



# Chimioréception de la saveur sucrée

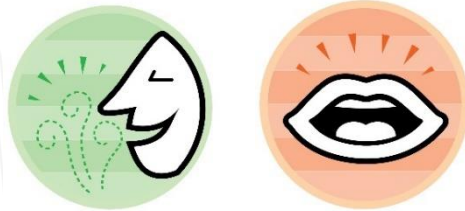
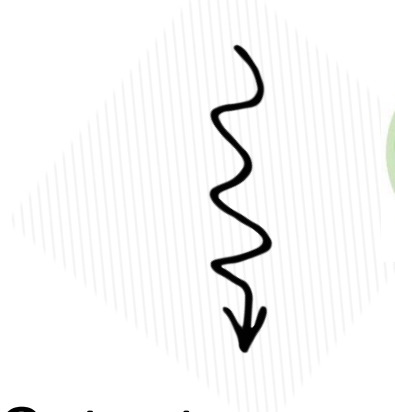
Dr. Sébastien Fiorucci

[Sebastien.Fiorucci@unice.fr](mailto:Sebastien.Fiorucci@unice.fr)

<http://chemosim.unice.fr/fiorucci>

# Odorat et goût : 2 sens chimiques

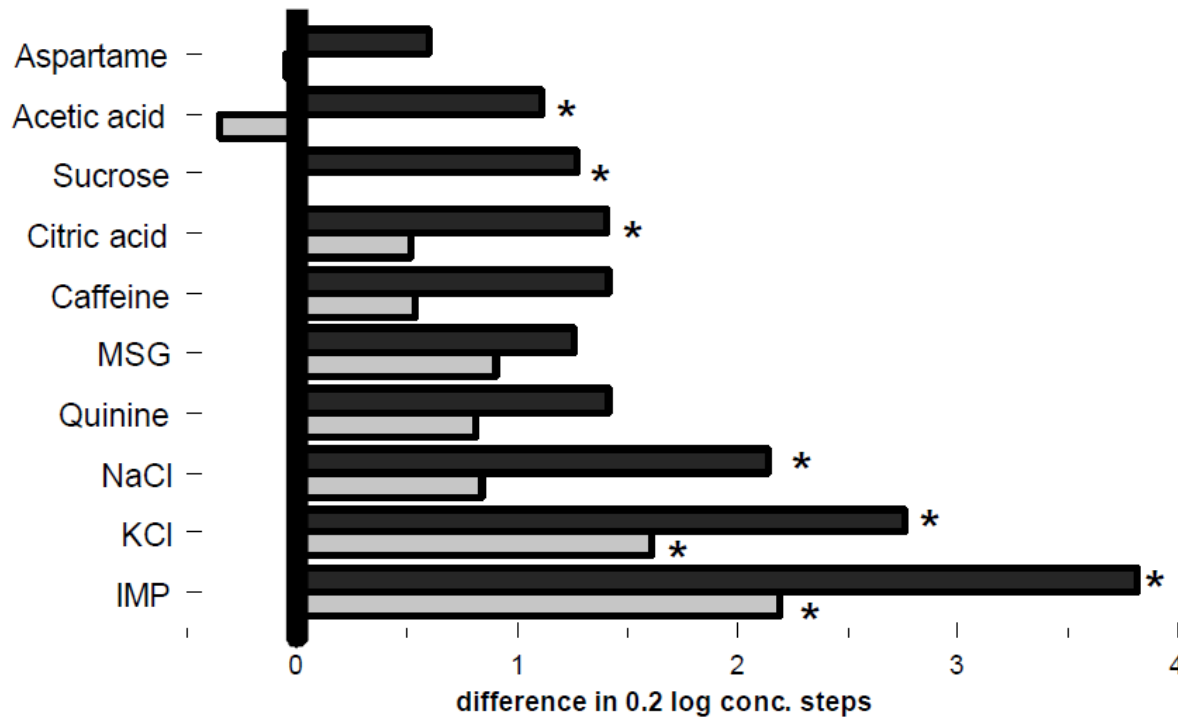
- Input = signal chimique ou physique



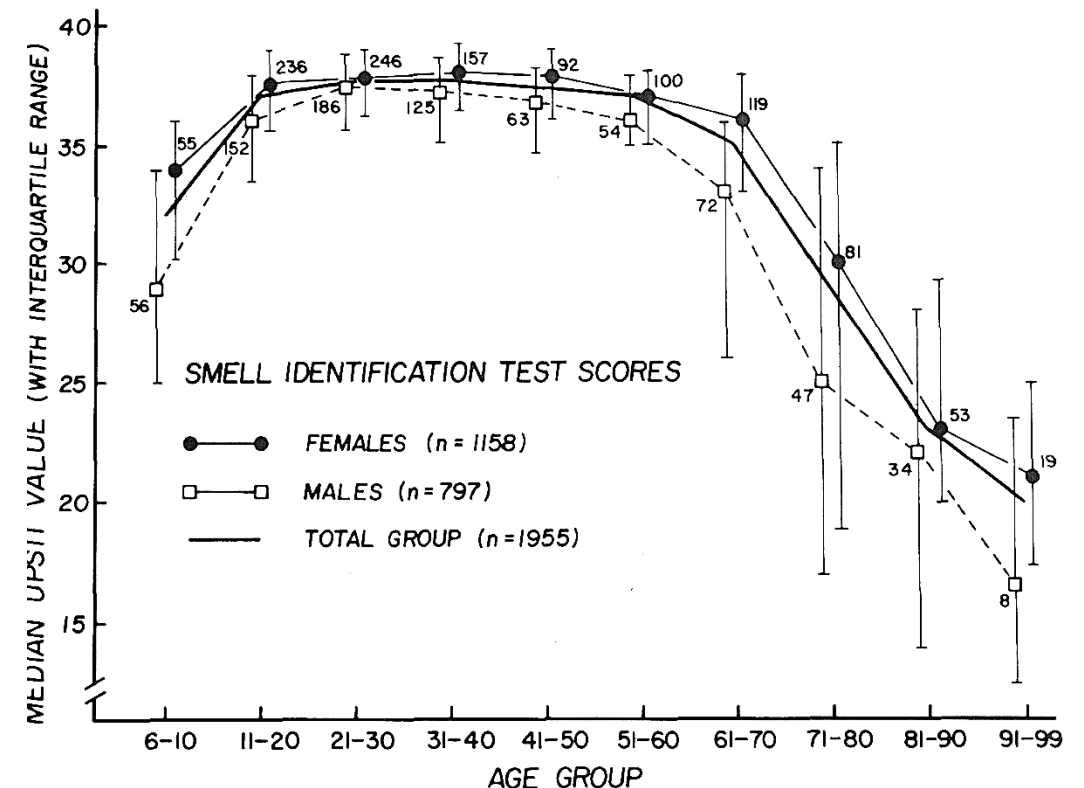
- Output =
  - @Neurone : signal électrique
  - @Cerveau : intégration du signal
  - @Humain : perception, émotion, cognition, souvenir, ...



# Perte des performances sensorielles avec l'âge



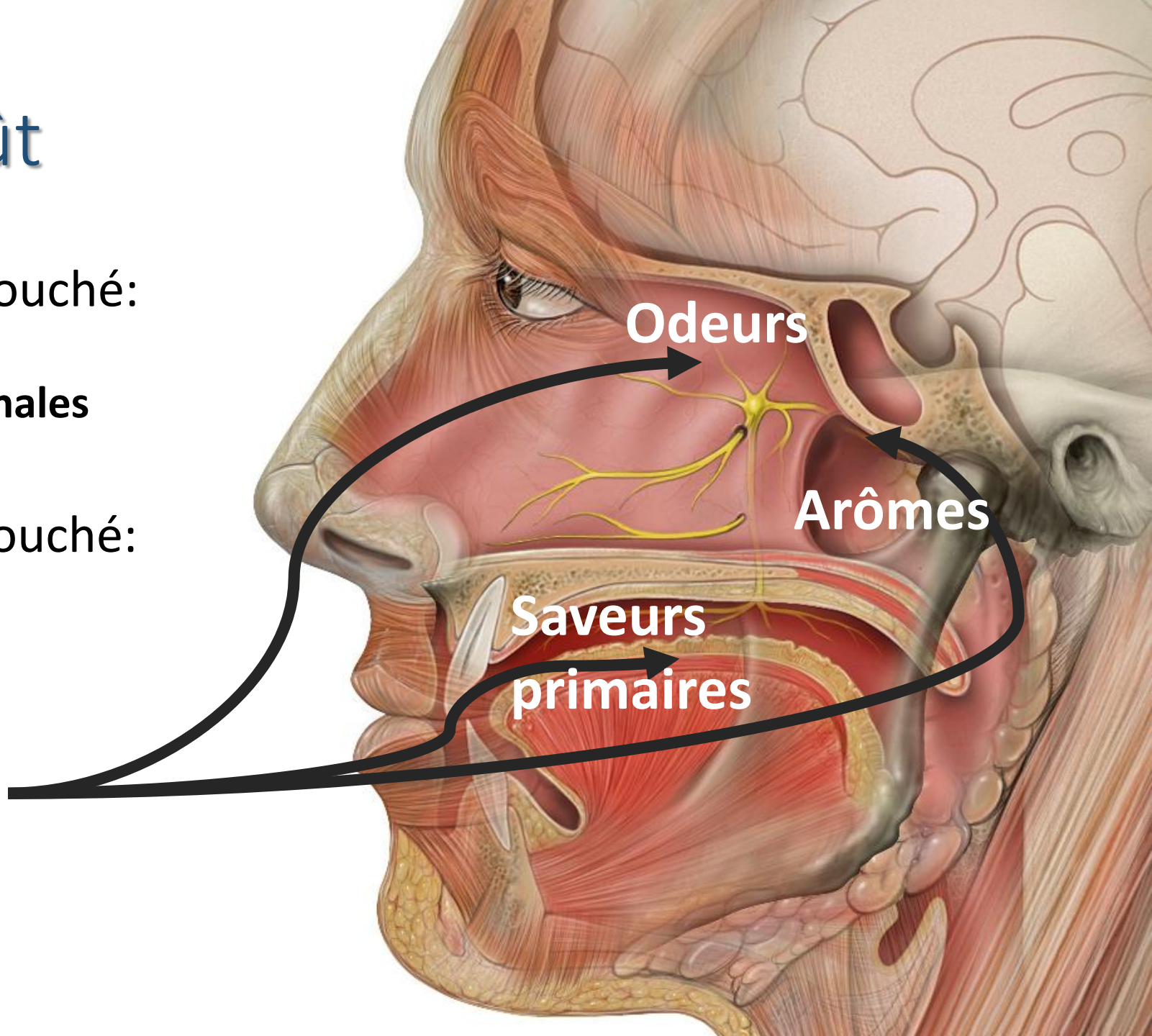
Mojet *et al.* Chem. Senses 2001



Doti *et al.* Physiol. Behav. 1984

# Physiologie du goût

- Goûter avec le nez bouché:  
**Saveurs primaires**  
**+ perceptions trigéminales**
- Goûter sans le nez bouché:  
**+ arômes**



# Le sens du goût

Saveurs  
primaires



sucré



salé



acide



amer



umami

Arômes (odeurs)



Perception  
trigéminal



Chaud



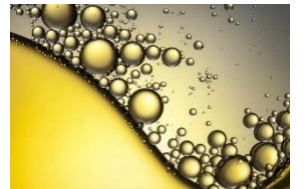
froid



astringence



métallique

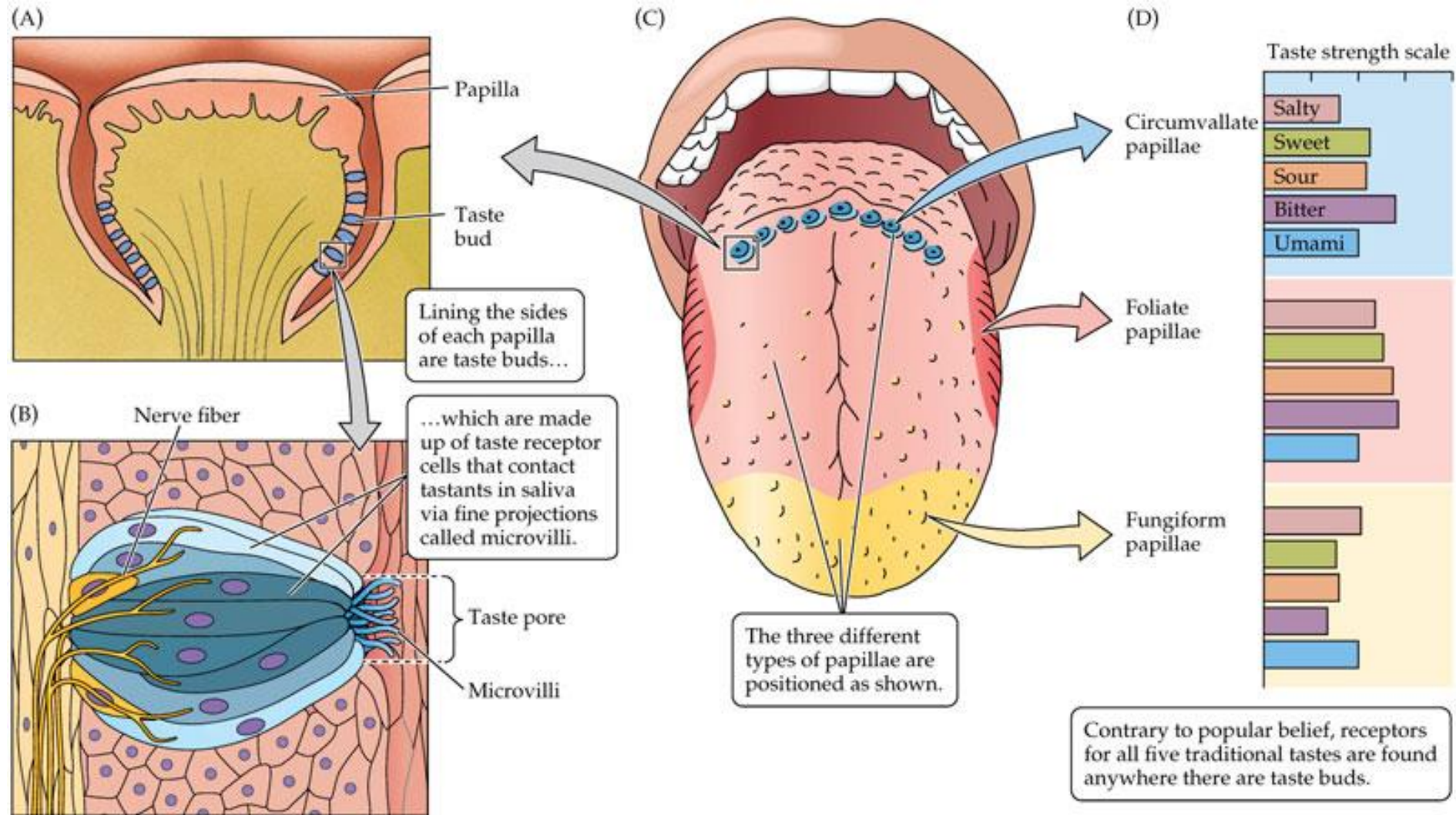


gras (saveur primaire?)



*Nos cinq sens (réal. S. Scala)*  
© Film Concept Associés

# Anatomie du système gustatif



# Les saveurs : des fonctions différentes

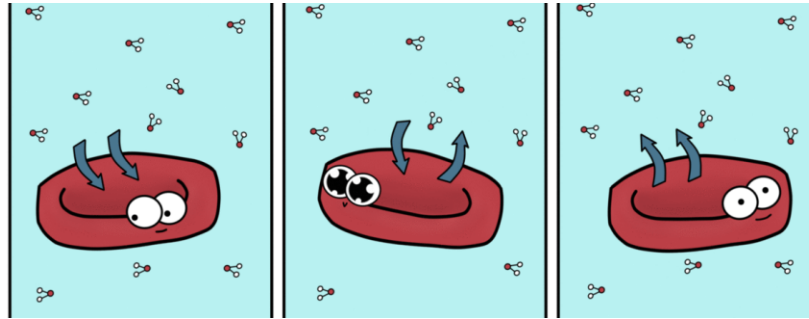
Sucrée



Acide



Salé



Umami



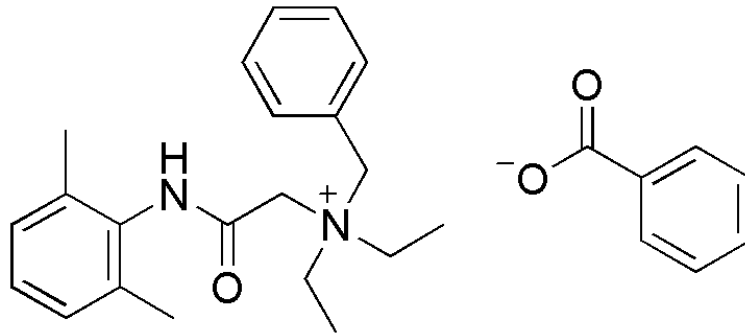
Amer



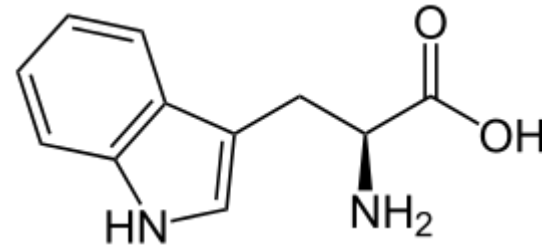
# Code combinatoire de la perception des saveurs

| Saveurs | Nombre de récepteur(s) | Seuils de détection                                                                                 |
|---------|------------------------|-----------------------------------------------------------------------------------------------------|
| Sucré   | 1 récepteur            | 0,01 M           |
| Salé    | 1 récepteur            | 0,01 M           |
| Umami   | 1 récepteur            | 0,001 M         |
| Acide   | 1 récepteur            | 0,0001 M       |
| Amer    | ~ 25-30 récepteurs     | 0,000000001 M  |

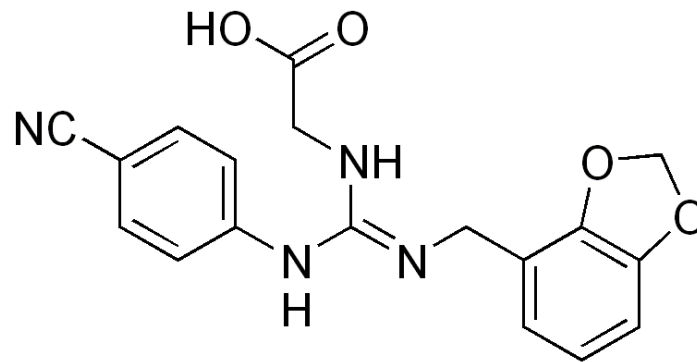
# Relations structure - goût



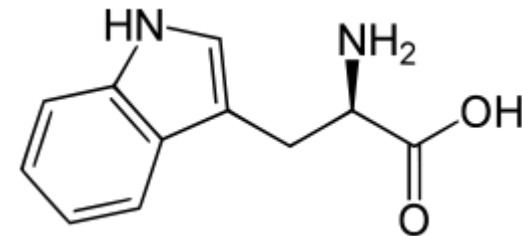
Benzoate de dénatonium  
(amer)



L-tryptophane  
(amer)

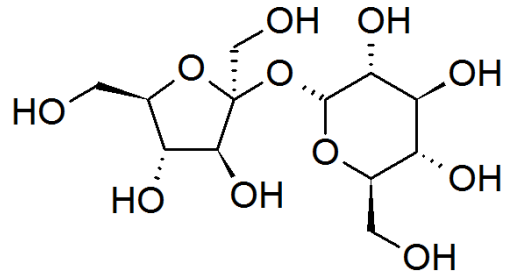


Lugduname  
(sucré)



D-tryptophane  
(sucré)

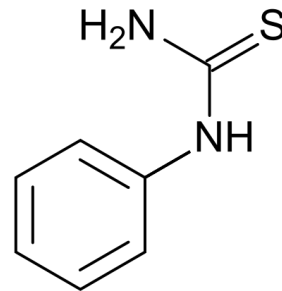
# Du récepteur au comportement alimentaire



Polymorphisme TAS1R2 impacte la perception du sucrose



Eni *et al.* Am. J. Clin. Nutr. 2010



Polymorphisme TAS2R38 impacte la perception PTC (phenylthiocarbamide)

Kim *et al.* Science 2003

# Récepteurs gustatifs

**PKD2L1 (2006)**

*Polycystic-Kidney-Disease-Like*  
Canal ionique perméant aux protons

**T1R2-T1R3 (2001)**

*Taste 1 Receptor*  
Récepteur gustatif  
de type 1 membres 2 et 3

**T1R1-T1R3 (2002)**

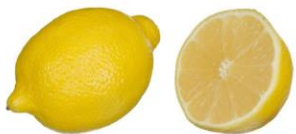
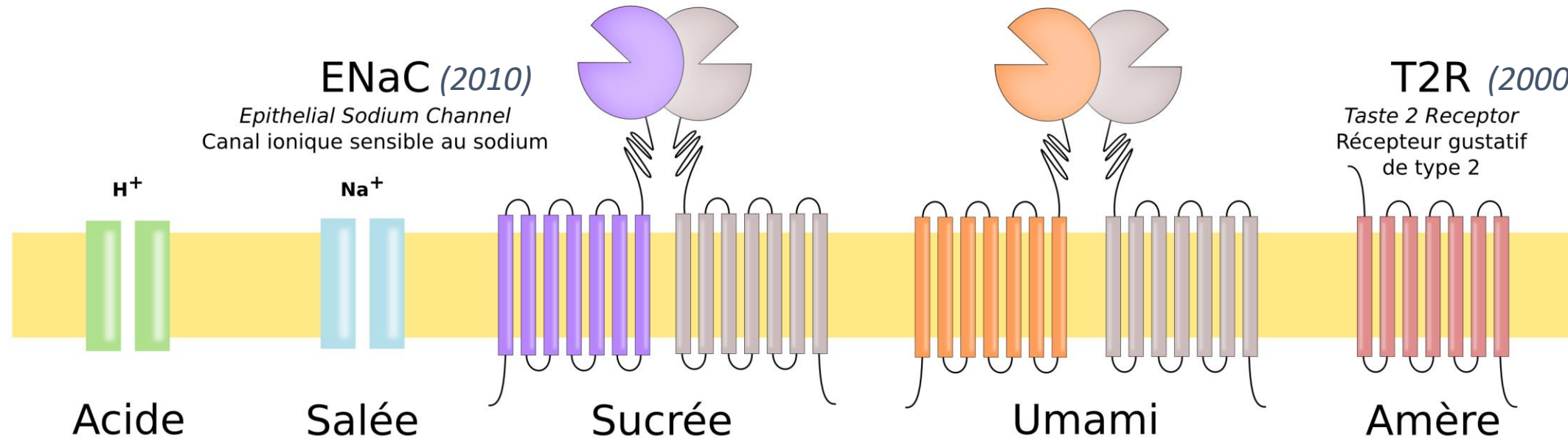
*Taste 1 Receptor*  
Récepteur gustatif  
de type 1 membres 1 et 3

**ENaC (2010)**

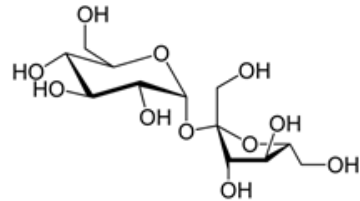
*Epithelial Sodium Channel*  
Canal ionique sensible au sodium

**T2R (2000)**

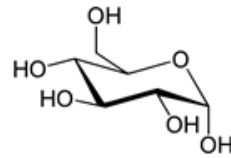
*Taste 2 Receptor*  
Récepteur gustatif  
de type 2



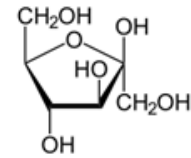
# Goût sucré : Un large espace chimique



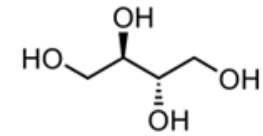
sucrose



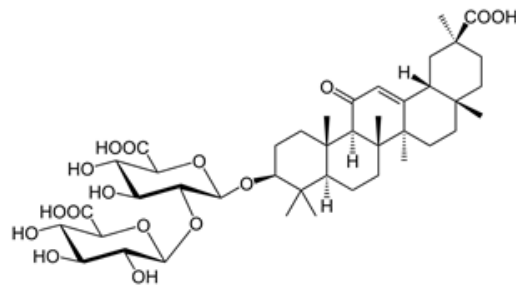
$\beta$ -D-glucose



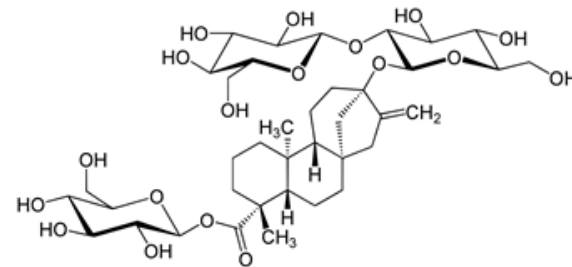
$\alpha$ -D-fructose



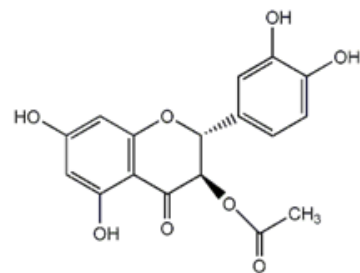
erythritol



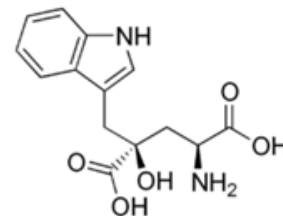
glycyrrhizin



stevioside



taxifolin 3-acetate

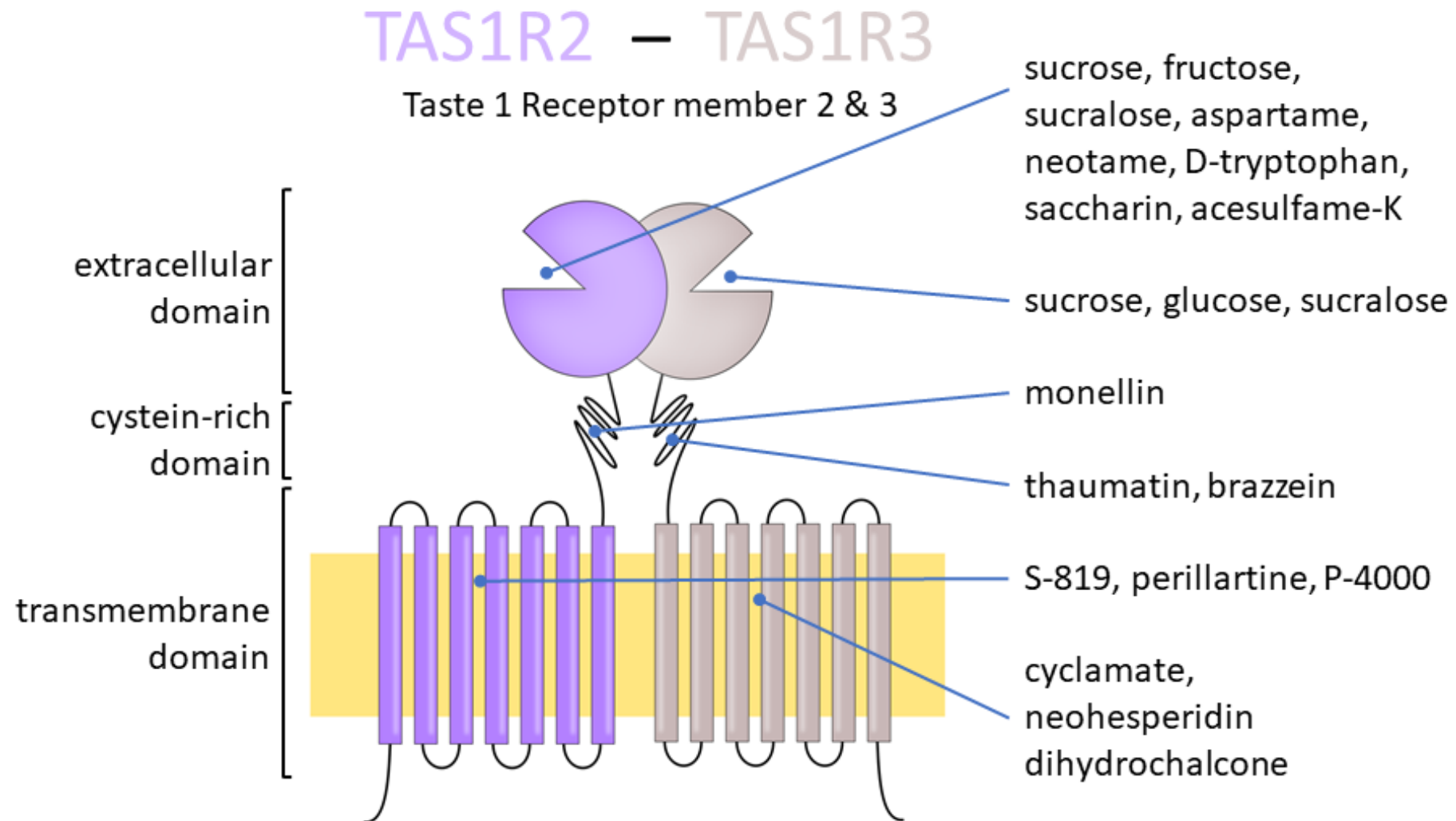


monatin



brazzein

# Goût sucré : un unique récepteur



# Protéines « sucrées » & récepteur gustatif

THE JOURNAL OF BIOLOGICAL CHEMISTRY  
© 2004 by The American Society for Biochemistry and Molecular Biology, Inc.

Vol. 279, No. 43, Issue of October 22, pp. 45068–45075, 2004  
Printed in U.S.A.

## The Cysteine-rich Region of T1R3 Determines Responses to Intensely Sweet Proteins\*<sup>§</sup>

Received for publication, June 17, 2004, and in revised form, August 4, 2004  
Published, JBC Papers in Press, August 6, 2004, DOI 10.1074/jbc.M406779200

Peihua Jiang<sup>‡</sup>, Qingzhou Ji<sup>§</sup>, Zhan Liu<sup>§</sup>, Lenore A. Snyder<sup>‡</sup>, Lumie M. J. Benard<sup>§</sup>,  
Robert F. Margolskee<sup>§¶</sup>, and Marianna Max<sup>‡¶</sup>

From the <sup>‡</sup>Department of Physiology and Biophysics and <sup>§</sup>Howard Hughes Medical Institute,  
Mount Sinai School of Medicine, New York, New York 10029

Jiang *et al.* J. Biol. Chem. 2004

## The anatomy of mammalian sweet taste receptors

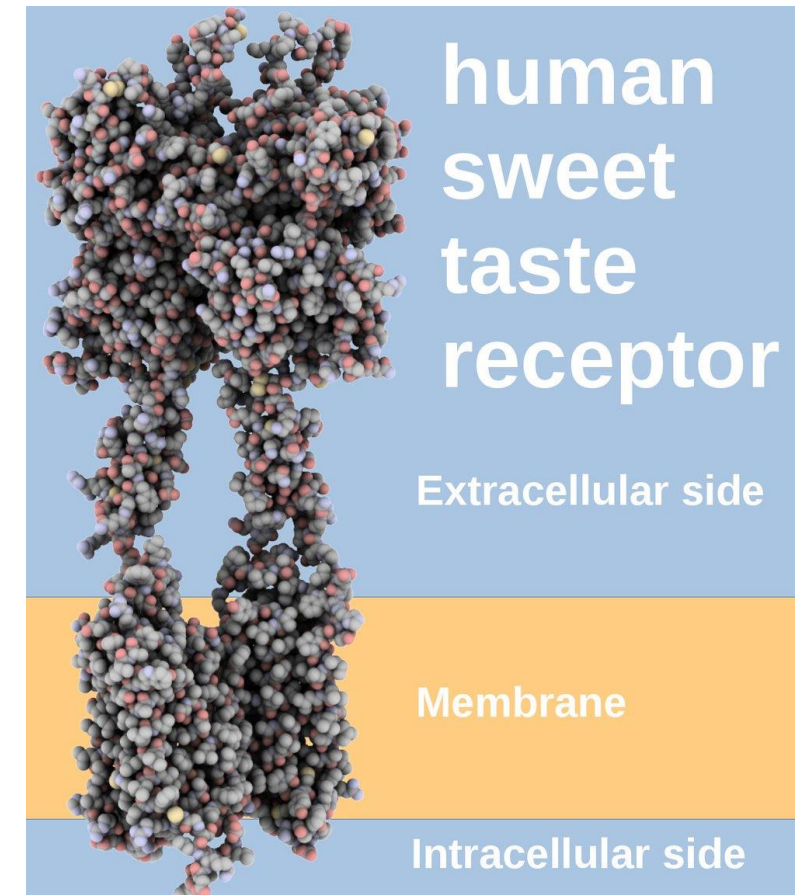


Jean-Baptiste Chéron,<sup>1</sup> Jérôme Golebiowski,<sup>1,2</sup> Serge Antonczak,<sup>1</sup> and Sébastien Fiorucci<sup>1\*</sup>

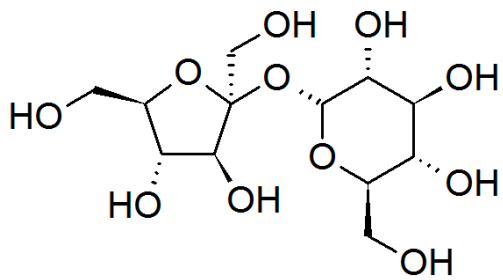
<sup>1</sup> Université Côte d'azur, CNRS, Institut de Chimie de Nice UMR7272, 06108 Nice, France

<sup>2</sup> Department of Brain and Cognitive Science, DGIST (Daegu Gyeongbuk Institute of Science & Technology), Daegu, Korea

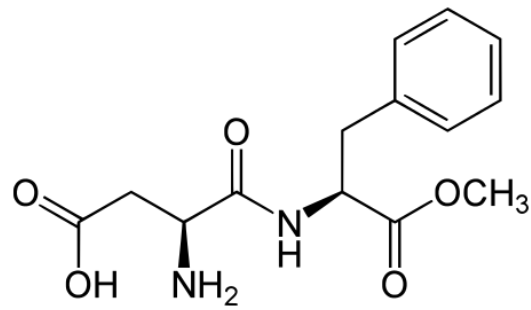
Chéron *et al.* Proteins. 2017



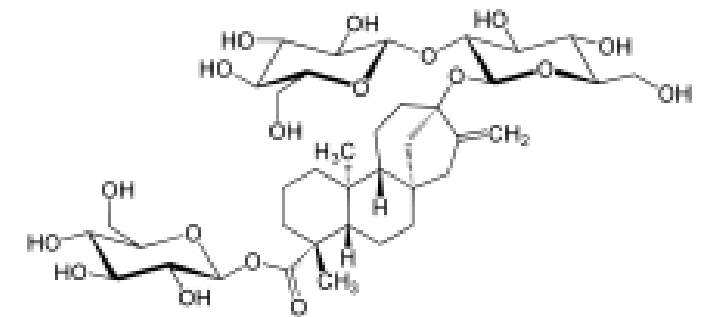
# Alternatives au saccharose



saccharose



aspartame



stévia (stévioside)

# Duper nos papilles ?



Miraculine (fruit du miracle)



Acide ?

# Duper nos papilles ?



Miraculine (fruit du miracle)



Sucré !

*« Les perceptions des sens et les jugements de l'esprit sont des sources d'illusion et des causes d'incertitudes »*

Anatole France

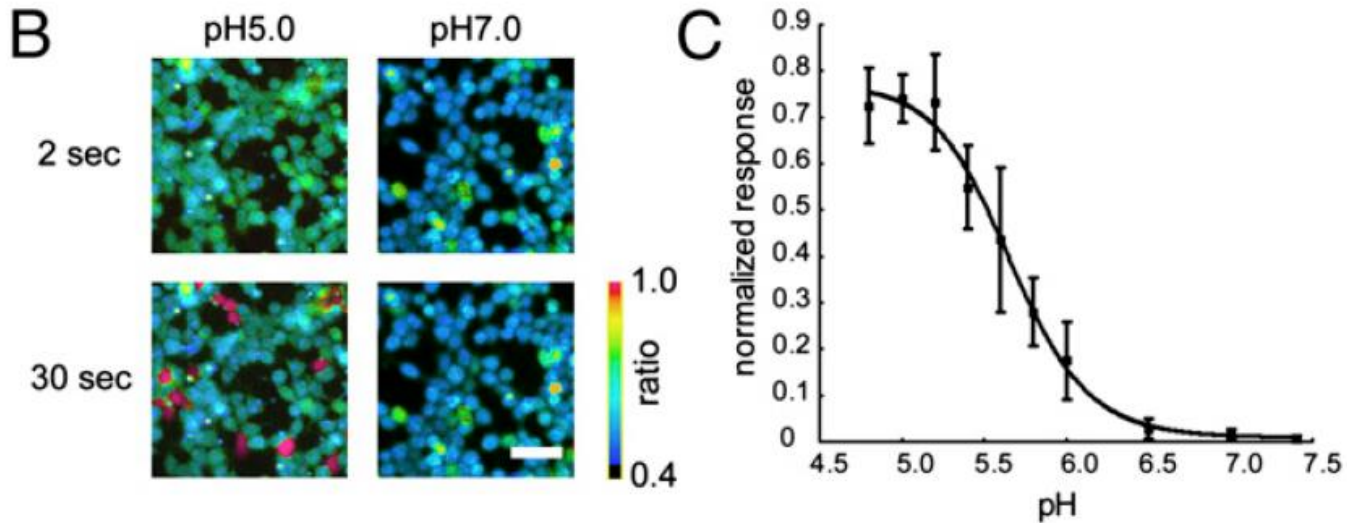
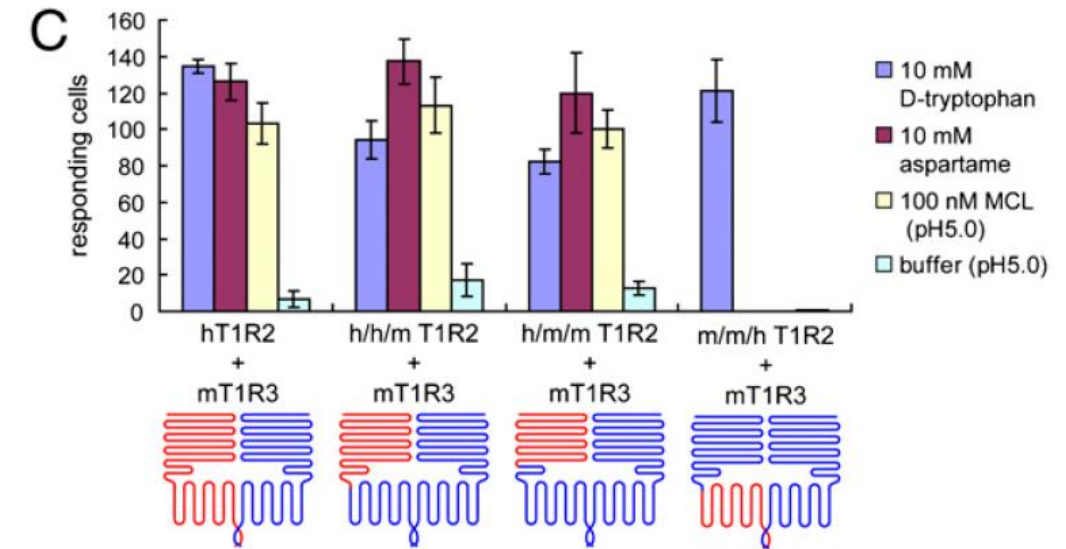
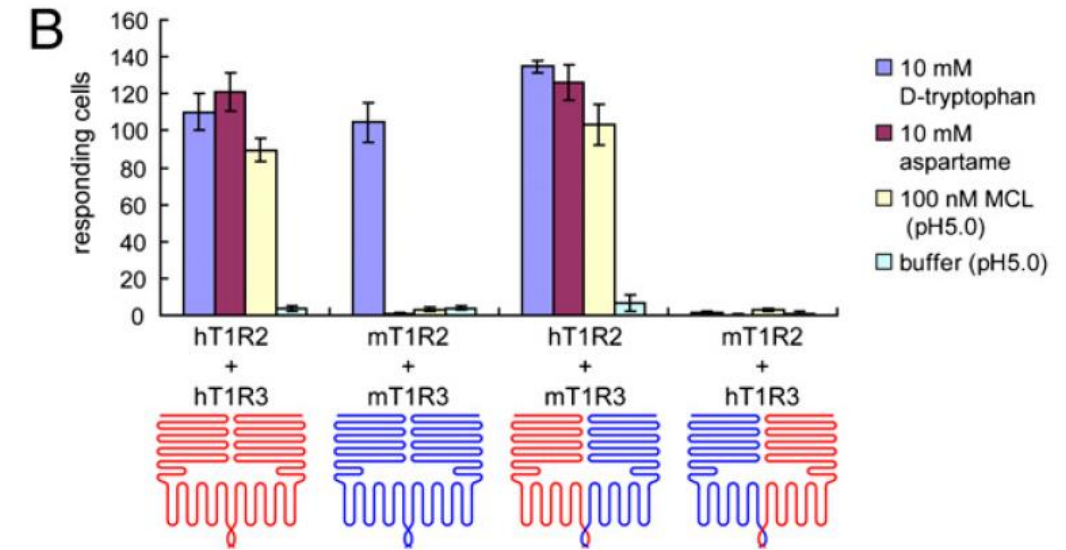
# Human sweet taste receptor mediates acid-induced sweetness of miraculin

Ayako Koizumi<sup>a</sup>, Asami Tsuchiya<sup>a</sup>, Ken-ichiro Nakajima<sup>a</sup>, Keisuke Ito<sup>a</sup>, Tohru Terada<sup>b</sup>, Akiko Shimizu-Ibuka<sup>a</sup>, Loïc Briand<sup>c</sup>, Tomiko Asakura<sup>a</sup>, Takumi Misaka<sup>a,1</sup>, and Keiko Abe<sup>a,d,1</sup>

<sup>a</sup>Department of Applied Biological Chemistry, and <sup>b</sup>Agricultural Bioinformatics Research Unit, Graduate School of Agricultural and Life Sciences, University of Tokyo, Bunkyo-ku, Tokyo 113-8657, Japan; <sup>c</sup>Centre des Sciences du Goût et de l'Alimentation, Unité Mixte de Recherche-6265 Centre National de la Recherche Scientifique, Unité Mixte de Recherche-1324 Institut National de la Recherche Agronomique, Université de Bourgogne, Agrosup Dijon, F-21000 Dijon, France; and <sup>d</sup>Health and Anti-Aging Project, Kanagawa Academy of Science and Technology, Takatsu-ku, Kawasaki 213-0012, Japan

Edited by David Julius, University of California, San Francisco, CA, and approved August 30, 2011 (received for review November 26, 2010)

Koizumi *et al.* PNAS. 2011



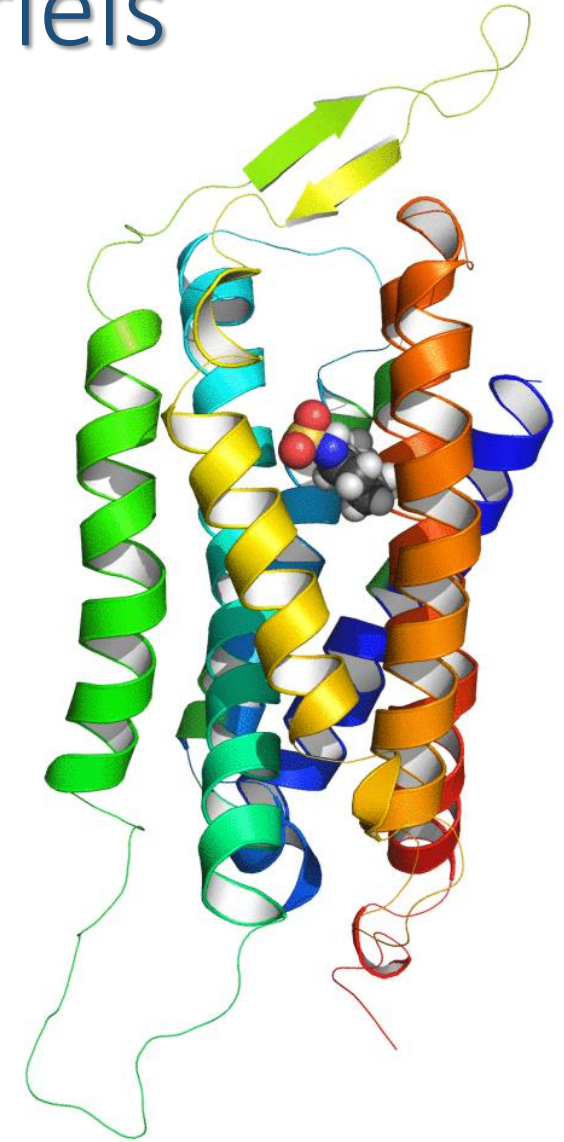
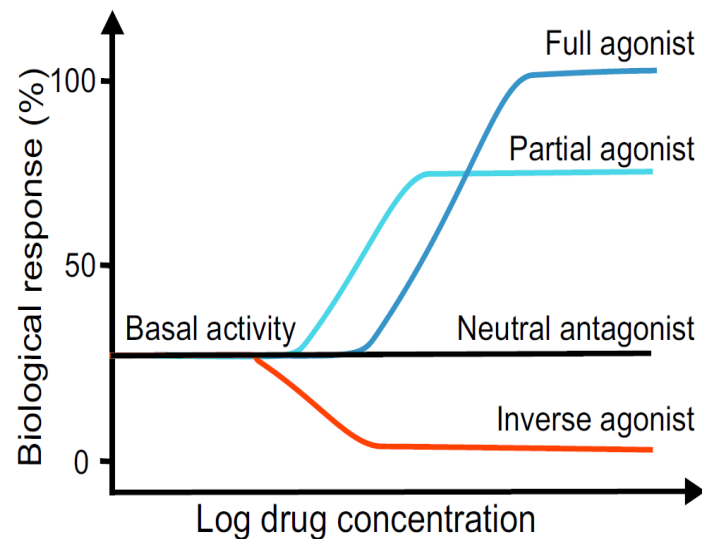
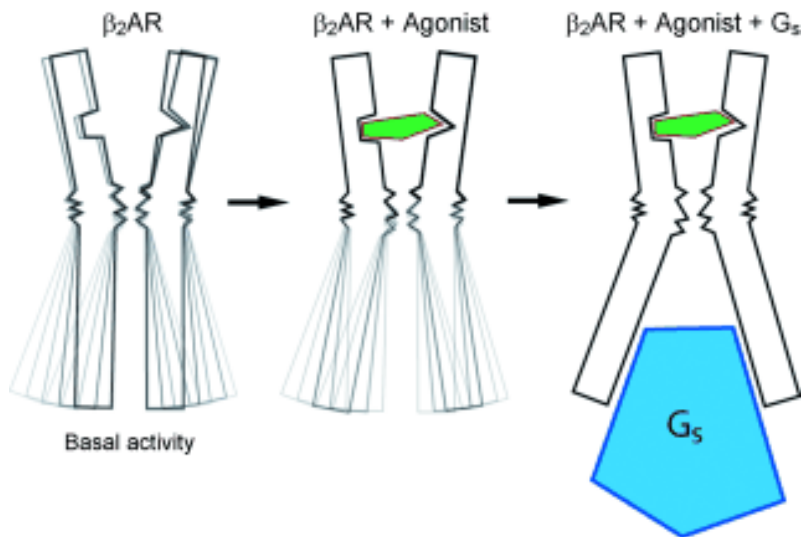
# Projets en cours :

Modèles numériques de la perception des saveurs

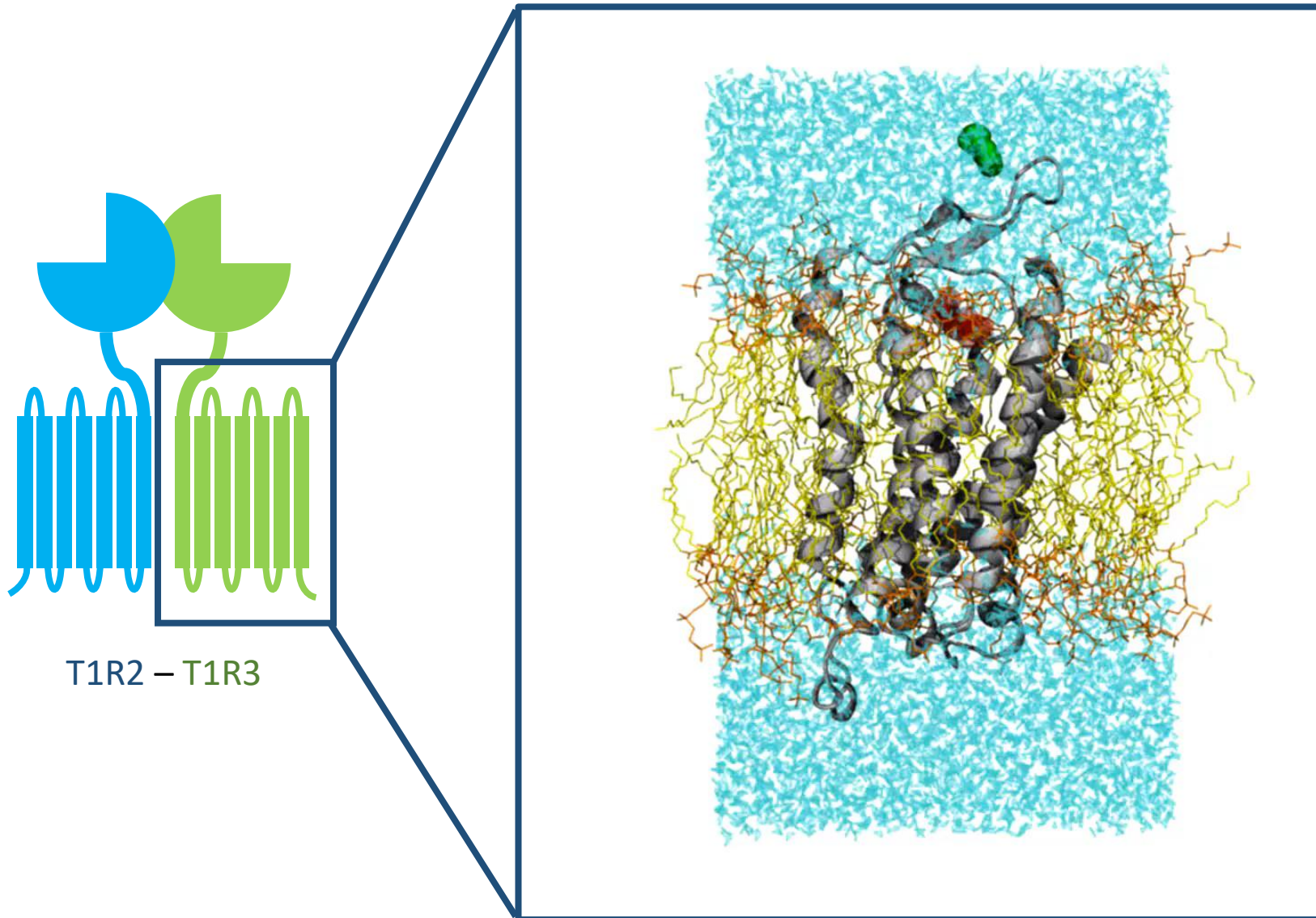
Décrypter les mécanismes moléculaires  
(modèle 3D & dynamique)

# Récepteurs chimio-sensoriels

- RCPG
- Domaine 7TM
- Traduction d'une information chimique en influx nerveux

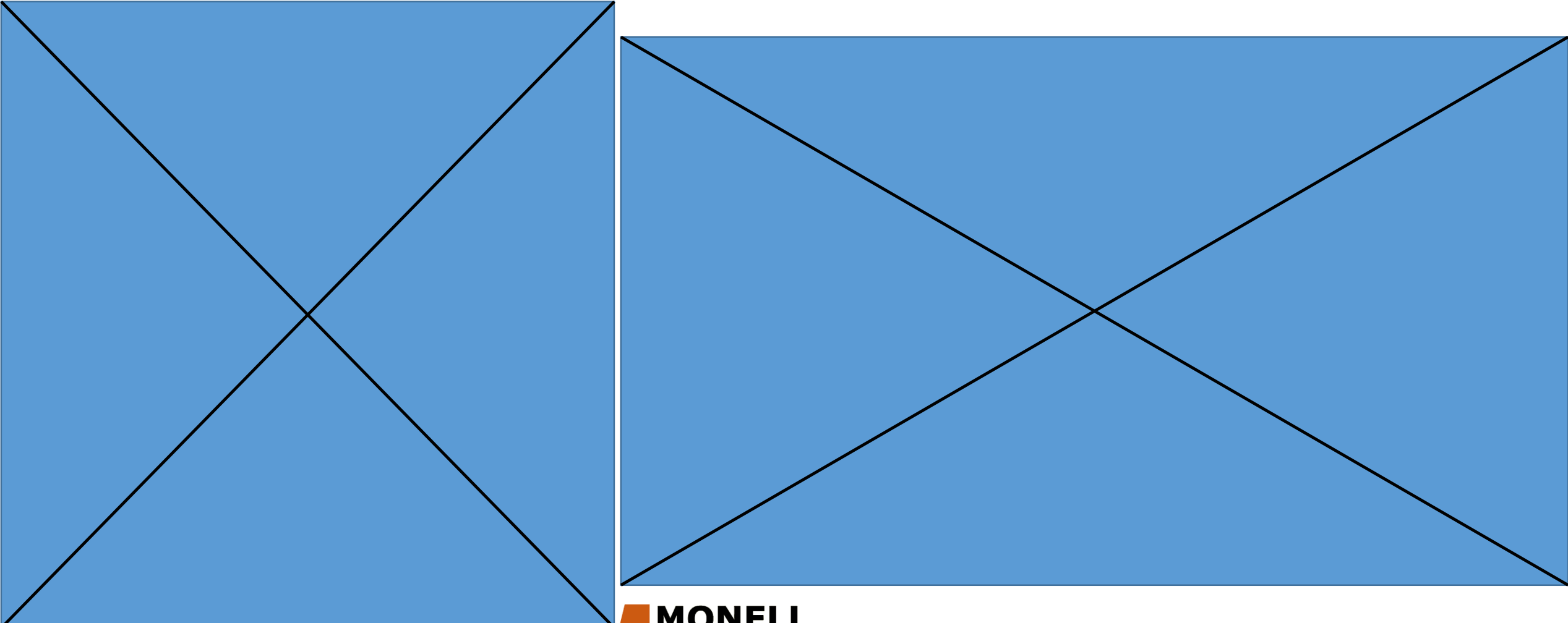


# Site allostérique du récepteur au goût sucré



MD simulations  
Amber16  
FF14SB  
15  $\mu$ s, NPT, TIP3P

# Mécanismes de modulation du goût

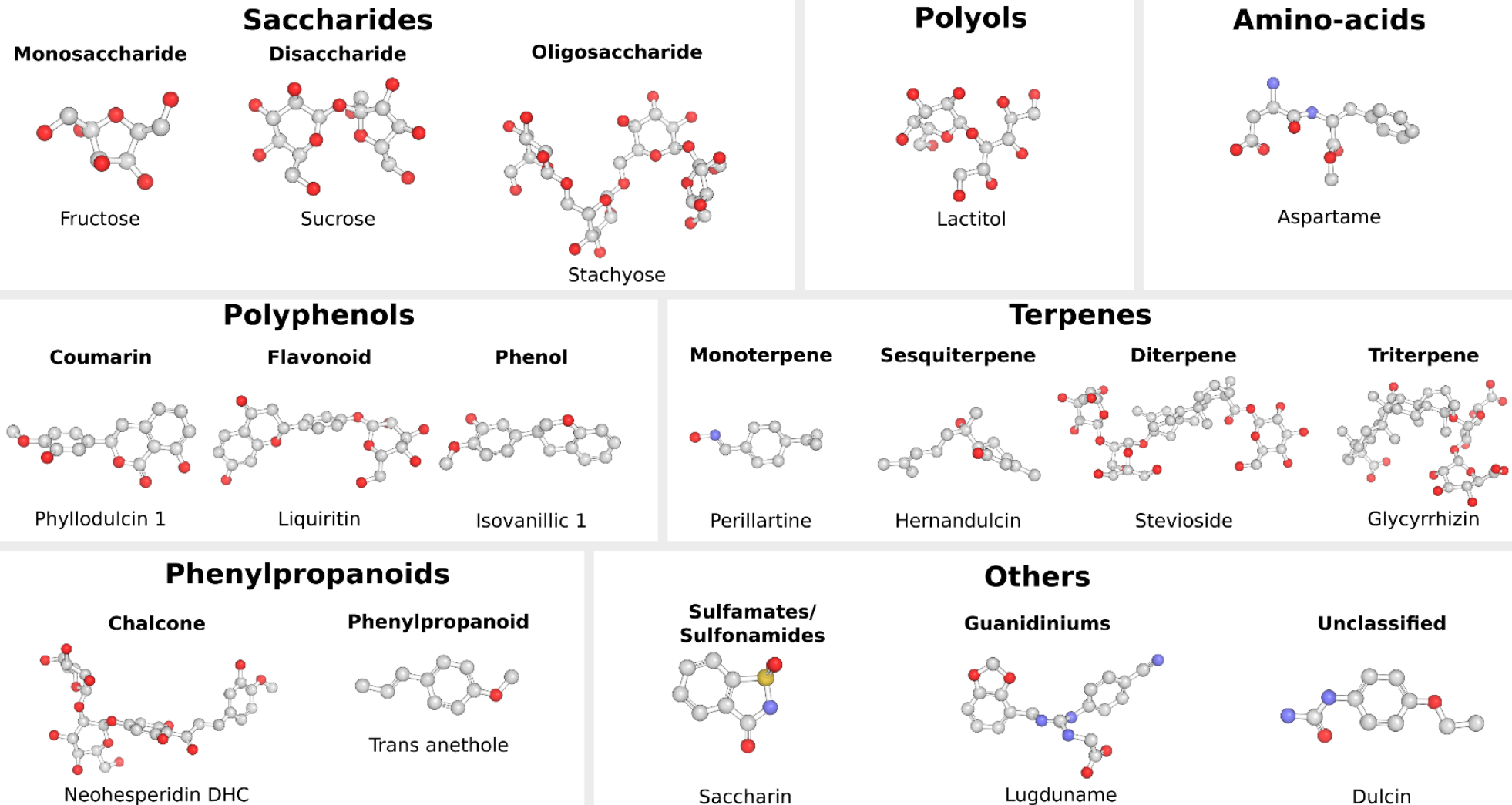


Explorer les espaces chimiques

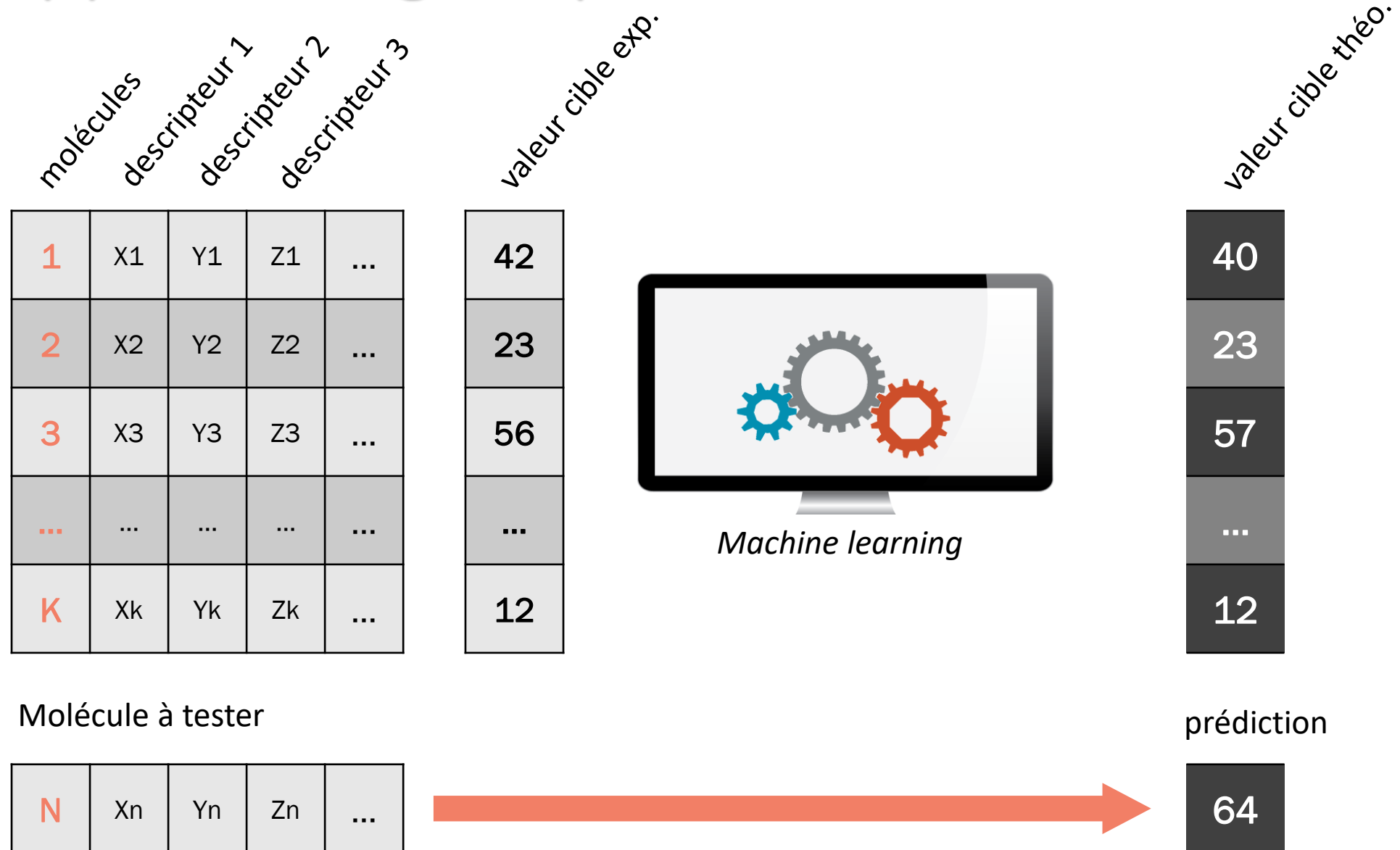
-

Relations structure - goût

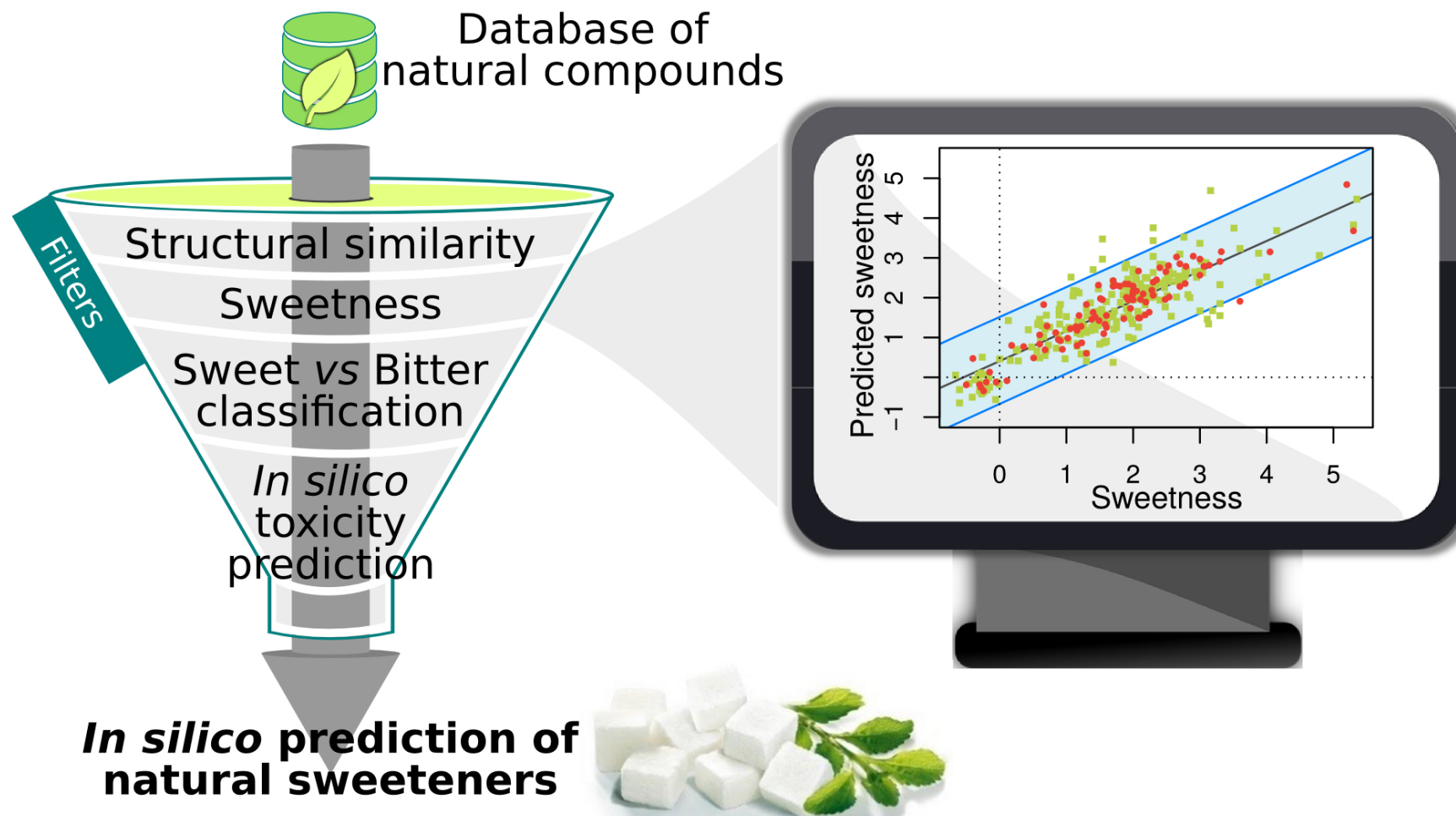
# SweetenersDB



# Apprentissage supervisé, les modèles QSAR



# Modèle de relations structure - goût sucré

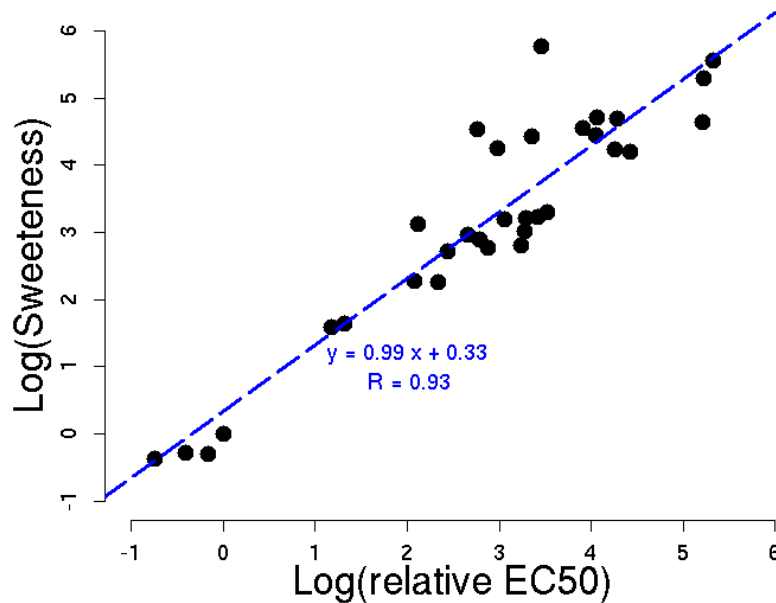


# Tests *in vitro*

- Contrôle vecteur vide (vv)
- Ligand (référence sucralose)

Indice de pouvoir sucrant:

- Saccharose (référence) : 1
- Sucralose : 600-650
- Molécule A : ~ 50 ?



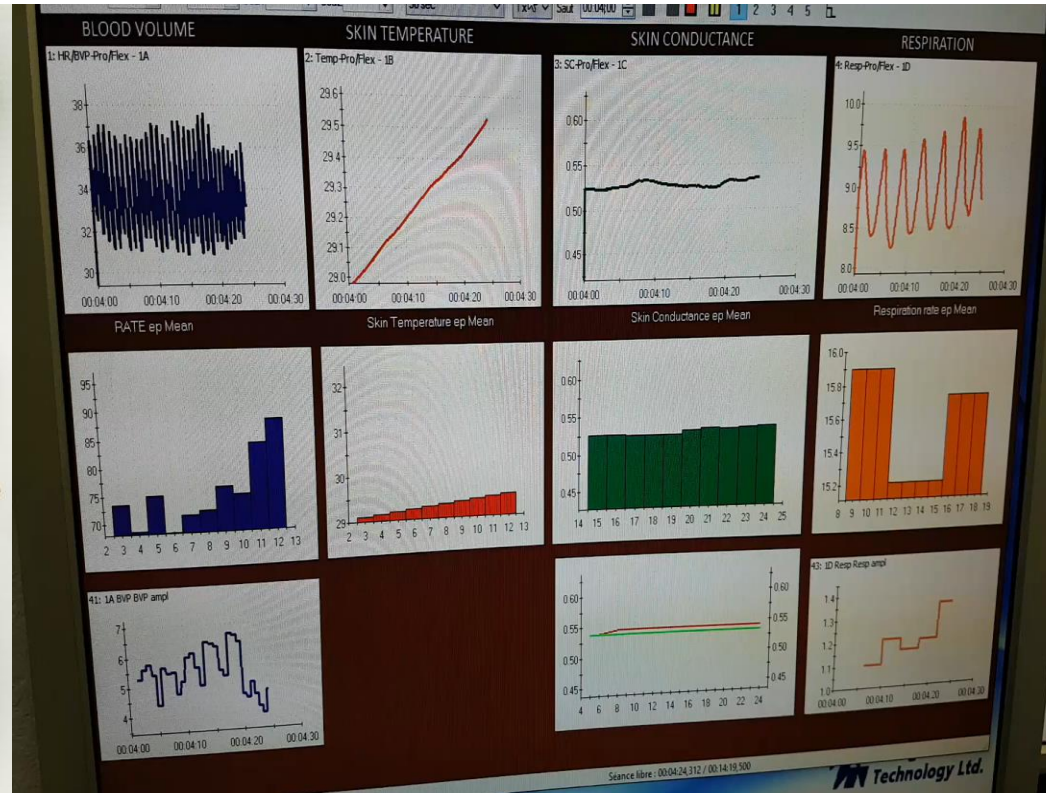
Données *In vitro* : L. Briand & C.Belloir (CSGA, Dijon)

Mesure des émotions

-

Réponse inconsciente de l'organisme à un  
stimulus sensoriel

# Stimulation sensorielle & mesures psychophysiques



# Remerciements



Prof. M. Zacharias



Technische Universität München



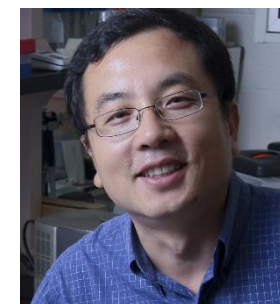
Dr. J. Waldispühl



McGill  
UNIVERSITY



Dr. L. Briand



Dr. P. Jiang



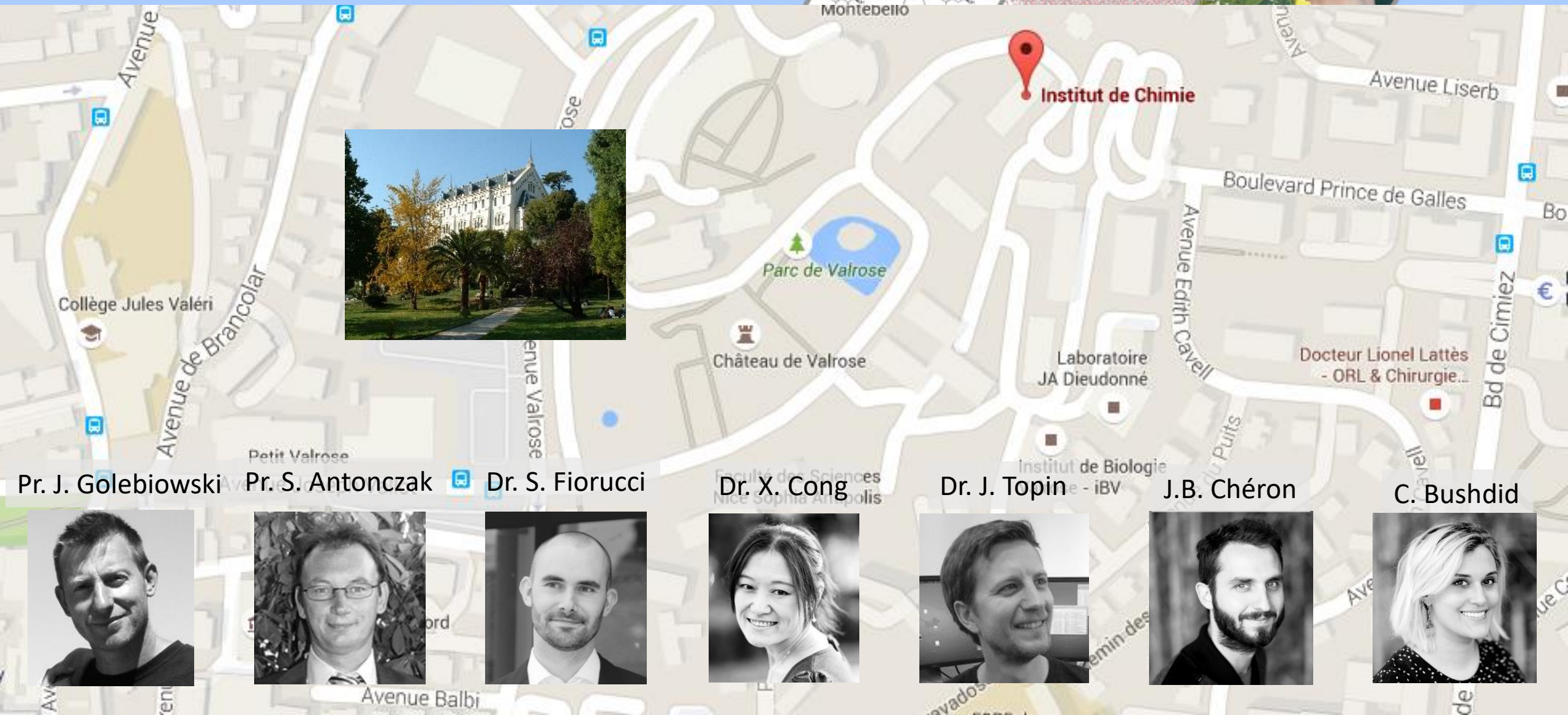
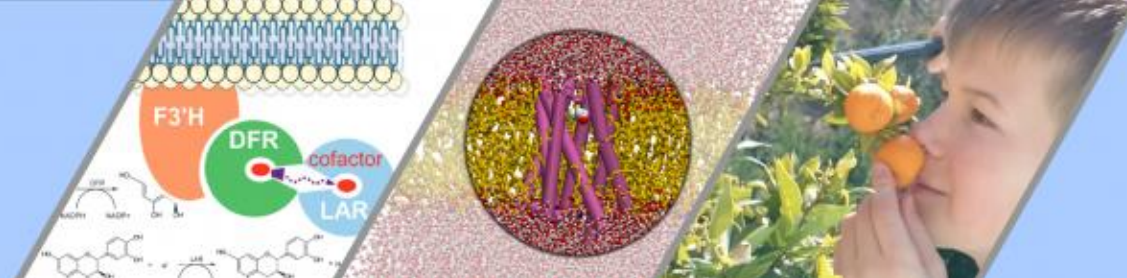
Dr. A. Marchal



# Chemosim Lab

*Chemoinformatics, Emotion & Simulation*

<http://chemosim.unice.fr>



Pr. J. Golebiowski Pr. S. Antonczak Dr. S. Fiorucci

Dr. X. Cong

Dr. J. Topin

J.B. Chéron

C. Bushdid

