants (KFOs)

#	KFO	Reaction	Odor quality	Threshold conc. (µg/kg water)
1	ethanol	fermentation	alcoholic	990000
2	(*R*)-limonene	biosynthesis	citrus-like	13
3	2-methoxy-4-vinylphenol	Maillard	smoky	5
4	(*E*,*E*)-2,4-decadienal	lipid oxidation	fatty, French fries-like	0.03
5	2-methyl-3-furanthiol	Maillard	Meaty, bouillon-like	0.00003



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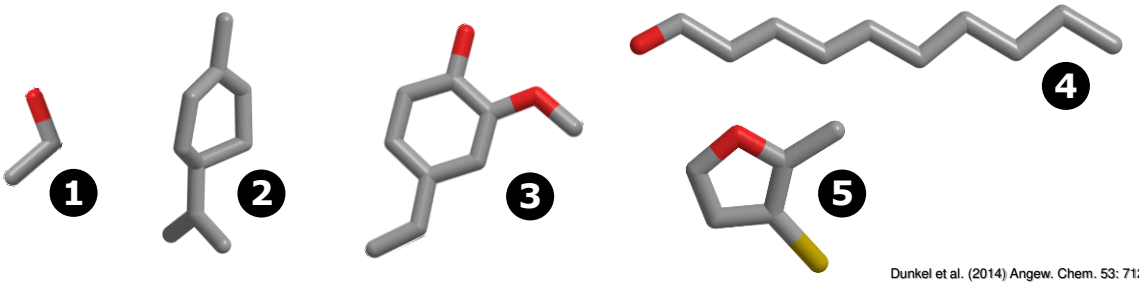
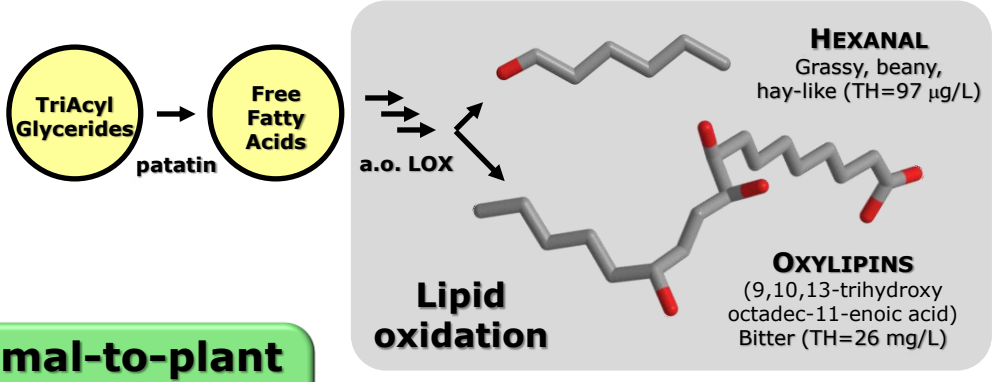


Dunkel et al. (2014) Angew. Chem. 53: 7124-7143.

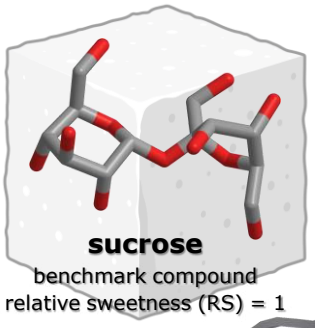
Reactions upon processing leading to off-flavor formation



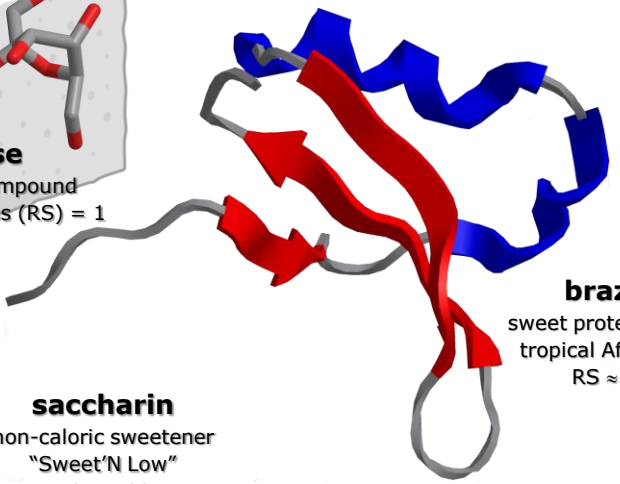
Animal-to-plant protein transition

Ernstgård et al. (2017) PLoS ONE 12: e0185479.
Gläser et al. (2020) J. Agric. Food Chem. 68: 10374-10387.

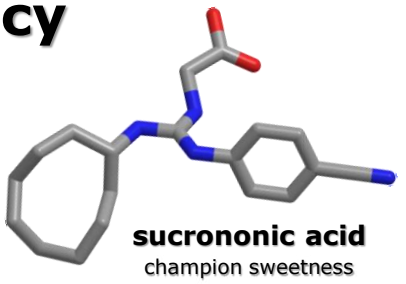
Sweet molecules can differ enormously in size and potency



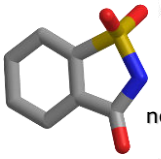
sucrose
benchmark compound
relative sweetness (RS) = 1



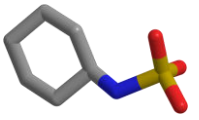
brazzein
sweet protein from fruit
tropical African shrub
RS ≈ 2,000



sucrononic acid
champion sweetness
RS ≈ 200,000

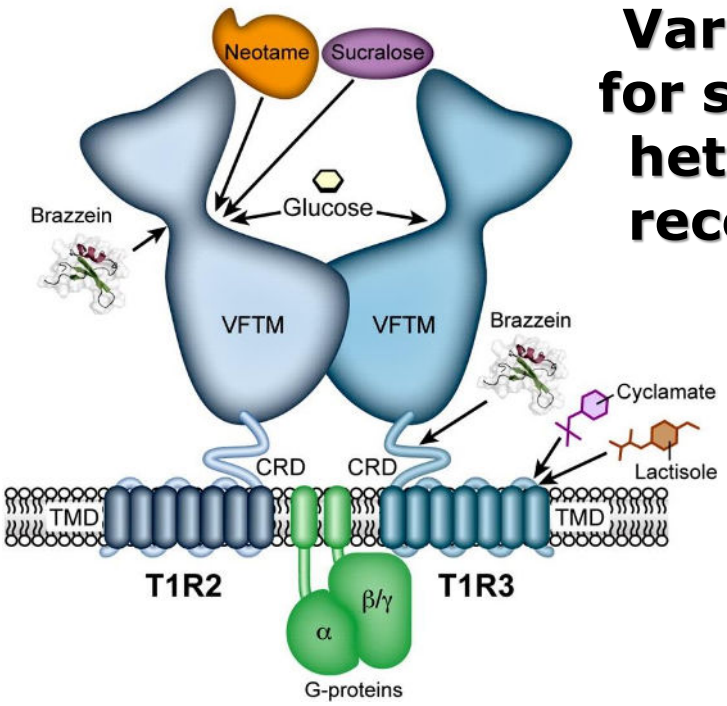


saccharin
non-caloric sweetener
"Sweet'N Low"
RS = 400



cyclamate
non-caloric sweetener
part of "Natreen"
RS = 30

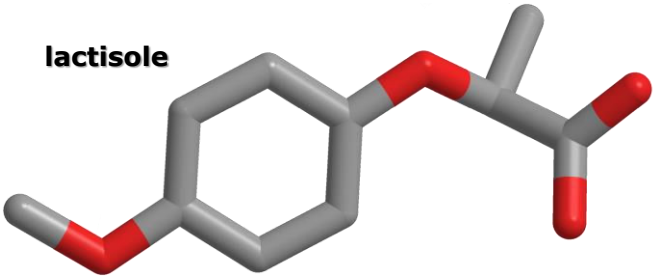
Various binding sites for sweet molecules in heterodimeric sweet receptor T1R2/T1R3



Can various sweeteners synergize, so that lower total concentrations can be used?

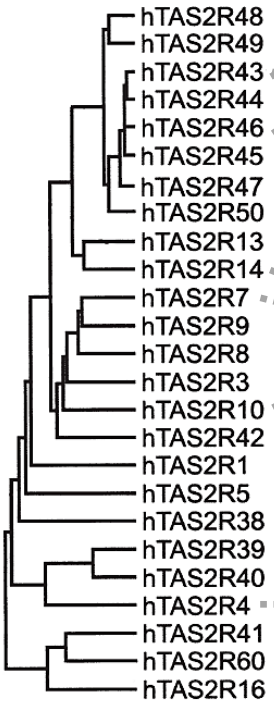
Assadi-Porter et al. (2010) J. Mol. Biol. 398: 584-599.

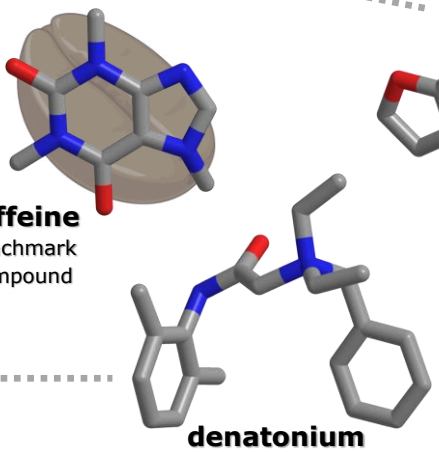
Sweet taste perception can be inhibited by the sweet blocker 'lactisole'



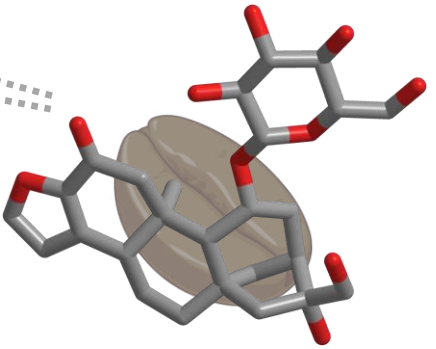
Are there also blockers for other types of receptors?

25 receptors (TAS2Rs) for detecting bitter taste





caffeine
benchmark compound

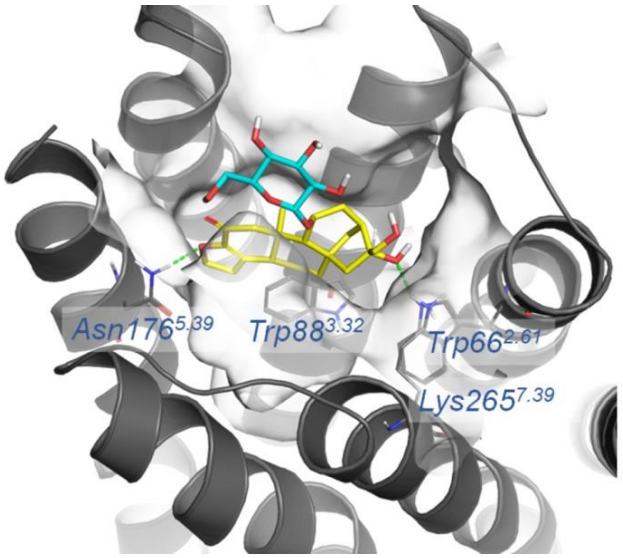


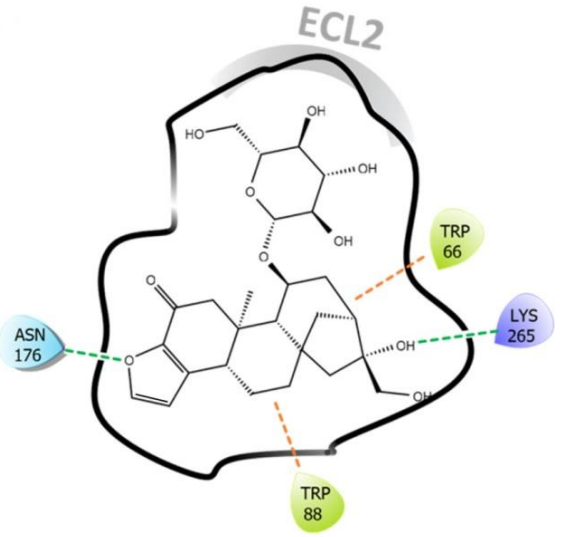
mozambioside
30x more bitter than caffeine

denatonium
most bitter compound known

Behrens and Meyerhof (2006) Cell. Mol. Life Sci. 63: 1501-1509.
Lang et al. (2020) J. Agric. Food Sci. 68: 6692-6700.

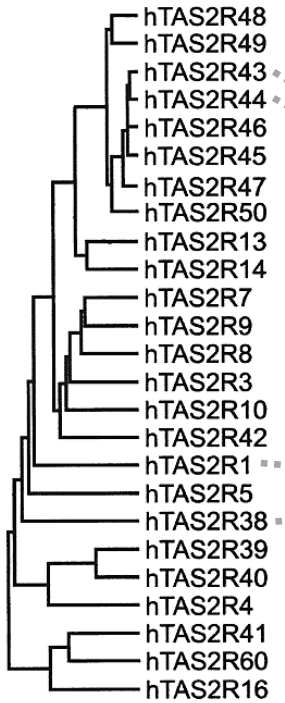
Docking of mozambioside into TAS2R43

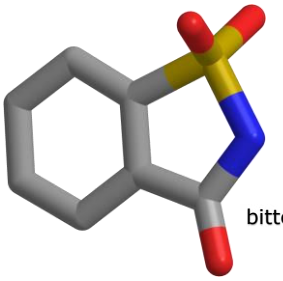




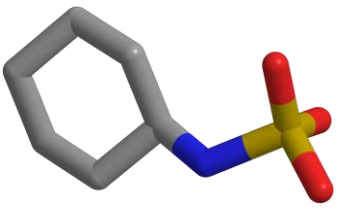
Lang et al. (2020) J. Agric. Food Sci. 68: 6692-6700.

Also non-caloric sweeteners are recognized by TAS2Rs





saccharin
non-caloric sweetener
"Sweet'N Low"
bitterness threshold ≈ 0.12 mM



cyclamate
non-caloric sweetener
part of "Natreen"
bitterness threshold ≈ 30 mM

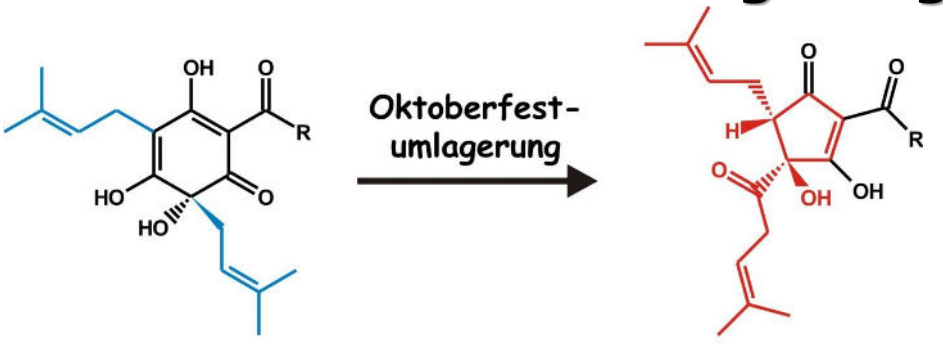
Behrens et al. (2017) Cell Chem. Biol. 24: 1199-1204.

Bitterness in beer is mediated by hop bitter acids

hop bitter acids activate 3 bitter receptors at concentrations of ~0.04-15 µM

Dunkel et al. (2020) J. Agric. Food Chem. 68: 10414-10423.

The "Oktoberfest Umlagerung"

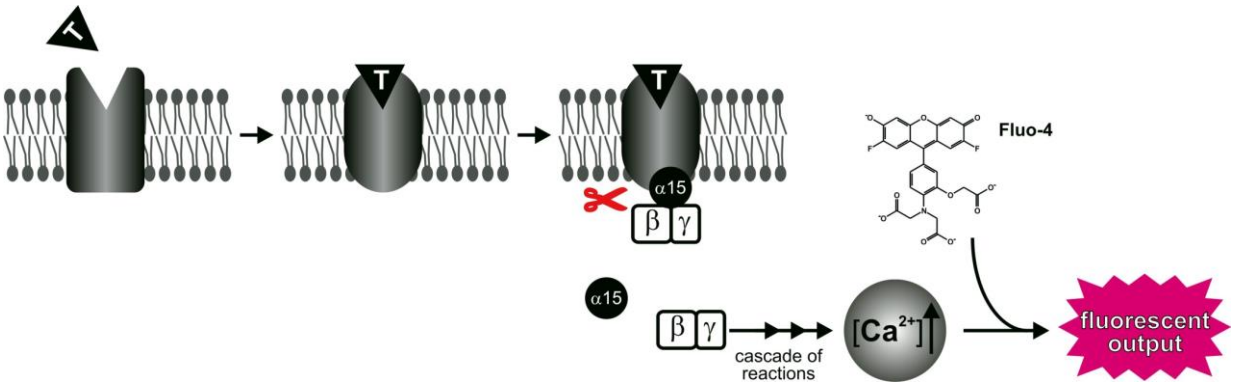


alpha-acids

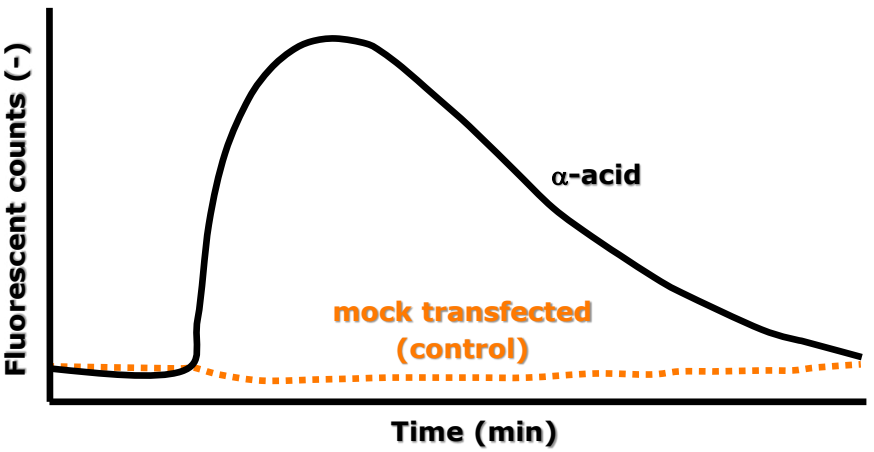
iso-alpha-acids

- Hop contains α-acids, which are <u>NOT</u> so bitter by themselves (in human panel tests!)
- During the brewing step (high T), they are converted to iso-α-acids, which are very bitter (taste threshold <1 ppm)!

Recombinant cells with bitter receptors as a "color assay" to determine bitterness

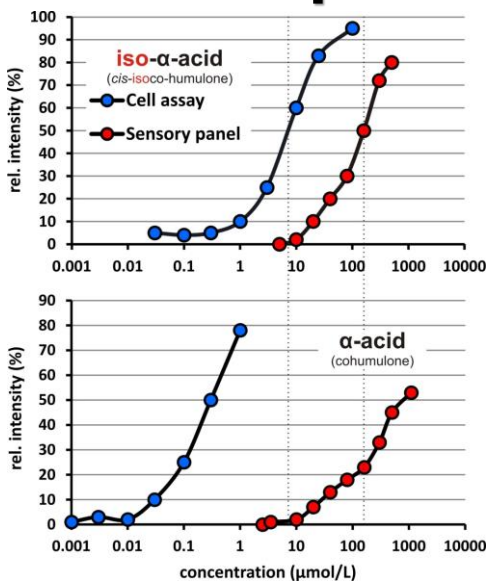


Response of recombinant TAS2R1 cells to α-acid from hop



Intelmann et al. (2009) Chem. Percept. 2: 118-132.

Cell assay- and sensory panel-based dose-response curves of bitter acids



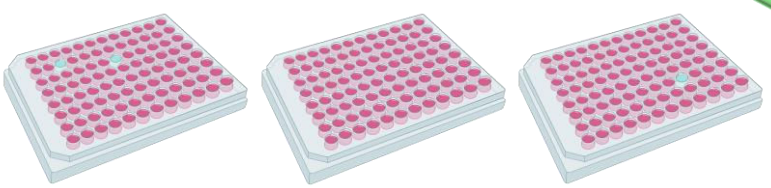
- Curves were used to determine the characteristic EC_{50} values (EC_{50} = half-maximal effective concentration)
- Note that human sensory panelists give high… EC_{50} scores (lower potenc… …ids AND iso-α-acids … …eptor cell assa…
- Note la… acids betwe… assay and human… experiment!

One cannot only rely on cell-based taste receptor assays

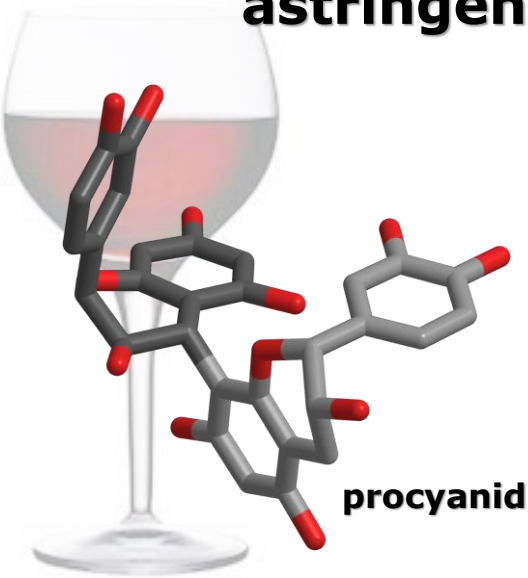
What is the importance of cell-based bitter taste receptor assays?

- Determine the intrinsic bitterness of compounds
- Better understand inter-individual variation in bitter perception
- Discovery of bitter blockers

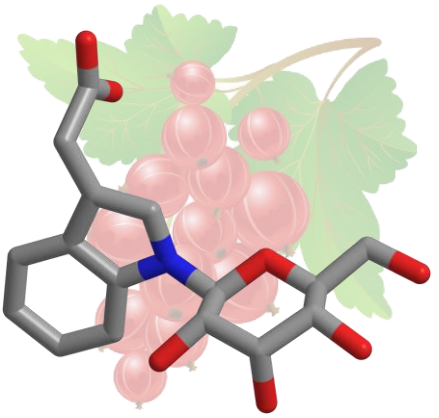
Cell-based taste receptor assays are powerful for high-throughput screening purposes



Different molecular signatures of astringent substances

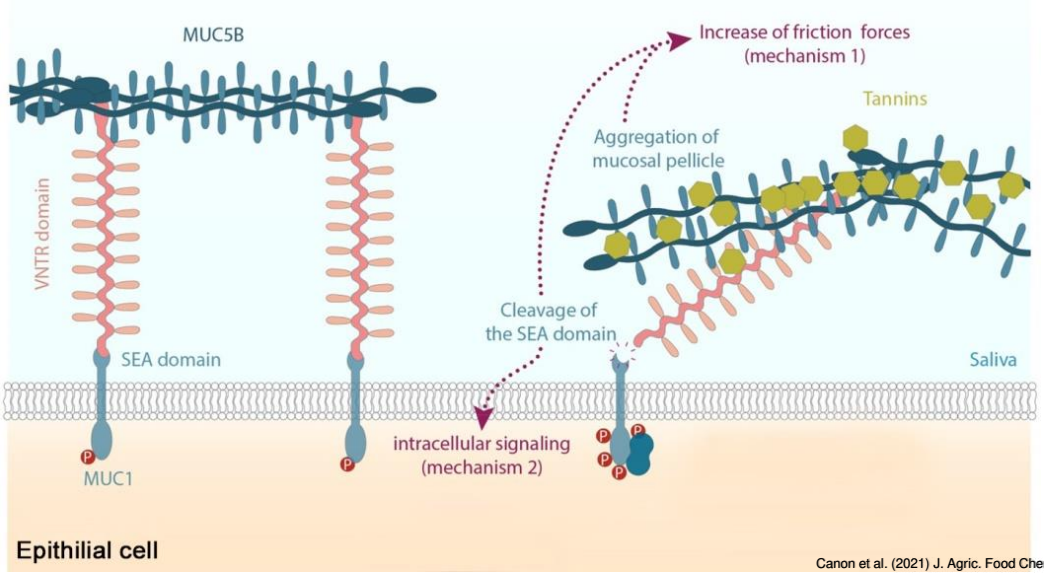


procyanidin



3-carboxymethyl-indole-1-*N*-β-D-Glc*p*

Hypothesis on the molecular mechanism underpinning astringency sensation



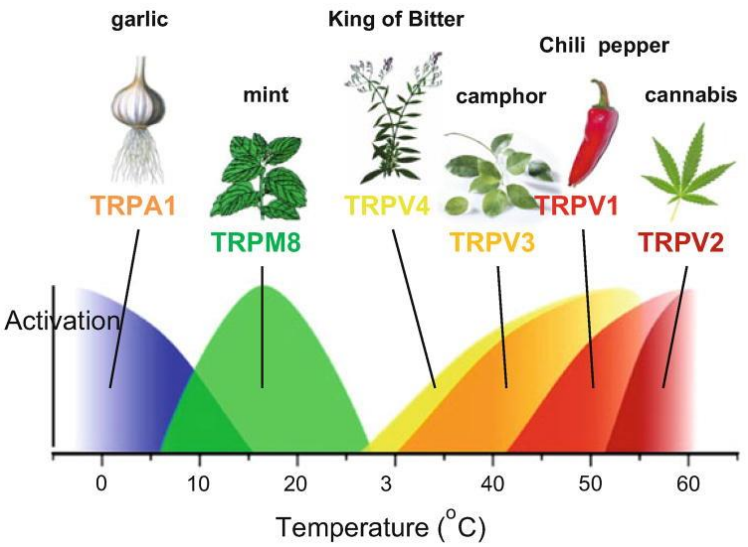
Canon et al. (2021) J. Agric. Food Chem. 69: 3822-3826.

Taste enhancement

- **Umami**
  - Taste of mono sodium glutamate (MSG)
  - Certain molecules can boost the umami taste of MSG, or the sweet or salty taste of sucrose an… respectively
- **Kokumi**
  - Often peptides
  - No intrinsic taste at all
  - Can boost the intensity of other taste …

- Strategy for salt reduction to combat hypertension
- Improve palatability of foods for elderly

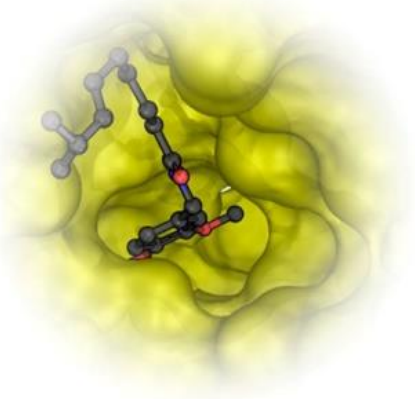
Sensors (TRP channels) for hot and cold also bind spicy and cooling molecules

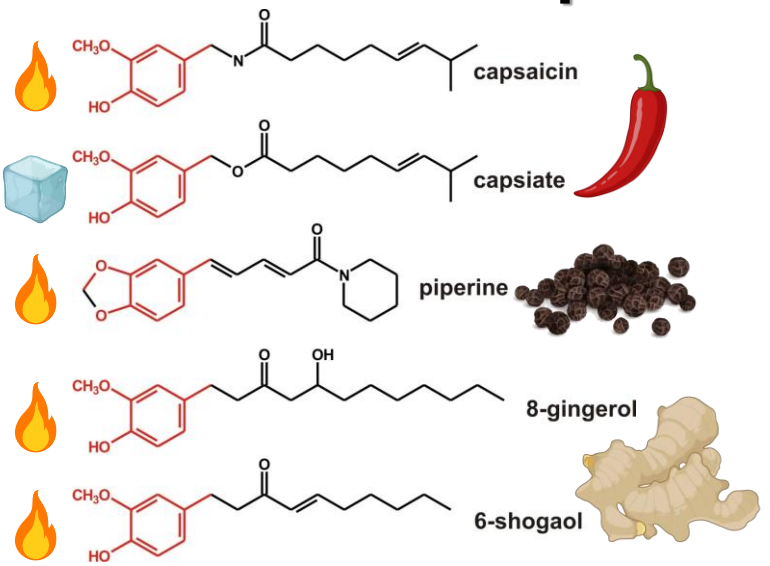


- Each TRP opens in a 'specific' temperature window
- Besides, each TRP recognizes a specific set of molecules associated with taste sensations

Roper (2014) Handb. Exp. Pharmacol. 223: 827-871.

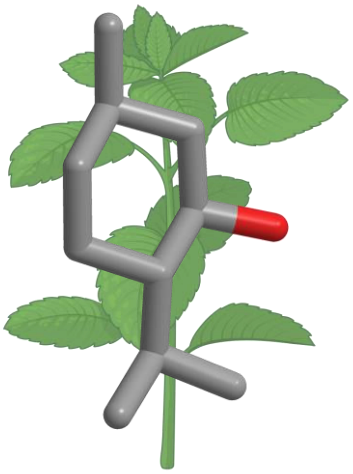
The homovanillyl group as a structural motif to bind to the TRPV1 receptor



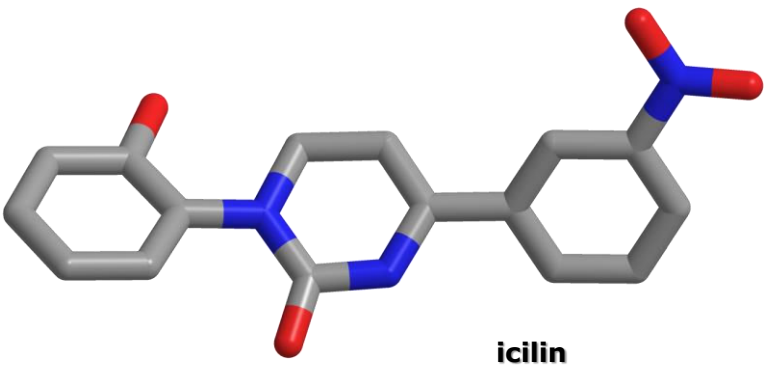


Examples of cooling compounds

Substances activate TRPM8 / TRPA1



(-)-menthol
peppermint
benchmark compound



icilin
synthetic
champion cooling

Cooling compounds formed during Maillard reaction

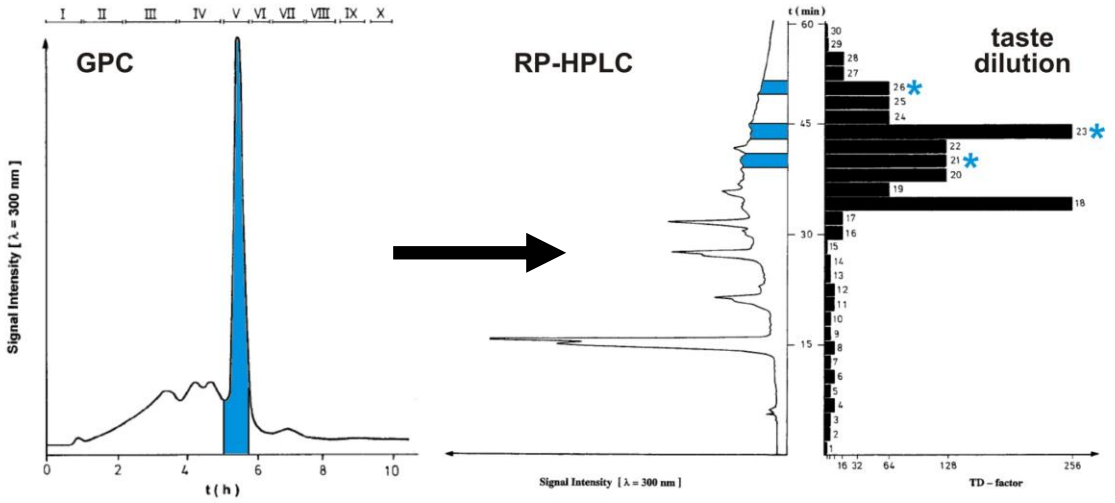
- During roasting of cereal grain (dark malt) Maillard reaction occurs
- Cereals contain high amount of proline and hexose
- Dry-heating of proline / glucose (equimolar) mixture (20 min, 190 °C)

Ottinger et al. (2001) J. Agric. Food Chem. 49: 1336-1344.

Principle of taste dilution assay (TDA)

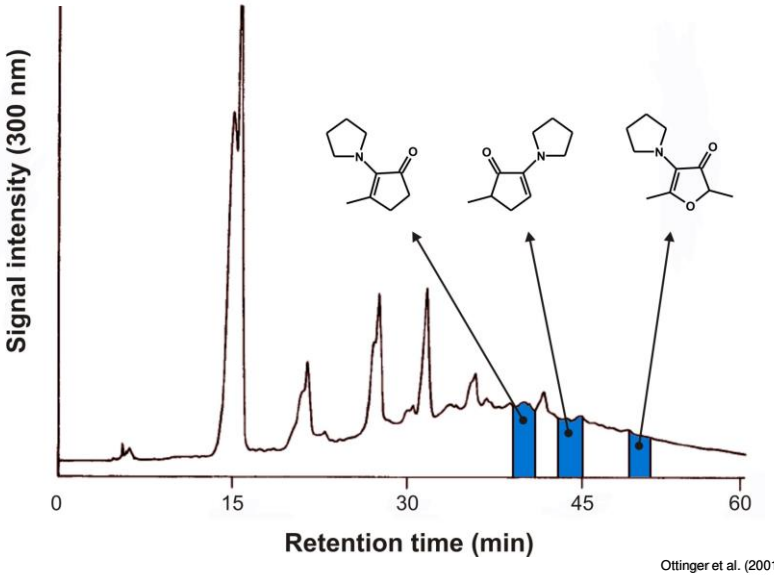
- Determination of the relative contribution of different compounds to the total taste of a mixture
- Mixture of compounds subjected to various kinds of chromatography
- Serial dilutions of the different fractions to determine the highest dilution at which a specific taste is still perceived (taste dilution factor, TDF)
- Repeated fractionation and TDA can identify taste-active compounds

Taste dilution assay to detect cooling compounds in dark malt-like products



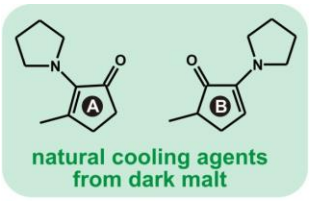
Ottinger et al. (2001) J. Agric. Food Chem. 49: 1336-1344.

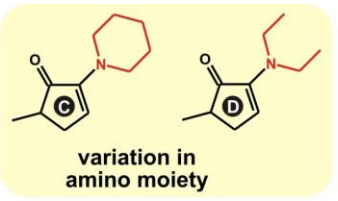
Structure of novel cooling compounds in dark malt (α-keto enamine motif?)

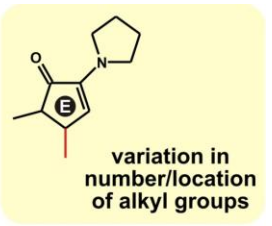


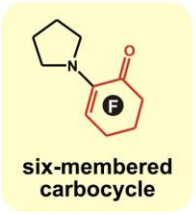
Ottinger et al. (2001) J. Agric. Food Chem. 49: 1336-1344.

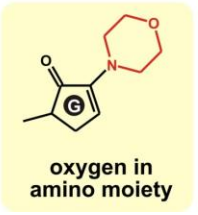
Better cooling compounds from leads of dark malt by organic synthesis?

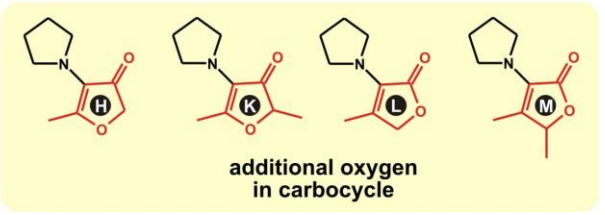










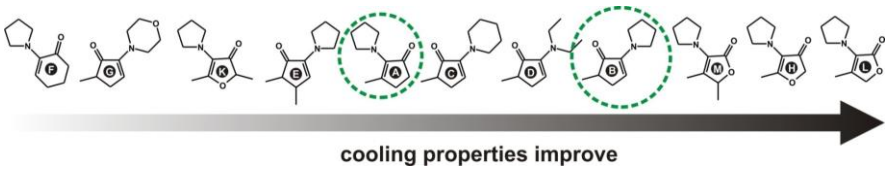


Ottinger et al. (2001) J. Agric. Food Chem. 49: 1336-1344.

Comparison of cooling and odor tresholds of α-keto enamines

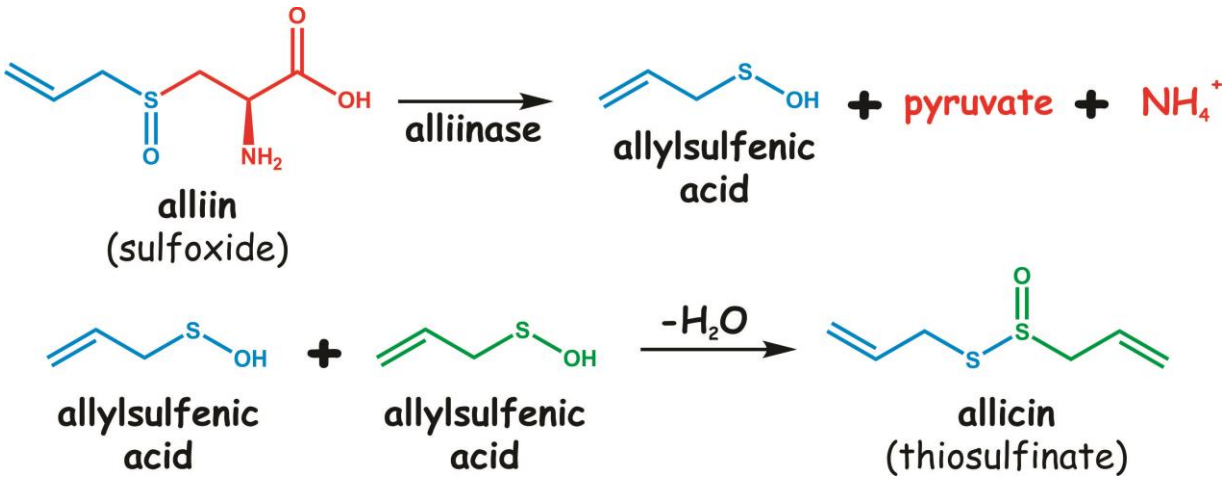
Compound	Cooling threshold (mg/kg)	Odor threshold (mg/kg)	Odor quality
F	715	80	rubber-like
G	585	1245	rubber-like
K	120	45	nutty, roasty
E	90	180	faintly mint-like
A	35	60	faintly amine-like
C	20	16	faintly mint-like
D	16	7.5	curcuma-like
B	6.7	3.9	faintly mint-like
M	3.0	50	faintly mint-like
H	2.2	-	odor-less
L	0.04	-	odor-less
(-)-menthol	1.5	0.2	mint-like

Note that the (minty) odor and cooling activity can be uncoupled

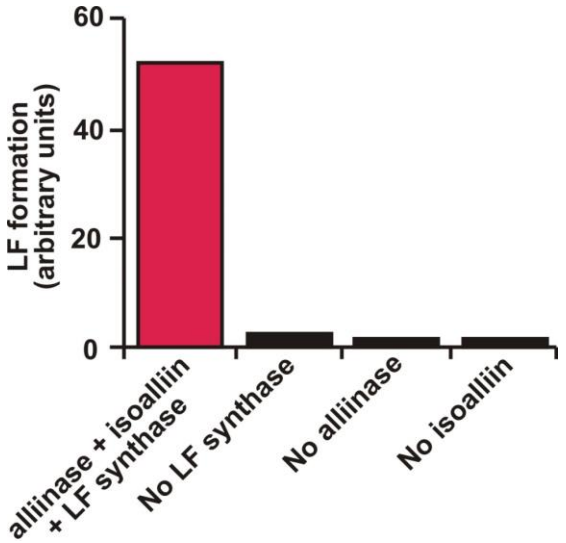


Ottinger et al. (2001) J. Agric. Food Chem. 49: 1336-1344.

Enzymatic (alliinase) conversion of onion precursors to flavor



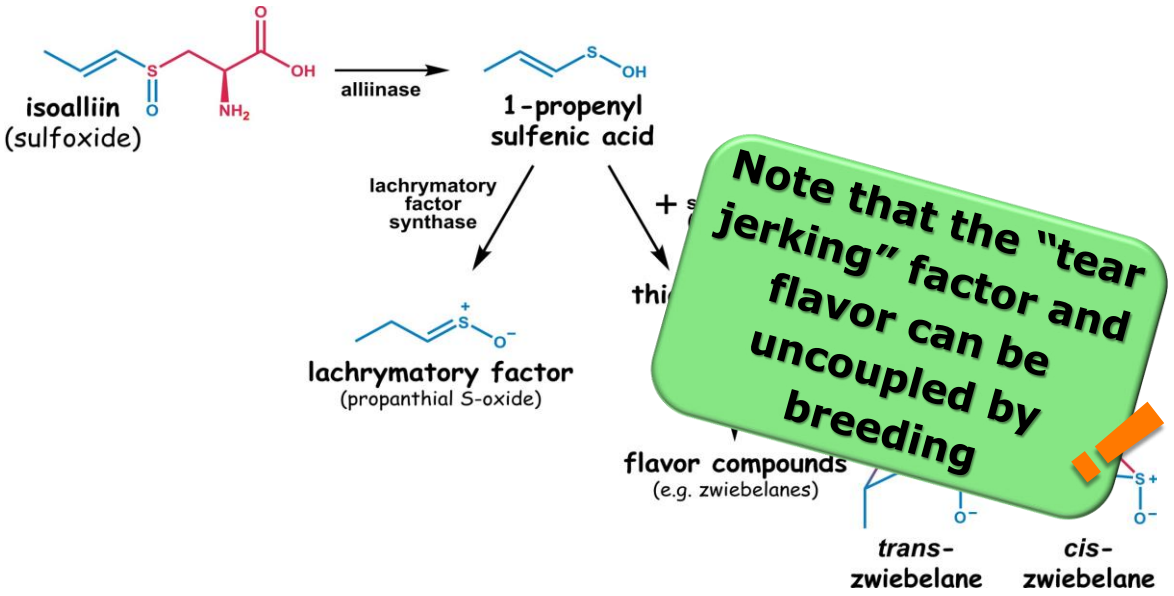
An enzyme is responsible for the lachrymatory or "tear-jerking" factor in onion



- Lachrymatory factor (LF) corresponds to propanthial S-oxide, a compound discovered in 2002
- The compound is formed by the enzyme LF synthase
- Breeding possibilities for flavorsome, user-friendly onion bulb

Imai et al. (2002) Nature 419: 685.

Reactions leading to lachrymatory factor



Imai et al. (2002) Nature 419: 685.

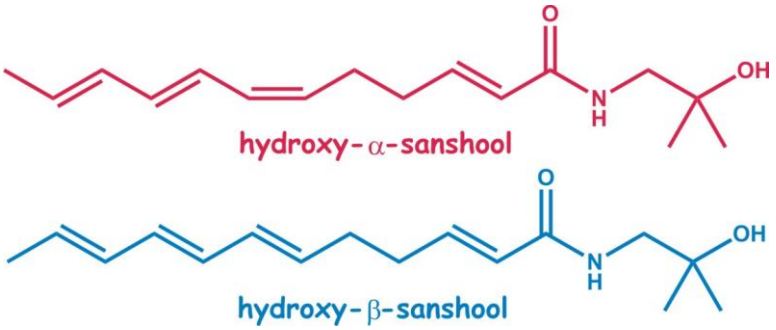
Tingling substances – the electric effect

Unsaturated alkyl amides activate TRPA1

Szechuan flower buttons

Sichuan peppercorns

"Subtle" structural differences influence perception of unsaturated alkyl amides

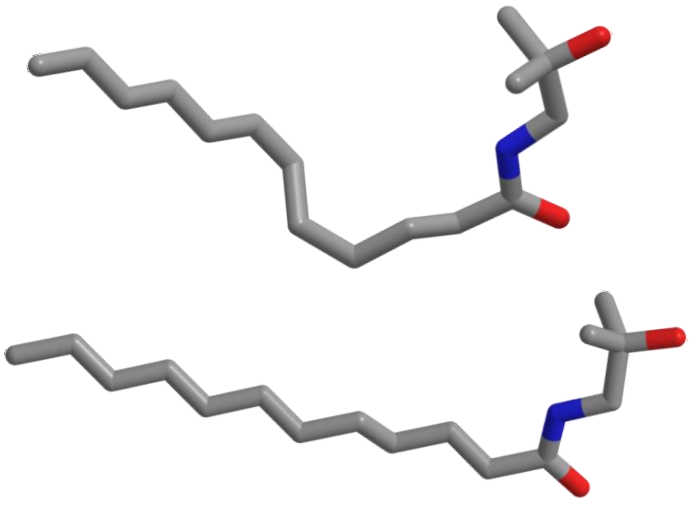


Tingling effect
Salivating

Numbing effect
Reduced salivation

Bader et al. (2014) J. Agric. Food Chem. 62: 2479-2488.

"Subtle" structural differences influence perception of unsaturated alkyl amides



Hydroxy-α-sanshool
Tingling effect
Salivating

Hydroxy-β-sanshool
Numbing effect
Reduced salivation

Bader et al. (2014) J. Agric. Food Chem. 62: 2479-2488.

Chewing gum with taste sensations

Encapsulation / slow release approaches allow to alter taste perception in time!

Take-home messages

- Detailed understanding of tastant-receptor interactions growing, but signal transduction to brain and cross-modal interactions remain challenging
- Deorphanizing olfactory receptors → more palatable foods and designer perfumes?
- Trends in food technology:
  - Healthy food (low-calorie, low salt, high antioxidant), tasty food for elderly
  - Animal-to-plant protein transition → mitigating off-flavor / improving flavor

… creating the right chemistry …

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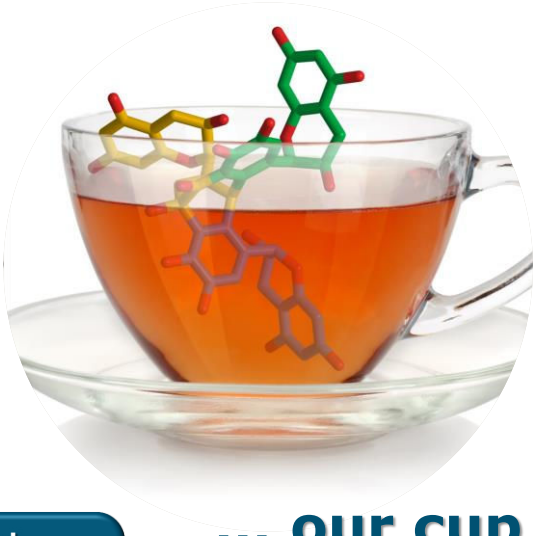

… our cup of tea …