

# Structuring foods to improve the delivery of bioactives and nutrients



**Dr Didier DUPONT**

INRA, Rennes, France



# Portrait

## The National Institute for Agronomic Research

- Set up in 1946
- A public, scientific and technological establishment
- Under the joint authority of the Ministries of Agriculture and Research
- Second largest French public research organisation with a staff of nearly 11000 and a budget of 680 millions euros
- Largest European organisation for agricultural research



DIET  
AGRICULTURE  
ENVIRONMENT

INRA



Science &  
Technology of  
Milk & Egg

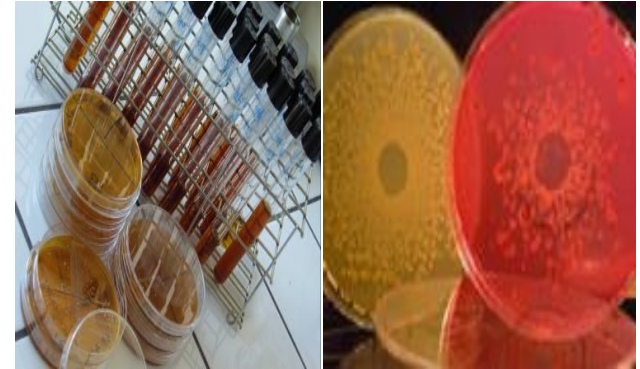
145 staff  
25 PhD students



## Multidisciplinary and multi-scale approaches, reinforced by two high-caliber facilities

Dairy Platform (Iso 9001)

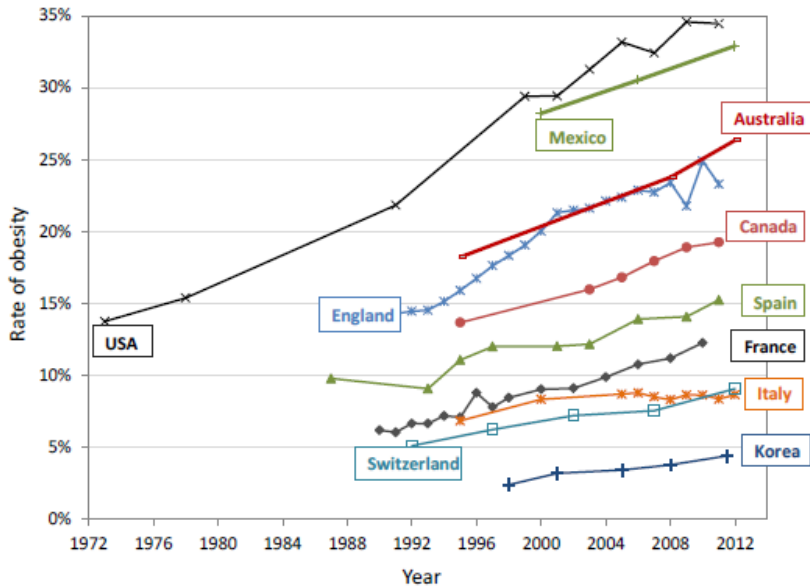
Biological Resource Center (Iso 9001)



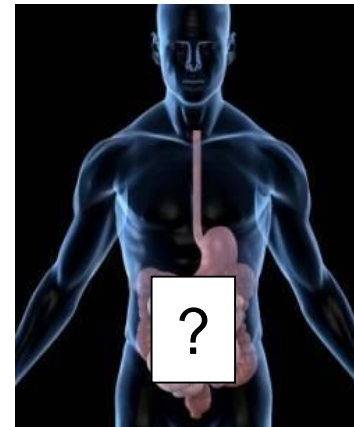
- ❑ **Structuration / disintegration mechanisms of food matrix:**  
*from structural characterization to digestion*
- ❑ **Dairy processing and cheese making:**  
*toward sustainable dairy systems*
- ❑ **Microbial interaction:**  
*food matrix and host cell*

**Please visit [http://www6.rennes.inra.fr/stlo\\_eng](http://www6.rennes.inra.fr/stlo_eng)**

# Why are we interested in understanding food digestion?



Diet-related diseases ↑  
Prevent these pathologies rather than cure them



**Gut = interface between food and human body**

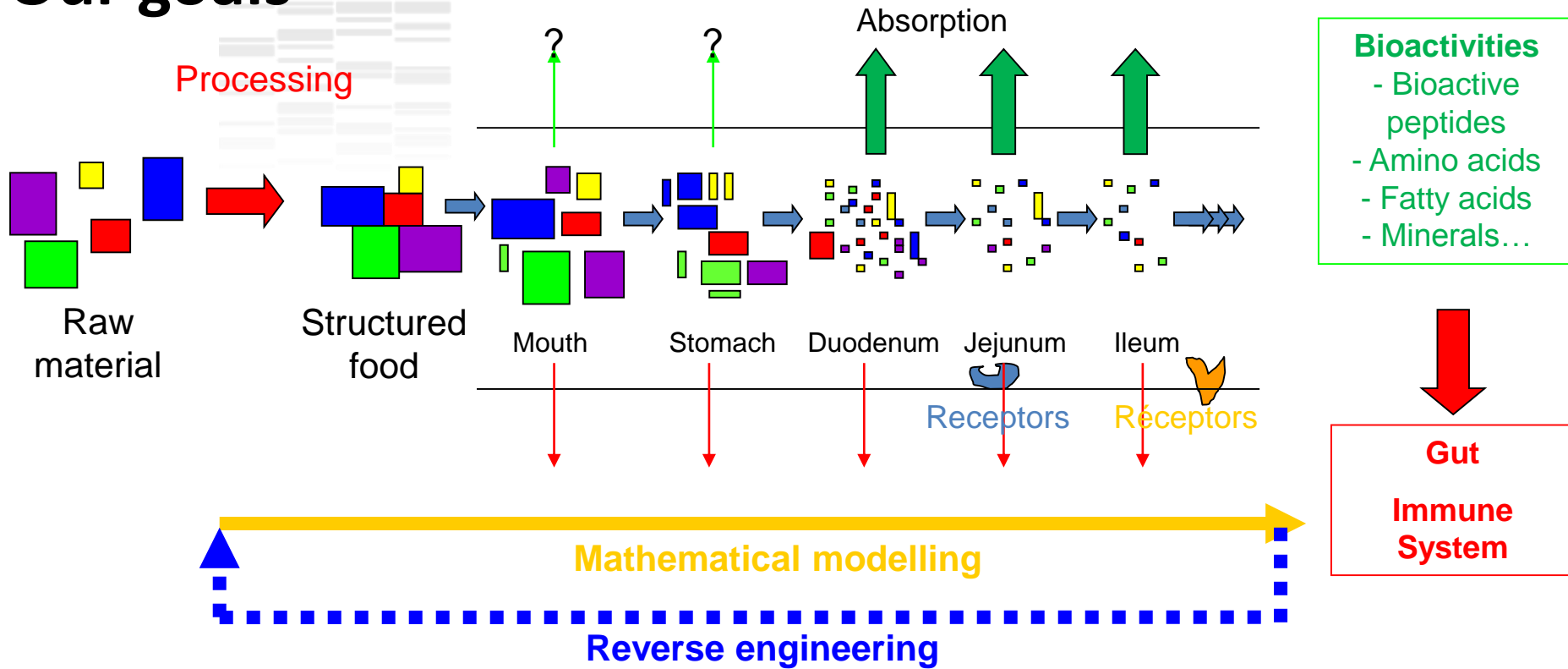
**Digestion releases food components that can have a beneficial or a deleterious effect on human health**

... but the mechanisms of food disintegration in the gastrointestinal tract remain unclear and the digestive process has been considered as a black box so far

**By increasing our knowledge on food digestion, we will increase our knowledge on the effect of food on human health**

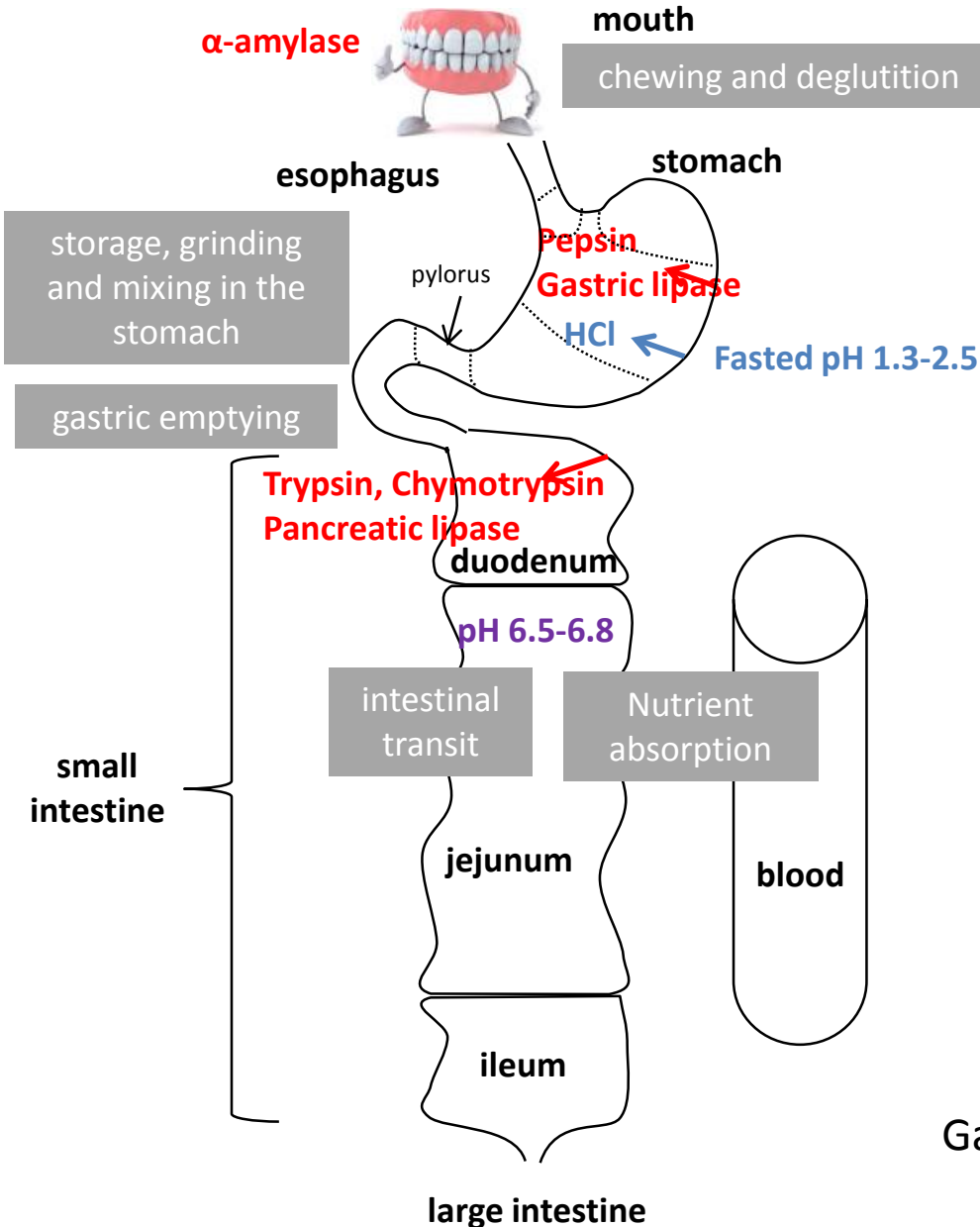
# Our goals

Healthy Adult/ Neonate/ Elderly

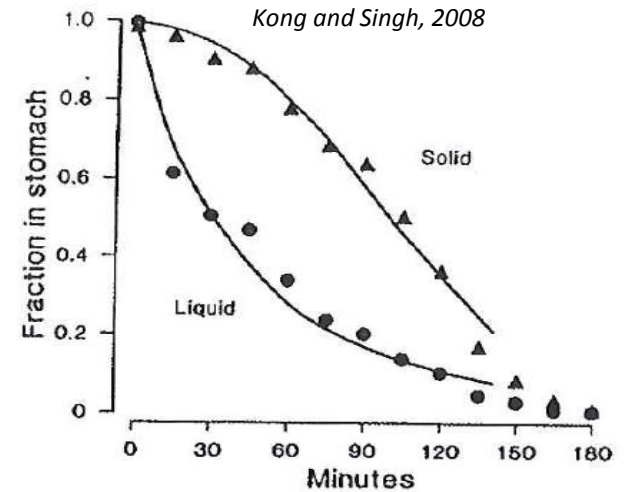


- ☞ To understand the mechanisms of breakdown of food matrices and their constituents in the gut and identify the beneficial/deleterious food components released during digestion
- ☞ To determine the impact of the structure of food matrices on these mechanisms
- ☞ To model these phenomena in order to develop a reverse engineering approach

# The digestive process



From Roger Lentle, Massey Univ. NZ



Gastric phase = a very complex but crucial step for the whole digestion process

# The structure of dairy products modulate the bioavailability of dietary amino acids



Barbé F.<sup>1</sup>, Ménard O.<sup>1</sup>, Le Gouar Y.<sup>1</sup>, Buffière C.<sup>2</sup>, Famelart M.-H.<sup>1</sup>, Laroche B.<sup>3</sup>, Le Feunteun S.<sup>4</sup>, Rémond D.<sup>2</sup> and **Dupont D.**<sup>1</sup>



<sup>1</sup> INRA STLO Rennes, France

<sup>2</sup> INRA UNH Clermont-Ferrand, France

<sup>3</sup> INRA MIA Jouy-en-Josas, France

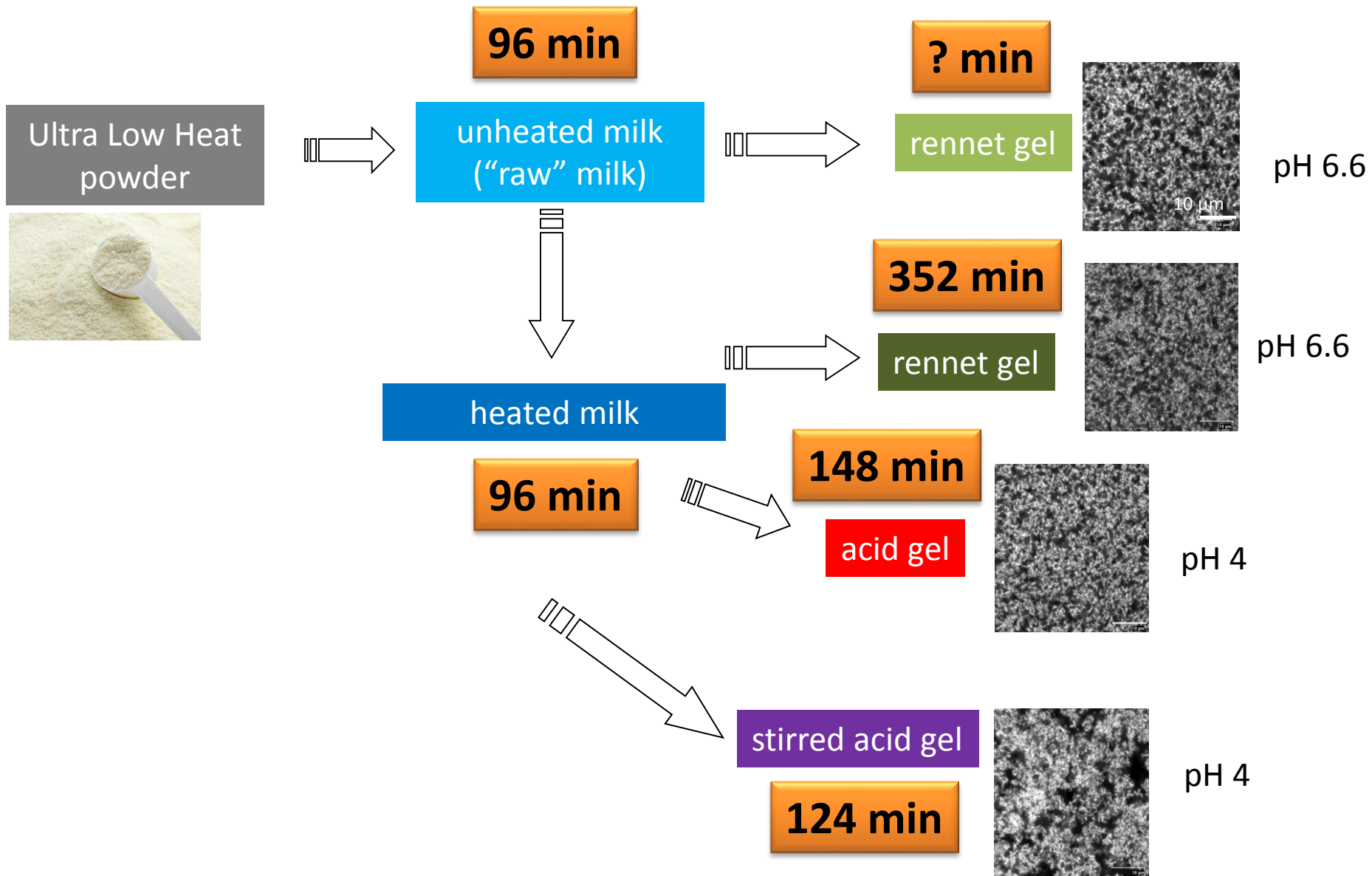
<sup>4</sup> INRA GMPA Grignon, France



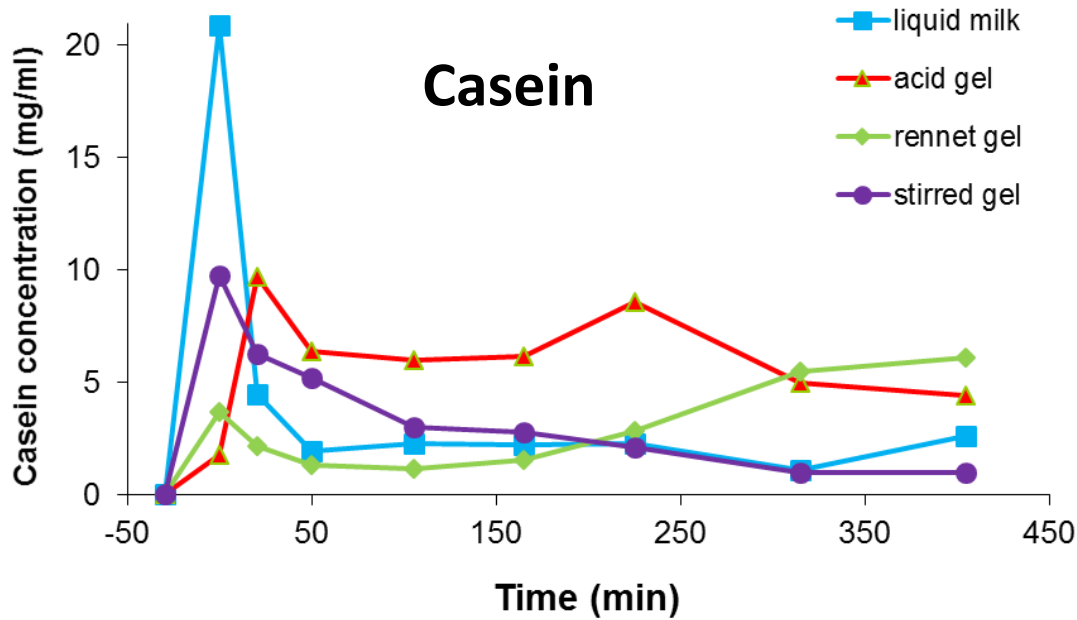




# Time of residence in the stomach

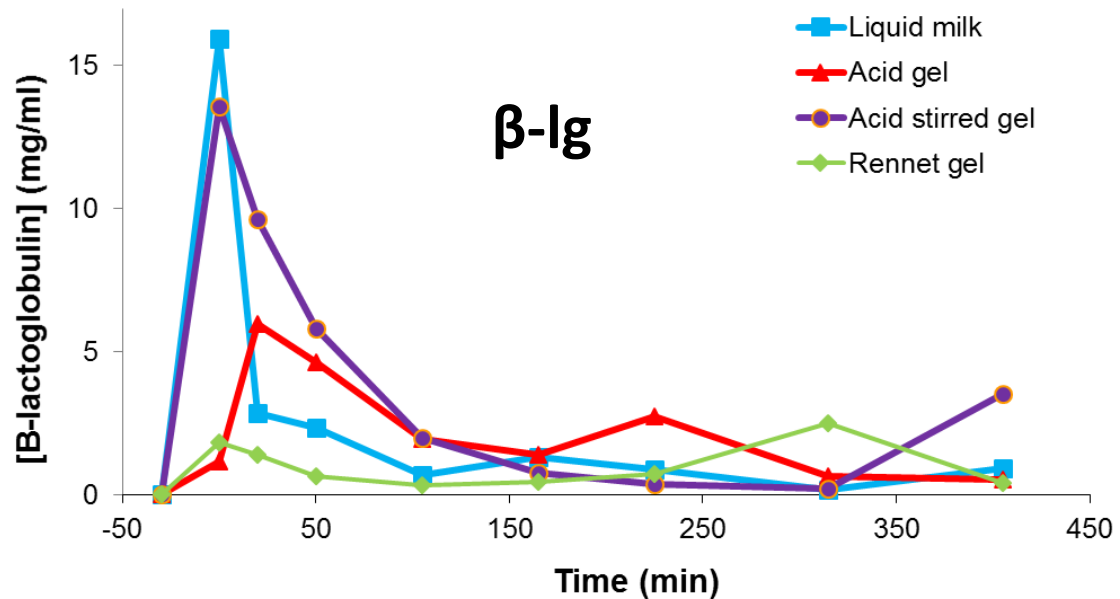


# Milk proteins in the duodenum (ELISA)



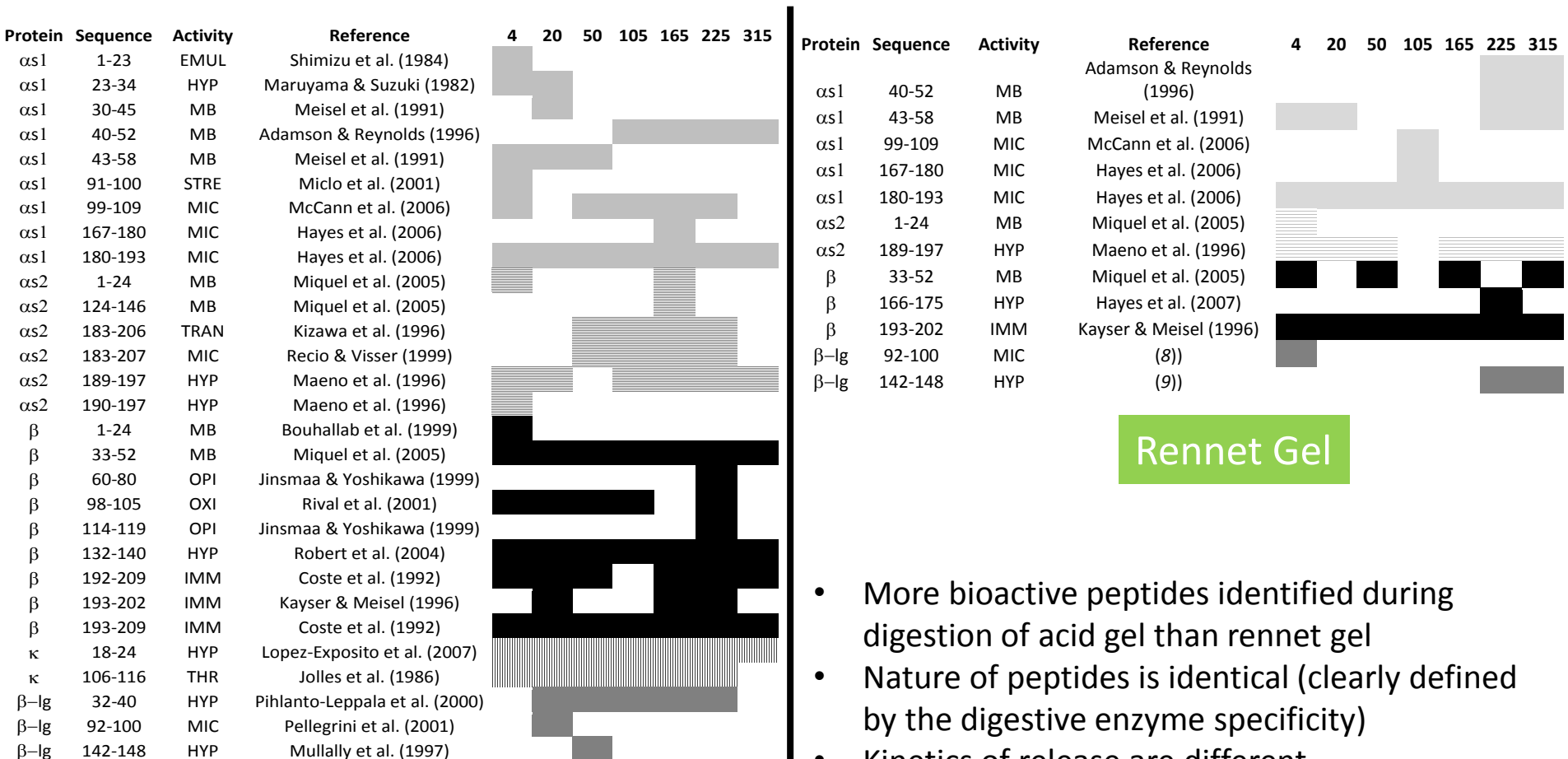
- Intense and early peak with milk
- Lower and delayed with gels
- Intermediate behaviour with stirred gel
- Low concentrations with rennet gel but casein release tends to increase over time

- Only traces of milk proteins found in the jejunum
- Dairy products remain highly digestible



# Bioactive peptides released during digestion differ from one matrix to another

More than 4000 peptides were identified in the gut lumen!!!



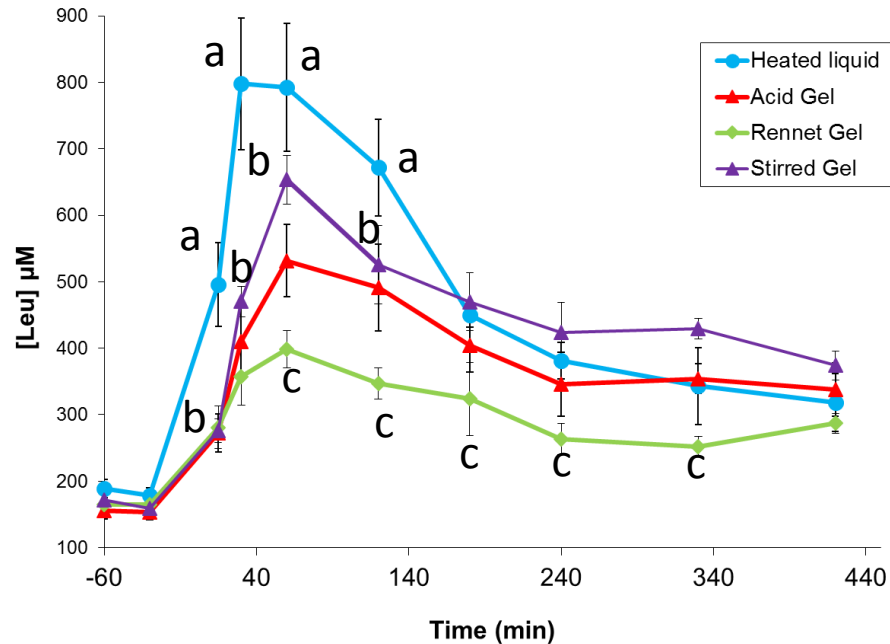
Rennet Gel

Acid Gel

Barbé et al. 2014  
Food Res Int

- More bioactive peptides identified during digestion of acid gel than rennet gel
- Nature of peptides is identical (clearly defined by the digestive enzyme specificity)
- Kinetics of release are different

## 2) effect on absorption

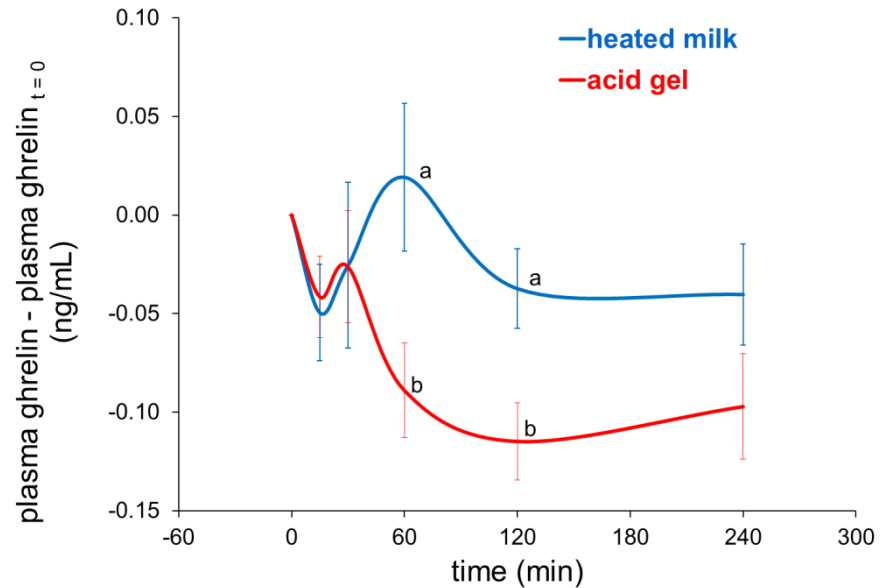


milk gelation:

- delayed proteins transit → delayed AA absorption
- ↘ maximal AA concentration in the plasma

## 3) potential effect on satiety

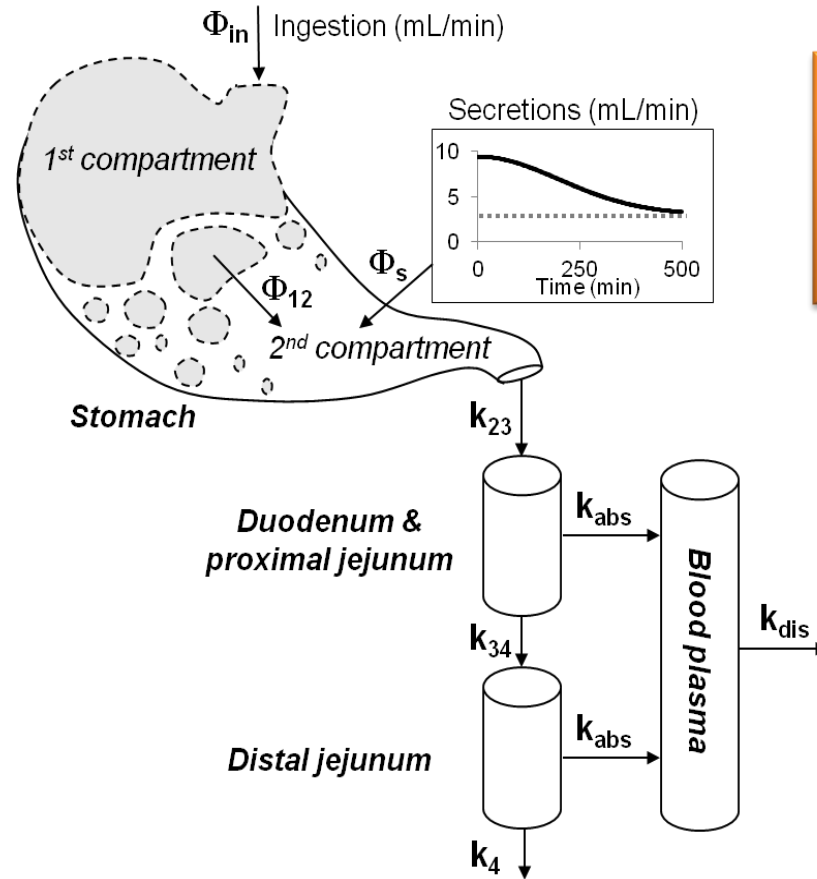
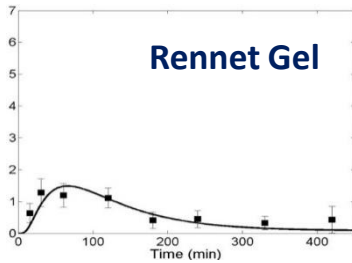
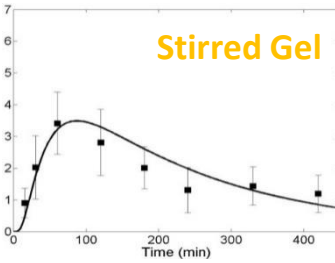
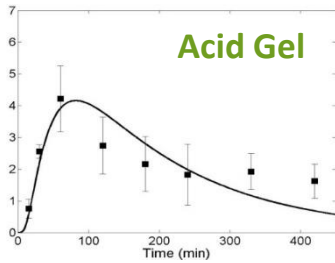
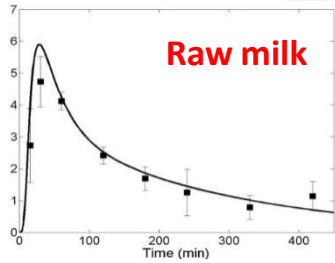
ghrelin (gastrointestinal hormone → appetite stimulation)



milk gelation:

- ↘ postprandial ghrelin concentration =
- ↗ satiety ?

# In silico model of transit and absorption



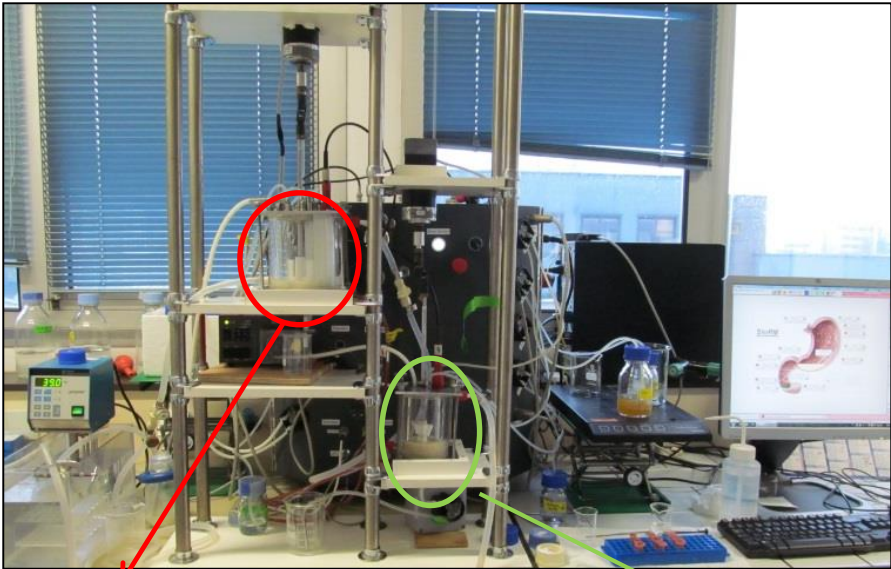
Le Feunteun  
et al. Food  
Bioprocess  
Tech 2014

Better understanding of the food behaviour in the stomach  
Predictive model???

# Differential behaviour of acid/rennet gels in gastric conditions

- ☞ Acid/Rennet gel: identical composition, similar rheological properties and pore size
- ☞ ≠ Time of residence in the stomach (Acid 148 min /Rennet 352 min)
  - ☞ How can we explain this difference? Dynamic *in vitro* digestion of the 2 gels

Ménard *et al.*  
Food Chem 2014



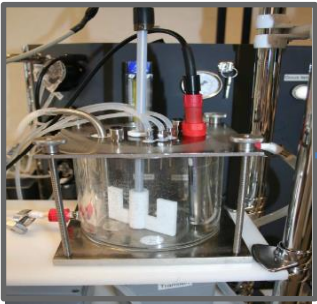
DIDGI®

StoRM® software

**Stomach**

**Small intestine**

- Pepsine
- Gastric lipase
- Simulated gastric fluid
- HCl



Emptying :  
Elashoff's model



- Pancreatin
- Bile
- Simulated intestinal fluid
- NaHCO<sub>3</sub>

Emptying :  
Elashoff's model



# Behaviour of acid and rennet gels in the stomach during *in vitro* dynamic digestion

Barbé et al.  
Food Chem. 2014



Formation of a strong coagulum with rennet gel → slow down the gastric emptying of caseins

**The structure that a food adopts in the stomach is essential to understand its digestion**



# Understanding the mechanisms of dairy gel particles degradation in the stomach



Floury J.<sup>1</sup>, Cardoso Bianchi T.L.<sup>1</sup>, Thévenot J.<sup>1</sup>, Dupont D.<sup>1</sup>, Jamme F.<sup>2</sup>, Lutton E.<sup>3</sup>,  
Panouillé M.<sup>3</sup>, Boué F.<sup>3</sup>, Le Feunteun S.<sup>4</sup>

<sup>1</sup> INRA STLO Rennes, France

<sup>2</sup> SOLEIL Synchrotron Gif-sur-Yvette, France

<sup>3</sup> INRA GMPA Grignon, France



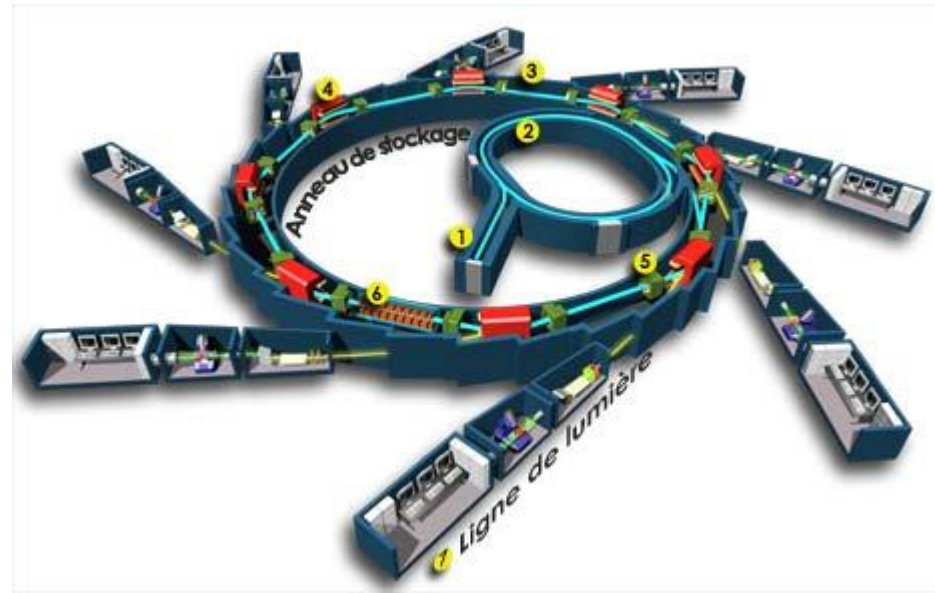


Soleil is a particle (electron) accelerator that produces the synchrotron radiation, an extremely powerful source of light that permits exploration of inert or living matter

DISCO

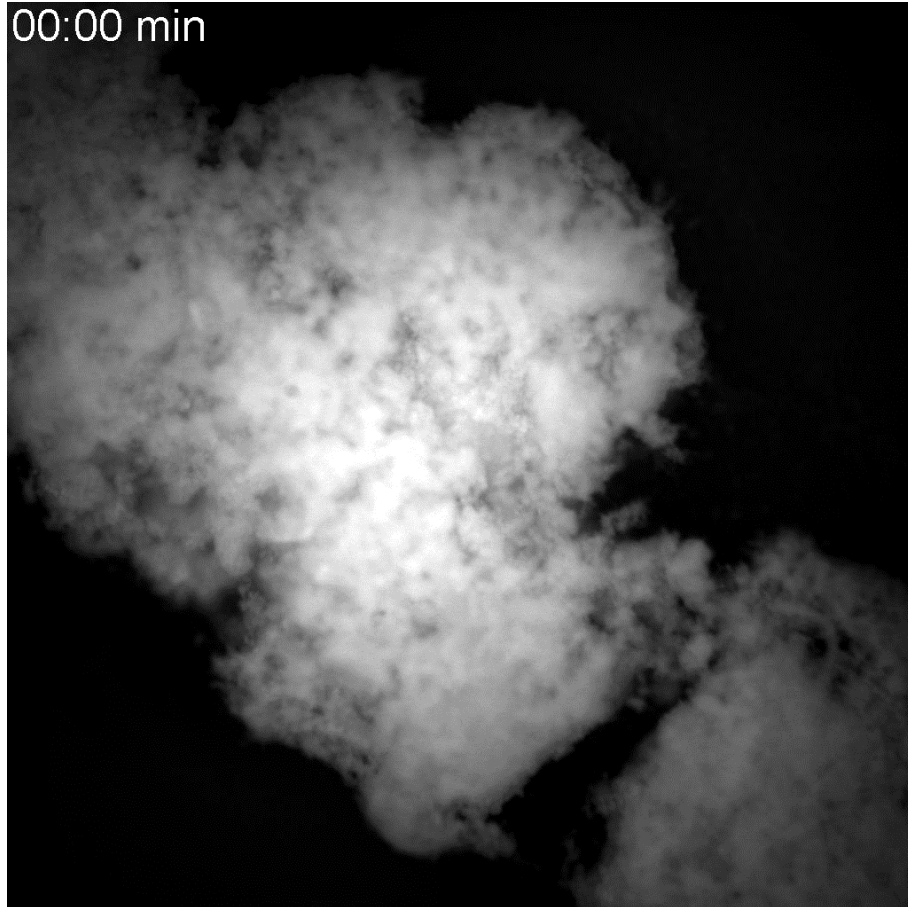
DISCO is a VUV to visible beamline dedicated to biochemistry, chemistry and cell biology. The spectral region is optimized between 60 and 700 nm with conservation of the natural polarization of the light

☞ Allow the imaging of protein intrinsic fluorescence with a UV microscope

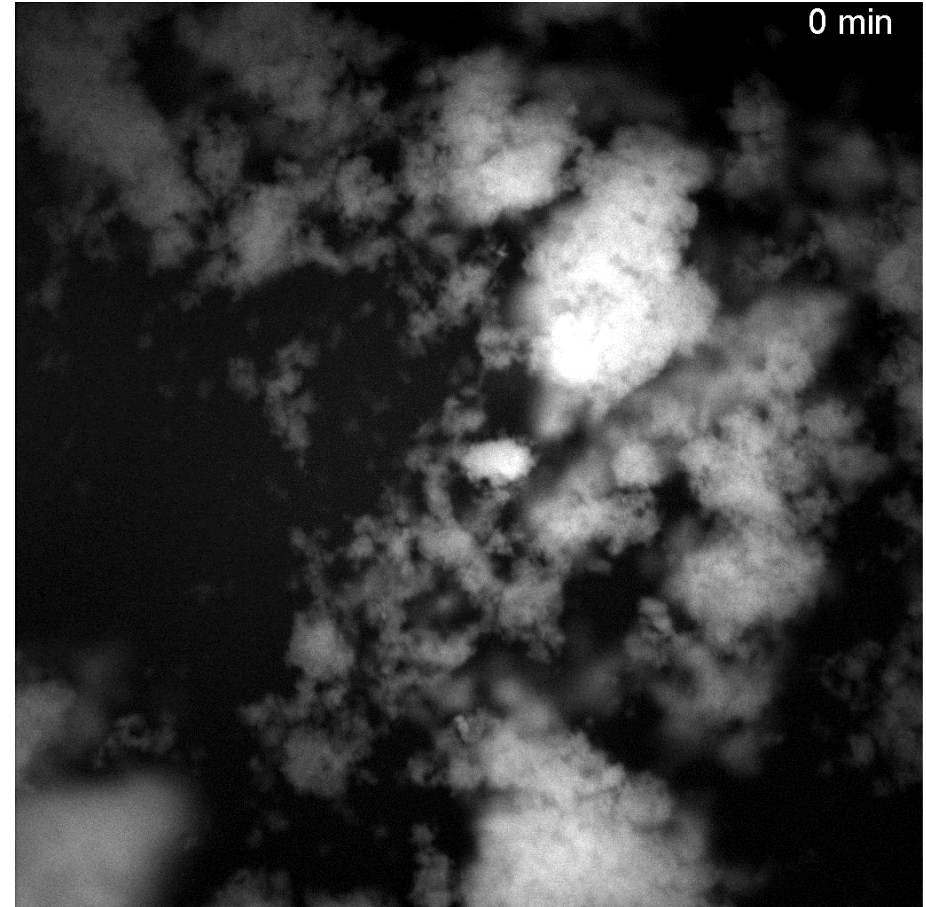




# Kinetics of gel particles disintegration: comparison of rennet/acid gel



**Rennet Gel**



**Acid Gel**



# Can the food structure be used to control the delivery of bioactives?



Pineda-Vadillo C., Le Gouar Y., Menard O., Guerin-Dubiard C., Nau F., Dupont D.<sup>1</sup>

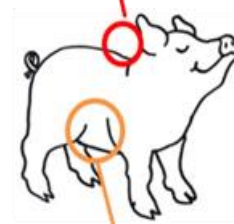


INRA STLO Rennes, France

# Evaluate the effect of the food matrix structure on the release and bioavailability of DHA during *in vivo* digestion

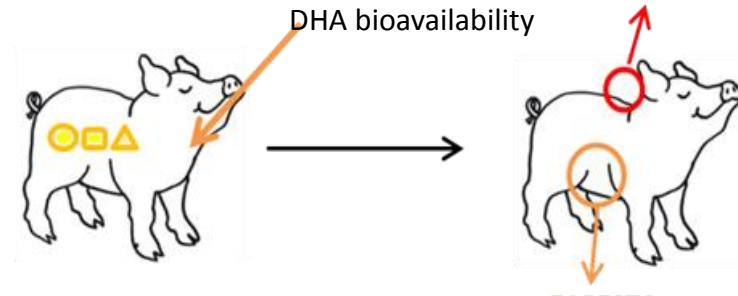
SANG	EFFLUENTS
"-15 min"	"-15 min"
	0 min (3min)
	+20 min
	+50 min
+1h	
	+1h 30min
+2h	
+3h	+3h
+4h	
	+4h 30min
+6h	+6h
	+7h 30min
+8h	
+10h	
+24h	
+48h	

YUGULAR CATHETER



DUODENAL CANULE

+ DHA  
① ② ③



DHA bioavailability

pH  
De visu characterization  
Proteolysis  
DHA quantification



# Food matrices of identical composition but different structure

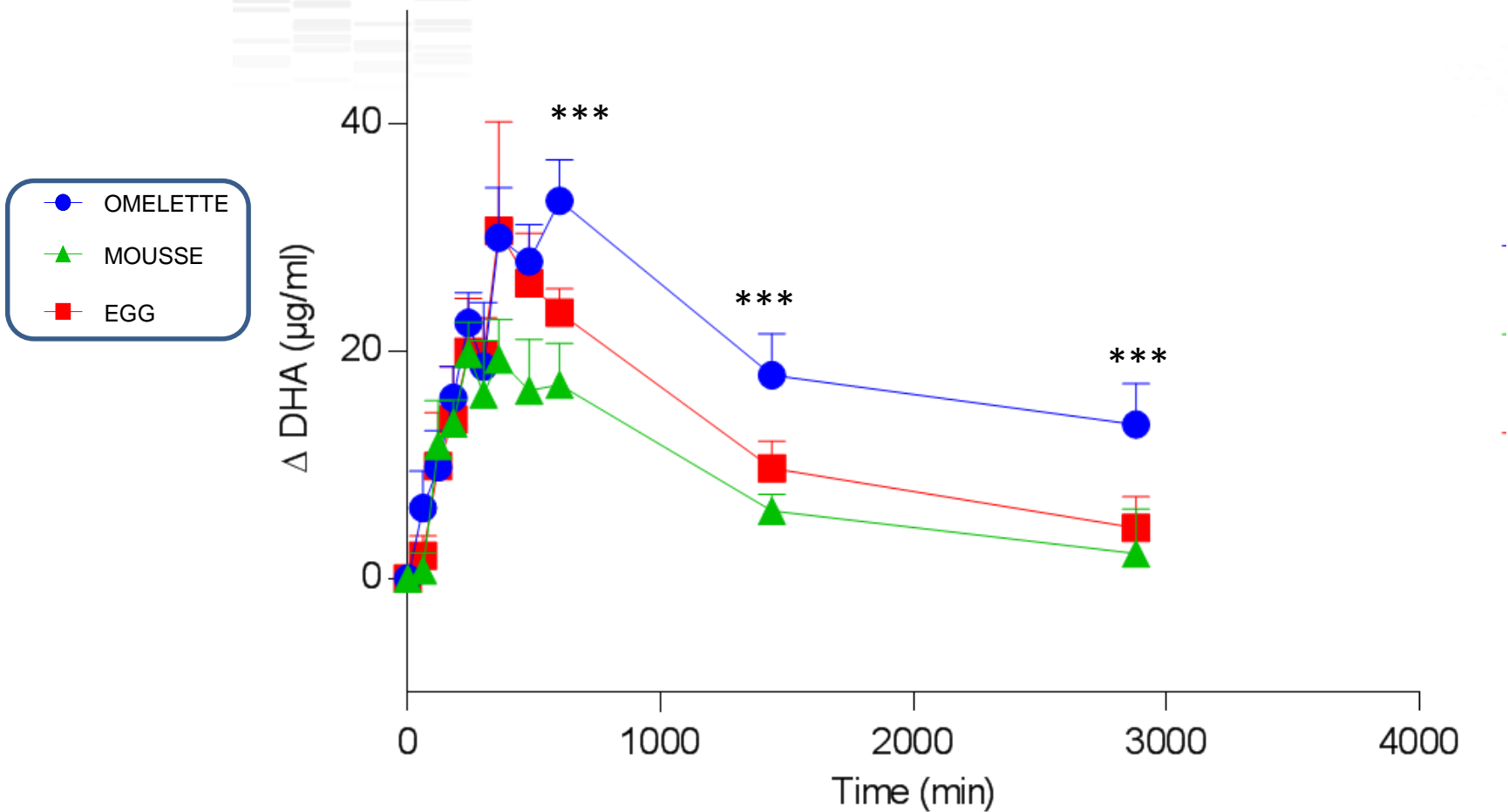
- 1** OMELETTE (Egg yolk and egg white **MIXED** and **COOKED**)
- 2** HARD BOILED- EGGS (Egg yolk and egg white **NOT MIXED** and **COOKED**)
- 3** MOUSSE (**FOAMED RAW** Egg white mixed with **RAW** egg yolk)



Egg yolk: egg white proportion identical as in real eggs 500g /intake **1.74 g of DHA**

**DHA recovery after cooking:** Omelette (99.4%) Boiled-eggs (104%) Mousse (91.7%)

# Quantification of DHA in plasma



Delivering DHA through omelette increases DHA bioavailability



# Infant formulas

Can we create lipid structures biomimetic of the native fat globule?



Le Huërou-Luron I.<sup>1</sup>, Bouzerzour K.<sup>2</sup>, Ferret-Bernard S.<sup>1</sup>, Ménard O.<sup>2</sup>, Le Normand L.<sup>1</sup>, Perrier C.<sup>1</sup>, Le Bourgot C.<sup>1</sup>, Jardin J.<sup>2</sup>, Bourlieu C.<sup>2</sup>, Carton T.<sup>3</sup>, Le Ruyet P.<sup>4</sup>, Cuinet I.<sup>4</sup>, Bonhomme C.<sup>4</sup>, Dupont D.<sup>2</sup>



<sup>1</sup> INRA ADNC Rennes, France

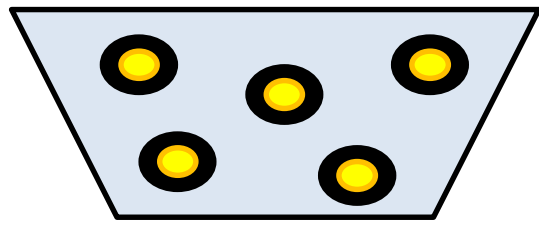
<sup>2</sup> INRA STLO Rennes, France

<sup>3</sup> BIOFORTIS, Saint-Herblain, France

<sup>4</sup> LACTALIS, Retiers, France

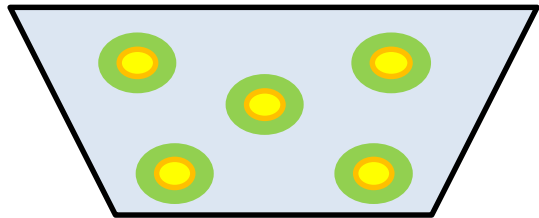
# Infant formulas: can we create lipid structures biomimetic on the native fat globule?

Formula T1



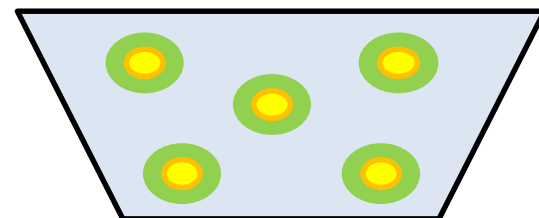
Interface 100 % Proteins  
100% vegetable oil

Formula T2

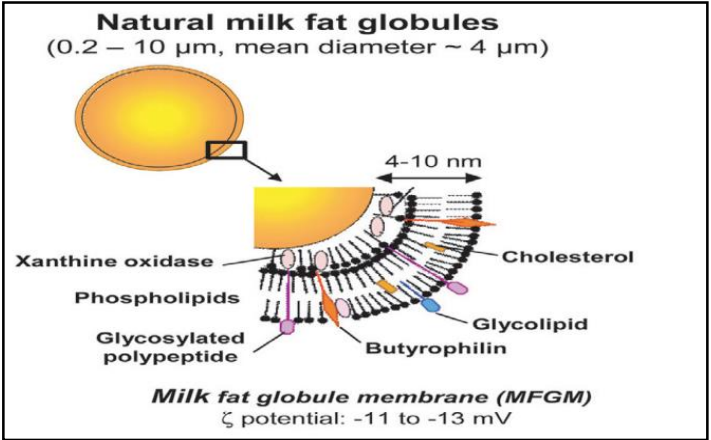


Interface 100 % phospholipids  
100% vegetable oil

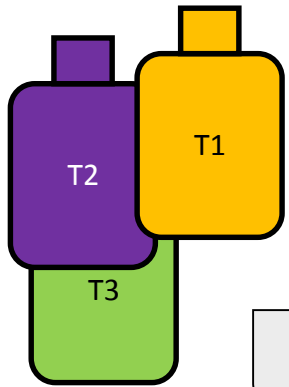
Formula T3



Interface 100 % phospholipids  
40% vegetable oil + 60% milk fat

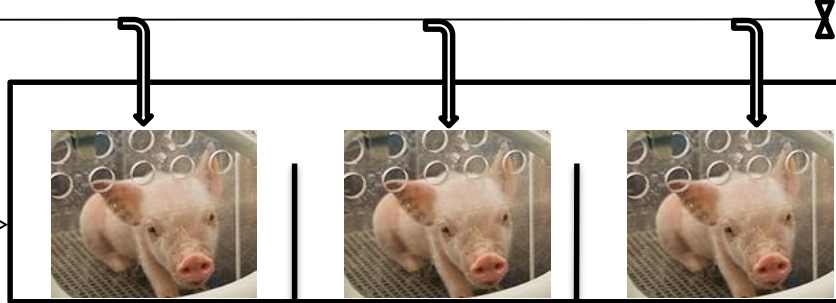


# Can the composition of Infant Formula modulate the physiological response of the neonate?



- Veg
- Veg + PL
- Dairy Fat + PL

Automatic meal delivery (10 meals/ day)



+  
Mother-fed piglets  
(MF = + control)



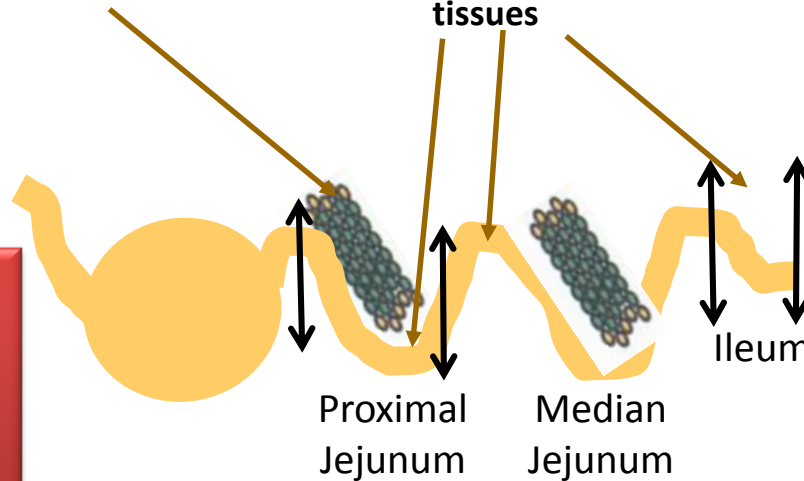
Slaughtering after

7 days

28 days

(90 min postprandial)

Mesenteric Lymph Nodes (MLN) Collect of effluents and tissues



Effluents:  
-SDS-PAGE  
-Elisa

Tissues:

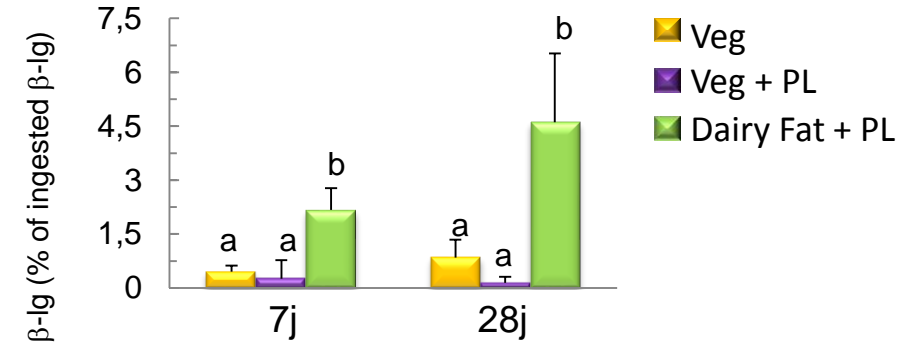
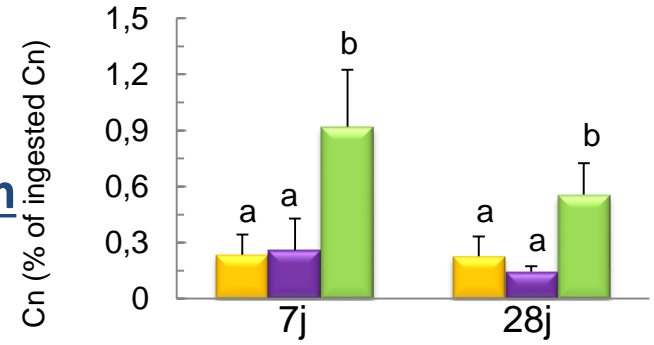
- Morphometry
- Enzyme Activities
- Intestinal Permeability
- Local immune response
- Microbiota

# Protein Digestion

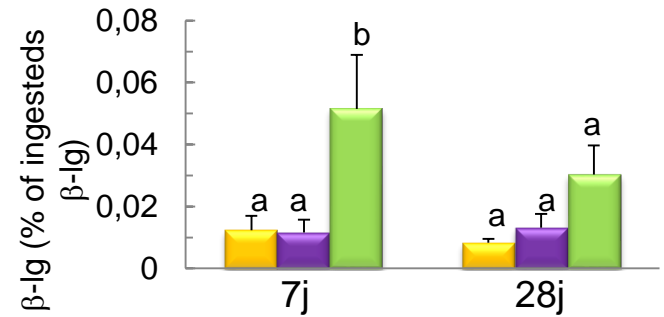
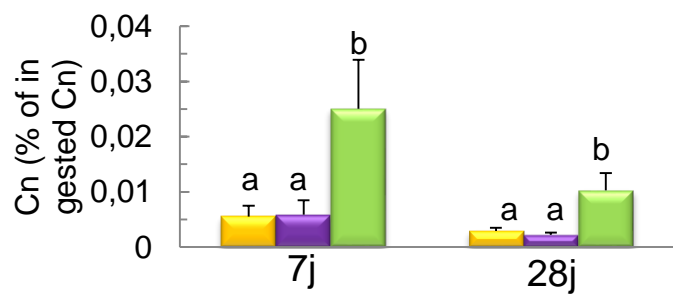
## Casein

## $\beta$ -lactoglobulin

Jejunum



Ileum



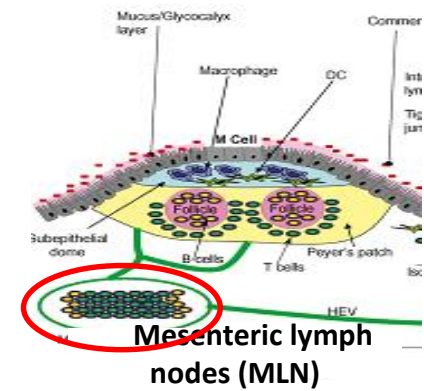
Milk Proteins better resist to intestinal digestion in the presence of dairy fat

➔ Modification of the interface

(Granger *et al* 2005; Davies *et al*, 2001)

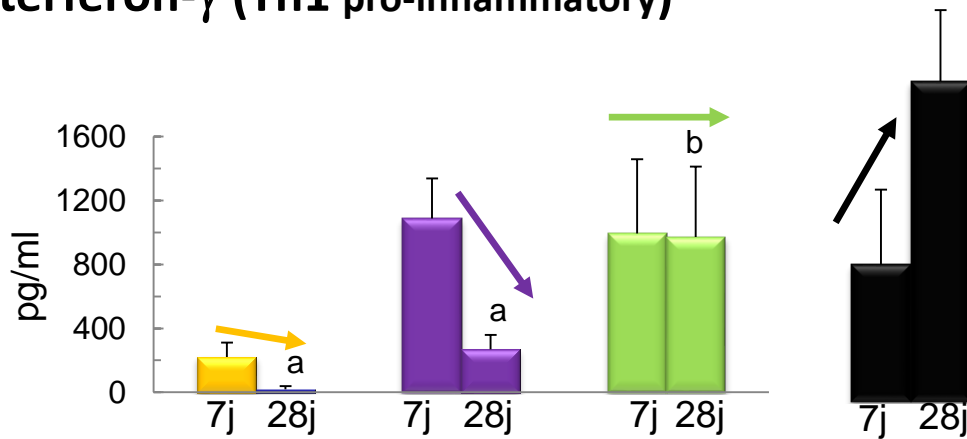


# Secretory activity of MLN

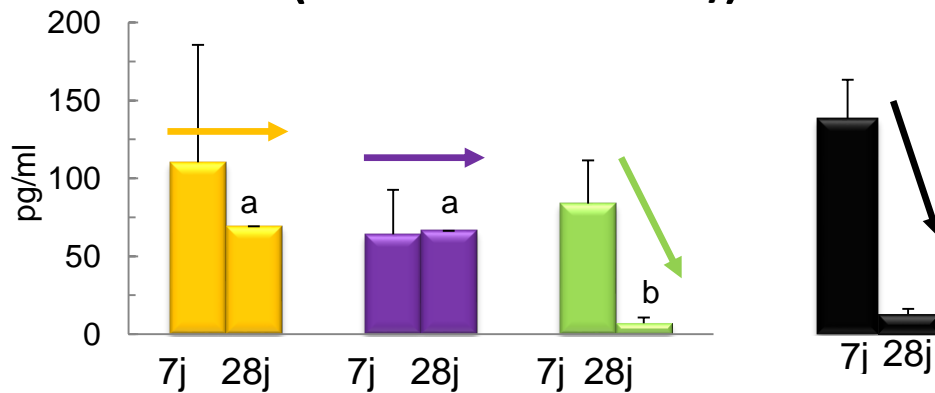


- Veg
- Veg + PL
- Dairy Fat + PL
- Porcelets SM

## Interferon- $\gamma$ (Th1 pro-inflammatory)



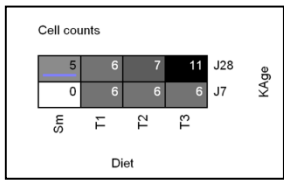
## Interleukine-10 (Th2 anti-inflammatory)



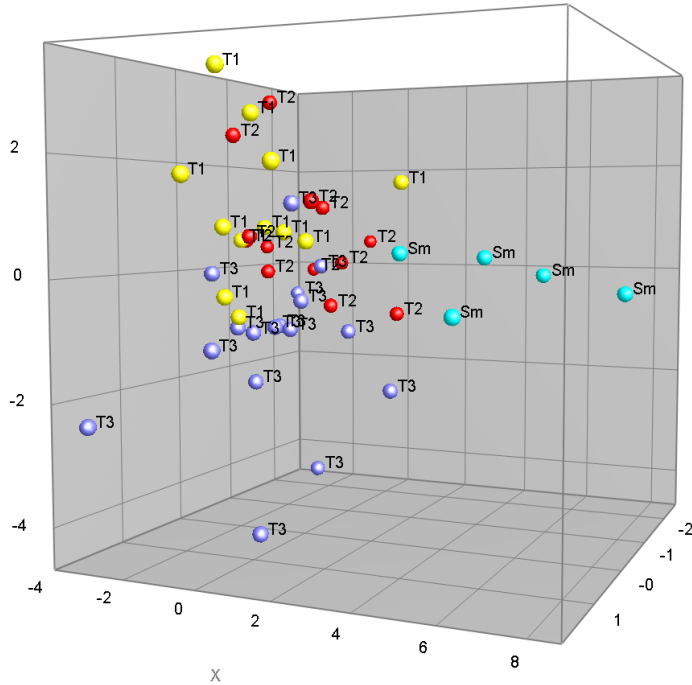
Milk lipids → maturation of the piglet's immune system more similar than with sow's milk

Le Herou-Luron et al.  
Eur J Nutr 2016

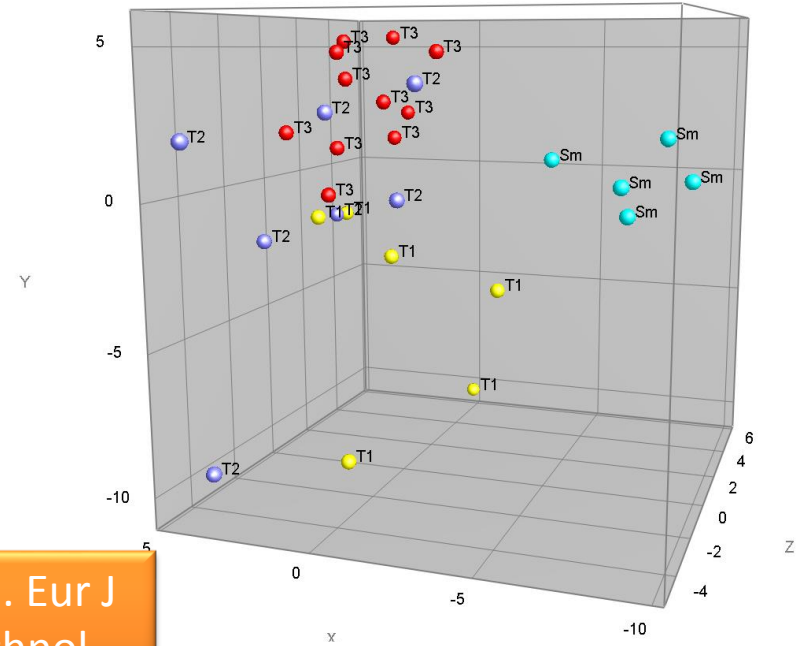
# Microbiota by DHPLC



D7 & D28



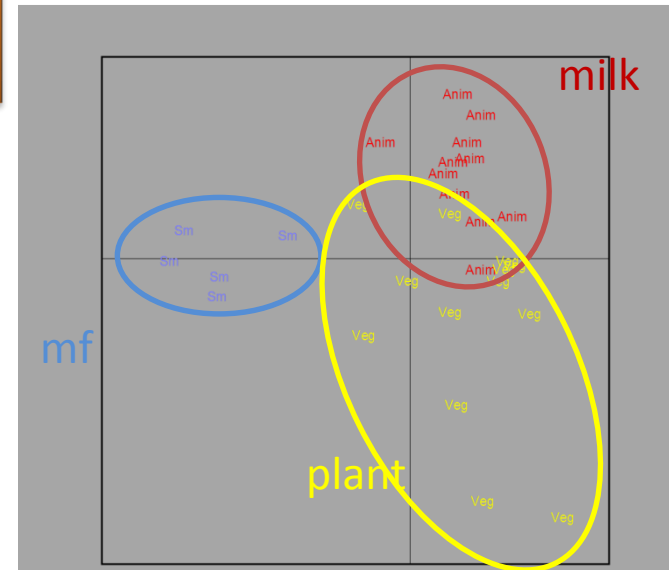
D28



Bourlieu et al. Eur J Lipid Sci Technol 2016

The composition/structure of the infant formula « orientates » the microbiota

More Proteobacteria with milk fat /  
More Firmicutes with plant oil



# Conclusion

Food structure regulates the kinetics of digestion and the release of nutrients and bioactives in the bloodstream

Gastric emptying rate will highly depend on the structure that the product will adopt in the stomach cavity

Understanding the mechanisms of food particle breakdown in the stomach is critical to control the structure a food will adopt in gastric conditions

Being able to design food structures for controlling the kinetics of hydrolysis of macronutrients will allow to obtain food particularly adapted to specific population



# The Bioactivity & Nutrition team



## Head

Didier DUPONT - Senior Scientist

## Scientists

Claire BOURLIEU – Junior Scientist  
Rachel BOUTROU – Junior Scientist  
Amélie DEGLAIRE – Lecturer  
Juliane FLOURY – Lecturer  
Catherine GUERIN - Lecturer  
Joëlle LEONIL – Senior Scientist  
Françoise NAU – Professor  
Jonathan THEVENOT – Post-doc



## PhD students

Samira de OLIVEIRA (2013-2016)  
Lucie LORIEAU (2016-2019)  
Linda LEROUX (2016-2019)  
Manon HIOLLE (2016-2019)  
Yohan REYNAUD (2016-2019)

## Technicians

Gwenaële HENRY  
Yann LE GOUAR

## Engineers

Julien JARDIN  
Olivia MENARD  
Jordane OSSEMOND

## Masters students

# Improving health properties of food by sharing our knowledge on the digestive process

COST Action FA1005

Dr. Didier DUPONT, Senior Scientist, INRA, France

●  
**INFOGEST**  
●



**June 2011 – May 2015**







**INFOGEST**  
International Conference  
Rennes, France  
April 2017

We are pleased to announce the next

## 5<sup>th</sup> International Conference on Food Digestion



**in Rennes, France, 4-6 April 2017**