



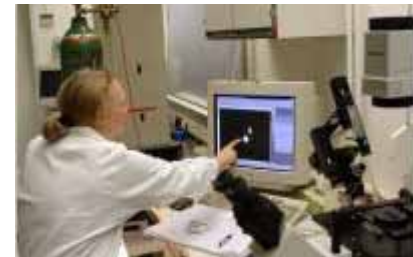
Süßgeschmackswahrnehmung als Grundlage für kalorienfreie Süßstoffe

*DECHEMA-Kolloquium
Luckenwalde, 1. November 2007*

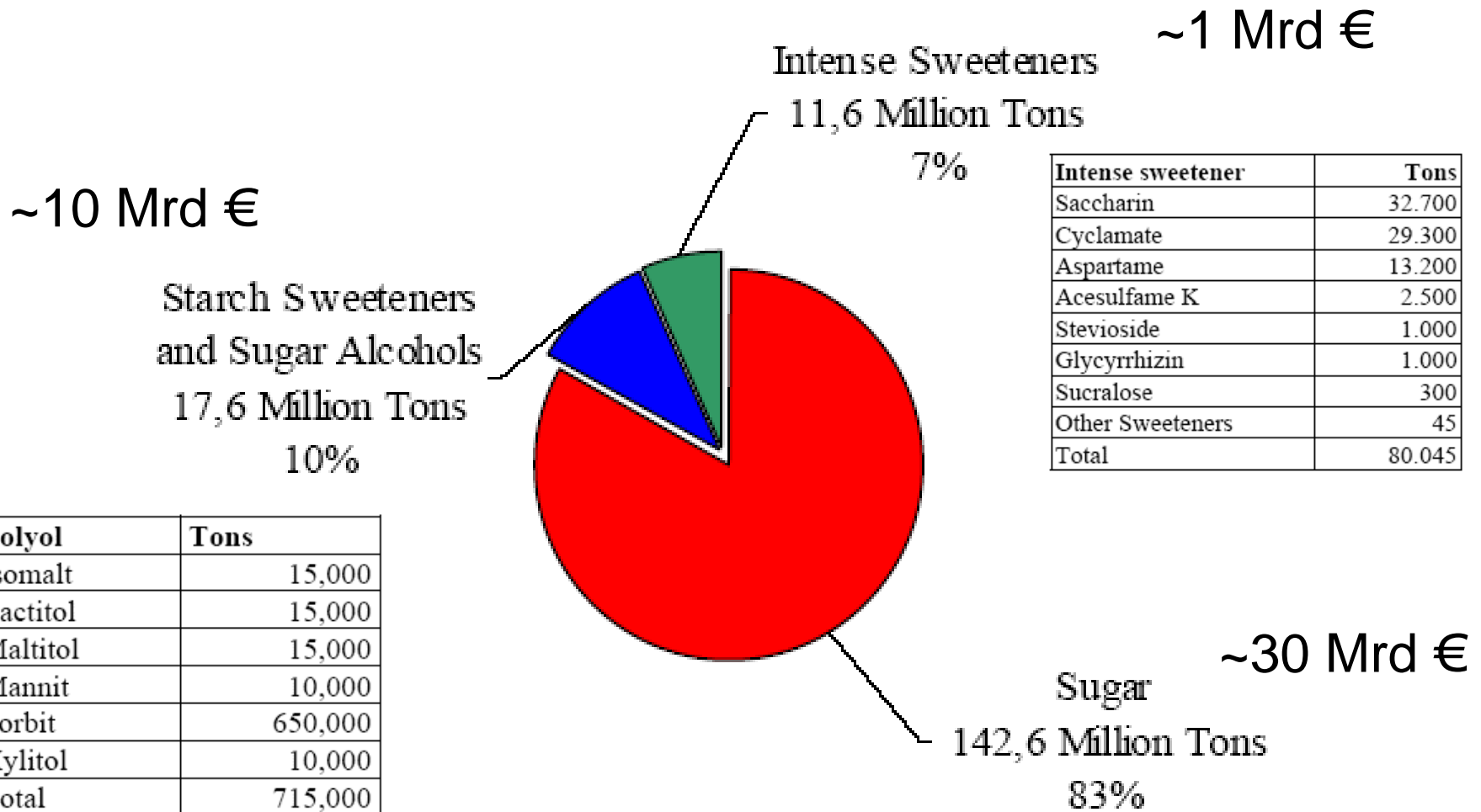
Wolfgang Meyerhof



**German Institute of
Human Nutrition
Potsdam-Rehbruecke**



World Production Volume of Sweeteners (2003) expressed in sugar equivalents



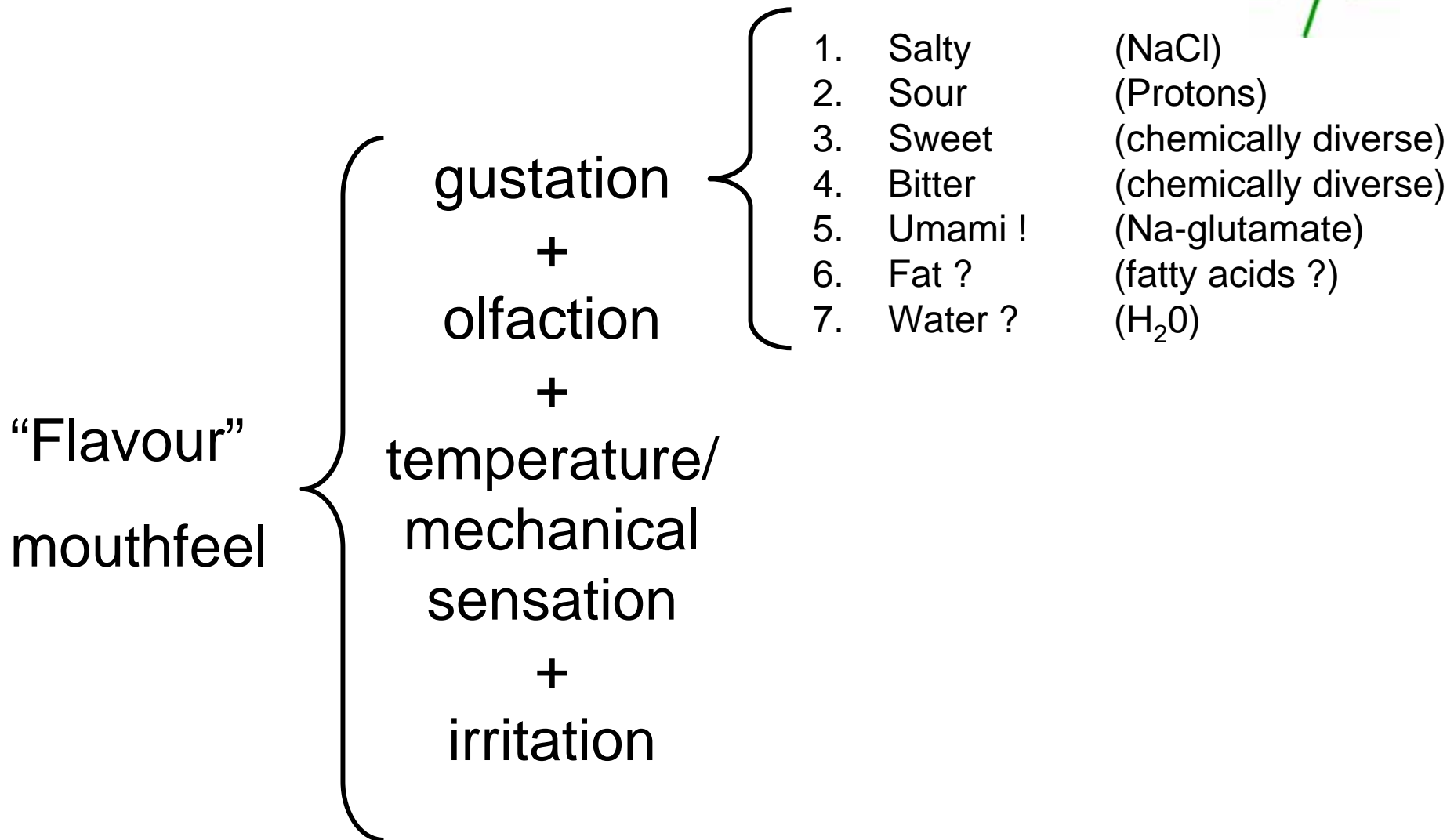
Disadvantages of starch sweeteners and polyols
<p>1. High caloric value As people become more health conscious and count calories demand for starch sweeteners may suffer.</p>
<p>2. Dental care As with sugar starch sweeteners are implicated in tooth decay.</p>
<p>3 Laxative effects of polyols In some cases the high volumes required in food production have a laxative effect when consuming the particular products. Regular consumption however, can lead to adaption and increased tolerance.</p>

Disadvantages of Intensive Sweeteners
<p>Health Some intensive sweeteners are suspected of having an adverse effect on health; while in most cases this will only be true if the intensive sweetener is consumed in excess, health warnings are sometimes obligatory on product labels: aspartame, saccharine</p>
<p>Taste Sweetness is a subjective phenomenon, perceived differently from individual to individual. Different intensive sweeteners produce different taste sensations, not all of them desirable, and some leave an unpleasant aftertaste.</p>

Sweetener	EU	USA	Canada	Japan	Australia
Saccharin	Allowed	Allowed	Not allowed	Allowed	Allowed
Aspartame	Allowed	Allowed	Allowed	Allowed	Allowed
Acesulfame K	Allowed	Limited	Allowed	Not allowed	Allowed
Cyclamate	Allowed	Not allowed	Limited	Not allowed	Allowed
NHDC	Allowed	GRAS	Not allowed	Allowed	Allowed
Thaumatococin	Allowed	GRAS	Allowed	Allowed	Allowed
Stevioside *	Not allowed	Dietary Supplement	Dietary Supplement	Allowed	Dietary Supplement
Glycyrrhizine	Not Allowed	Not allowed	Not allowed	Allowed	Not allowed
Alitame	Not Allowed	Allowed	Allowed	Allowed	Allowed
Sucralose	Allowed	Allowed	Allowed	Allowed	Allowed

Multiple sensations but only 5 basic qualities

D/E



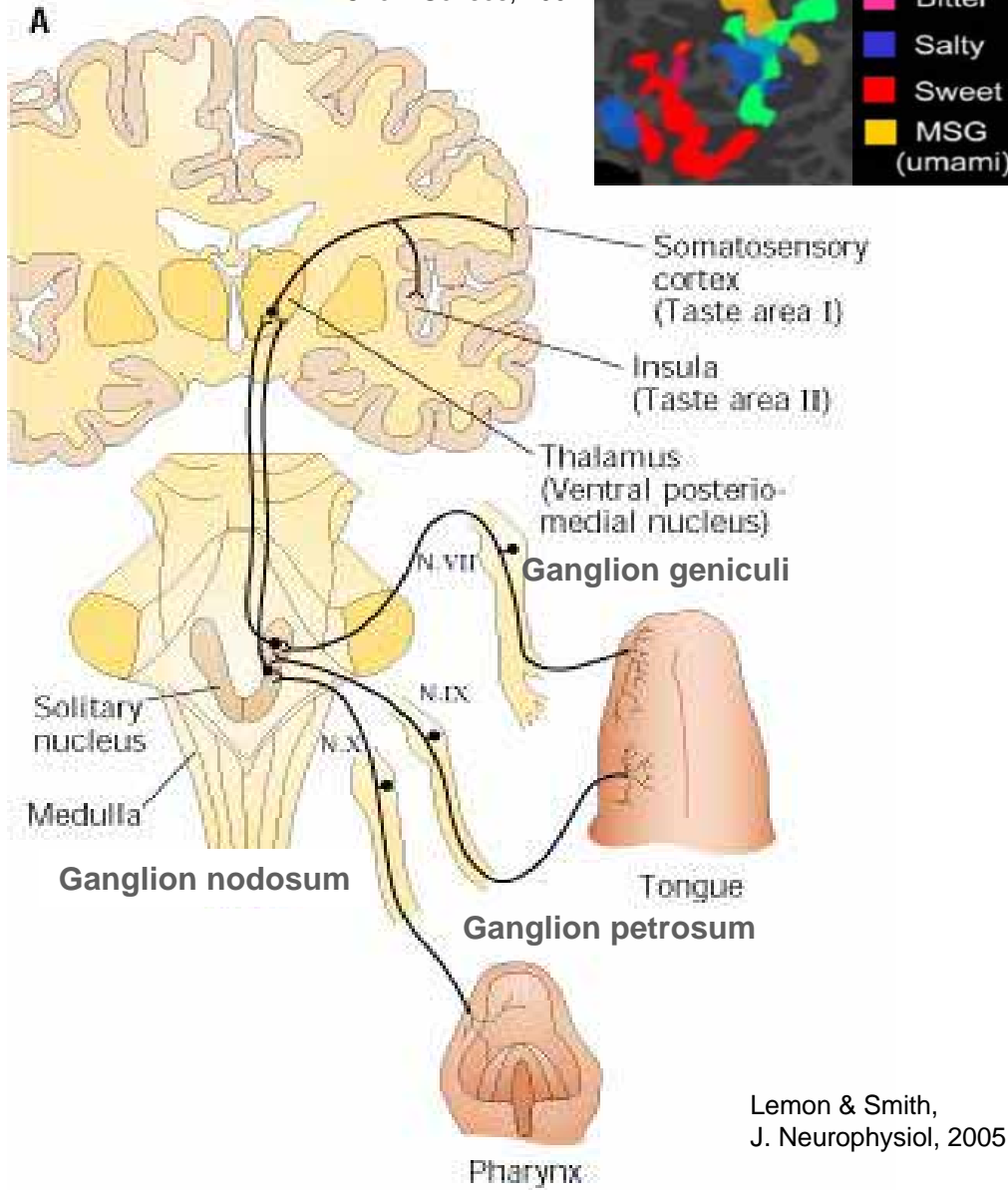
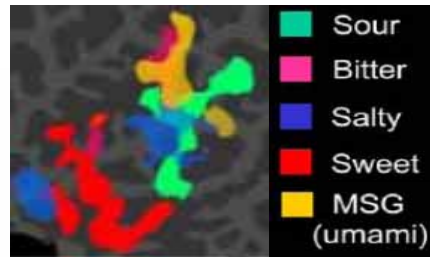
Taste modalities



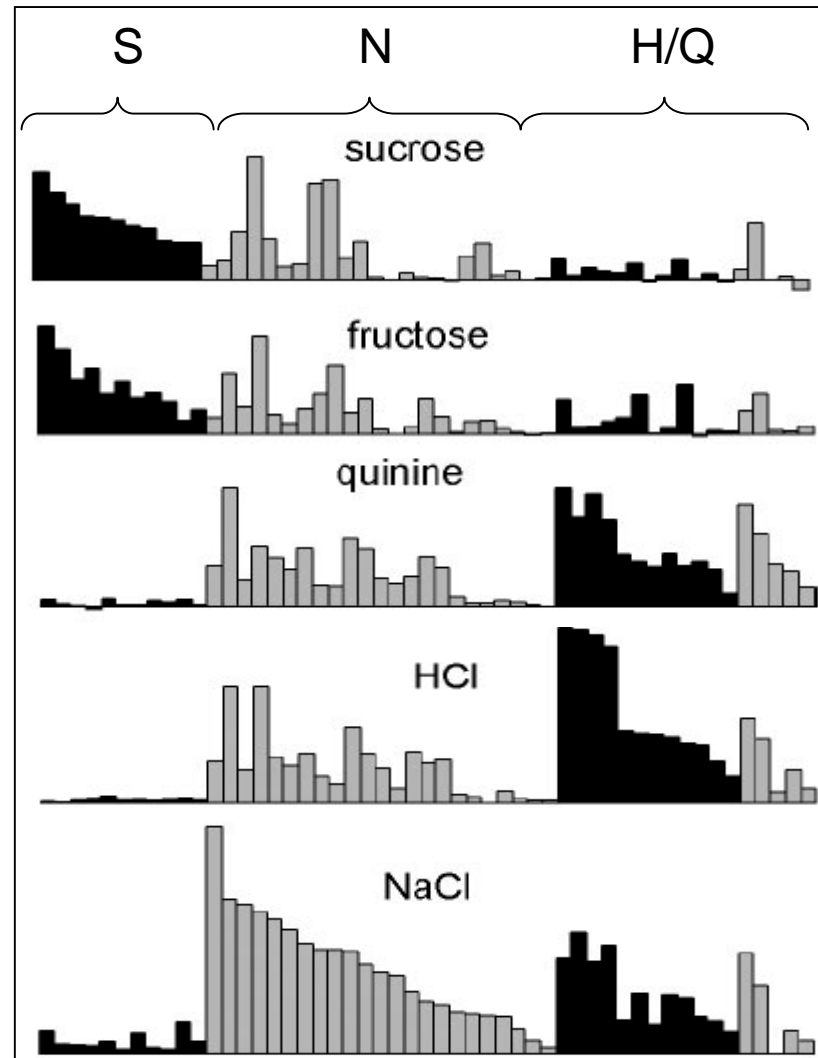
Modality	Function	Hedonic	Substance	Threshold (mol/l)
Bitter	Warning	Aversive	Quinine sulfate	0.000008
			Nicotin	0.000016
Sour	Warning	Aversive ↑	HCl	0.0009
		Attractive ↓	Citrate	0.0023
Sweet	Calorie detector	Attractive	Sucrose	0.01
			Glucose	0.08
Salty	Osmo-regulation	Attractive	NaCl	0.01
Umami	Calorie detector	Attractive	Na-glutamate	0.01

Central taste anatomy

Schoenfeld et al.,
Chem Senses, 2004

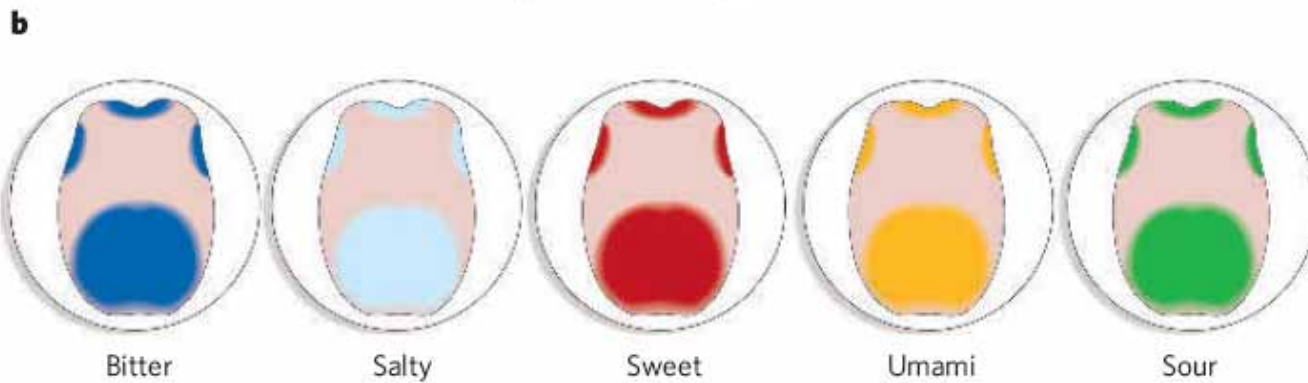
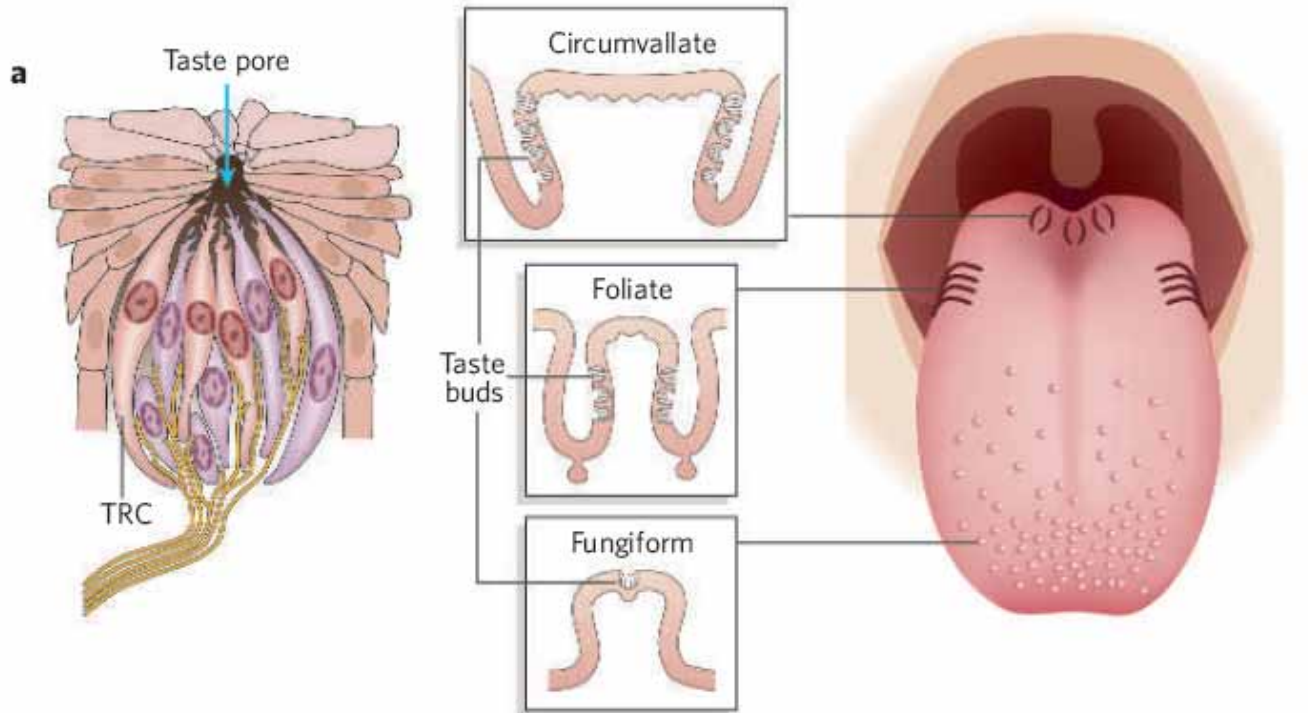


Lemon & Smith,
J. Neurophysiol, 2005



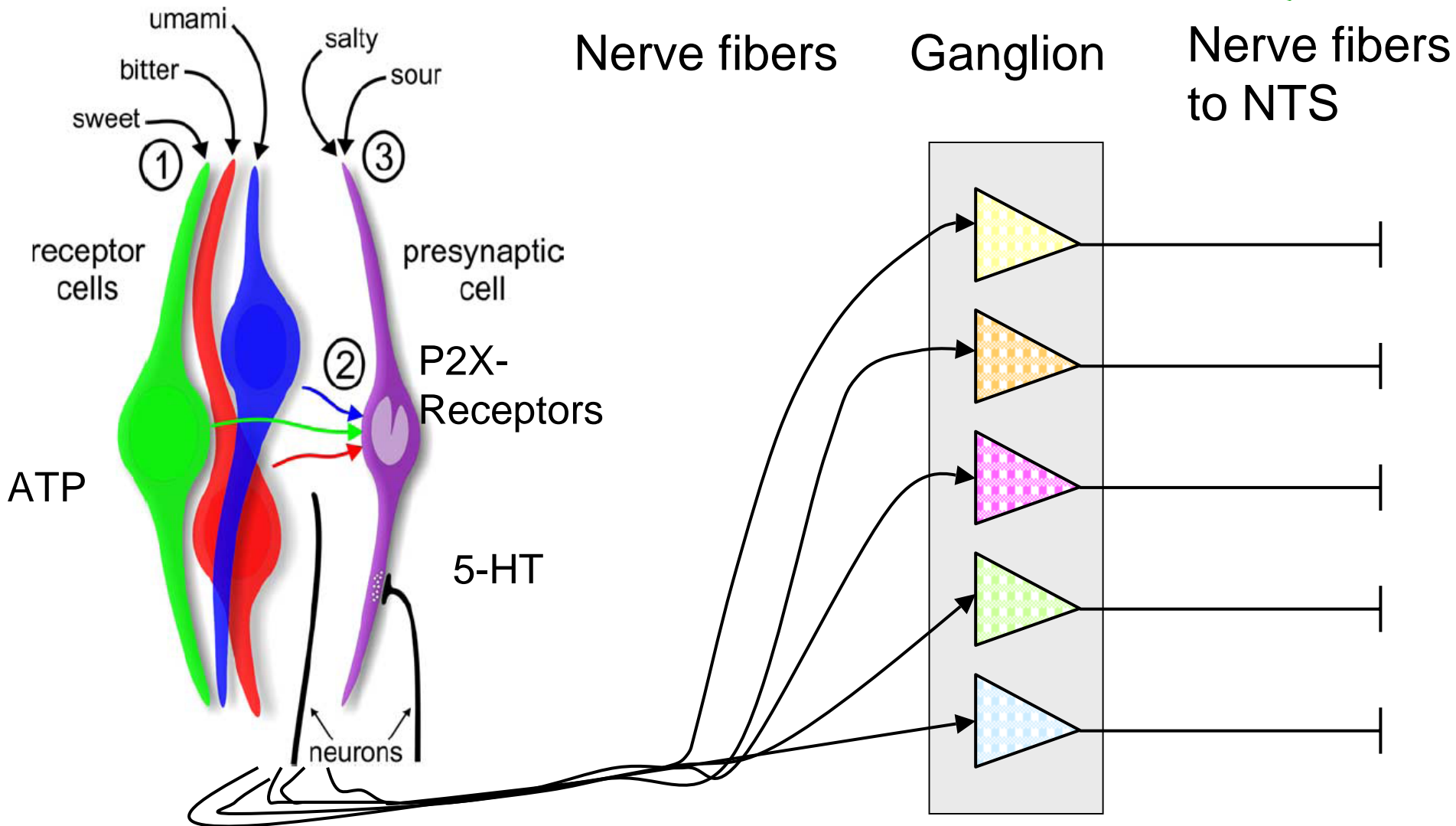
Peripheral taste anatomy

D/E



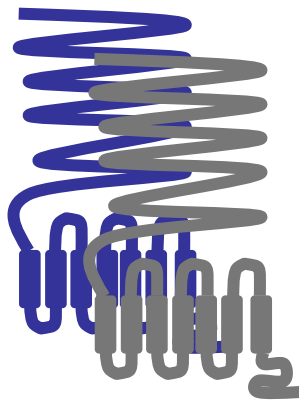
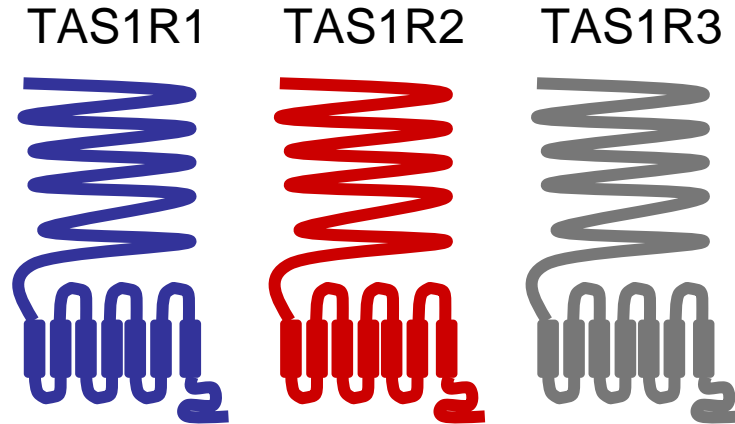
Peripheral taste quality coding II

D/E-

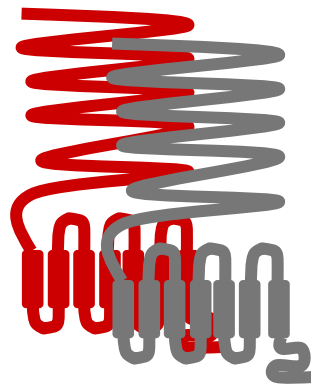


T1R Receptors

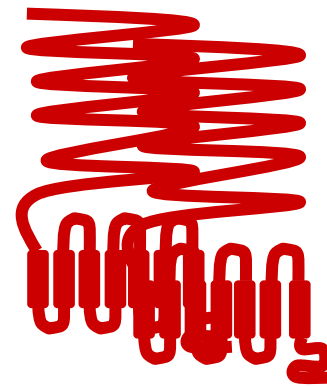
D/E



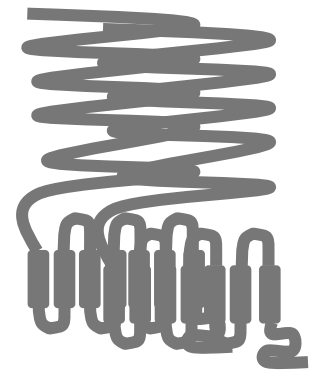
amino acid



sweet



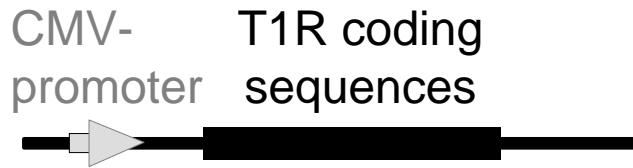
sweet



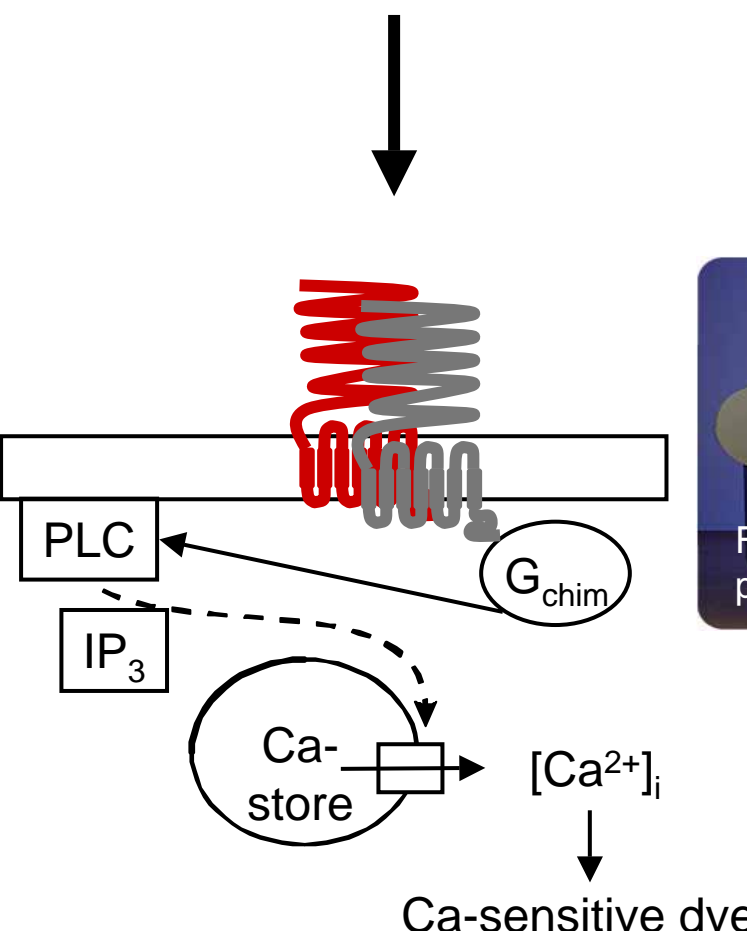
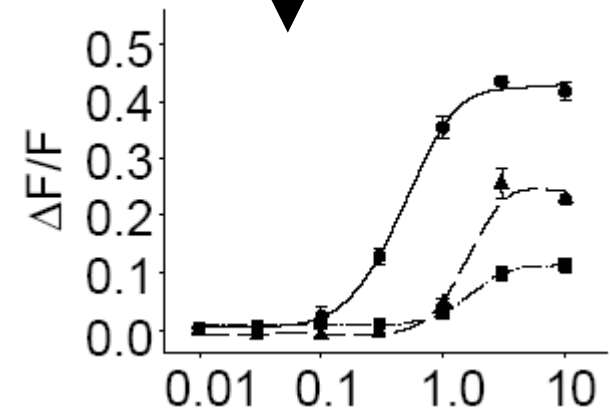
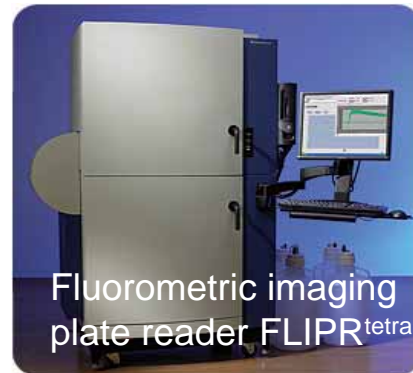
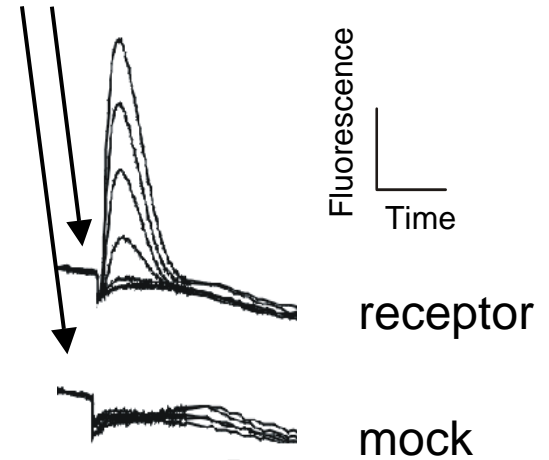
sweet

Functional expression assay of T1Rs

DIFE

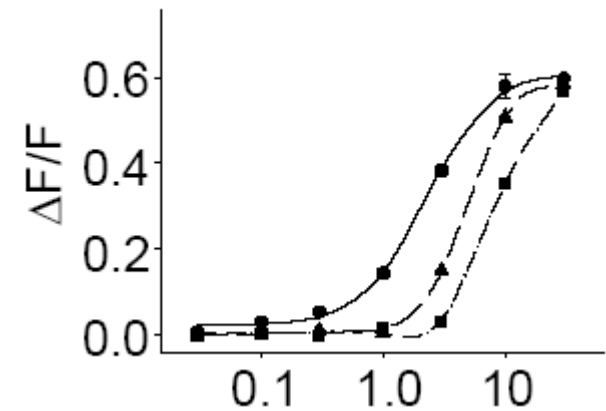
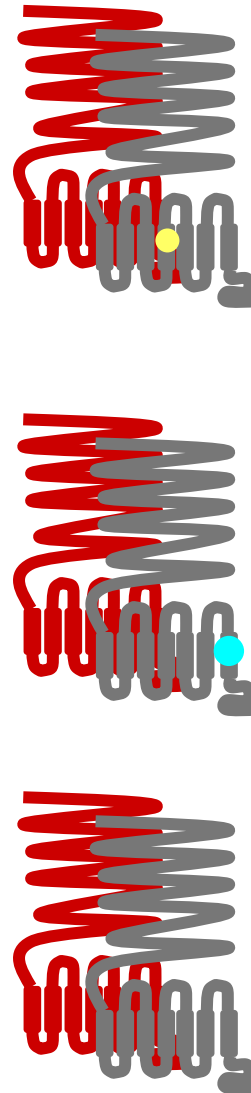
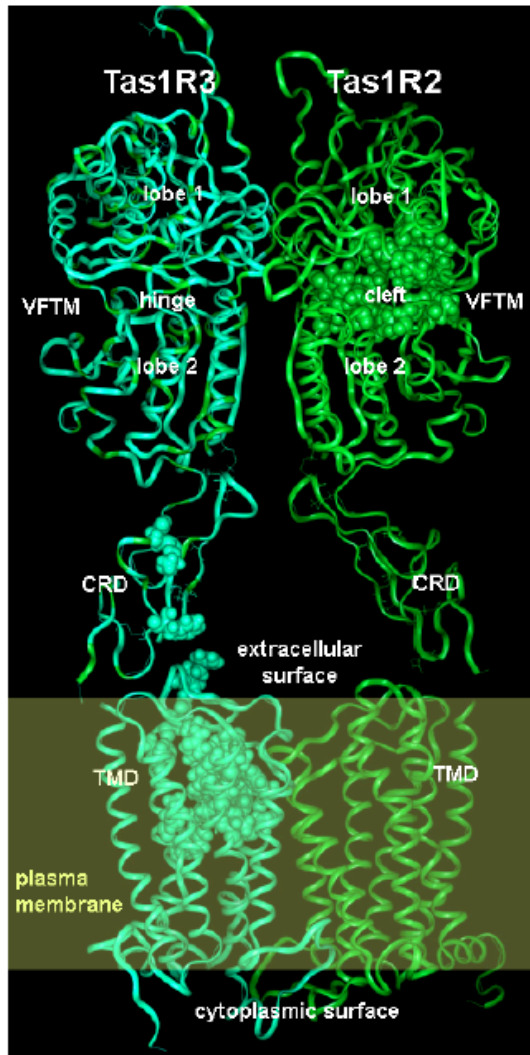


Various sweeteners at increasing concentrations



Molecular modeling of T1R2-T1R3 in combination with mutational analysis

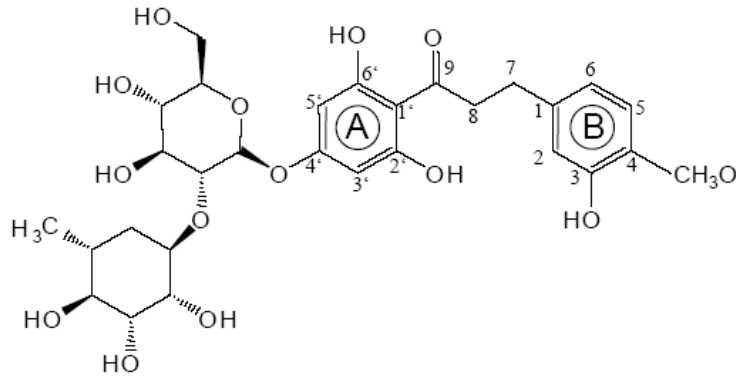
D/E-



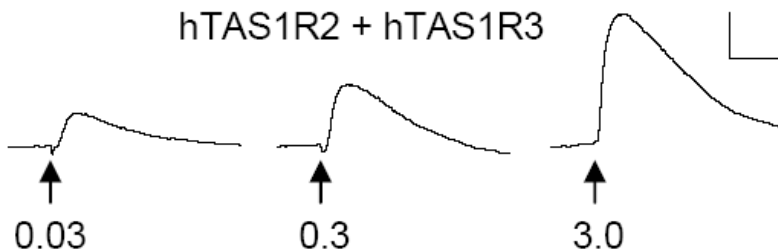
Experimental approach to identify the binding site for NHDC

D/E-

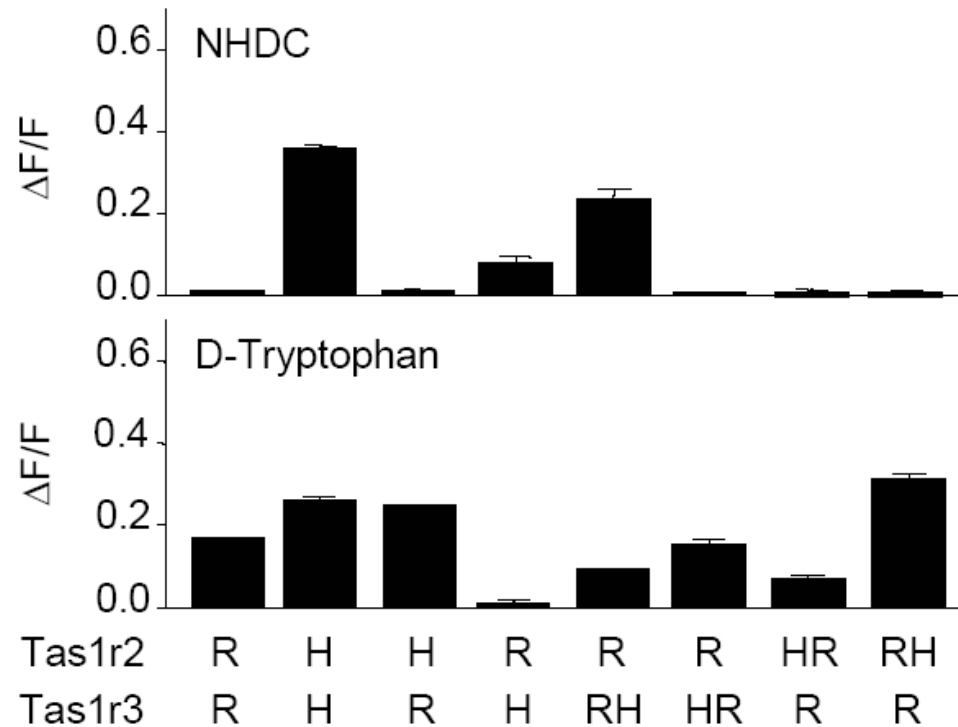
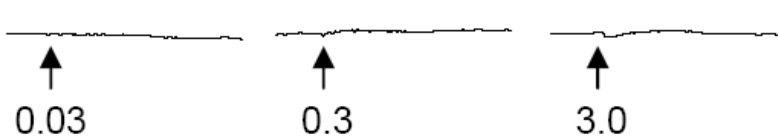
neohesperidin dihydrochalcone



hTAS1R2 + hTAS1R3

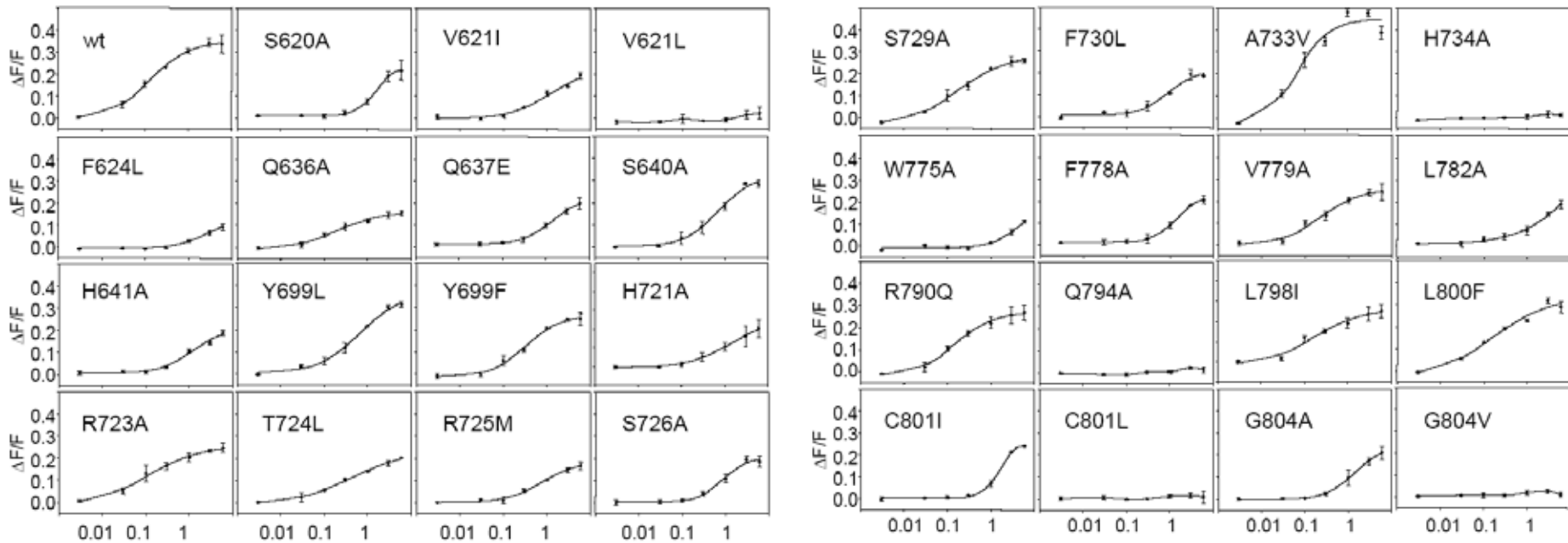


rTas1r2 + rTas1r3



Effects of mutations in human T1R3 after coexpression with wild type T1R2 on responses to neohesperidin dihydrochalcone

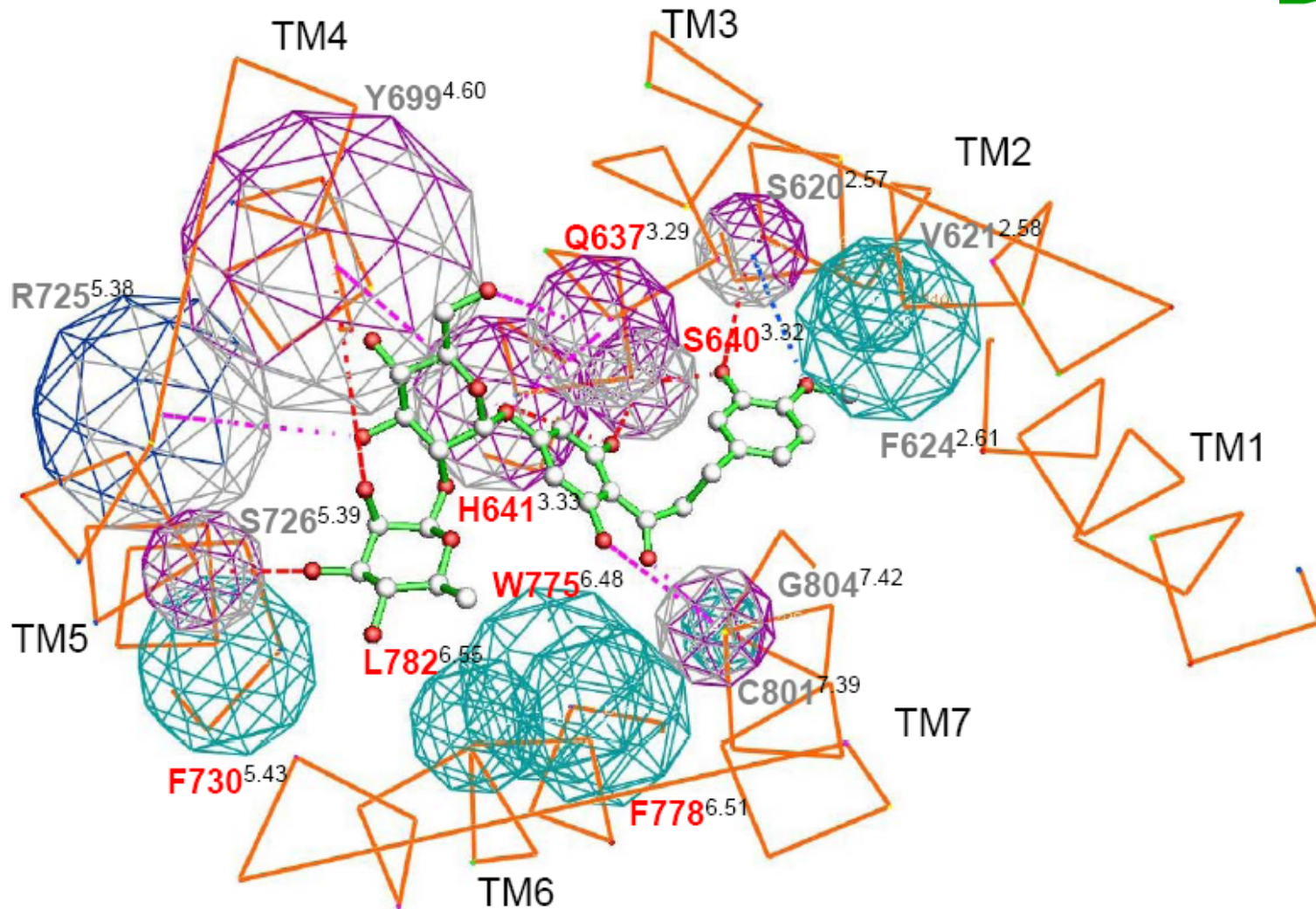
D/E-



[NHDC]

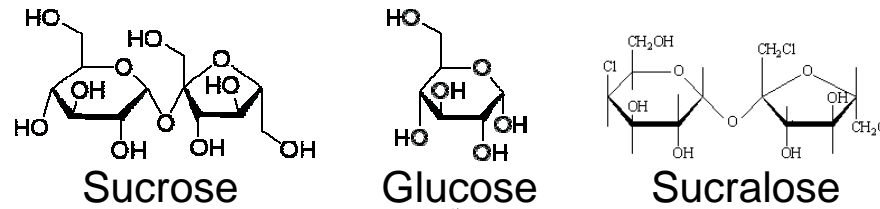
The binding site for NHDC at humn T1R2-T1R3

D/E-

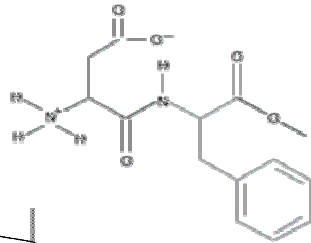


Ligand interaction sites of the sweet taste receptor

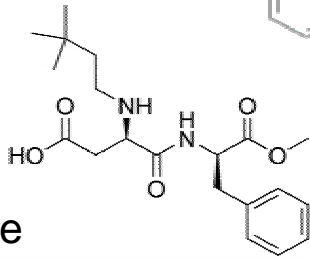
D/E-



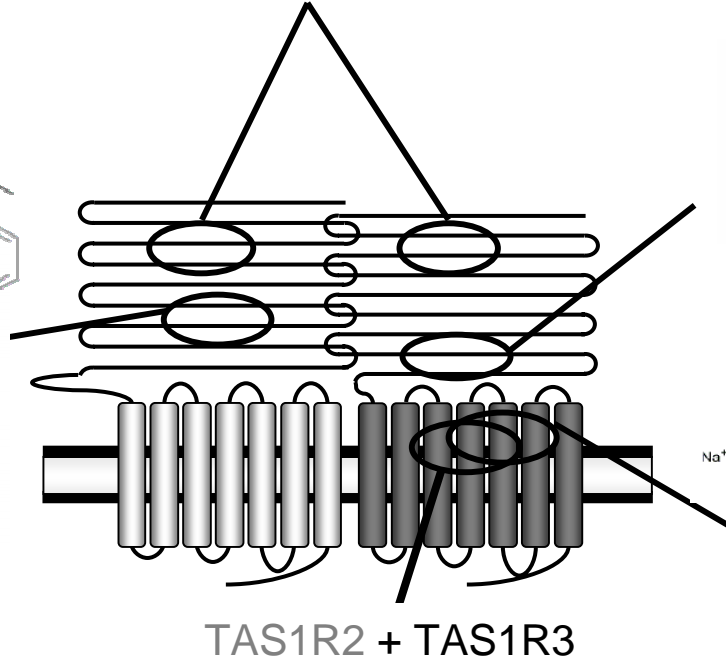
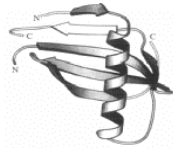
Aspartame



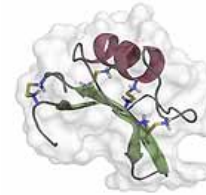
Neotame



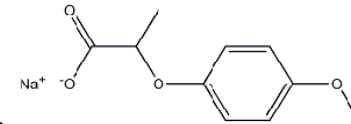
Monellin



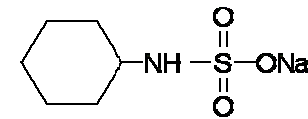
TAS1R2 + TAS1R3



Brazzein

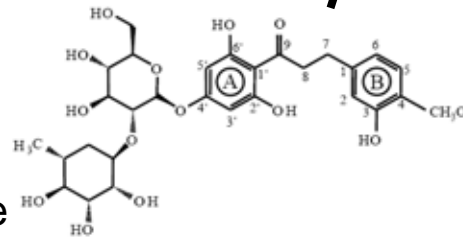


Lactisole



Cyclamate

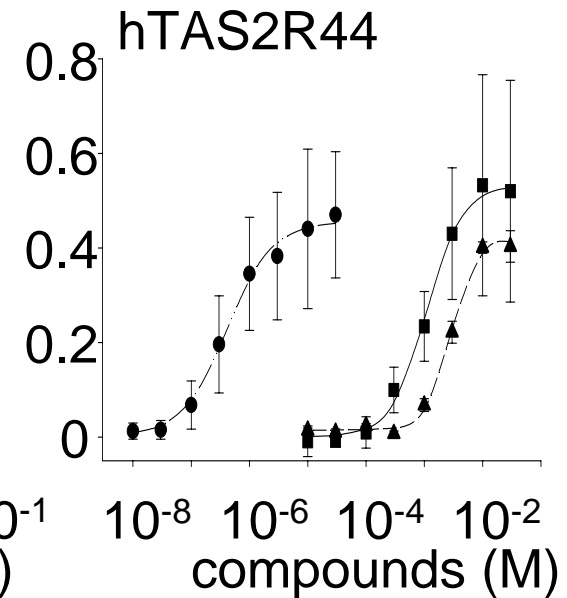
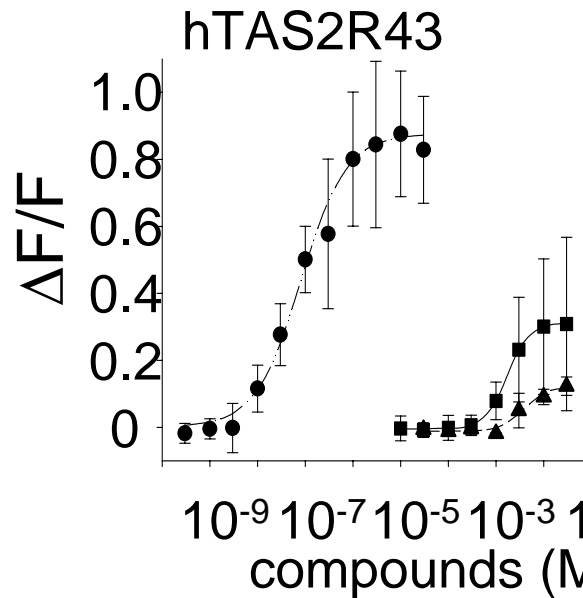
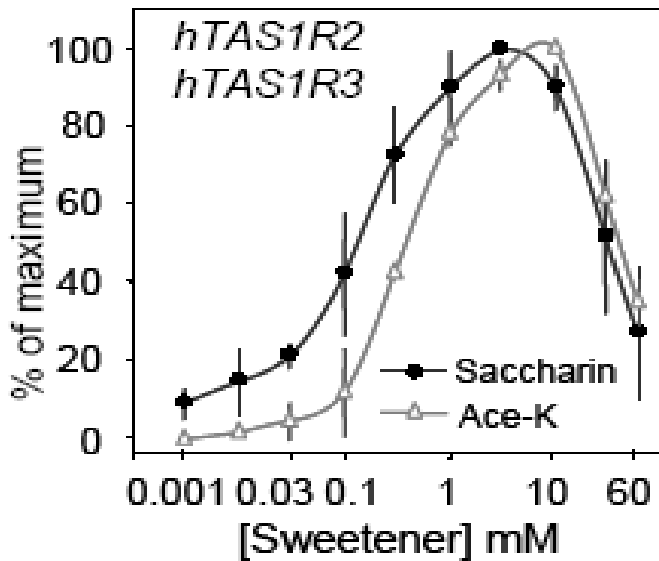
Neohesperidin Dihydrochalcone



Li et al, PNAS, 2002
 Zhao et al, Cell, 2003
 Xu et al, PNAS, 2004
 Jiang et al, JBC, 2004
 Jiang et al, JBC, 2005
 Winning et al, BMC Neurosci, 2005
 Winnig et al, BMC Struct Biol, 2007

Receptor mechanisms highlight sensory problems of sulfonyl amide sweeteners

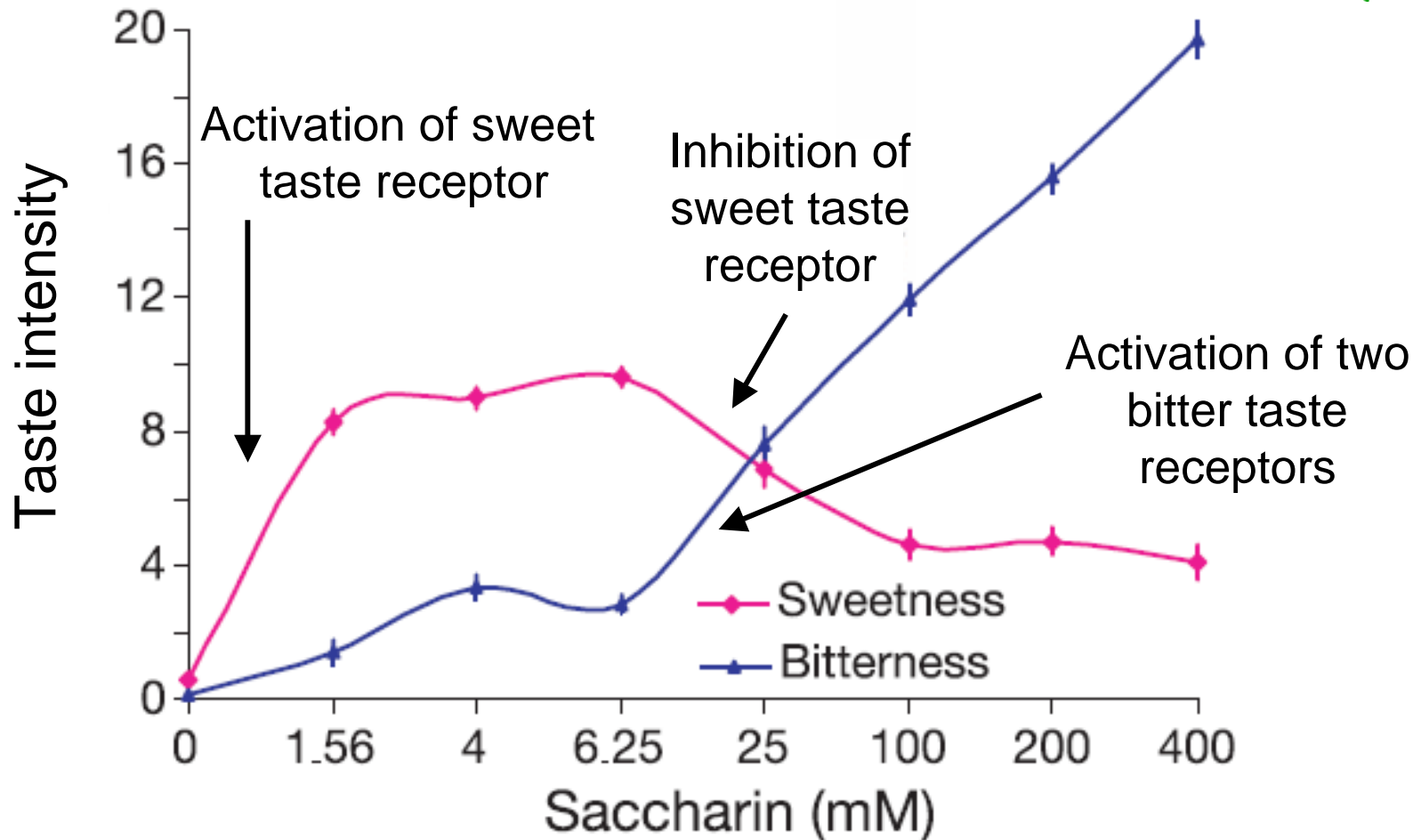
D/E



- Aristolochic acid
- Saccharin
- ▲ Acesulfame-K

Receptor mechanisms explain gustatory perception

D/E



Screening assays for taste-active compounds

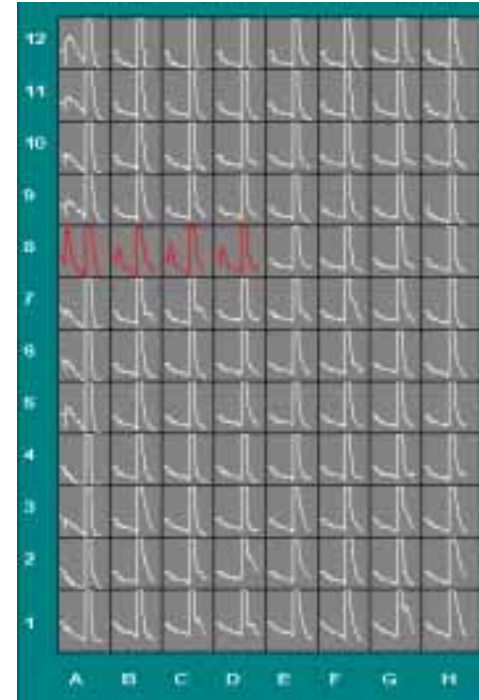
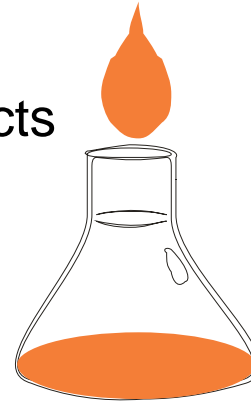
D/E-

Taste panels

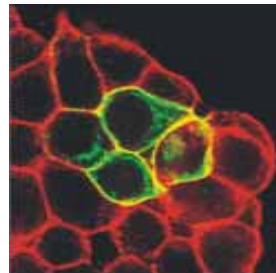


Receptor-based searches

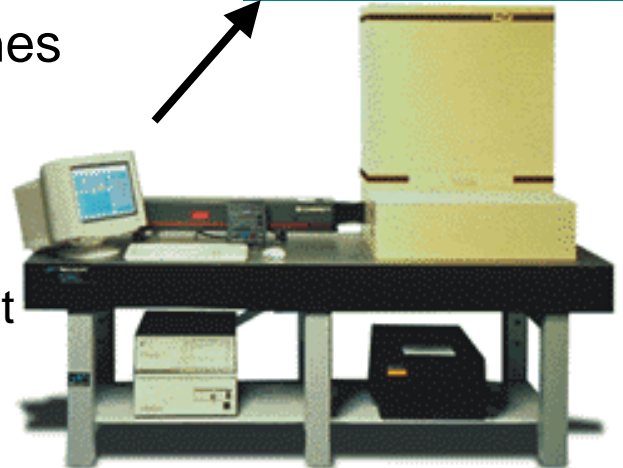
Crude extracts



Engineered cell lines



High throughput screens



	1	2	3	4	5	6	7	...
A	📧	🟪	🟪	🟢	🌀	🟡	🌙	
B	🟡	📧	🌀	🟢	📧	🟡		
C	🌙	🟢	🟡	🟢	🌙			
D	📧	🟡	🌙	🌀				
E	🟢	🌙	🌀					
F	🌀	📧						

Compound libraries



Thank you for your attention !