



Dairy food structures influence the rates of nutrient digestion

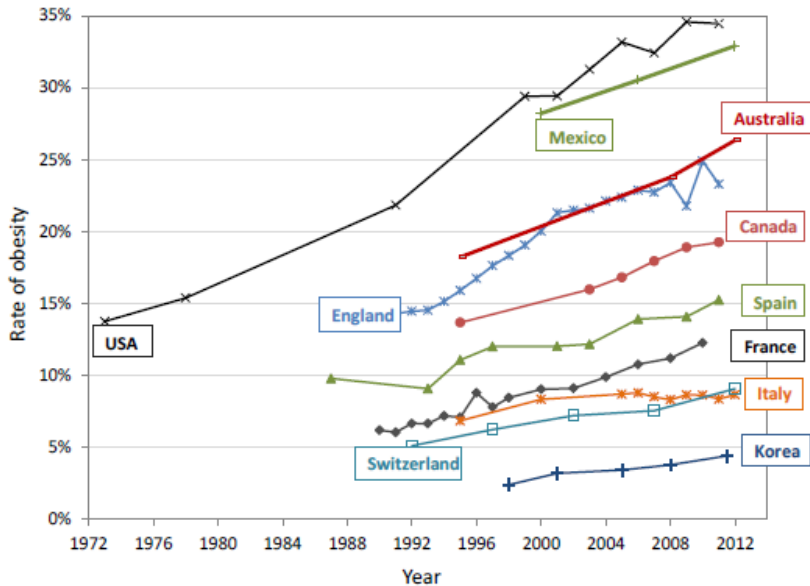


Dr Didier DUPONT

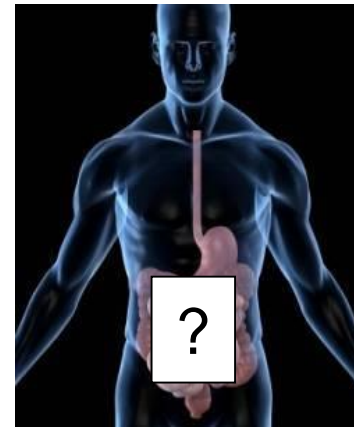
INRA, Rennes, France



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

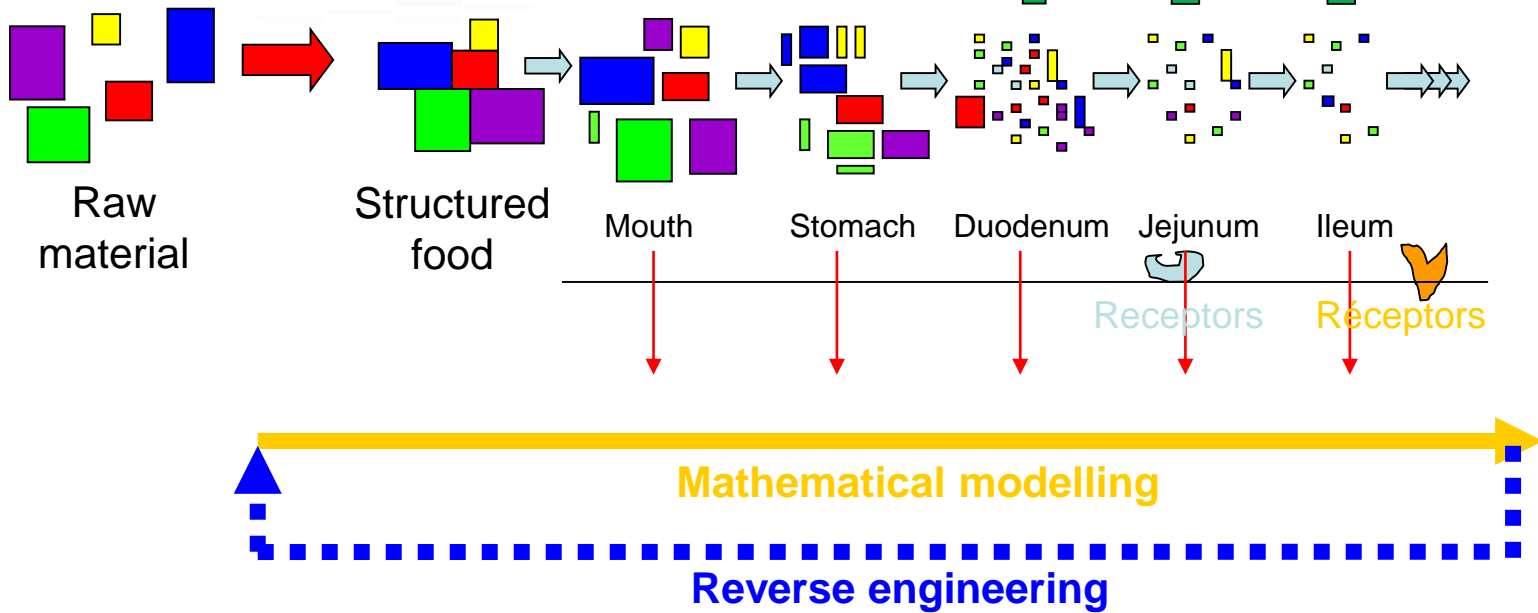
Digestion releases food components that can have a beneficial or a deleterious effect on human health

... 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

Processing

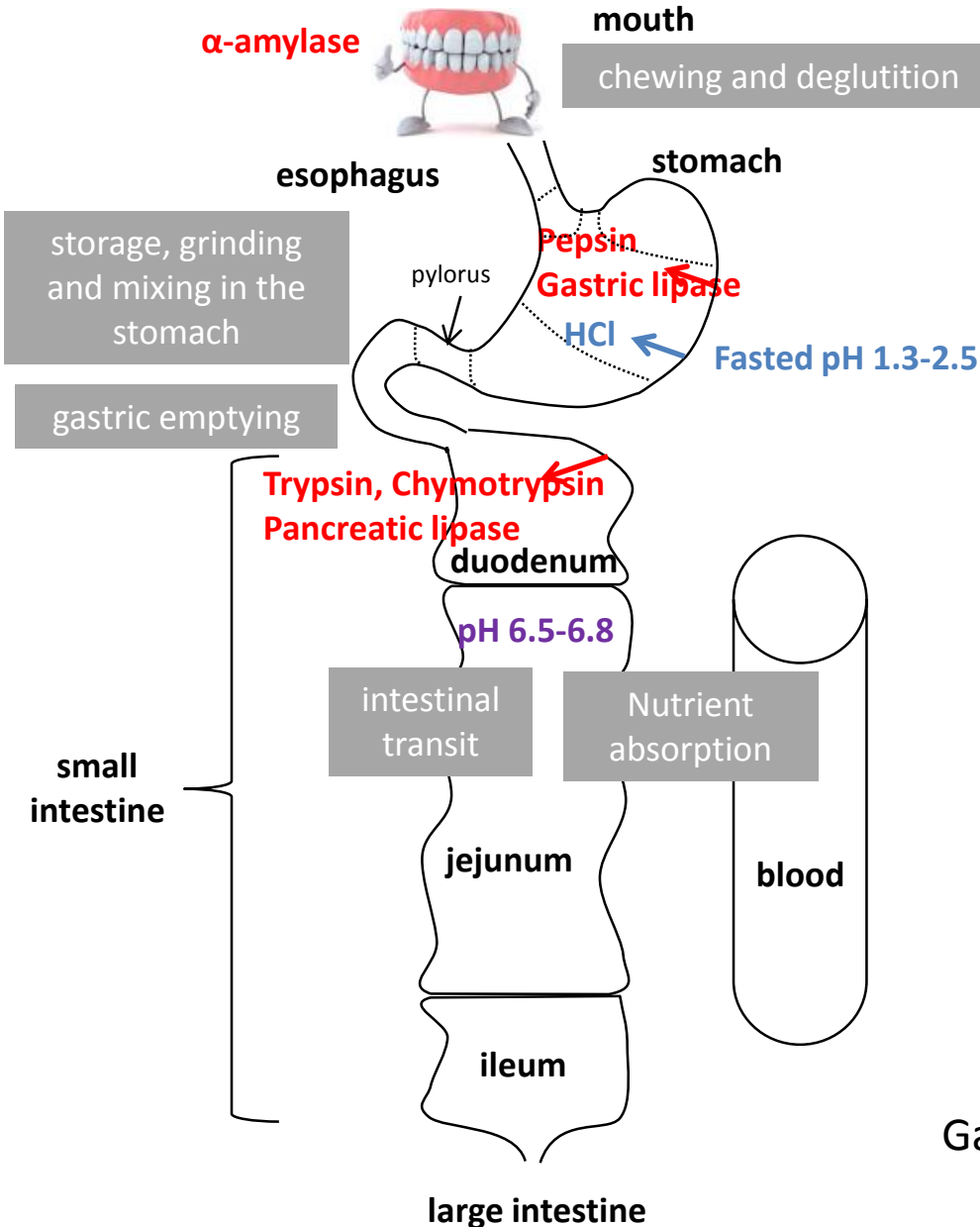


- Bioactivities**
- Bioactive peptides
 - Amino acids
 - Fatty acids
 - Minerals
 - Vitamins...

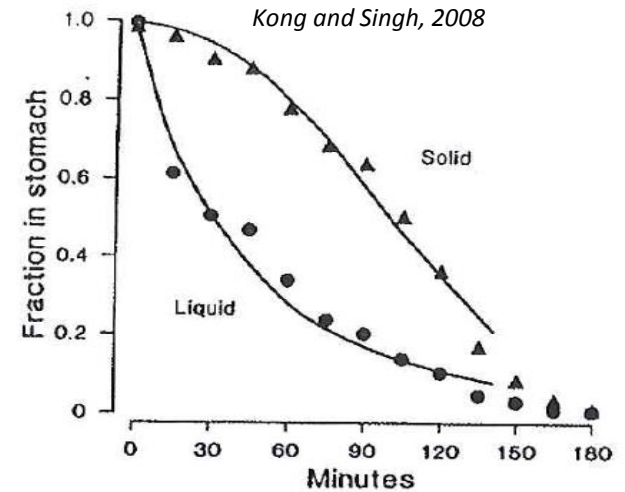
- Gut**
- Immune System
 - Intestinal microbiota

- ☞ 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 nutrient bioavailability
- ☞ To model these phenomena in order to develop a reverse engineering approach

The digestive process

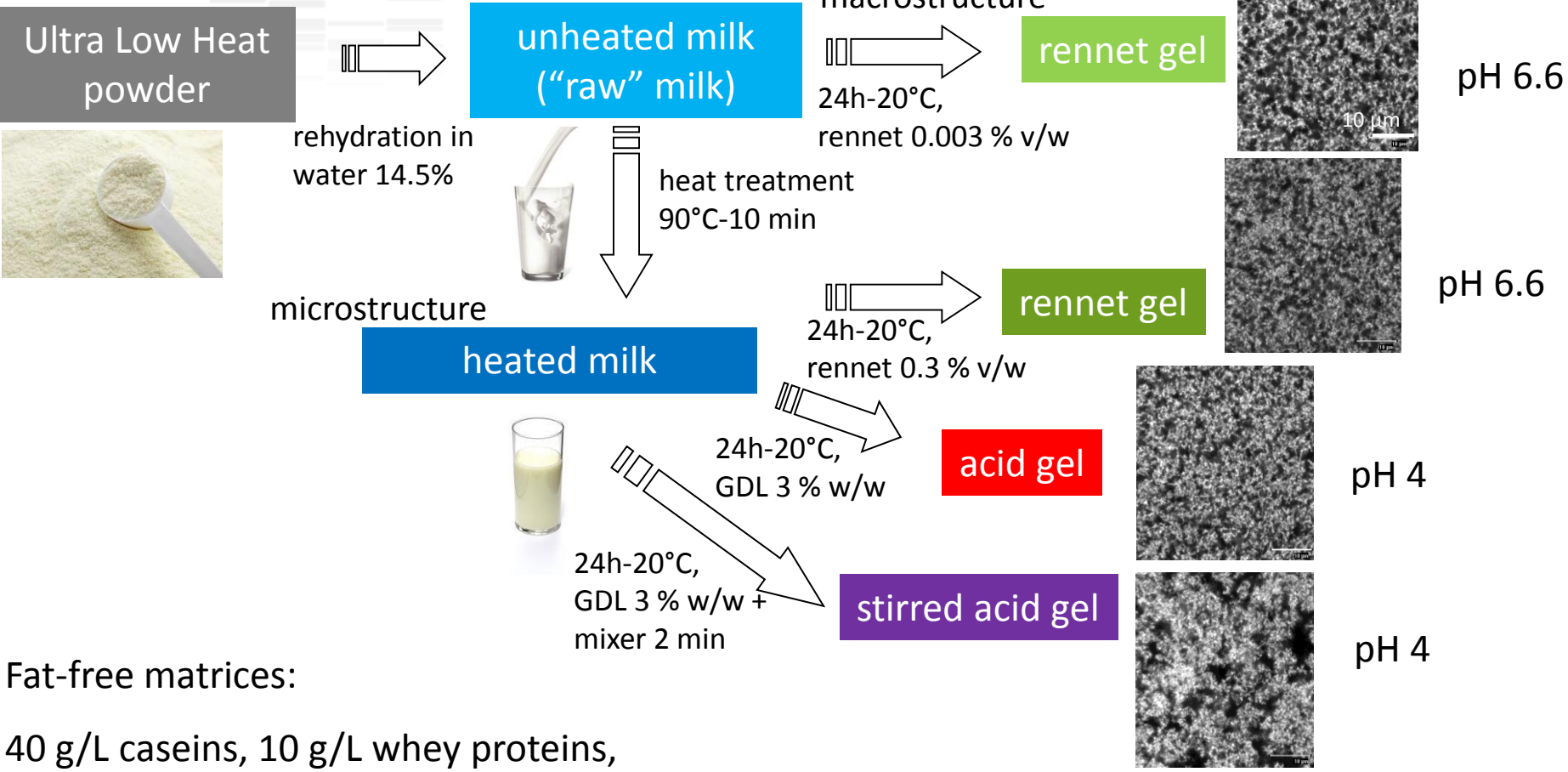


From Roger Lentle, Massey Univ. NZ



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

Do dairy products of identical composition but different structure exhibit similar kinetics of digestion?



Fat-free matrices:

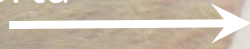
40 g/L caseins, 10 g/L whey proteins,
95 g/L lactose and minerals

+ marker of the meal transit (Cr^{2+} -EDTA) → Mean Retention Time in the stomach

The multi-cannulated mini-pigs

6 minipigs (20 ± 1kg)

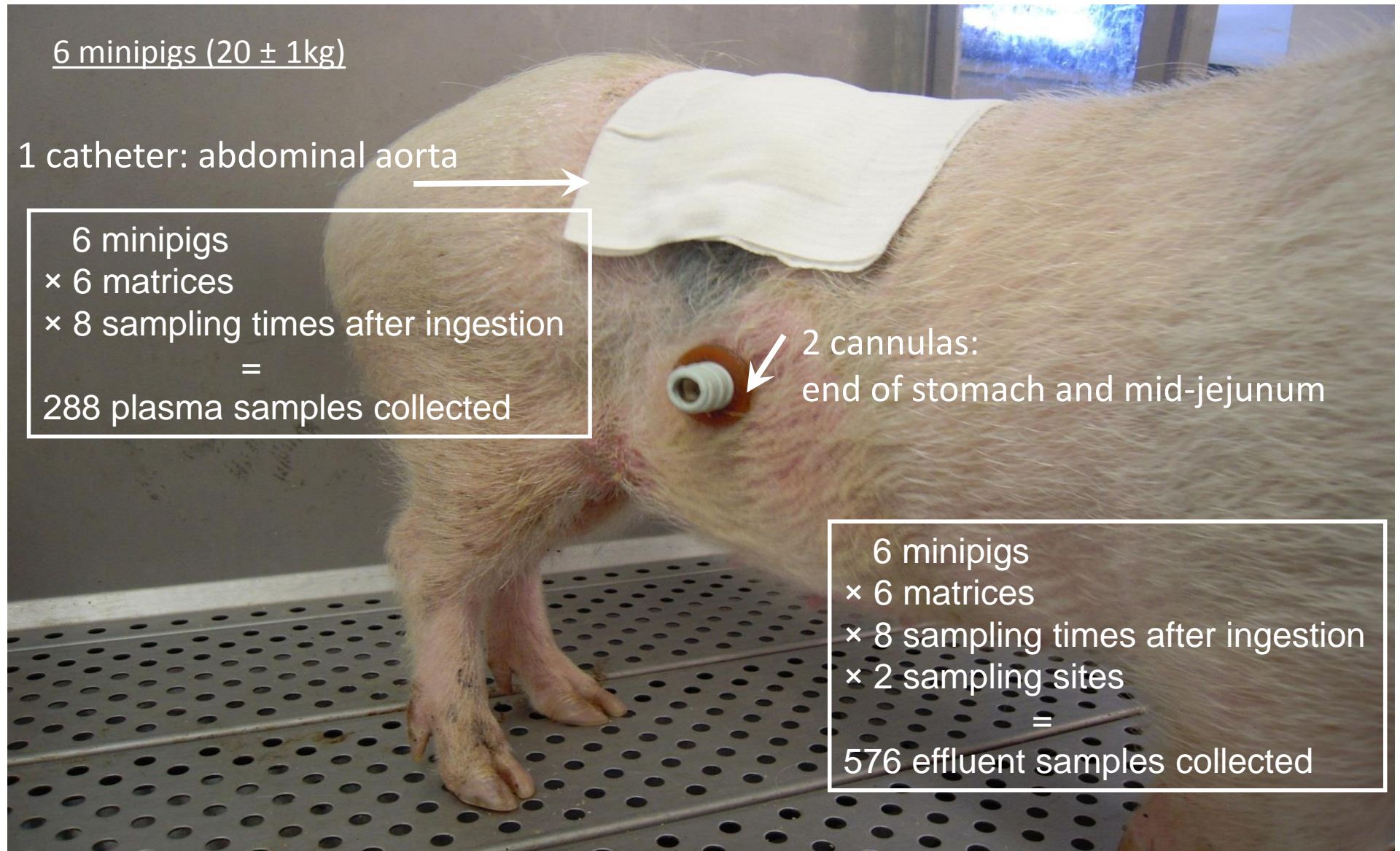
1 catheter: abdominal aorta



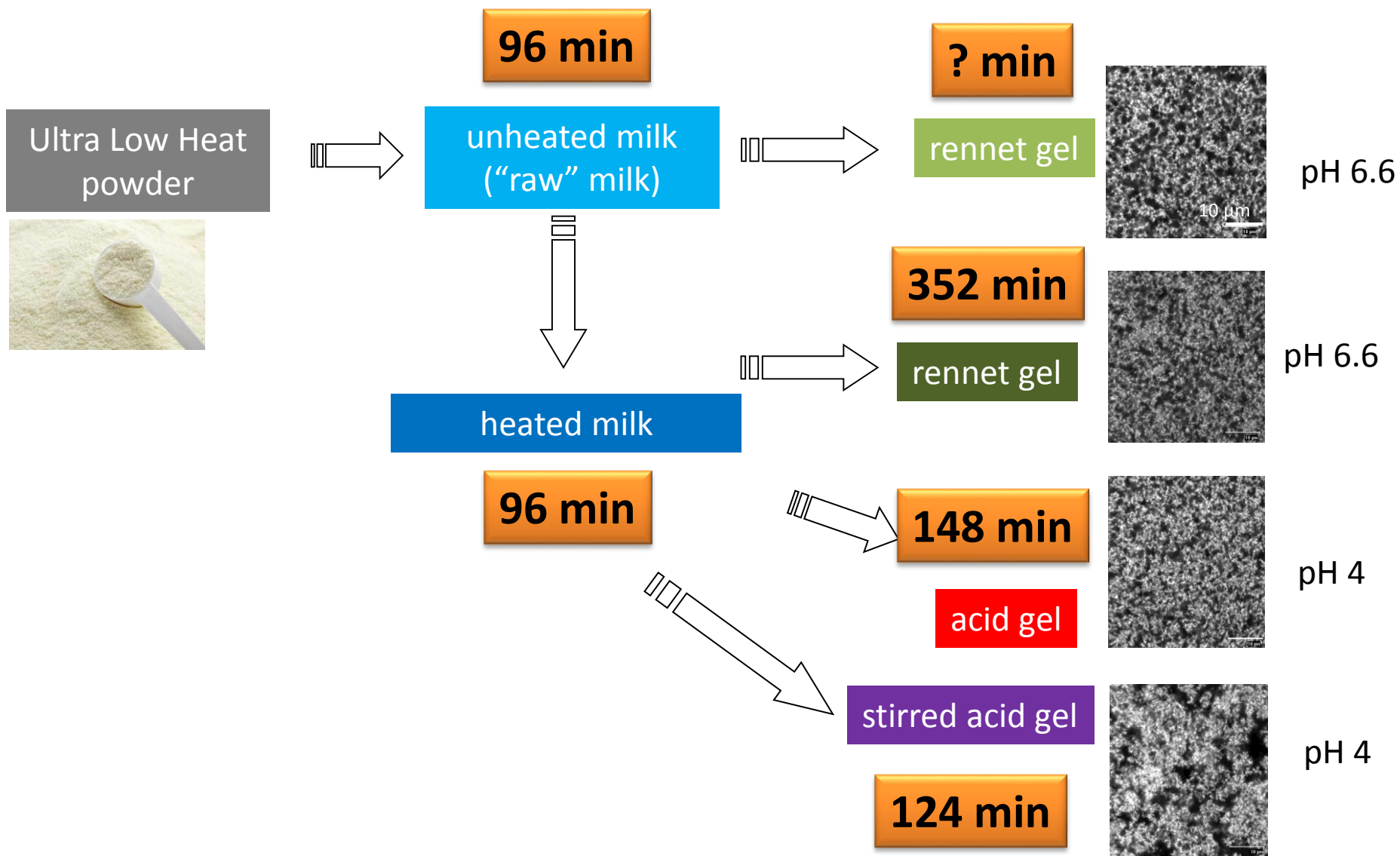
6 minipigs
× 6 matrices
× 8 sampling times after ingestion
=
288 plasma samples collected

2 cannulas:
end of stomach and mid-jejunum

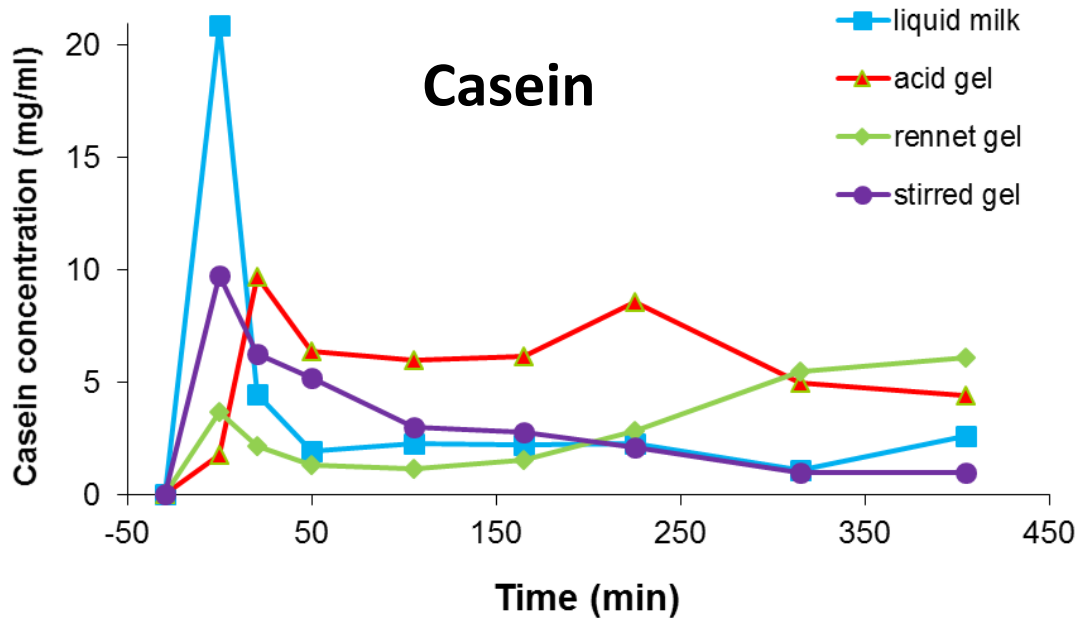
6 minipigs
× 6 matrices
× 8 sampling times after ingestion
× 2 sampling sites
=
576 effluent samples collected



Time of residence in the stomach

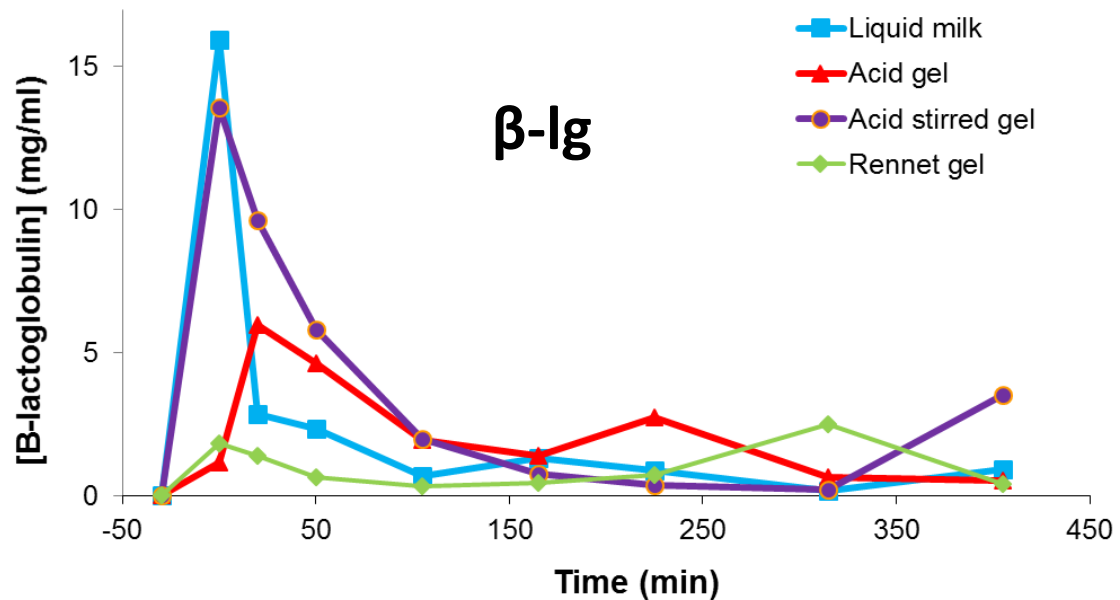


Milk proteins in the duodenum (ELISA)



- 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 16000 peptides were unambiguously identified!

Protein	Sequence	Activity	Reference	4	20	50	105	165	225	315
α s1	1-23	EMUL	Shimizu et al. (1984)	█						
α s1	23-34	HYP	Maruyama & Suzuki (1982)	█	█					
α s1	30-45	MB	Meisel et al. (1991)		█					
α s1	40-52	MB	Adamson & Reynolds (1996)				█	█	█	█
α s1	43-58	MB	Meisel et al. (1991)	█	█					
α s1	91-100	STRE	Miclo et al. (2001)							
α s1	99-109	MIC	McCann et al. (2006)	█	█					
α s1	167-180	MIC	Hayes et al. (2006)				█	█	█	█
α s1	180-193	MIC	Hayes et al. (2006)				█	█	█	█
α s2	1-24	MB	Miquel et al. (2005)	█	█					
α s2	124-146	MB	Miquel et al. (2005)							
α s2	183-206	TRAN	Kizawa et al. (1996)				█	█	█	█
α s2	183-207	MIC	Recio & Visser (1999)				█	█	█	█
α s2	189-197	HYP	Maeno et al. (1996)				█	█	█	█
α s2	190-197	HYP	Maeno et al. (1996)				█	█	█	█
β	1-24	MB	Bouhallab et al. (1999)	█	█					
β	33-52	MB	Miquel et al. (2005)	█	█					
β	60-80	OPI	Jinsmaa & Yoshikawa (1999)				█	█	█	█
β	98-105	OXI	Rival et al. (2001)				█	█	█	█
β	114-119	OPI	Jinsmaa & Yoshikawa (1999)				█	█	█	█
β	132-140	HYP	Robert et al. (2004)				█	█	█	█
β	192-209	IMM	Coste et al. (1992)				█	█	█	█
β	193-202	IMM	Kayser & Meisel (1996)				█	█	█	█
β	193-209	IMM	Coste et al. (1992)				█	█	█	█
κ	18-24	HYP	Lopez-Exposito et al. (2007)	█	█					
κ	106-116	THR	Jolles et al. (1986)	█	█					
β -lg	32-40	HYP	Pihlanto-Leppala et al. (2000)				█	█	█	█
β -lg	92-100	MIC	Pellegrini et al. (2001)				█	█	█	█
β -lg	142-148	HYP	Mullally et al. (1997)				█	█	█	█

Acid Gel

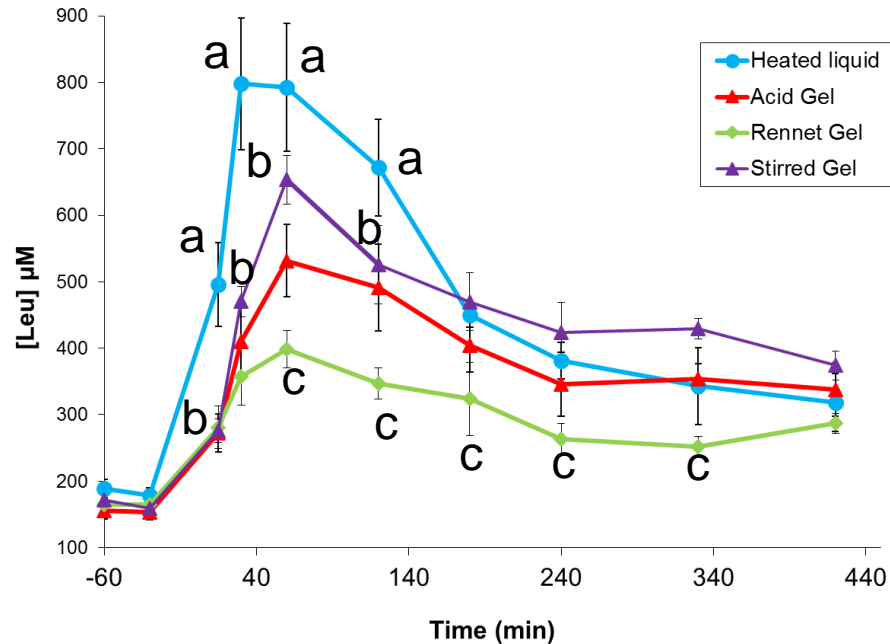
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α s1	99-109	MIC	McCann et al. (2006)				█	█	█	█
α s1	167-180	MIC	Hayes et al. (2006)				█	█	█	█
α s1	180-193	MIC	Hayes et al. (2006)				█	█	█	█
α s2	1-24	MB	Miquel et al. (2005)	█	█					
α s2	189-197	HYP	Maeno et al. (1996)				█	█	█	█
β	33-52	MB	Miquel et al. (2005)	█	█					
β	166-175	HYP	Hayes et al. (2007)				█	█	█	█
β	193-202	IMM	Kayser & Meisel (1996)				█	█	█	█
β -lg	92-100	MIC	(8)				█	█	█	█
β -lg	142-148	HYP	(9)				█	█	█	█

Rennet Gel

- 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

Barbé et al. 2014
Food Res Int

2) effect on absorption



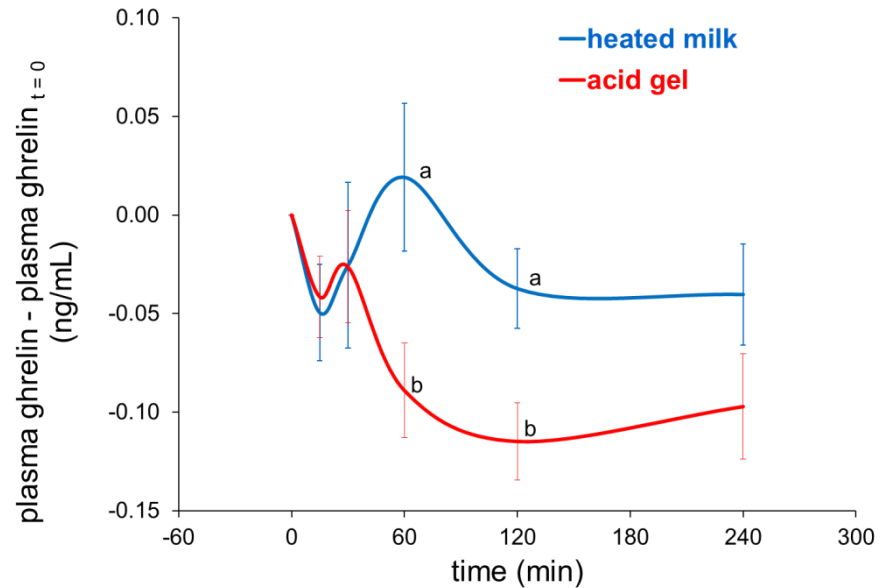
milk gelation:

→ delayed proteins transit → delayed AA absorption

↘ maximal AA concentration in the plasma

3) potential effect on satiety

ghrelin (gastrointestinal hormone → appetite stimulation)



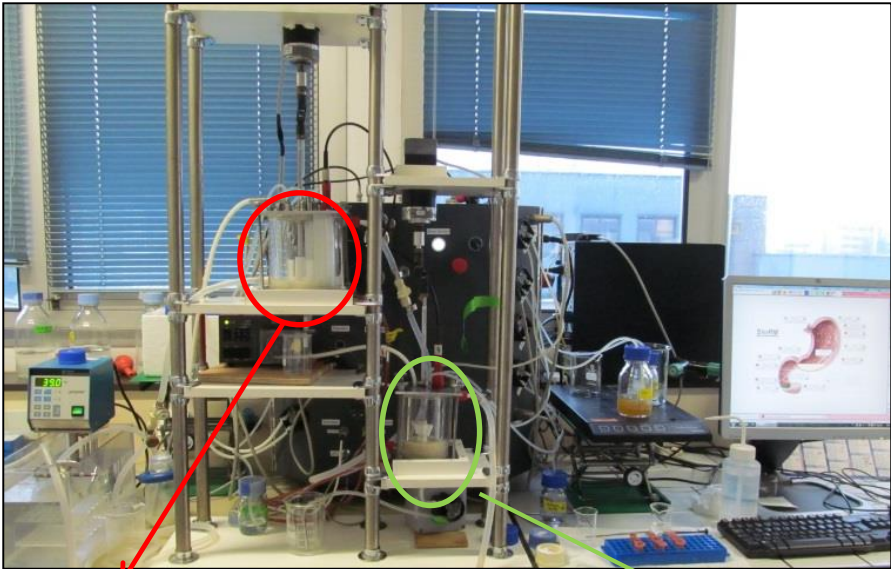
milk gelation:

↘ postprandial ghrelin concentration =
↑ satiety ?

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**



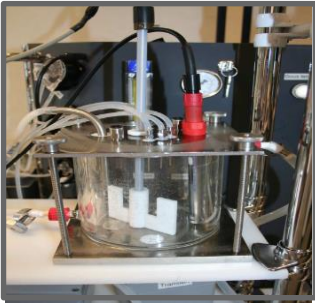
DIDGI®

StoRM® software

Stomach

Small intestine

- Pepsine
- Gastric lipase
- Simulated gastric fluid
- HCl



**Emptying :
Elashoff's model**



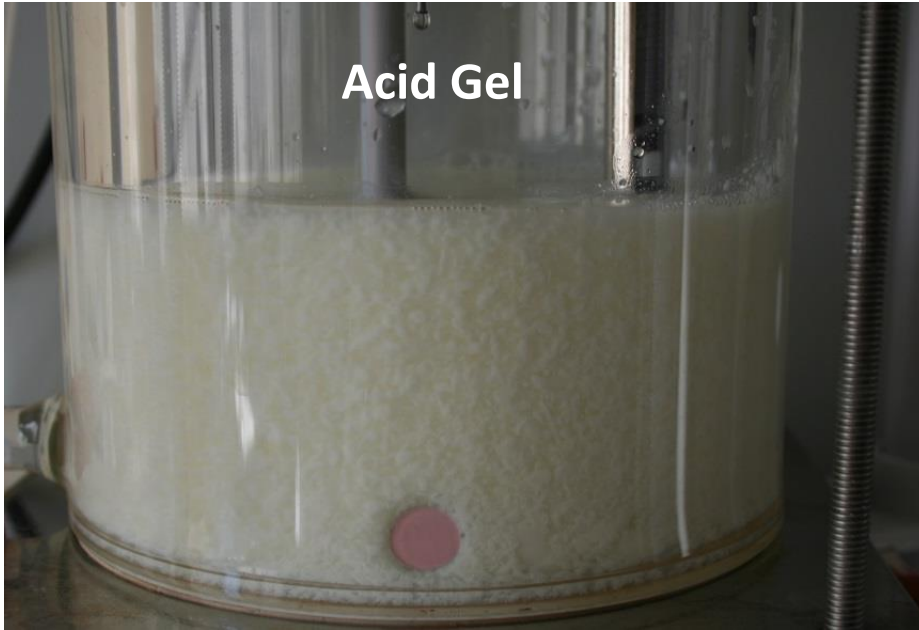
- Pancreatin
- Bile
- Simulated intestinal fluid
- NaHCO₃

**Emptying :
Elashoff's model**

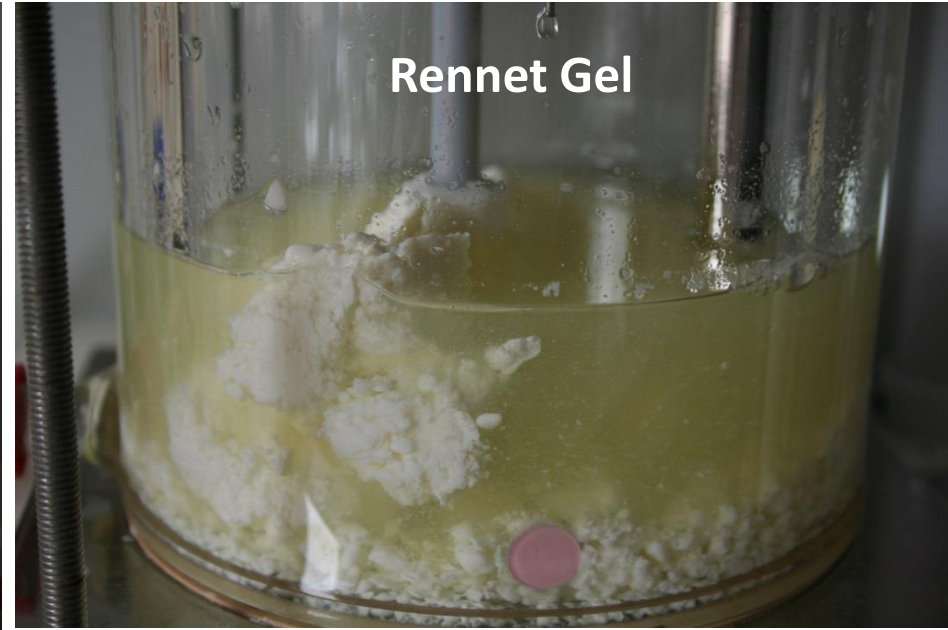
Behaviour of acid and rennet gels in the stomach during *in vitro* dynamic digestion

Barbé et al.
Food Chem. 2014

Acid Gel



Rennet Gel



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



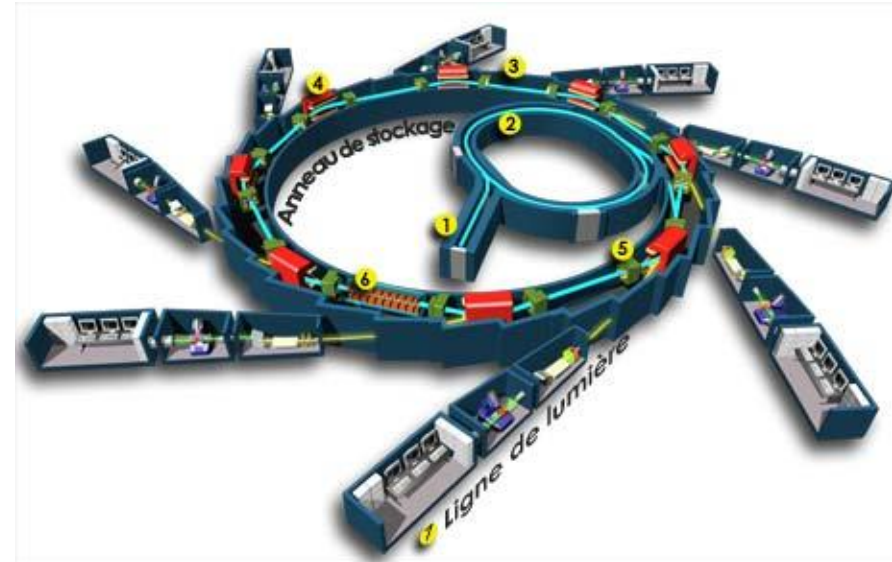
Understanding the mechanisms of dairy gel particles degradation in the stomach

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



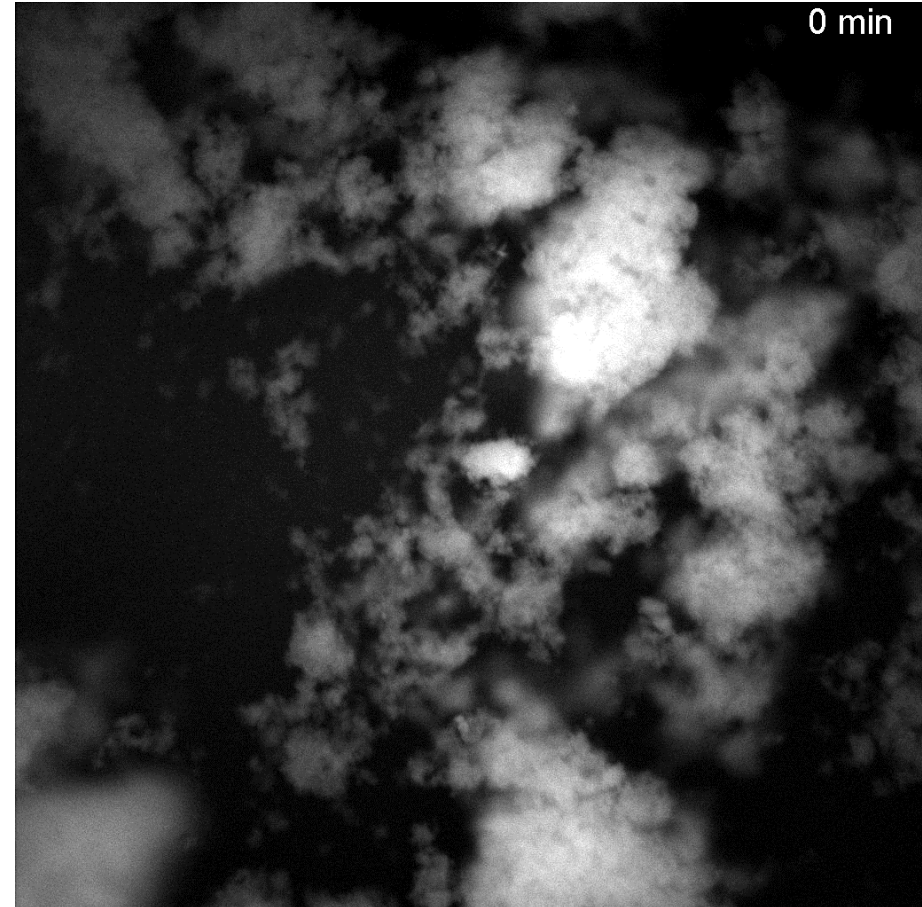
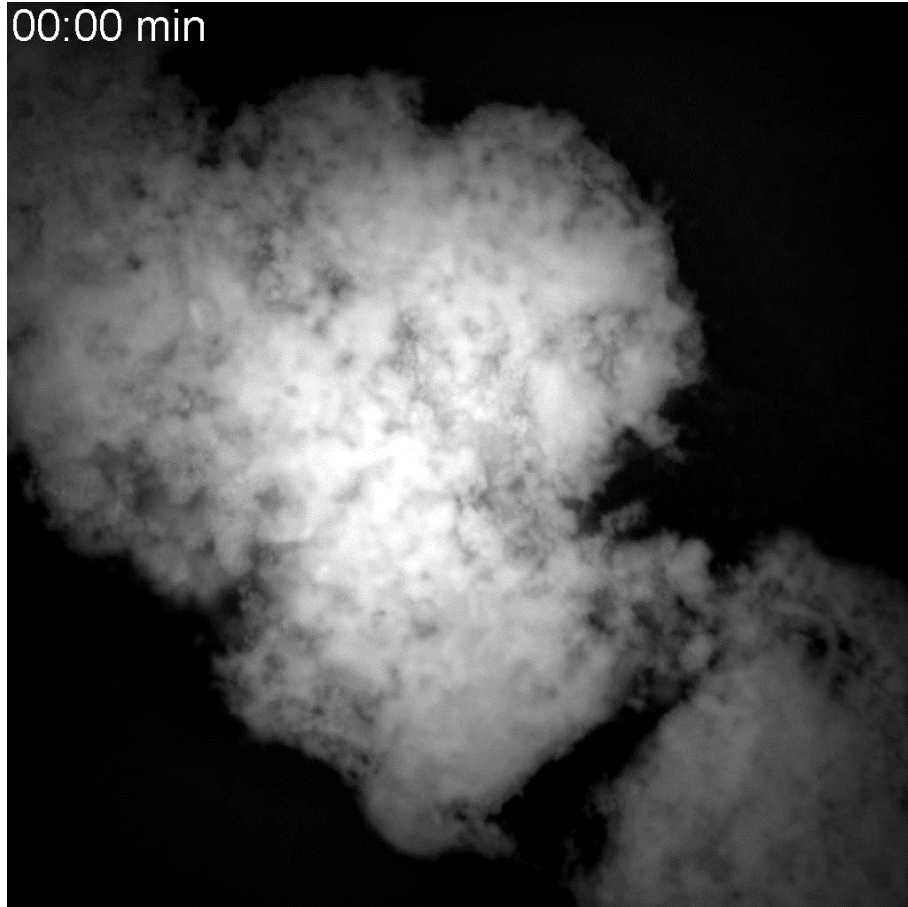
DISCO is a VUV to visible beamline dedicated to biochemistry, chemistry and cell biology. The spectral region is optimized between 60 and 700 nm with conservation of the natural polarization of the light

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



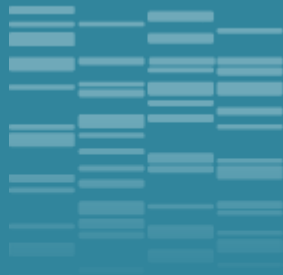
Kinetics of gel particles disintegration

Floury et al.
Food Chem. 2017



Rennet Gel

Acid Gel



Understanding how structures of human milk are disintegrated during digestion to create new biomimetic infant formula



Preterm hospitalized infants
Feeding nasogastric tube
Fed every 3 hours

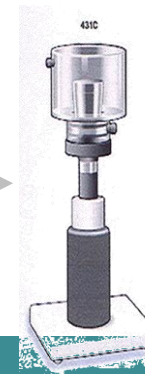
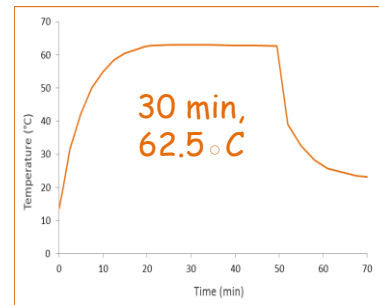
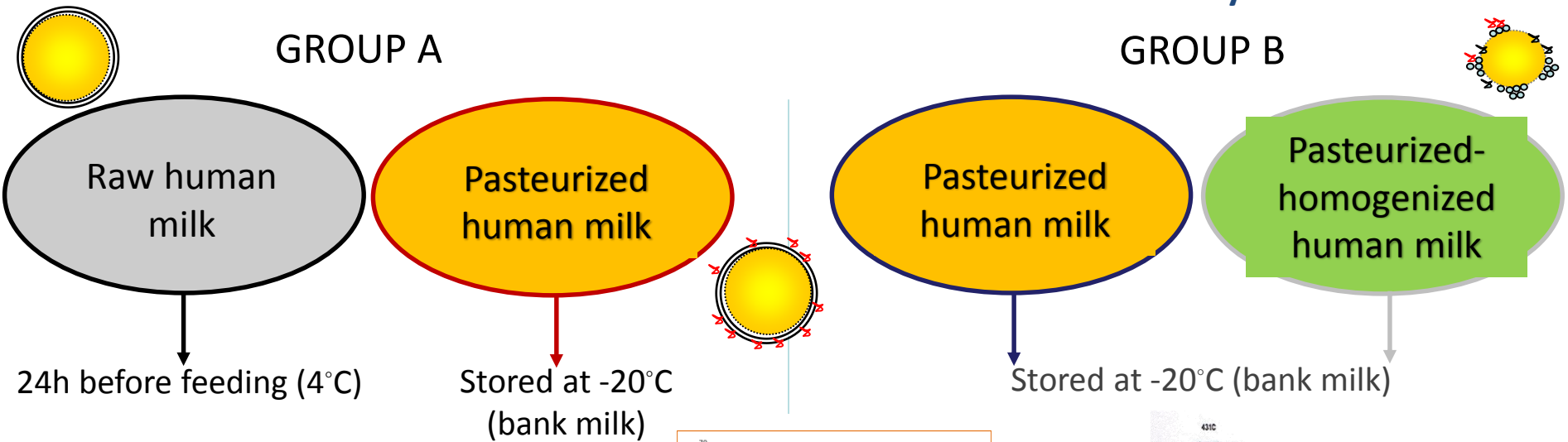
Aim: to compare meals with similar composition but different structure

Human milk from their **own mother**

Human milk from **anonymous donor**

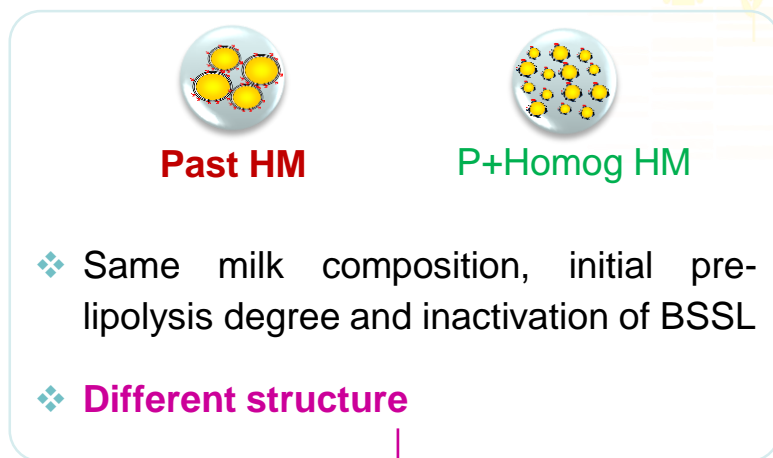
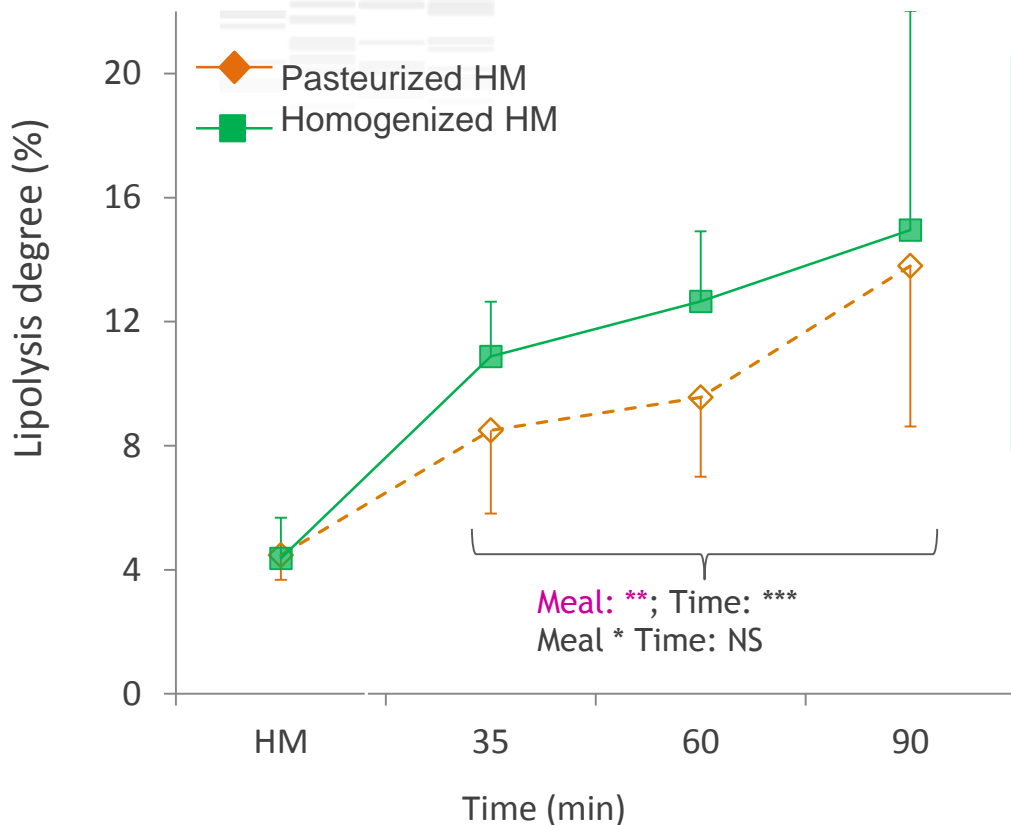
GROUP A

GROUP B



Homogenization by sonication

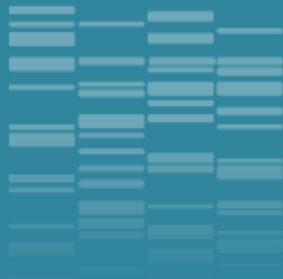
Homogenization impacted gastric lipolysis



➔ Increase of specific surface of droplets facilitating HGL adsorption

**De Oliveira et al.,
Clin Nutr 2017**
**De Oliveira et al.
Am J Clin, Nutr 2017**

Homogenization of human milk: a new way of stimulating the growth and development of pre-term neonate?

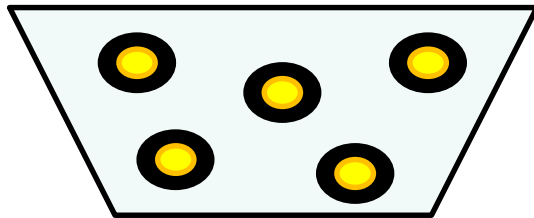


Infant formulas:
Can we create lipid structures
biomimetic on the native fat globule?



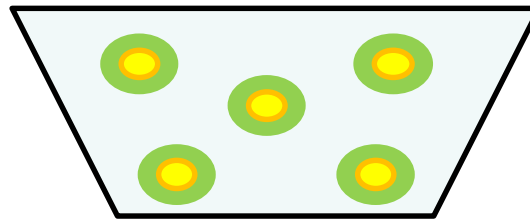
Infant formulas: can we create lipid structures biomimetic on the native fat globule?

Formula
T1



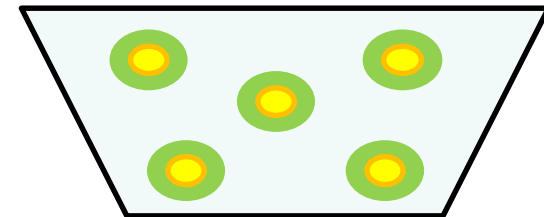
Interface 100 % Proteins
100% vegetable oil

Formula
T2

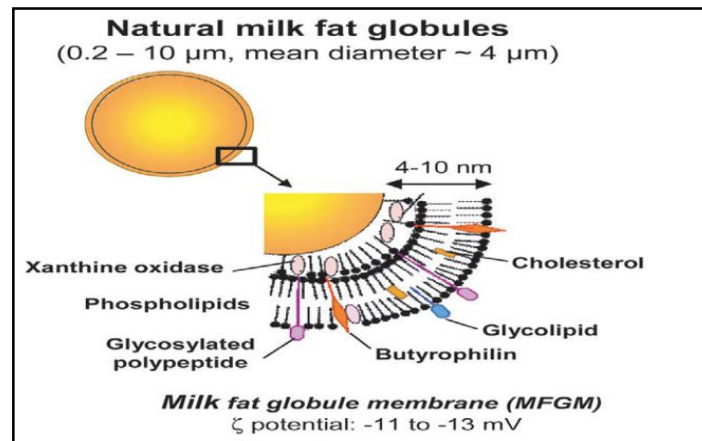


Interface 100 % phospholipids
100% vegetable oil

Formula
T3

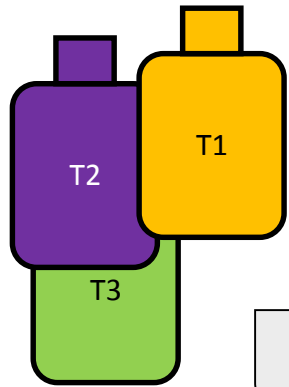


Interface 100 % phospholipids
40% vegetable oil + 60% milk fat



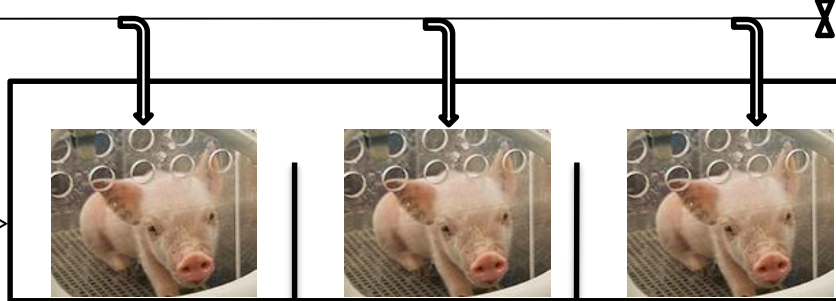
Lopez, (2007)

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

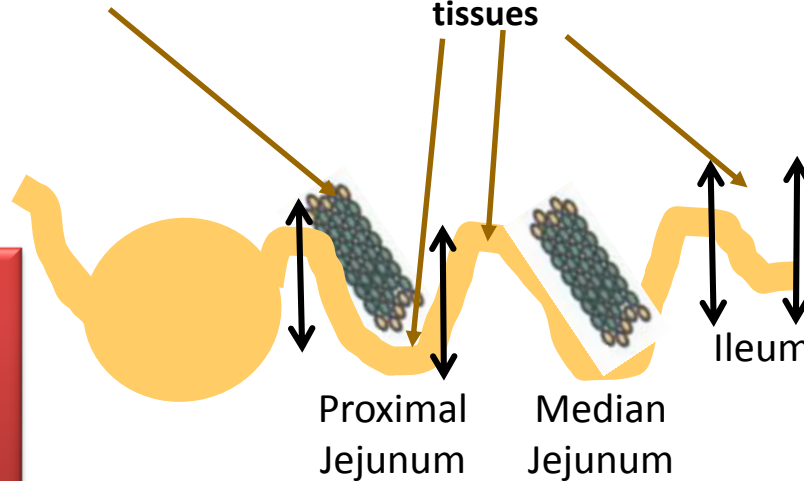
7 days

28 days

(90 min postprandial)

Mesenteric Lymph Nodes (MLN)

Collect of effluents and tissues

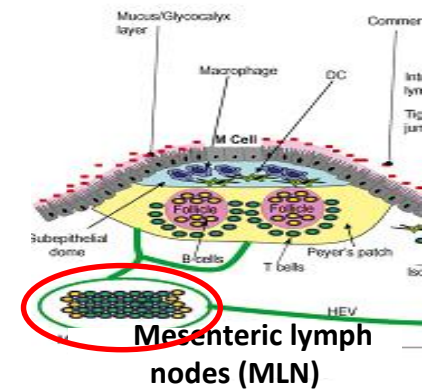


Effluents:
-SDS-PAGE
-Elisa

Tissues:

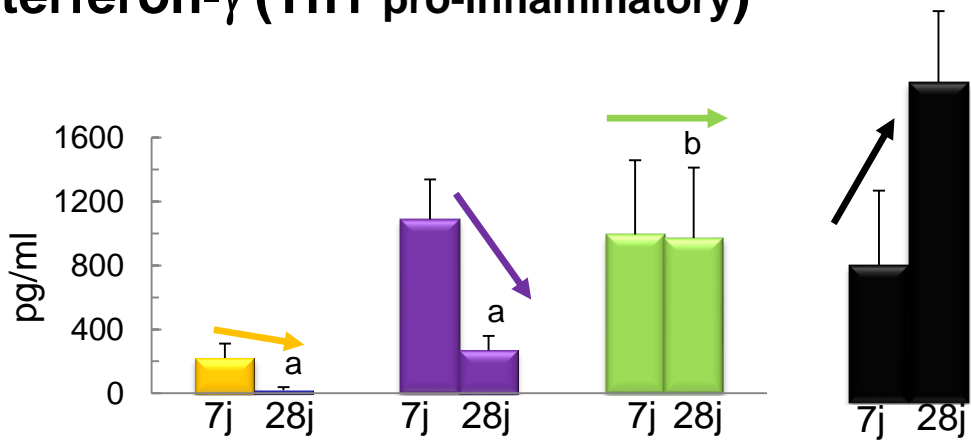
- Morphometry
- Enzyme Activities
- Intestinal Permeability
- Local immune response
- Microbiota

Secretory activity of MLN

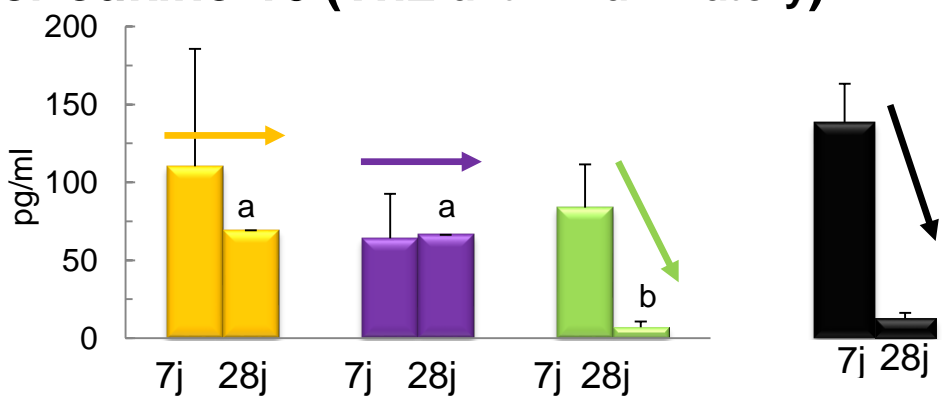


- Veg
- Veg + PL
- Dairy Fat + PL
- Porcelets SM

Interferon- γ (Th1 pro-inflammatory)



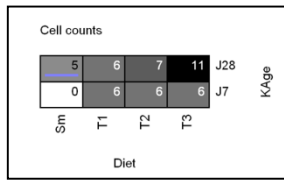
Interleukine-10 (Th2 anti-inflammatory)



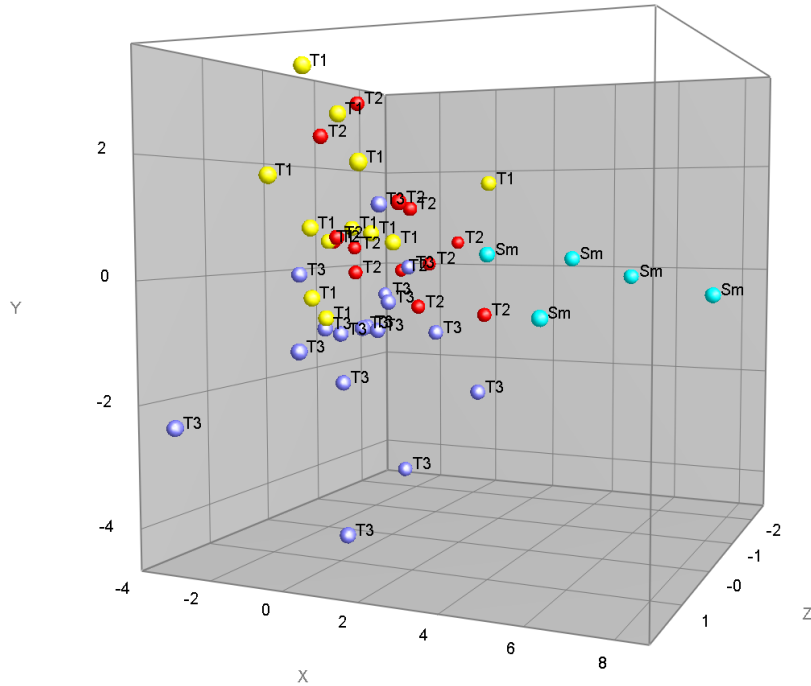
Milk lipids \rightarrow maturation of the piglet's immune system more similar than with sow's milk

**Le Huerou et al.
Eur J Nutr 2017**

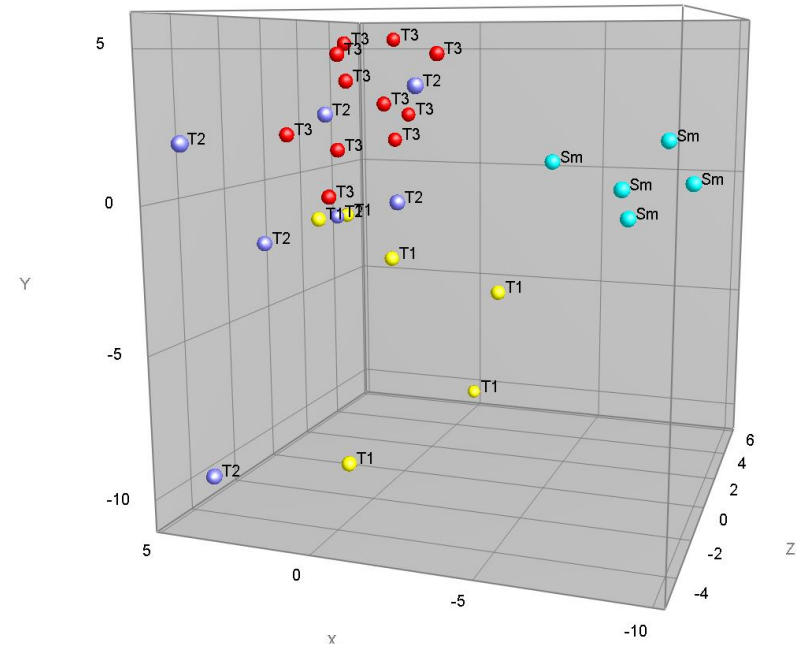
Microbiota by DHPLC



D7 & D28

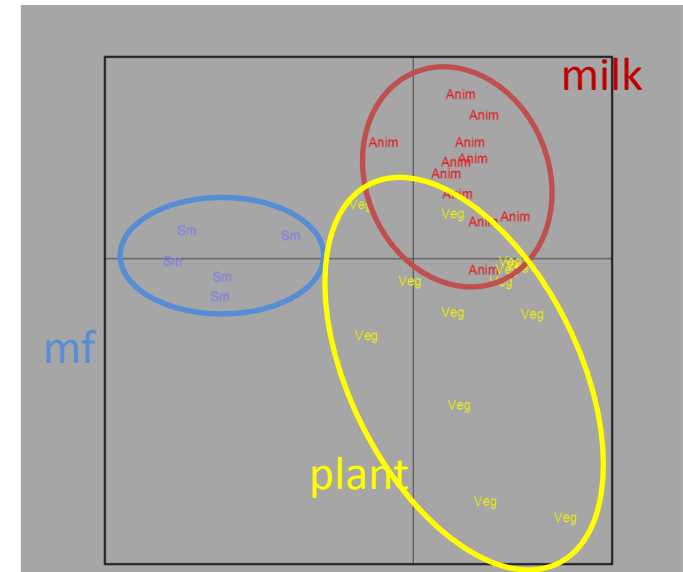


D28



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 2016

Conclusion

The structure/composition of food regulate the kinetics of protein and lipid 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 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

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Amélie DEGLAIRE – Lecturer

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Catherine GUERIN - Lecturer

Joëlle LEONIL – Senior Scientist

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Masters students

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

International Network

Dr. Didier DUPONT, Senior Scientist, INRA, France

●
INFOGEST
●



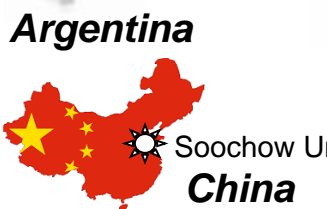


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Montenegro
 Ege Univ



USA
 Pom Med Univ
 Univ California Davis



New Zealand
 Riddett Inst
 Plant Food Res



China
 Soochow Univ

372 scientists - 140 institutes – 39 countries

Industry involvement

42 private companies are following INFOGEST





Chair
Didier Dupont - France



Vice-chair
Alan Mackie - UK

INFOGEST



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In vitro/in vivo correlations
WG1

In vitro semi-dynamic model of digestion
WG2

Models for specific populations
WG3

Digestive lipases and lipid digestion
WG4

Digestive amylases and starch digestion
WG5

In silico models of digestion
WG6



Didier Dupont



Alan Mackie



Uri Lesmes



Myriam Grundy



Nadja Siegert



Choi-Hong Lai

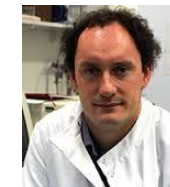


Guy Vergeres

The "Mind-the-Gap" group



Frederic Carriere



Fred Warren



Steven Le Feunteun



INFOGEST
International Conference
Granada, Spain
April 2019

We are pleased to announce the next
6th International Conference on Food Digestion



in Granada, Spain, 2-4 April 2019