INRAE, because our need for research is greater than ever

Didier Dupont

▶ **To cite this version:**

Didier Dupont. INRAE, because our need for research is greater than ever. ADSA annual meeting 2023, American dairy Science Association, Jun 2023, Ottawa, Canada. hal-04154049

HAL Id: hal-04154049
https://hal.inrae.fr/hal-04154049

Submitted on 6 Jul 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

science for people, life & earth

INRAE

French national research institute for
agriculture, food & environment

INRAE, because our need for research is greater than ever

Major global concerns
Climate change, biodiversity loss, environmental degradation (soil, air, water), fossil fuel depletion, pollution, urban population growth, malnutrition...

Tackling scientific challenges related to **agriculture**, **food production**, and the **environment** requires an integrated approach:

- Ecological transition
- Sustainable production of healthy food for all
- Complementary uses of bioresources, the bioeconomy
- Biodiversity and adaptive resource management

A world leader

No. 1 research institute in the world specialising in agriculture, food, and the environment

3rd in the agricultural sciences*
4th in the plant and animal sciences*
4th in food science*
10th in ecology and the environmental sciences*

*International rank based on scientific publications

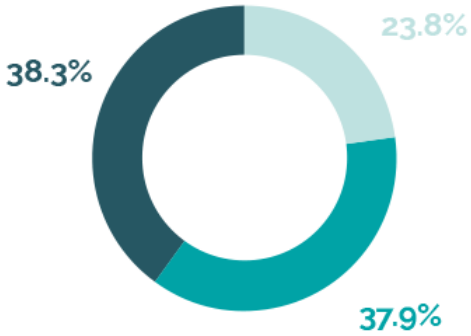
Key figures

INRAE 2020

8,341
permanent staff
(i.e., full-time positions)

49,2% men
50,8% women

2,811
contractual staff
(i.e., full-time positions)



- 1,990 researchers
- 3,165 engineers and assistant engineers
- 3,186 technicians

Budget of more than **€1 billion**
Public subsidies from the French government 78.3%
- External revenue 21.7%

First research institute to obtain
the certification Equality and Diversity at Work

L'INSTITUT agro

THE FRENCH INSTITUTE FOR **AGRICULTURE, FOOD** AND **ENVIRONMENT**

01 To facilitate bridges between…

EDUCATION

RESEARCH

INNOVATION

… to educate future actors of transitions at an international level

04

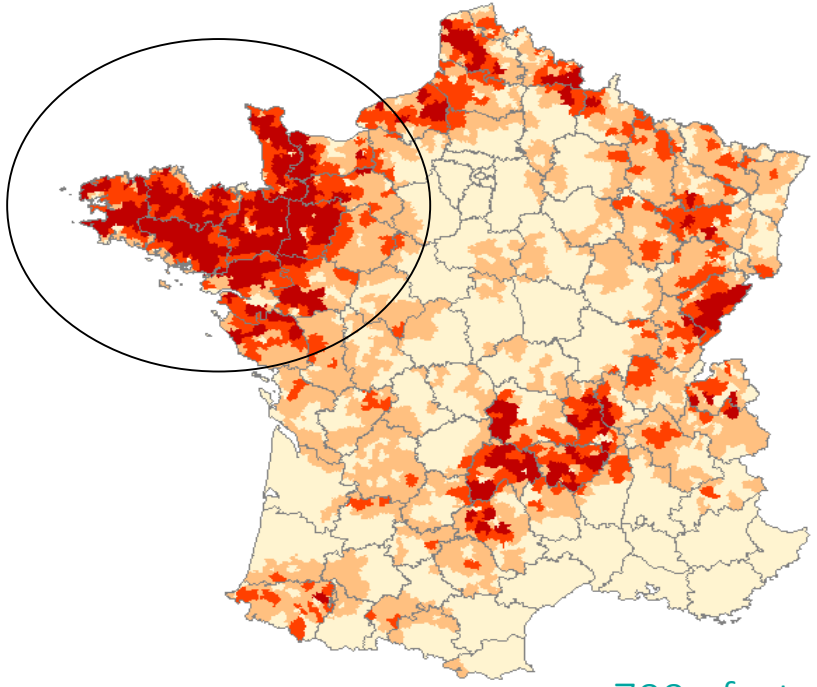
KEY FIGURES

06	14	310	4,700
CAMPUSES	DEPARTMENTS	ASSOCIATE-PROFESSORS	STUDENTS

Some economic aspects

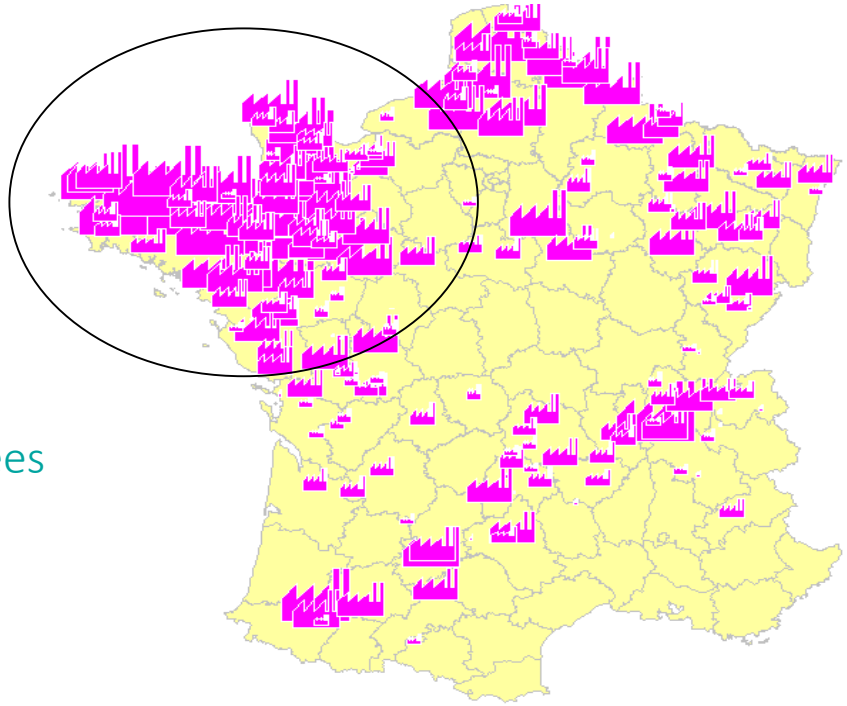
Milk production in France

(3.7 millions of dairy cows)



57,000 dairy farms
23.8 billions of liters
160,000 direct jobs

Treatment & transformation



700+ factories
60,000 employees

Source: CNIEL-French Dairy Board (2018)

PEGASE

(Physiology, Environment and Genetics for the Animal and livestock SystEms)

Head: Ludovic Brossard

Deputy Heads: Bénédicte Lebret, Vanessa Lollivier

PEGASE

Staff

<u>107 permanent staff members</u>

(95 from INRAE, 12 from AO)

47 scientists (CR, DR, EC & IR)

9 support engineers (IE)

51 “technicians” (AIBC)

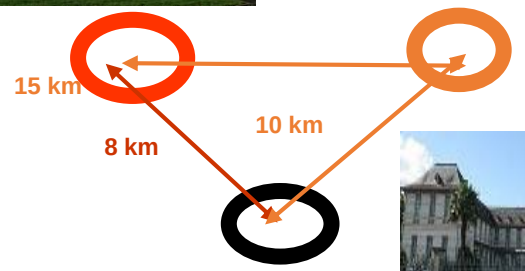
<u>About 90 non-permanents each year</u>

~165 persons daily

3 sites around Rennes (France)

PEGASE research
UE3P- Experimental unit (pigs)

PEGASE teaching



PEGASE
Experimental unit
(dairy cows and goats)

Pegase conducts research on animal biology and livestock systems with the ultimate goal to improve the sustainability and the competitiveness of animal production systems

STLO

Milk & Egg Science and Technology

Departments: MICA, CEPIA, P3AN
Carnot Institute « Qualiment » (since 2016)

140 people
80 tenure staff (34 researchers and professors; 42 technicians and engineers)

~25 Docs and Post-Docs / year

~15 Students (Master)

16 members of R&D dept (private sector)

Our playgrounds

Food and raw materials, milk and egg

- Composition
- Structure
- Quality

But also plant-based matrices

- Protein components
- Quality

Transformation Processes

Mastering the functionalities

- Process management
- Eco-efficiency
- Ecoconception

Fermentation, heat treatment, drying, membrane fractionation, Dairy technology

Human food

- Digestion

Food matrices

Design of foods safe, secure, adapted to human needs and sustainable

The Dairy Platform

Process in Platform (1000 m^2) > whole range of dairy technologies

- Heat treatment (pasteurization to UHT-sterilization)
- Homogenization, cream separation, melting…
- Membrane separation modules :
  - ✓ Microfiltration
  - ✓ Ultrafiltration
  - ✓ Reverse osmosis
- Two cheese production lines (soft- and hard-type cheeses)
- Spray drying facilities: pilot (1-7 kg of water per hour) and semi-industrial (BIONOV) units

The platform uses the analytical facilities as well as the expertise of the STLO research teams



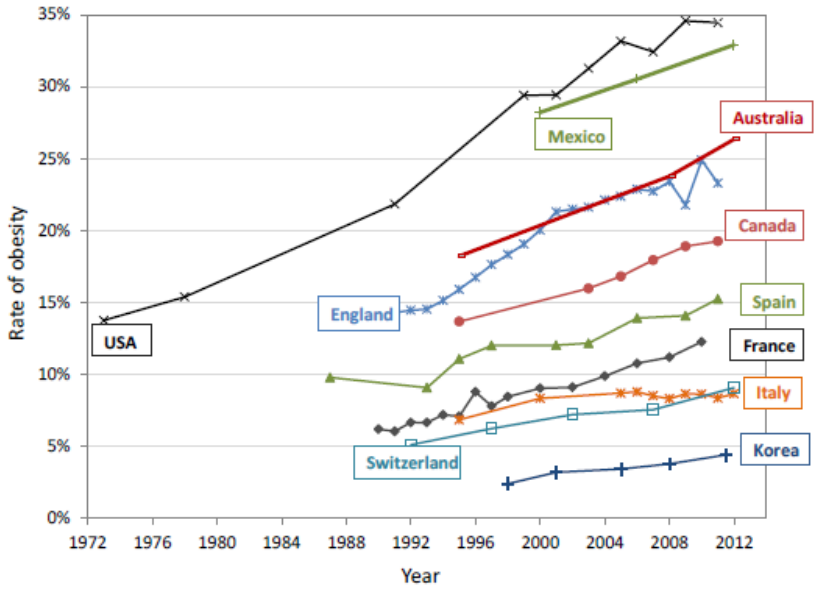

The structure of dairy products at different length scales drives the mechanisms of digestion and the nutrient bioavailability

Dr Didier DUPONT, INRAE, STLO, Rennes, France

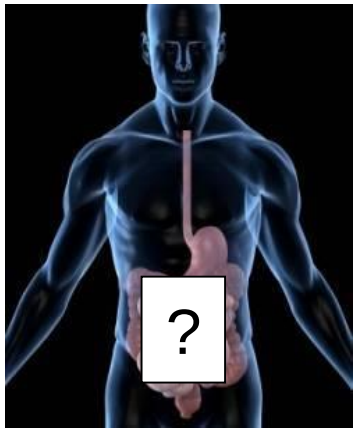
RÉPUBLIQUE FRANÇAISE
Liberté
Égalité
Fraternité

INRAE

Food and human health: the key role of 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

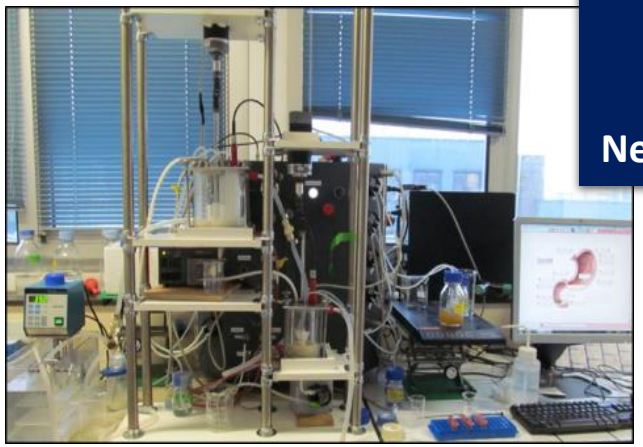
By increasing our knowledge on food digestion, we will increase our knowledge on the effect of food on human health

Models available at INRAE for simulating digestion

Menard et al. 2018, 2023
Wang et al. 2022

INFOGEST

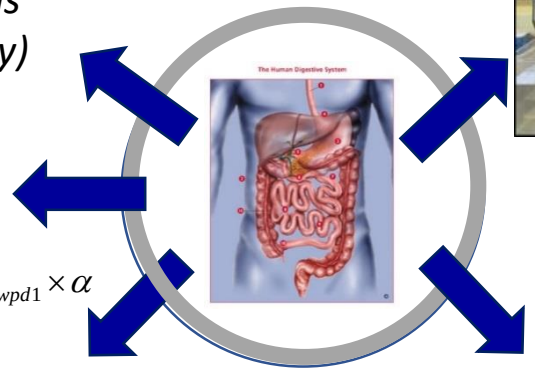
Peng et al. 2021
Halabi et al. 2021
Giribaldi et al. 2021
Chauvet et al. 2023
Nebbia et al. 2022, 2023



In vitro dynamic models (infant, adult, elderly)

In vitro static models (infant, adult, elderly)

In silico models



Le Feunteun et al. 2014, 2020

$$\Phi_{12} = k_{12whey} \times \left(V_1 - m_{caswpd1} \times \alpha\right) + k_{12aggr} \times m_{caswpd1} \times \alpha$$

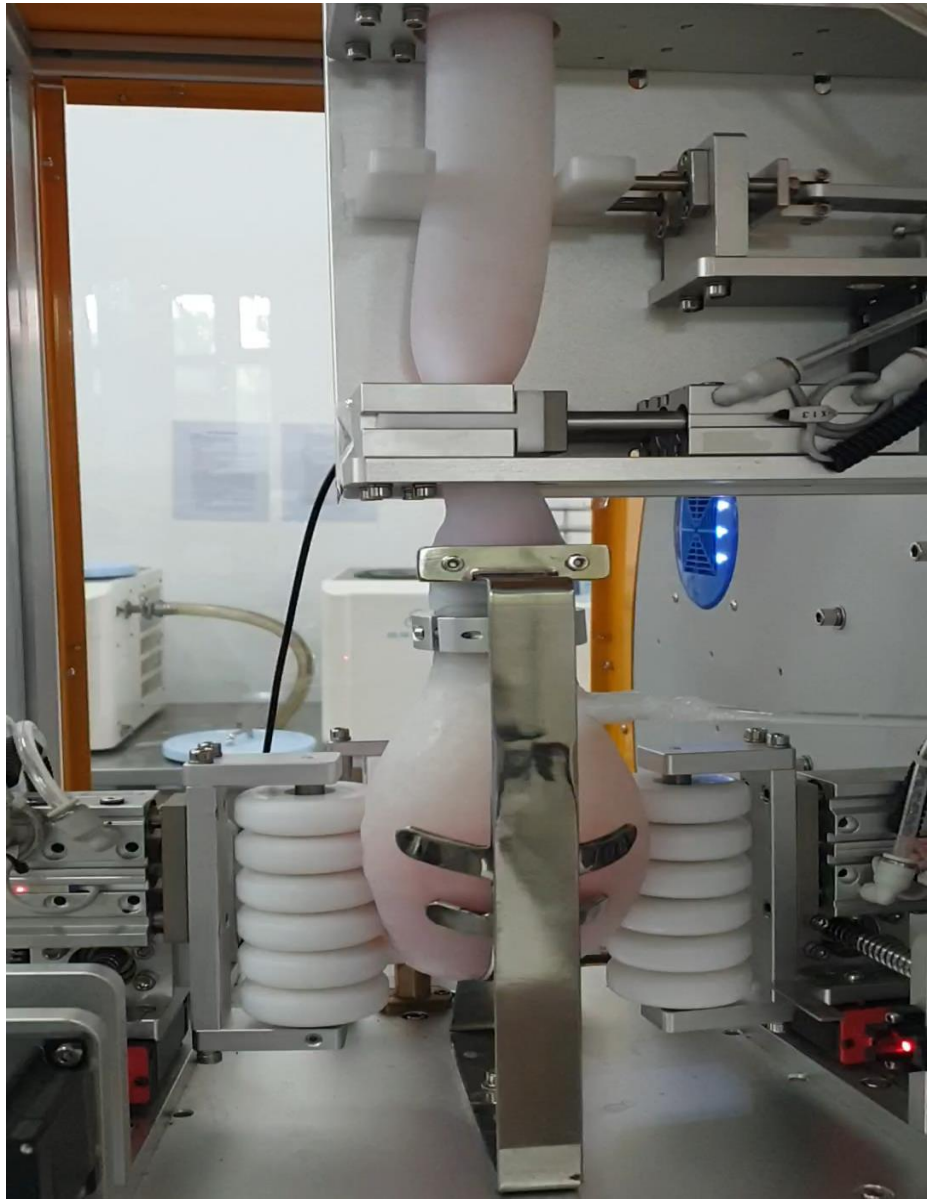
Human models

Animal models

De Oliveira et al. 2016
De Oliveira et al. 2017
Buffière et al. 2020
Boulier et al. 2023

Lemaire et al. 2021
Nau et al. 2022
Jimenez-Barrios et al. 2023
Charton et al. 2022, 2023

NERDT™ : the NEar Real Digestive Tract



STOMACH

Xiao Dong Pro-Health
Smart Digestion
Suzhou University

INSTITUT CARNOT QUALIMENT

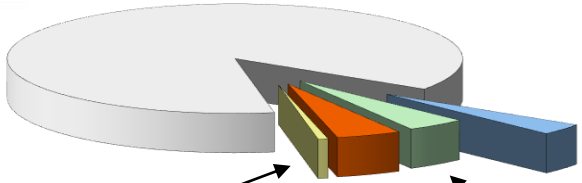
The supramolecular structure of caseins affects the kinetics of digestion

Dupont D.

INRAE, Rennes, France

Milk

Water (870-875)



Proteins (32-35 g/L)

Caseins (80%)
αs_1, αs_2, β, κ

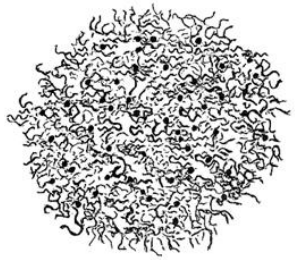
Whey Proteins (20%)
β-lg, α-la

Minerals (8-9 g/L), vitamins, …

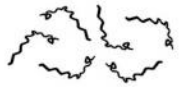
Lactose (48-50 g/L)

Lipids (34-44 g/L)

ø~200 nm
(Holt, 1994)



Casein organized into a supramolecular structure: the **casein micelle (CM)**



ø~11 nm
~15 casein molecules;
(Thomar *et al*. 2013)

Casein can also be extracted after acidification followed by neutralization: the **caseinate (CS)**

Objective

1 Investigate gastric emptying of an isoproteic solution of CM and CS (exp. 1)

2 Characterize the structure of the resulting chyme and determine if CM and CS are differently metabolized (exp. 2)

Experiment 1 – Determination of Gastric Emptying

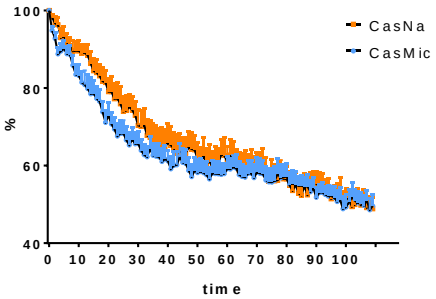
96 g of CM or CS rehydrated in 800 ml of water

+12 g of glucose

+ ^{99m}Tc-colloidal (25Mbq)

9 pigs (20-25 kg)

γ-scintigraphy over 120 min

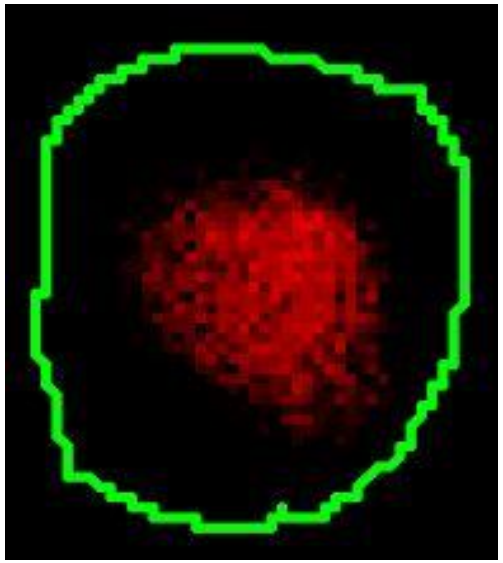


Gastric emptying half-time ($T_{1/2}$) and shape of the curve (β)

But a differential behaviour of CS and CM in the stomach

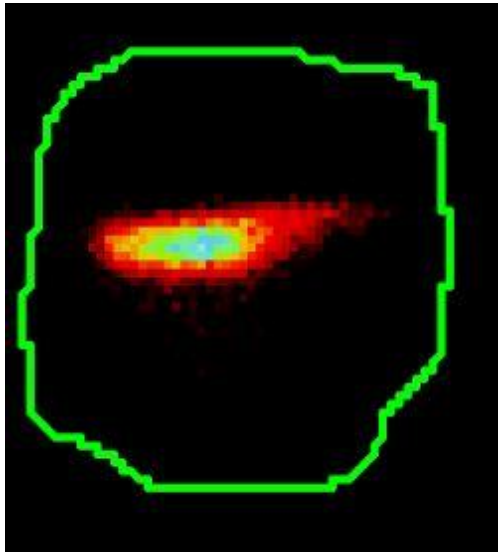
Exemple scintigraphic images at the beginning of gastric emptying (5-10 min after ingestion)

CM



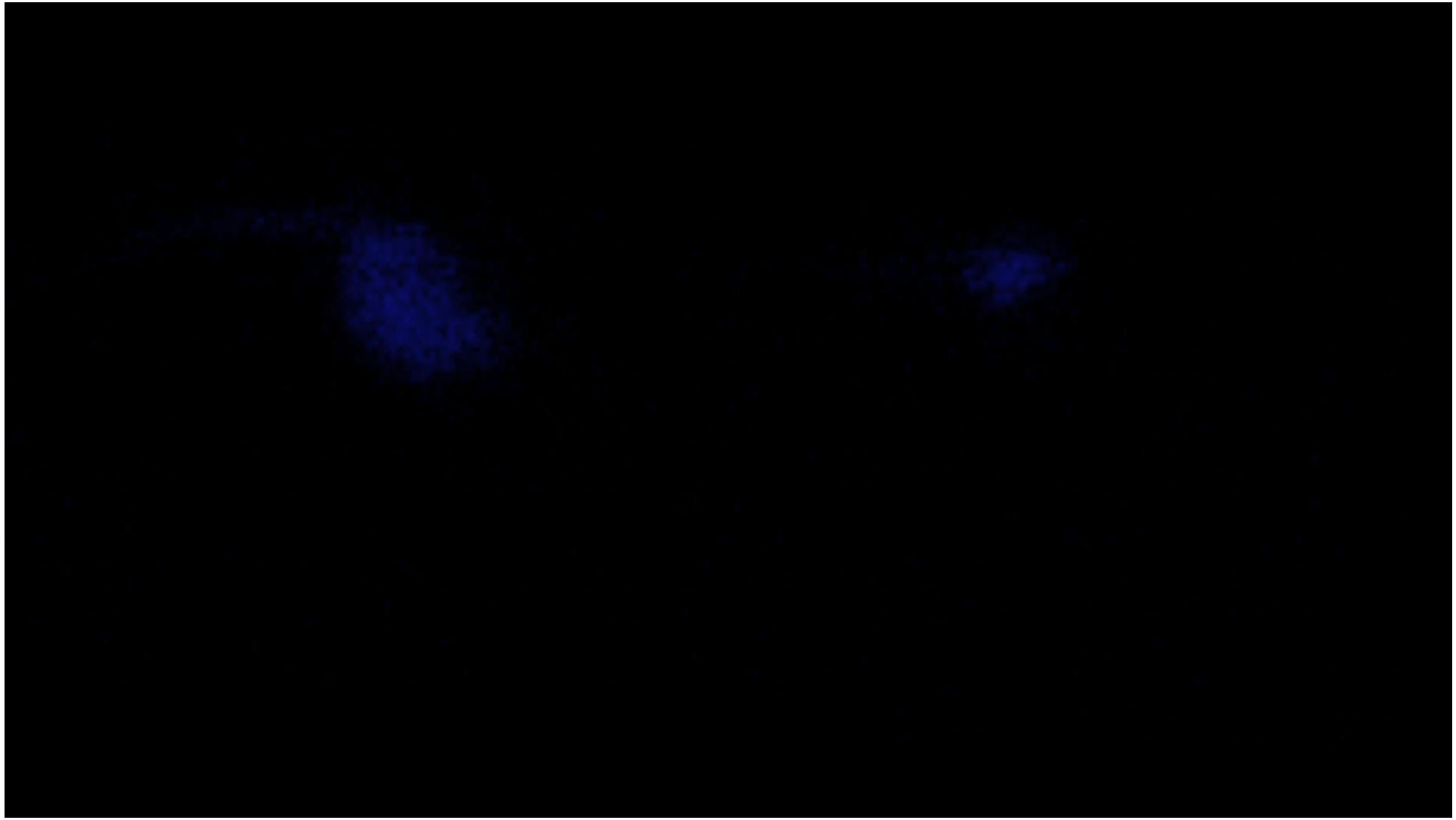
Radioactivity fully fills the stomach

CS



Radioactivity is highly concentrated in the proximal part of the stomach

Gastric emptying



Objective

1 Investigate gastric emptying of an isoproteic solution of CM and CS (exp. 1)

2 Characterize the structure of the resulting chyme and determine if CM and CS are differently metabolized (exp. 2)

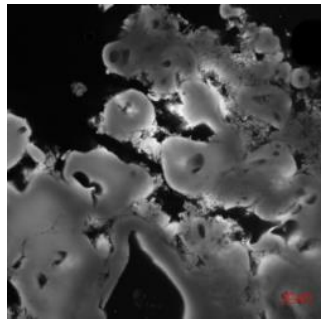
Experiment 2 – Chyme structure and protein metabolism

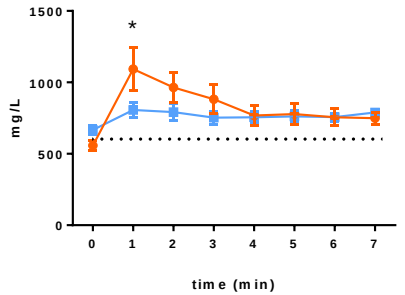
96 g of CM or CS rehydrated in 800 ml of water

+12 g of glucose

10 catheterized pigs (20-25 kg)

Characterization of the chyme structure (slaughtering after 10 min, n=4)





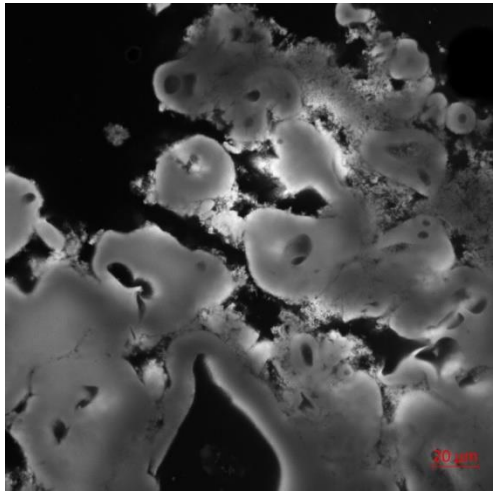
Free plasma amino acids over 7h n=6

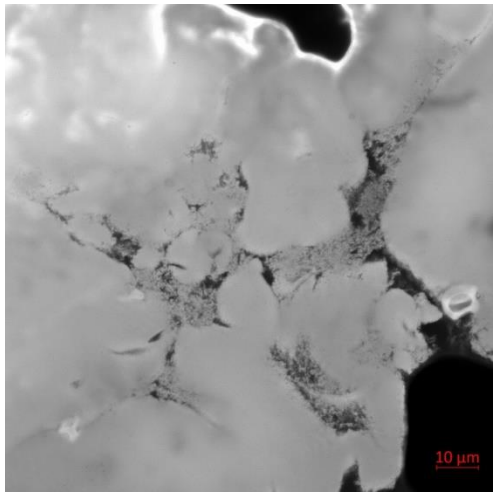
Collection of the stomach contents

CM forms a large coagulum in the stomach whereas CS mainly remains in the liquid form

Microstructure of gastric chymes

CM





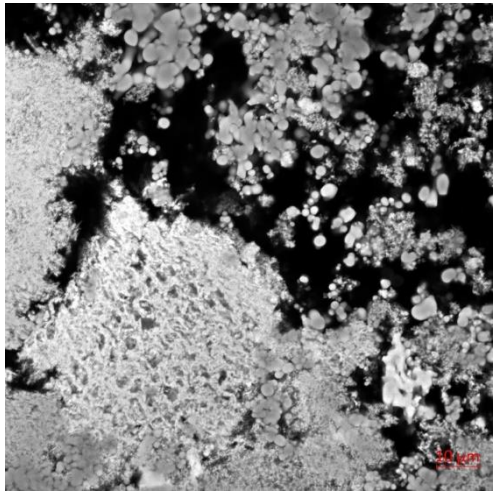
CM Gels (left) are compact and dense =

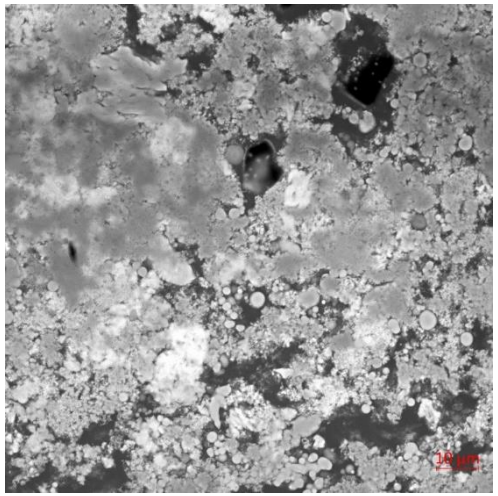
Strong coagulum

CS Gels (right) are an agglomerate of spherical particles that can easily dissociate. The gel have a very « loose » structure =

Protein precipitate

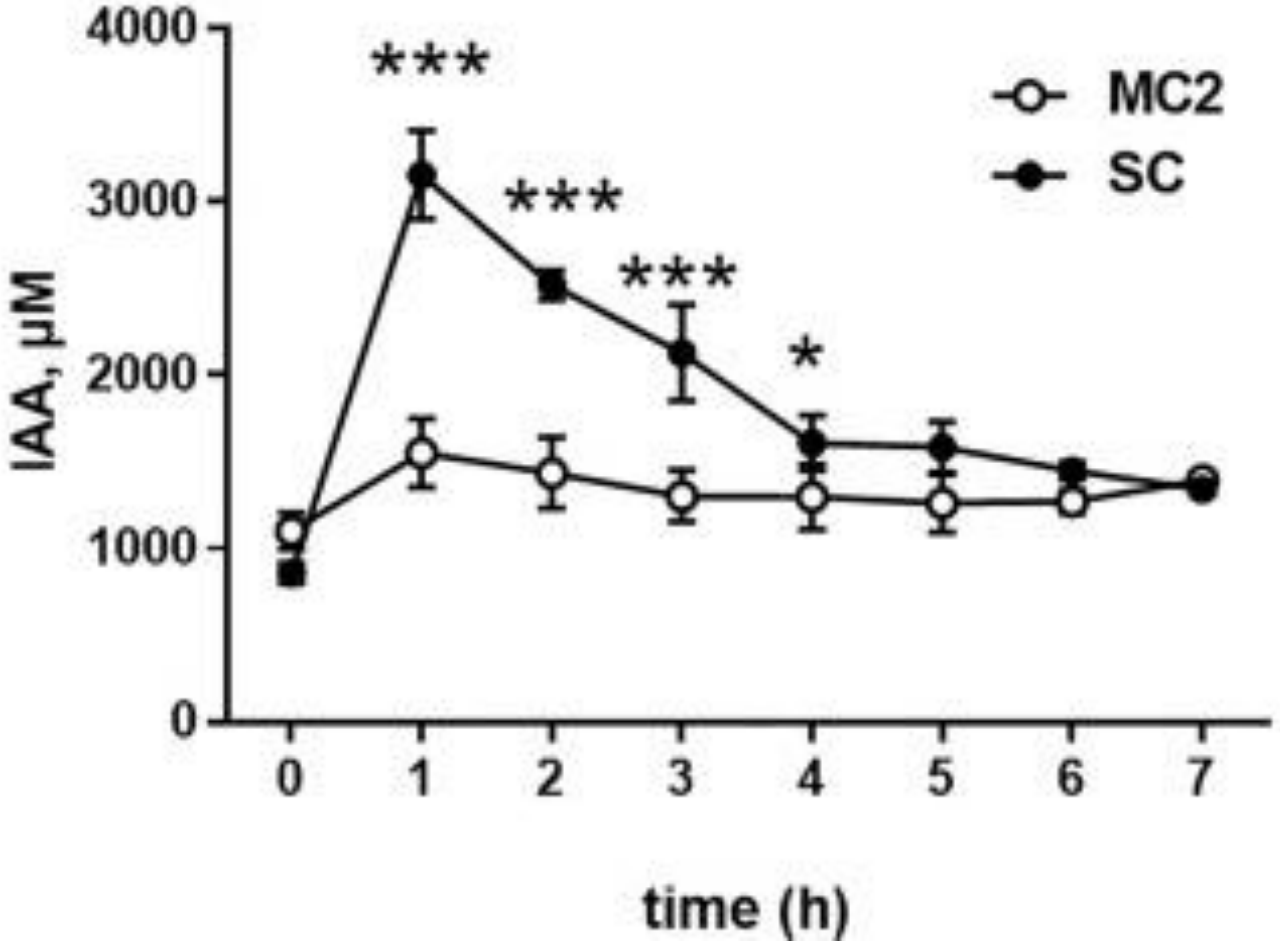
CS





Plasma indispensable amino acids

Boulier *et al.*
Food Chem. 2023



AA peak after 1h for CS whereas the concentration remains stable for CM

CM = slow caseins, CS = fast caseins

The macrostructure of dairy products, as modified by processing, affects the kinetics of protein digestion

Dupont D.

INRAE, Rennes, France

Comparison of 6 dairy products of identical composition but different structure

Ultra Low Heat powder

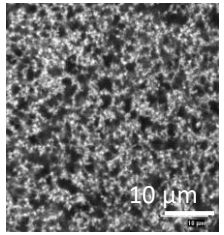
rehydration in water 14.5%

unheated milk ("raw" milk)

macrostructure

24h-20°C, rennet 0.003 % v/w

rennet gel



pH 6.6

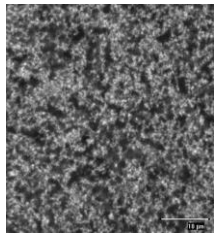
heat treatment 90°C-10 min

microstructure

heated milk

24h-20°C, rennet 0.3 % v/w

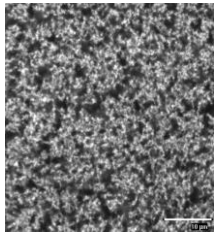
rennet gel



pH 6.6

24h-20°C, GDL 3 % w/w

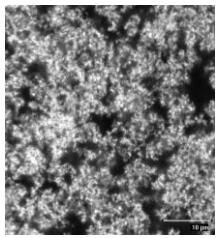
acid gel



pH 4

24h-20°C, GDL 3 % w/w + mixer 2 min

stirred acid gel



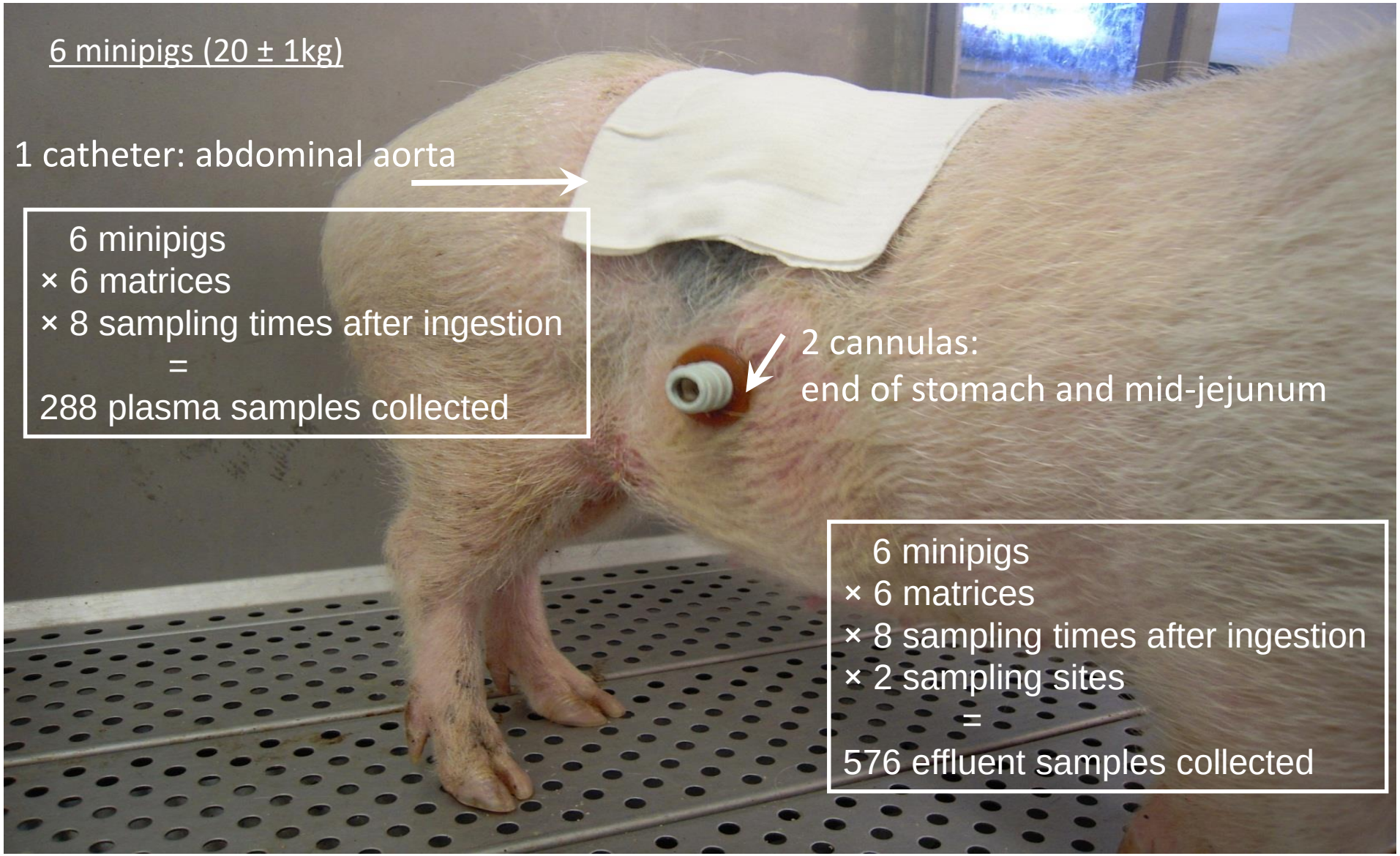
pH 4

Fat-free matrices:

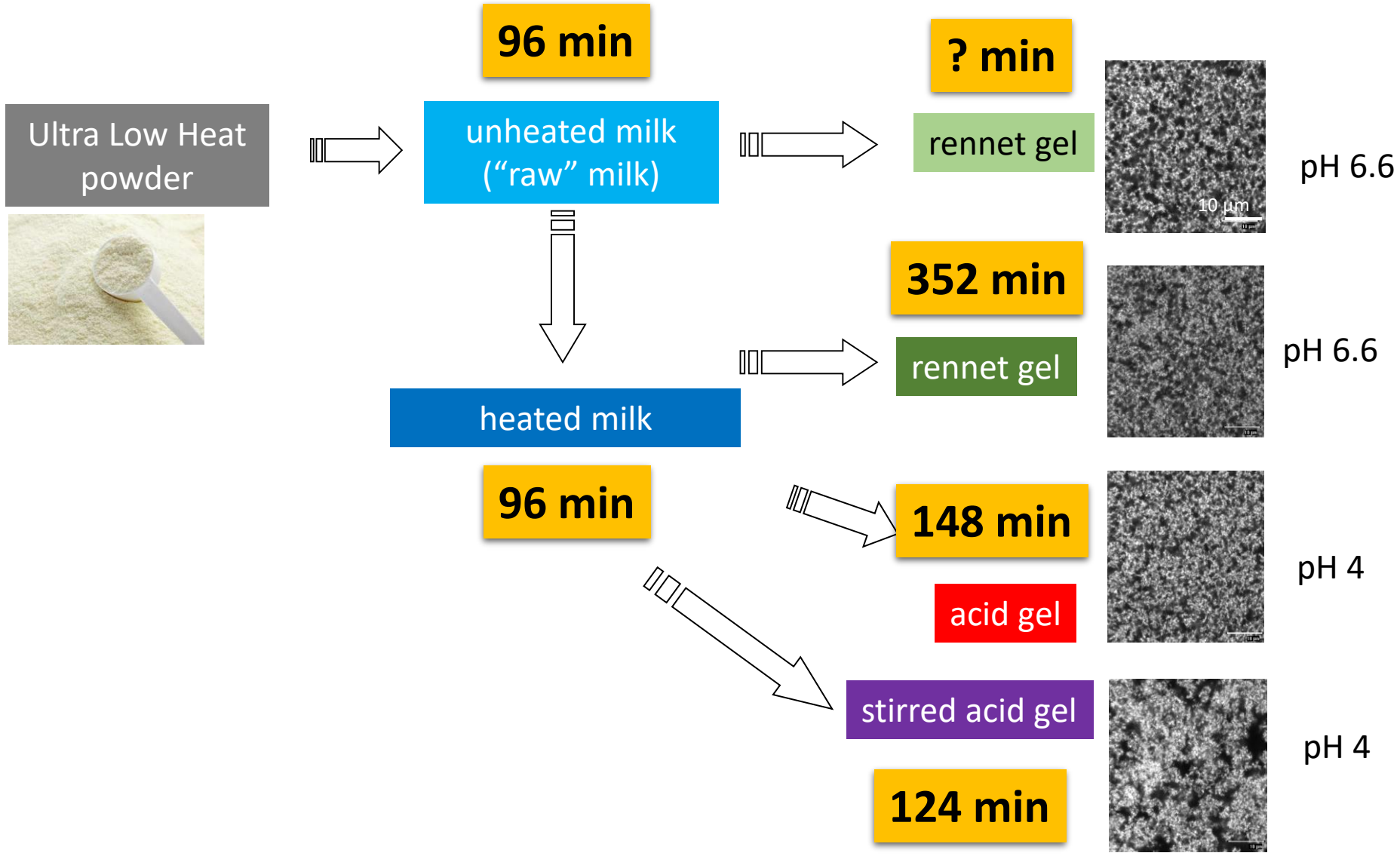
40 g/L caseins, 10 g/L whey proteins,
95 g/L lactose and minerals

+ marker of the meal transit (Cr^{2+}-EDTA) → Gastric emptying half-time

The multi-canulated mini-pigs



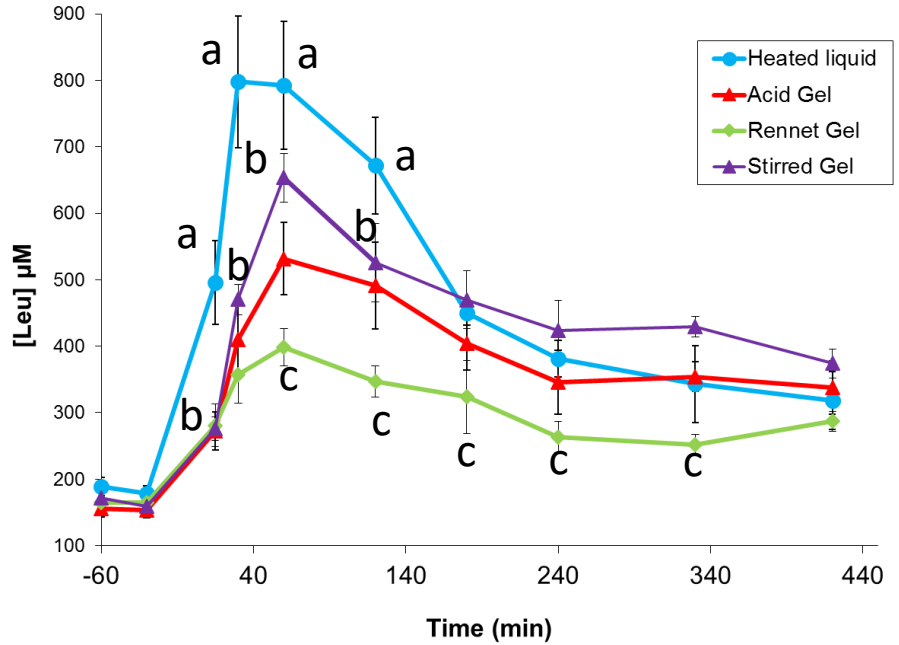
Gastric emptying half time



The liquid-gel transition

Barbé *et al.*
Food Chem 2013

Effect on absorption



milk gelation:

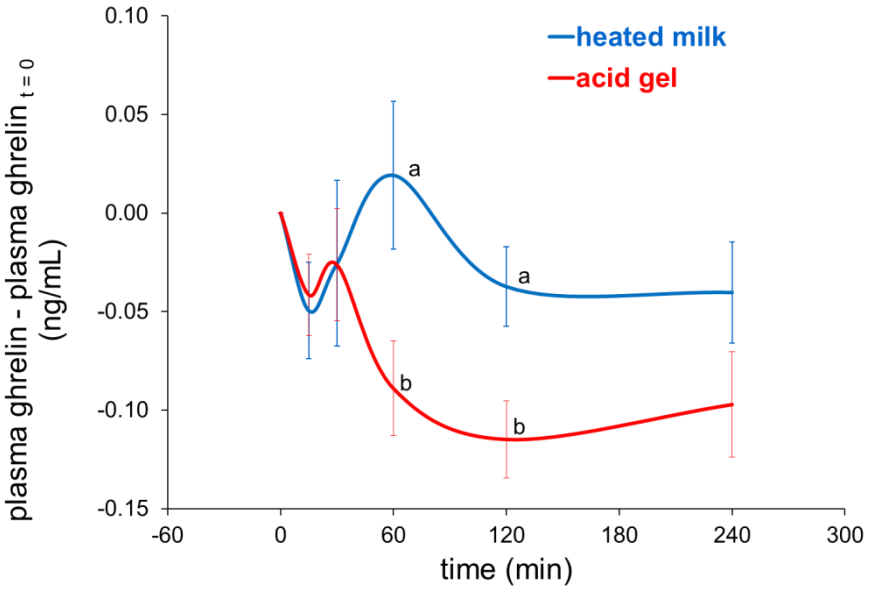
→ delayed proteins transit → delayed AA absorption

maximal AA concentration in the plasma

↘

Potential effect on satiety

ghrelin (gastrointestinal hormone → appetite stimulation)



milk gelation:

↘ **postprandial ghrelin concentration =**

↗ **satiety ?**

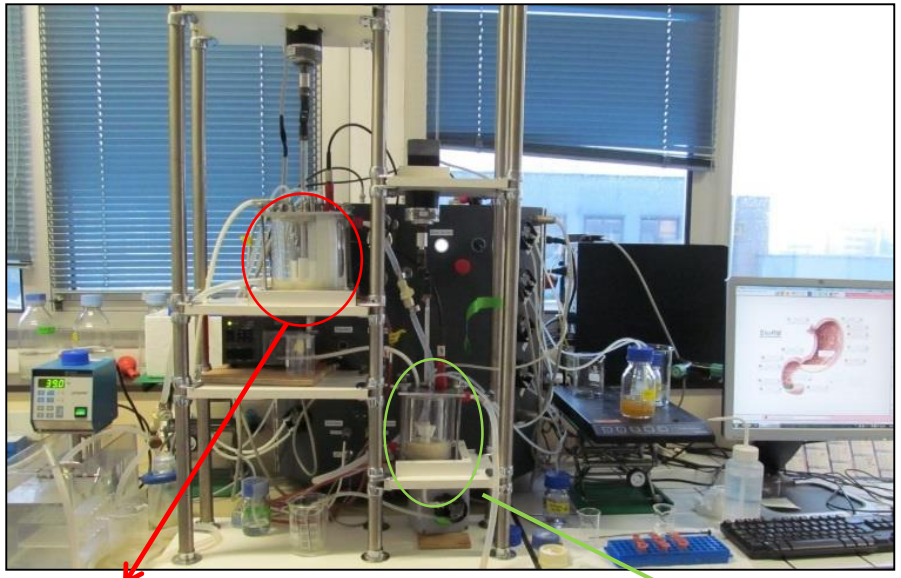
Differential behaviour of acid/rennet gels in gastric conditions

☞ 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

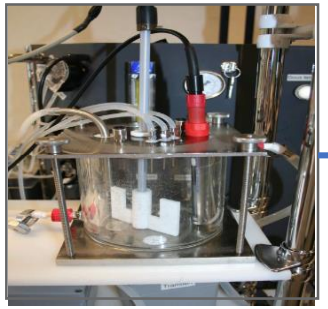
Ménard *et al.*
Food Chem 2014



DIDGI®

StoRM® software

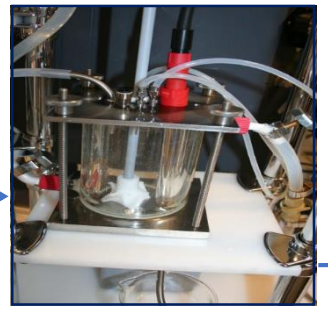
Stomach



- Pepsine
- Gastric lipase
- Simulated gastric fluid
- HCl

Emptying : Elashoff's model

Small intestine

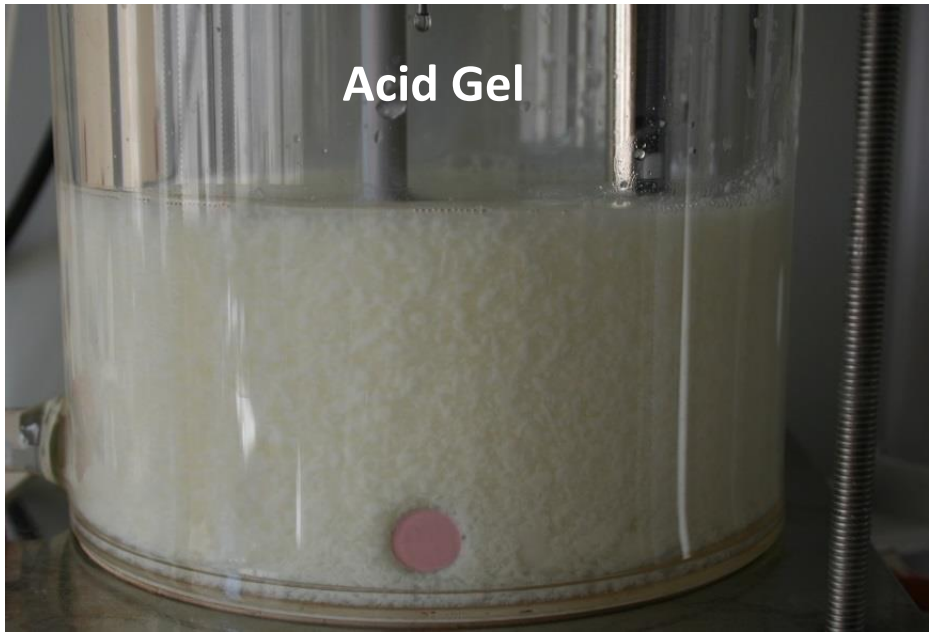


- Pancreatin
- Bile
- Simulated intestinal fluid
- $NaHCO_3$

Emptying : Elashoff's model

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

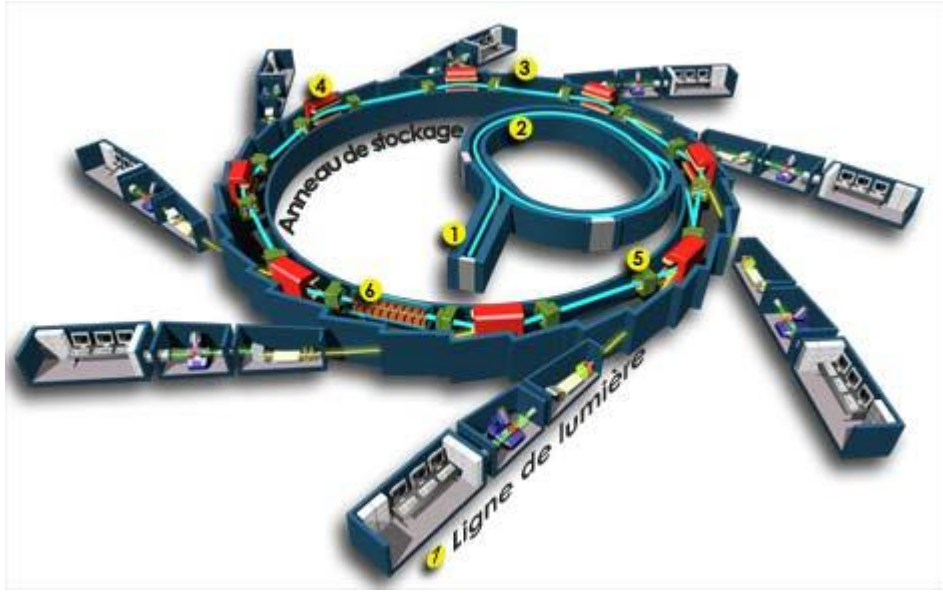
Barbé et al.
Food Chem. 2014



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

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

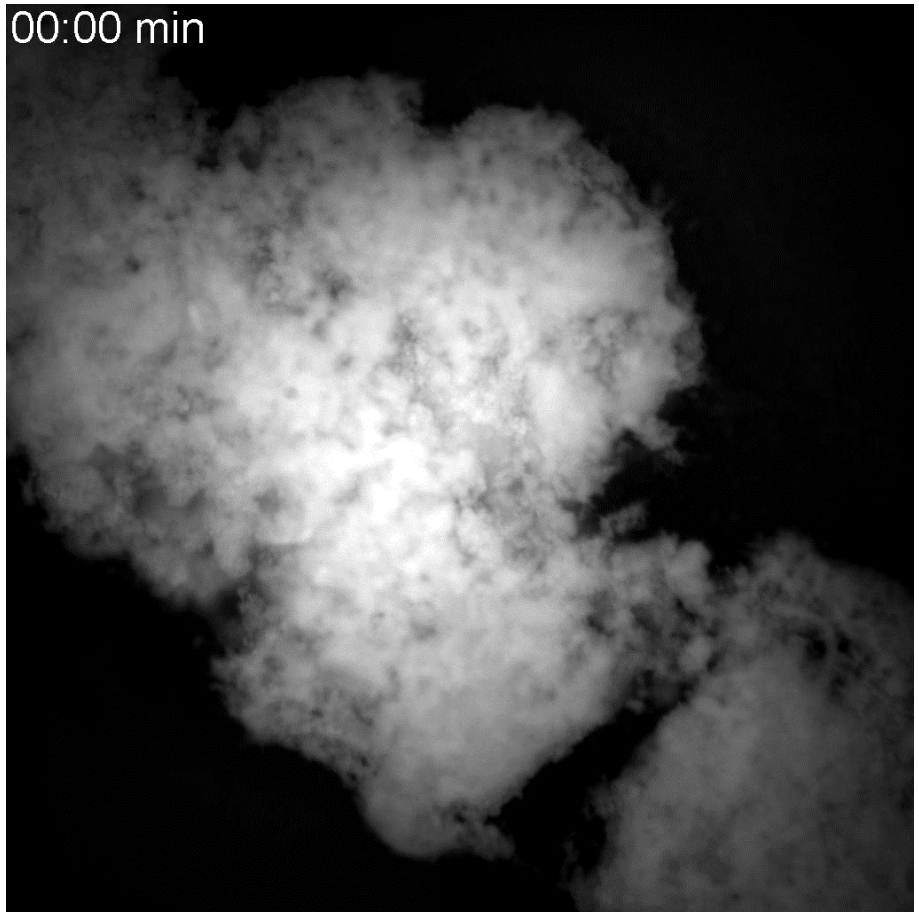


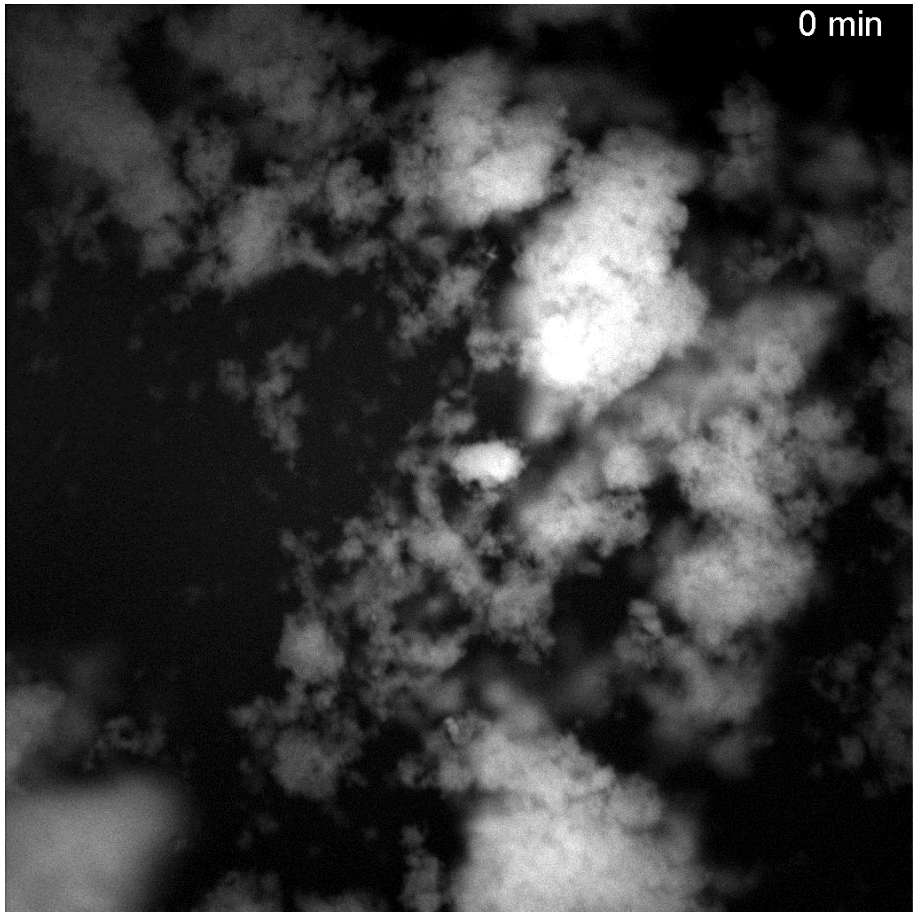
DISCO is a VUV to visible beamline dedicated to biochemistry, chemistry and cell biology. The spectral region is optimized between 60 and 700 nm with conservation of the natural polarization of the light

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

Kinetics of gel particles disintegration

Floury et al.
Food Chem. 2018





Rennet Gel

Acid Gel

Understanding human milk digestion to design new infant formulas that will have the same behaviour in the GI tract

Deglaire A., Menard O., De Oliveira S., Bourlieu C. & Dupont D.

INRAE, Rennes, France

Human milk / Infant Formula

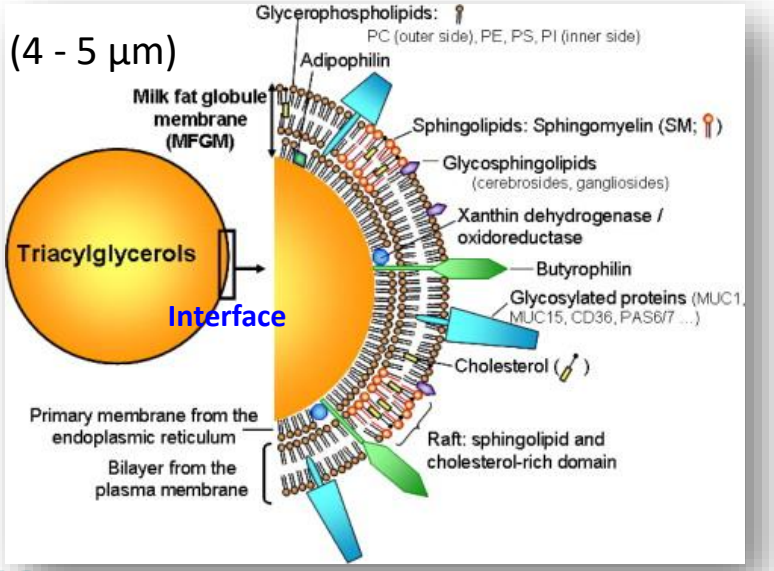
Lipid globule structure

Human milk

Bovine milk

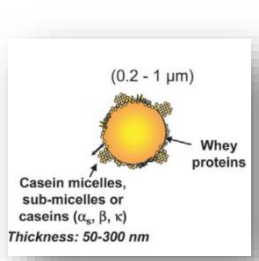
Infant Formula

Native milk fat globule



(Lopez, 2010)

Lipid droplets

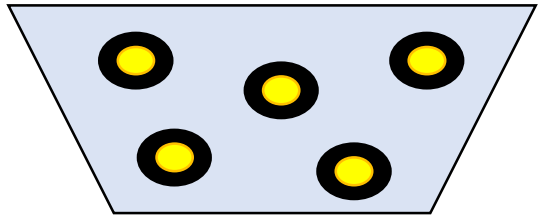


(0,2 - 1 µm)

(Lopez and Briard-Bion, 2007)

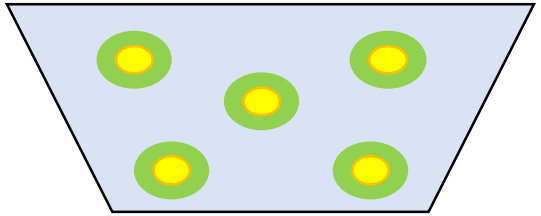
Infant formulas: can we create lipid structures biomimetic on the native fat globule?

Formula T1



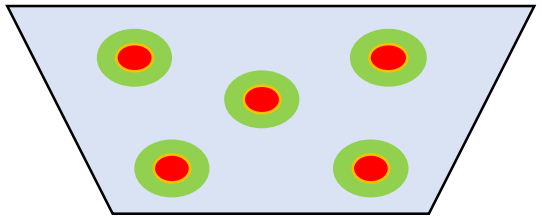
Interface 100 % Proteins
100% vegetable oil

Formula T2

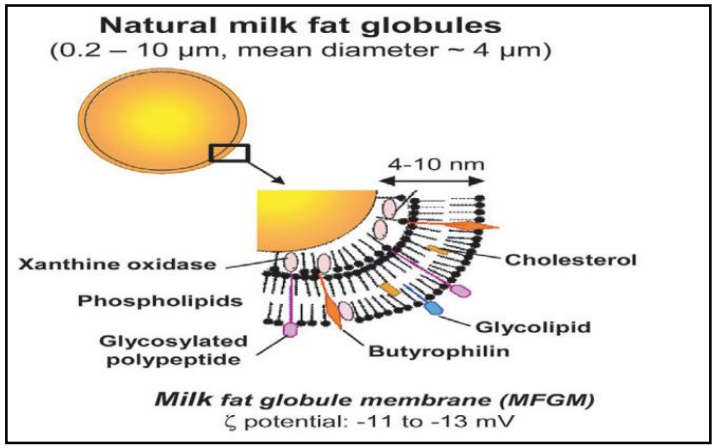


Interface 100 % phospholipids
100% vegetable oil

Formula T3

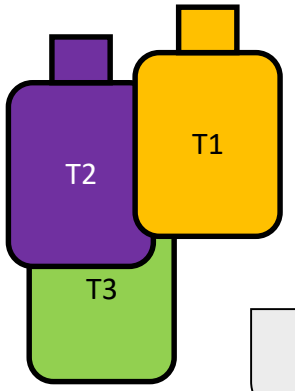


Interface 100 % phospholipides
40% vegetable oil + 60% milk fat



Lopez, (2007)

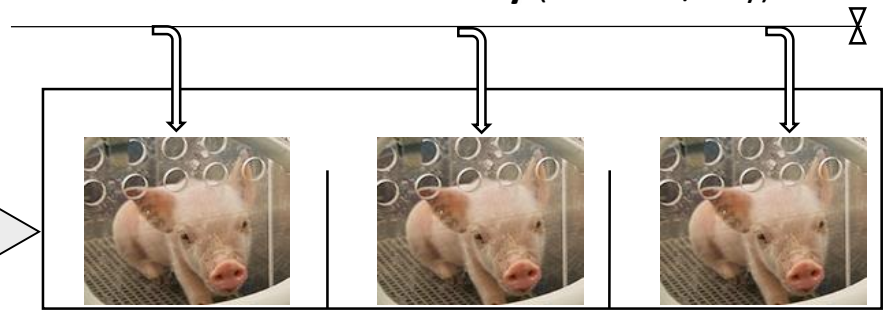
Can the composition of infant formula modulate the physiological response of the neonate?



Veg
Veg + PL
Dairy Fat + PL

Rehydration at 20%

Automatic meal delivery (10 meals/ day)



\+

Mother-fed piglets (MF = + control)

Slaughtering after

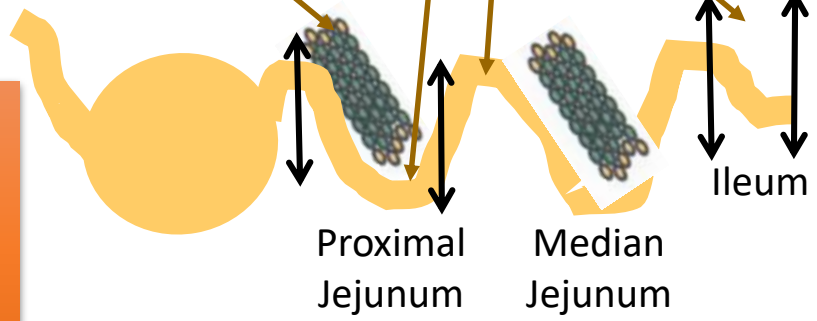
7 days

28 days

(90 min postprandial)

Mesenteric Lymph Nodes (MLN)

Collect of effluents and tissues

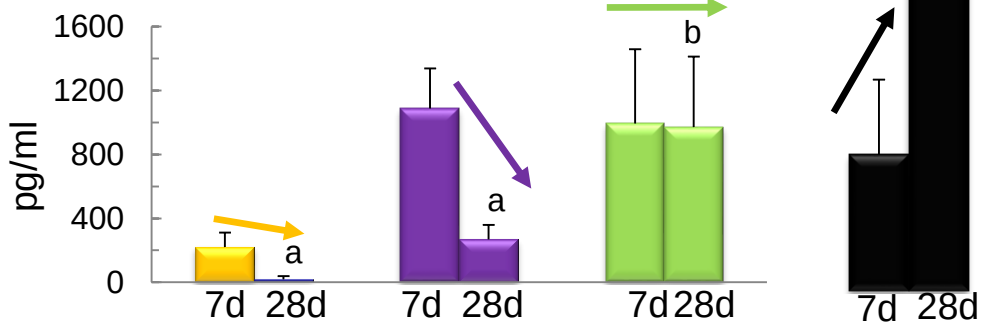


Effluents:
-SDS-PAGE
-Elisa

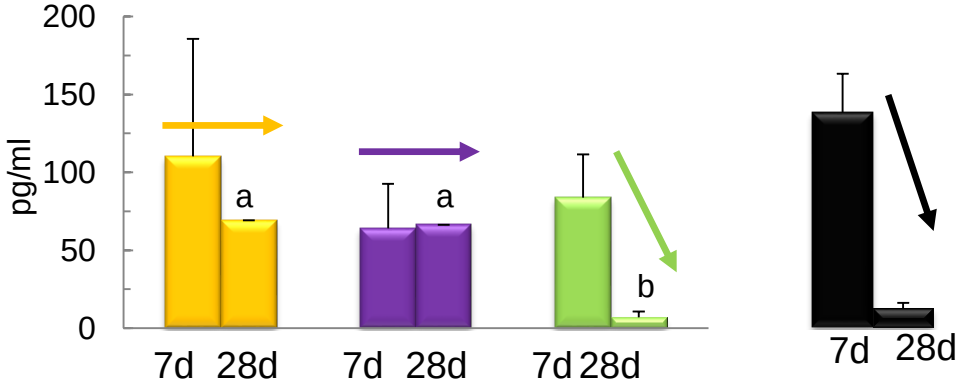
Tissues:
-Morphometry
-Enzyme Activities
-Intestinal Permeability
-Local immune response
-Microbiota

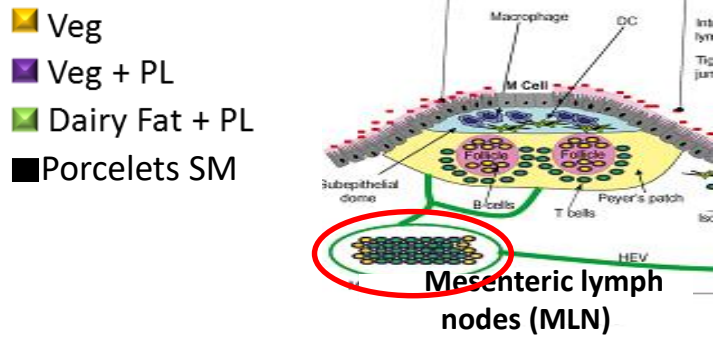
Secretory activity of MLN

Interferon-g (Th1 pro-inflammatory)



Interleukine-10 (Th2 anti-inflammatory)



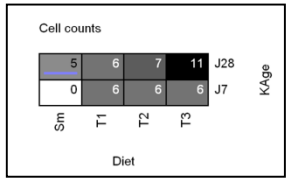


Mesenteric lymph nodes (MLN)

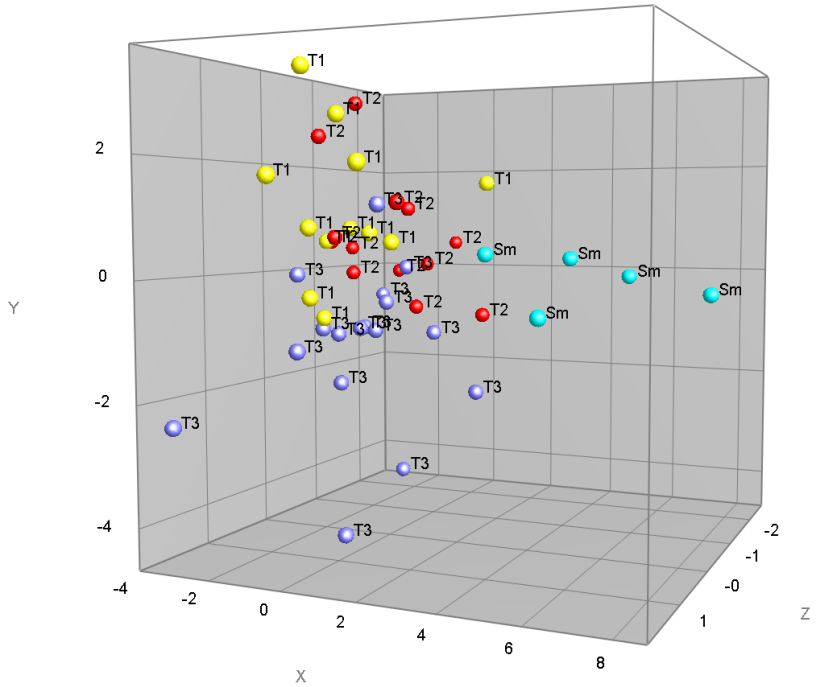
Milk lipids ➔ maturation of the piglet's immune system more similar than with sow's milk

Le Huerou et al. Eur J Nutr 2018

Microbiota by DHPLC



D7 & D28

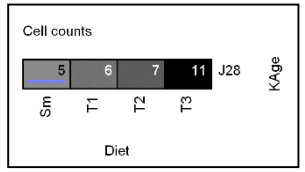


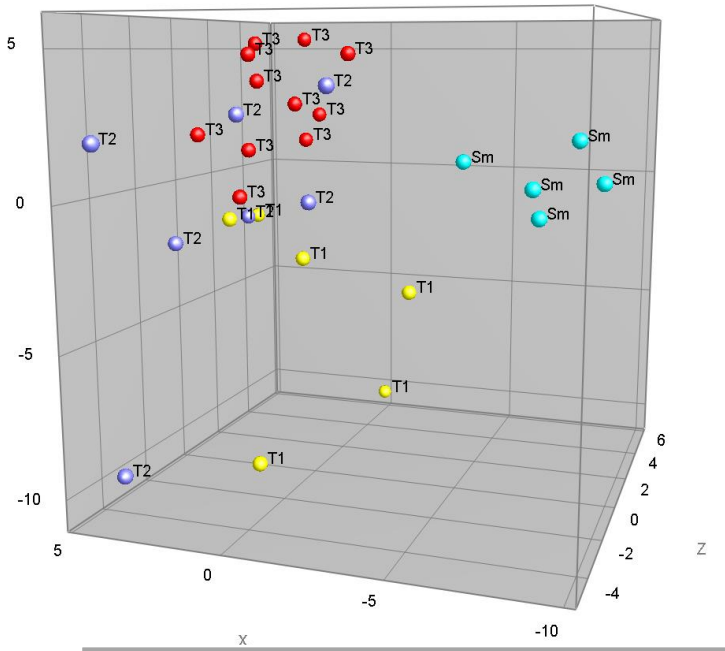
The composition/structure of the infant formula « orientates » the microbiota

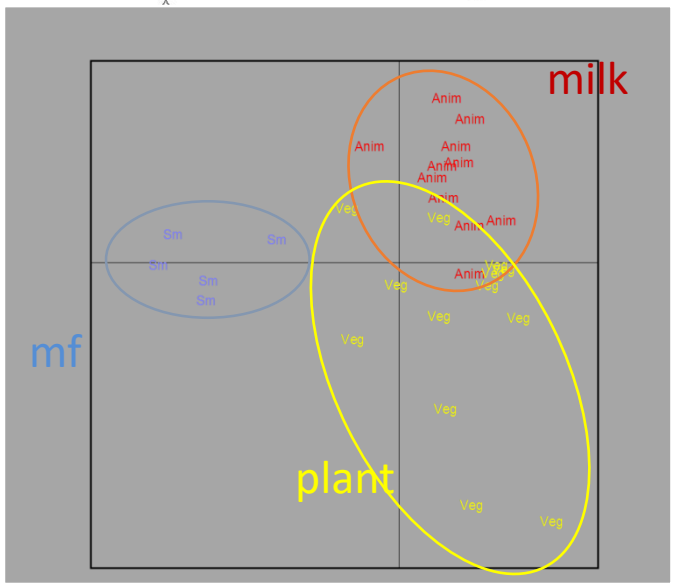
More Proteobacteria with milk fat /
More Firmicutes with plant oil

Bourlieu et al. Eur J Lipid Sci Technol 2015

D28

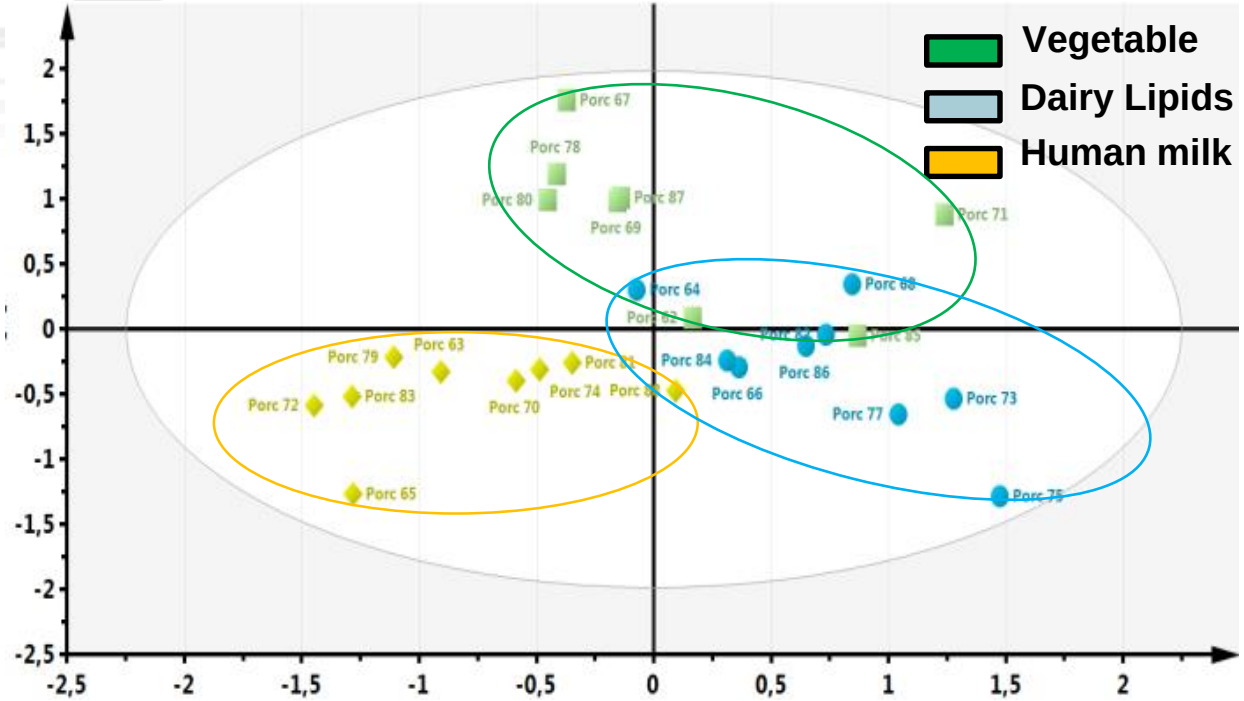






What happens when they become older (140 d)?

Lemaire *et al.*
Under publication



Some differences remain in:

* the microbiota composition
* the metabolome of the feces with 5 discriminating metabolites (including propionate)
* the immune system with a reduced susceptibility to inflammation with milk lipids (lower TNFα and IL8 with dairy lipids)

Conclusion

The structure/composition of dairy products regulate the kinetics of protein digestion and the release of amino acids 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 uderstand of foods are metabolized

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 at INRAE-STLO Rennes

Head
Didier DUPONT- Senior Scientist

Scientists
Amélie DEGLAIRE – *Lecturer*
Juliane FLOURY – *Lecturer*
Catherine GUERIN - *Lecturer*
Steven LE FEUNTEUN – *Senior Scientist*
Joëlle LEONIL – *Senior Scientist*
Martine MORZEL – *Senior Scientist*
Françoise NAU – *Professor*
Frédérique PEDRONO – *Lecturer*

Xiaoxi YU – *Post-doc*
Guilherme FURTADO – *Post-doc*

Technicians
Gwenaële HENRY
Yann LE GOUAR
Nathalie MONTHEAN

Engineers
Julien JARDIN
Olivia MENARD
Jordane OSSEMOND

PhD students
Yohan REYNAUD *(2016-2019)*
Amira HALABI *(2017-2020)*
Jun WANG *(2018-2021)*
Lea SALLELES *(2018-2021)*
Elise CHARTON *(2019-2022)*
Lucile CHAUVET *(2019-2022)*
Ousmane SUWAREH *(2019-2022)*

Masters students

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

International Research Network

Dr. Didier DUPONT, Senior Scientist, INRAE, France

INFOGEST

Scientific objectives

- Compare the existing digestion models, harmonize the methodologies and propose guidelines for performing experiments
- Validate *in vitro* models towards *in vivo* data (animal and/or human) and develop *in silico* approaches. Develop new models of digestion for specific populations (infant, elderly)
- Identify the beneficial/deleterious components that are released in the gut during food digestion
- Determine the effect of the matrix structure on the bioavailability of food nutrients and bioactive molecules

But these goals can only be reached by…

- Gathering scientists from different disciplines (food science, nutrition, gastroenterology, immunology…) to share and improve our knowledge on food digestion

INFOGEST
cost

Tech Univ Denmark
Univ Aarhus
Univ Copenhagen
MTT
Univ Oulu
Univ Eastern Finland
Norwegian Univ Life Sci
Chalmers Univ Tech
VTT
Nofima
Riga Stradin Univ
Univ Ljubljana
Univ Zagreb
NIZO
TNO
Lund Univ
Wageningen UR
Anabio
Iceland
Rothamsted Res
Teagasc
Univ Reading
James Hutton Inst
Univ Leeds
Univ College Cork
Univ Manchester
Univ Birmingham
Univ Glasgow
Cent Rech Lippmann
Univ Greenwich
Univ Nottingham
Univ Ghent
Agroscope Posieux
Inst Food Res
Agrocampus Ouest
Leatherhead Food Res
ACW
FiBL
Univ Sevilla
Univ Greifswald
Univ Valencia
IRD
Max Rubner-Institut
INRA
CNRS
Univ Basque Country
AgroParisTech
CTCPA
Univ Murcia
CSIC
Univ Granada
NIH Ricardo Jorge
Univ Alto Douro
ITQB
Milan State Univ
FEM
CNR
Univ Bologna
Univ Roma
Univ Milan
Univ Naples
Ege Univ
Agric Univ Tirana
Deakin Univ
Univ Queensland
Univ Medellin
Soochow Univ
Laval Univ
Univ Guelph
Czech Univ Prague
Inst Chem Technol
KTU Food Inst
Lithuanian Univ HS
Gdansk Univ Tech
Maize Res Inst
NGO
Univ Belgrade
Polish Academy of Sci
Univ Novi Sad
Aristote Univ Thessaloniki
Centr Food Res Inst
Ben Gurion Univ
Technion
Pom Med Univ
Univ California Davis
Riddett Inst
Plant Food Res
Nagoya Univ

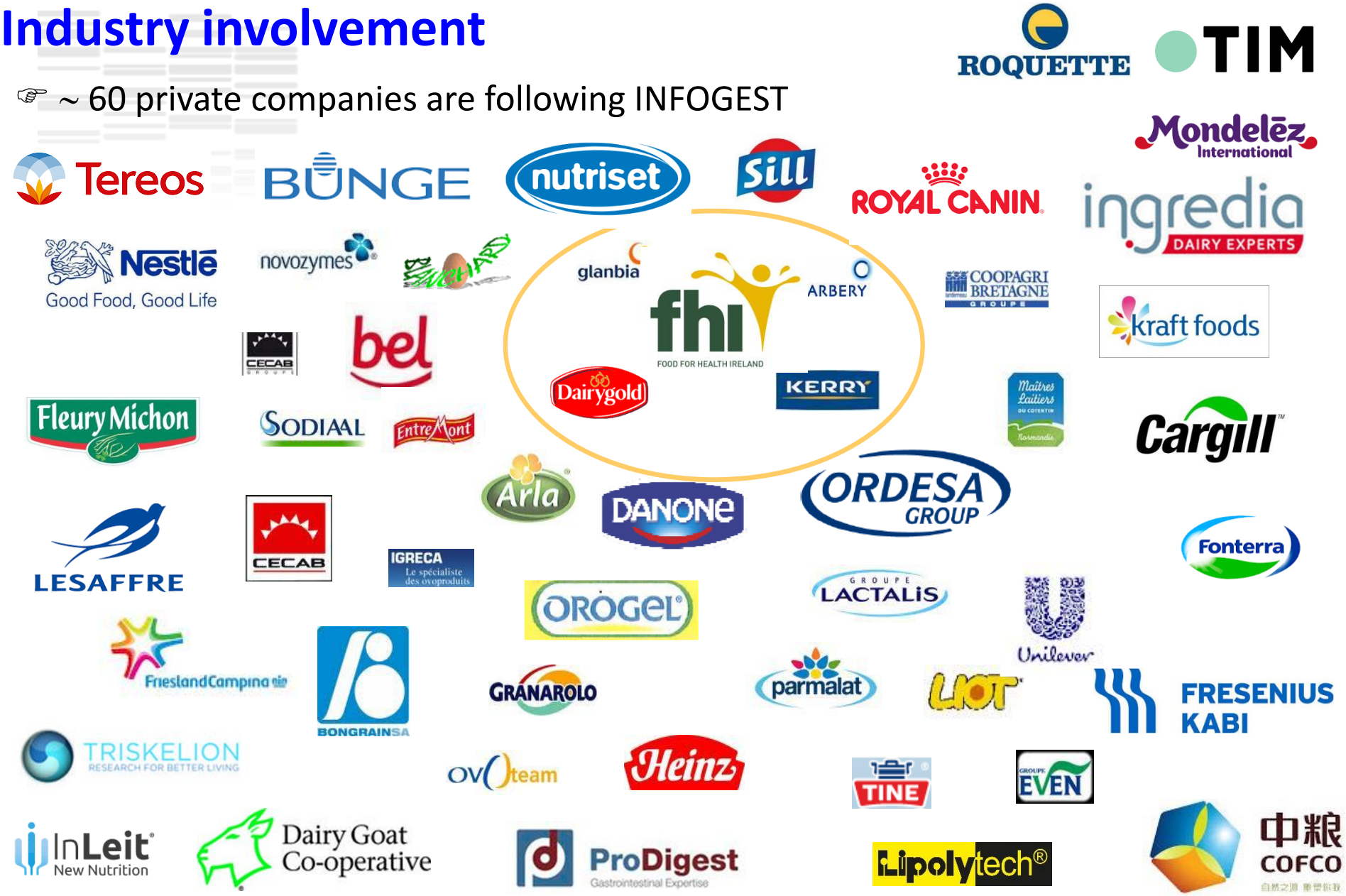
Sweden
Finland
Norway
Russia
Est.
Latvia
Belarus
Poland
Germany
Ukraine
France
Romania
Spain
Italy
Bulgaria
TURKEY
Greece

Canada
South Afrika
India
Kenya
Sri Lanka
Iran
New Zealand
Thailand
Peru
The Philippines
Mexico
Argentina
China
Australia
Albania
Montenegro
Chile
Tunisia
Colombia
Brazil
USA
Japan
Tanzania

715 scientists - 250 institutes – 56 countries

Industry involvement

☞ ~ 60 private companies are following INFOGEST



INFOGEST

Chair
Didier Dupont - France
didier.dupont@inrae.fr

Vice-chair
Alan Mackie - UK

www.cost-infogest.eu

In vitro models of digestion WG1

Isidra Recio

Food interaction – meal digestion WG2

Pasquale Ferranti

Absorption models WG3

Linda Giblin

Digestive lipases and lipid digestion WG4

Frederic Carriere

Digestive amylases and starch digestion WG5

Daniela Freitas

In silico models of digestion WG6

Steven Le Feunteun

Imaging Technologies applied to digestion WG7

Paul Smeets

Andre Brodkorb

Lotti Egger

Uri Lesmes

Brigitte Graf

Marion Letisse

Leslie Couedelo

Choi-Hong Lan

Luca Marciani

Some output – A consensus static in vitro digestion model

Minekus et al. 2014
Food & Function
~3000 citations
Highly Cited

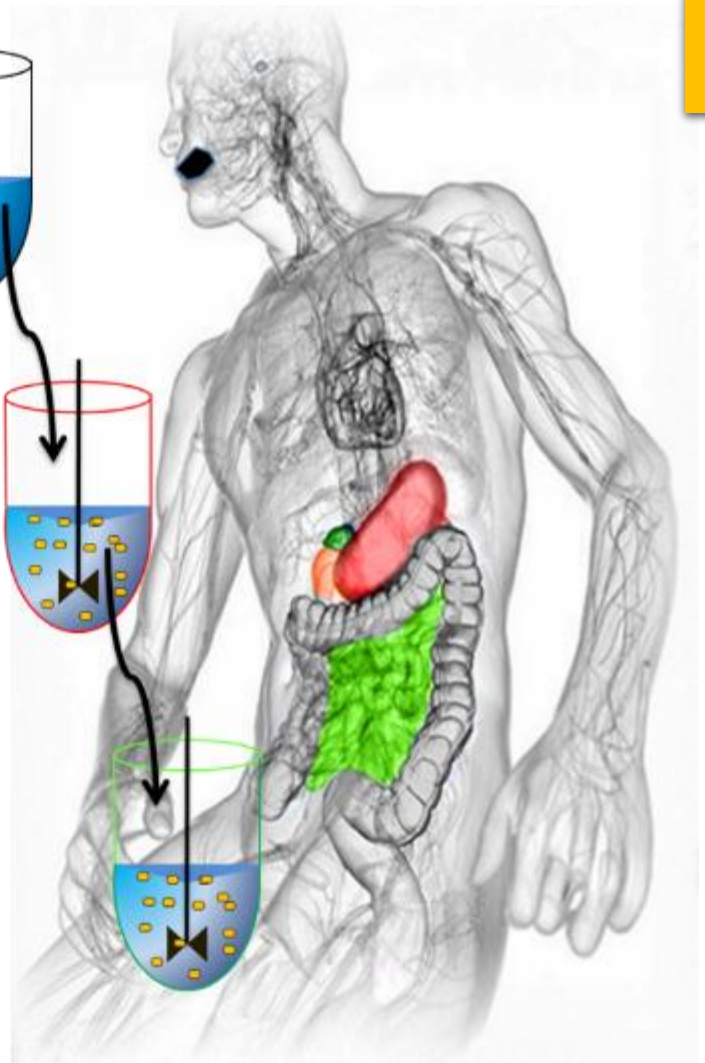
Brodkorb et al. 2019
Nature Protocols
~1150 citations
Highly Cited

Oral phase
Mix 1:1 with Simulated Salivary Fluid (SSF)
salivary amylase (75 U/mL)
2 min, pH 7

Gastric Phase
Mix 1:1 with Simulated Gastric Fluid (SGF)
Pepsin (2000 U/mL)
2h, pH 3

Intestinal Phase
Mix 1:1 with Simulated Intestinal Fluid (SIF)
Enzymes
- Pancreatin (based on trypsin 100 U/mL) or
- Pure enzymes

Bile (10mM)
2h, pH 7



YouTube

Training schools in Oslo, Granada, Madrid (2) and Santiago

INFOGEST
International Conference
Porto, Portugal
2024

We are pleased to announce the next

8th International Conference on Food Digestion

in Porto, Portugal, 9-11 April 2024