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Food structure affects the kinetics of food digestion and the bioavailability of nutrients

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Submitted on 5 Jun 2020

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Food structure affects the kinetics of food digestion and the bioavailability of nutrients

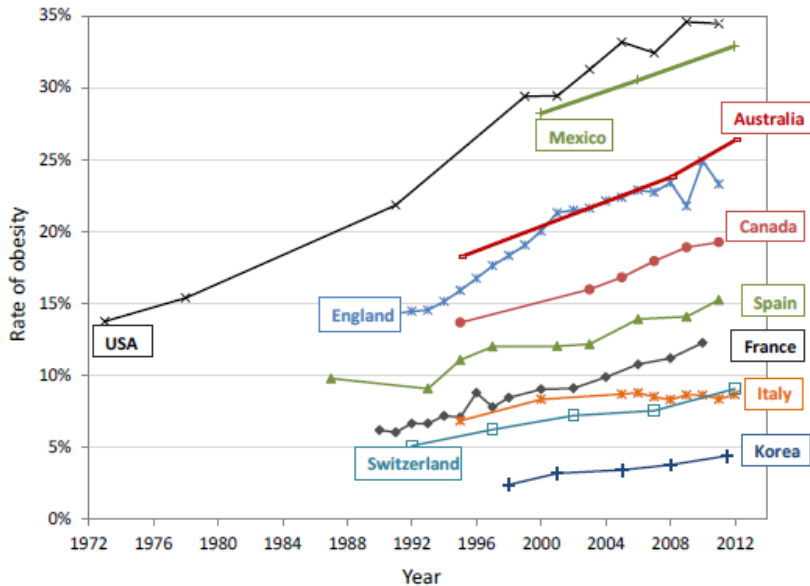


Dr Didier DUPONT

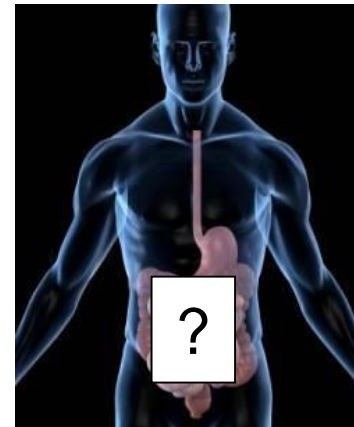
INRA, Rennes, France



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

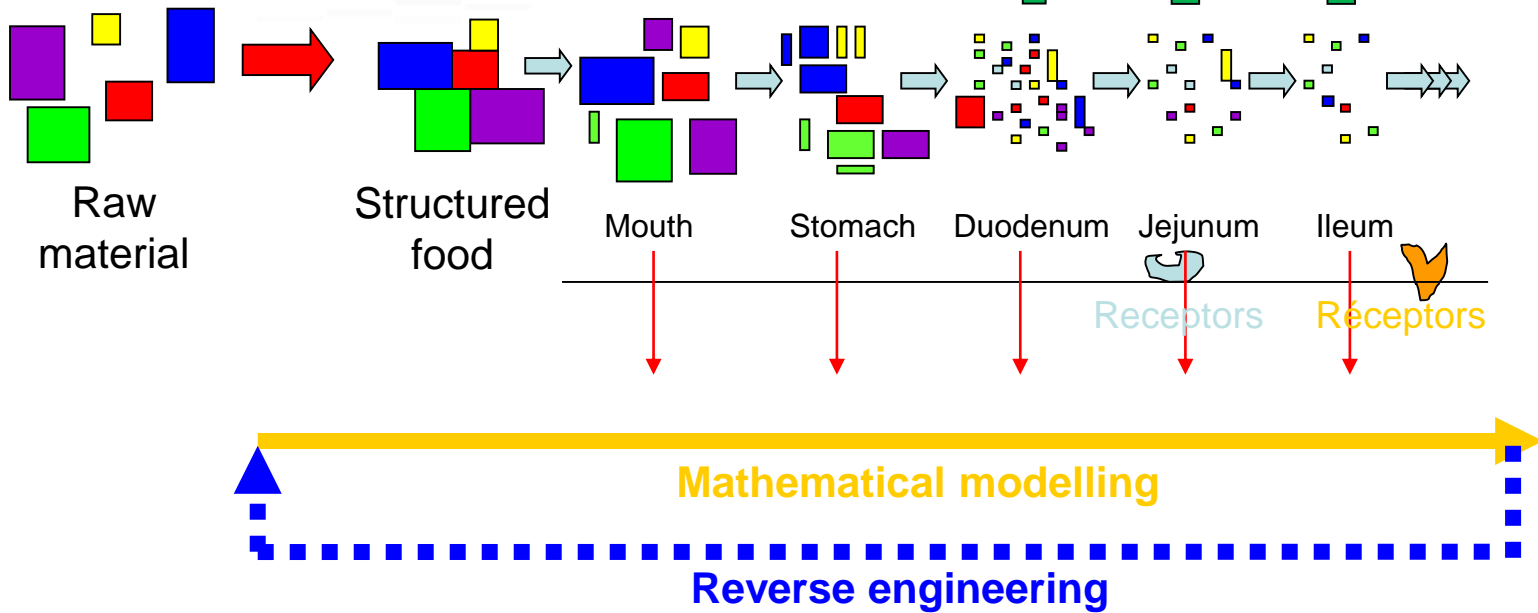
Digestion releases food components that can have a beneficial or a deleterious effect on human health

... 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

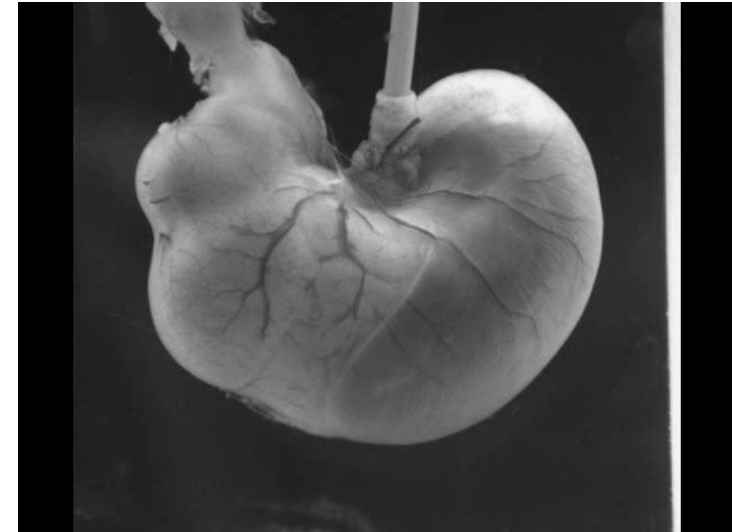
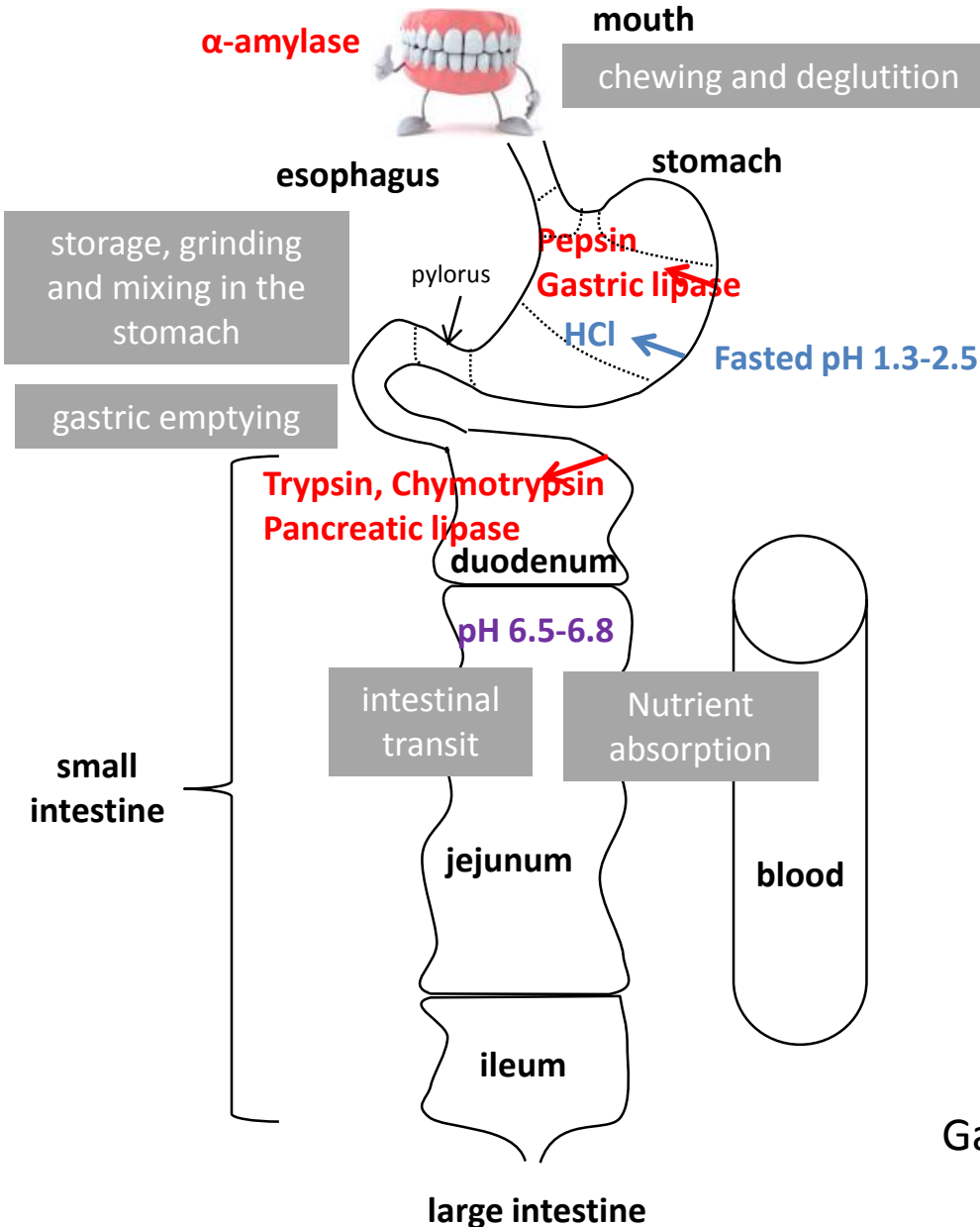


- Bioactivities**
- Bioactive peptides
 - Amino acids
 - Fatty acids
 - Minerals
 - Vitamins...

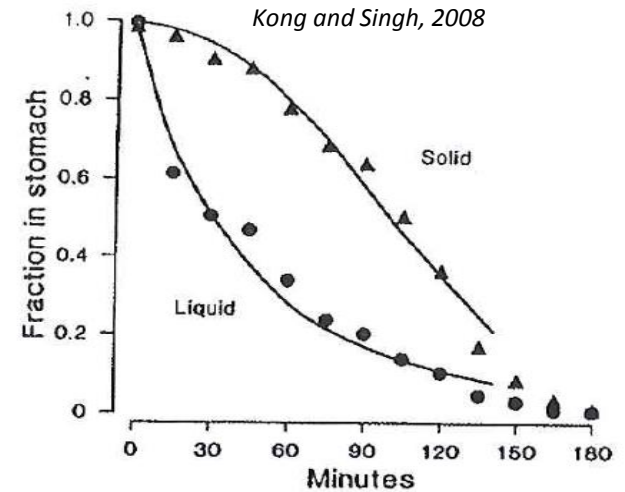
- Gut**
- Immune System
 - Intestinal microbiota

- ☞ 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

Models available at INRA for simulating digestion

Dupont et al. 2010ab,
Mol Nutr Food Res
Minekus et al. 2014
Food Funct

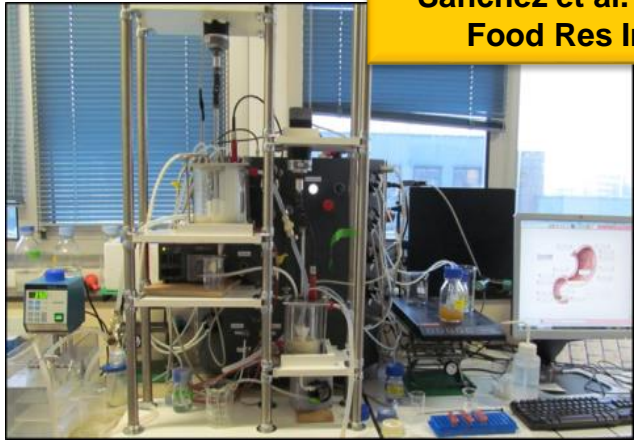


*In vitro static models
(infant, adult)*

Le Feunteun et al. 2014
Food Bioprocess Tech

*In silico
models*

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



*In vitro dynamic models
(infant, adult, elderly)*

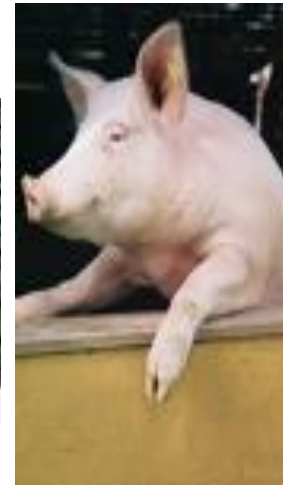
Menard et al. 2014,
Food Chem
Sanchez et al. 2015
Food Res Int



*Human
models*

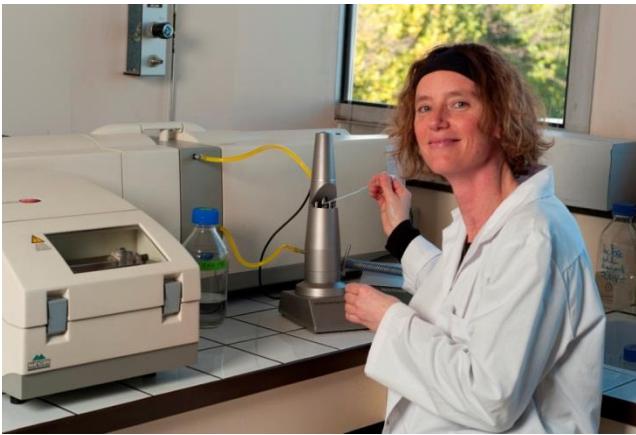


Animal models



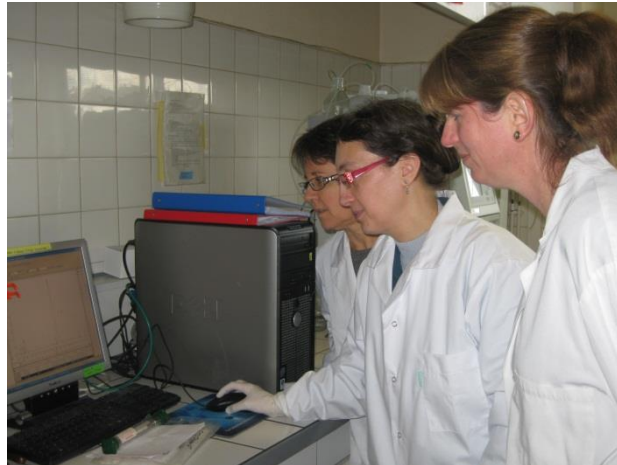
Barbé et al. 2013, 2014
Food Chem
Le Huerou-Luron et al.
2016 Eur J Nutr

De Oliveira et al. 2016
Am J Clin Nutr
De Oliveira et al. 2017
Clin Nutr



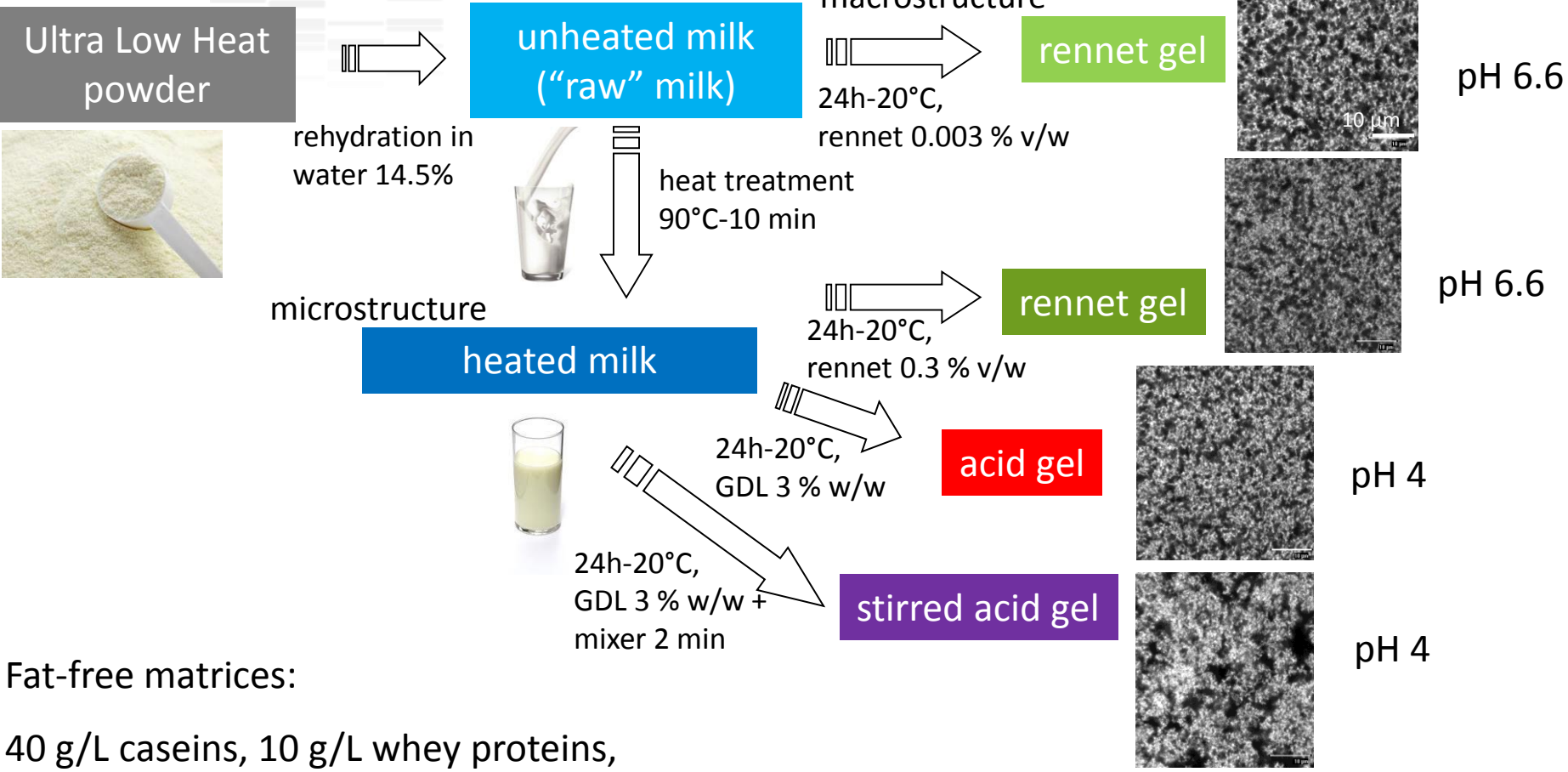
Period 2012-2017

Main achievements



Bioactivity & Nutrition

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



Fat-free matrices:

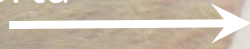
40 g/L caseins, 10 g/L whey proteins,
95 g/L lactose and minerals

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

The multi-cannulated mini-pigs

6 minipigs (20 ± 1kg)

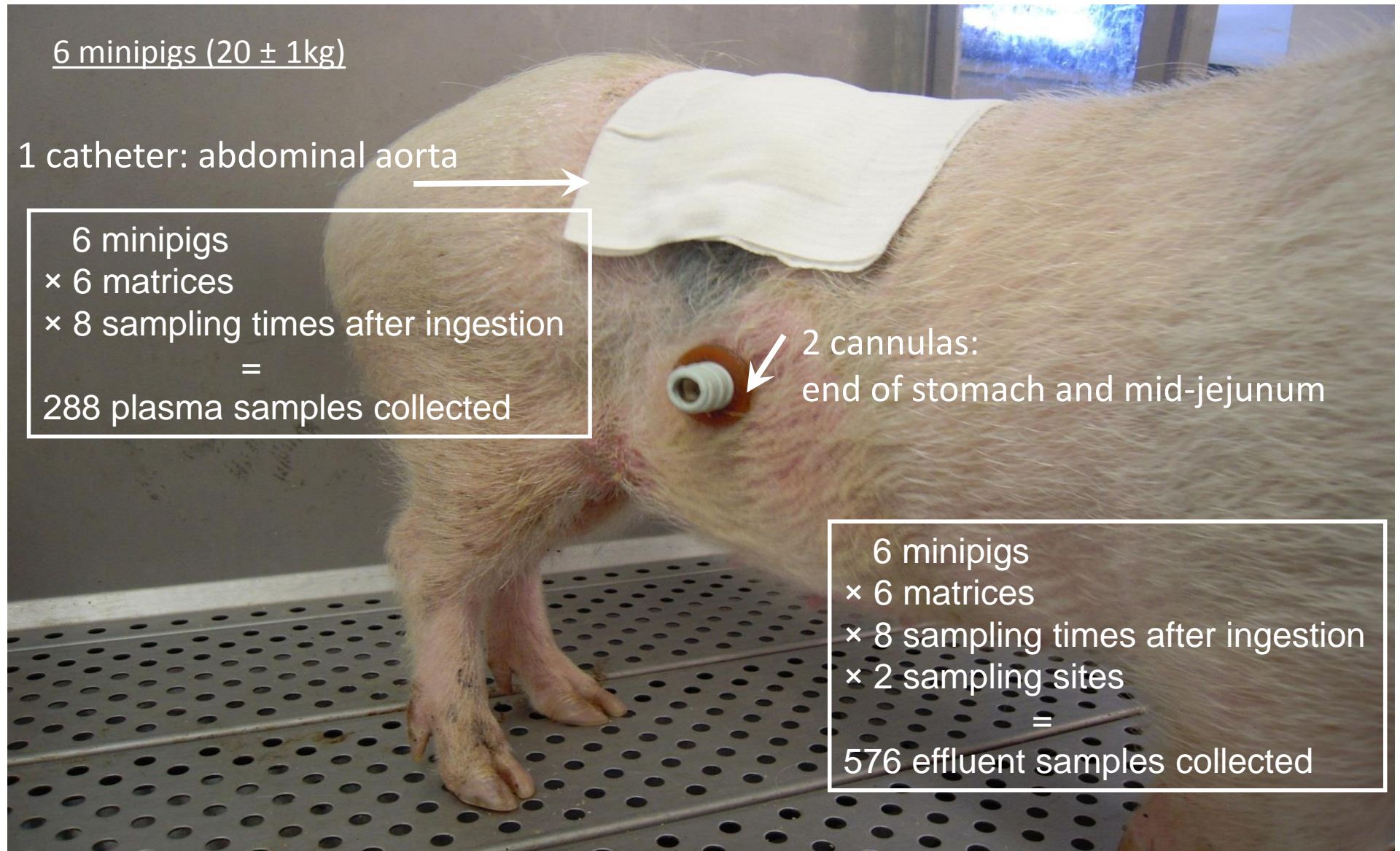
1 catheter: abdominal aorta



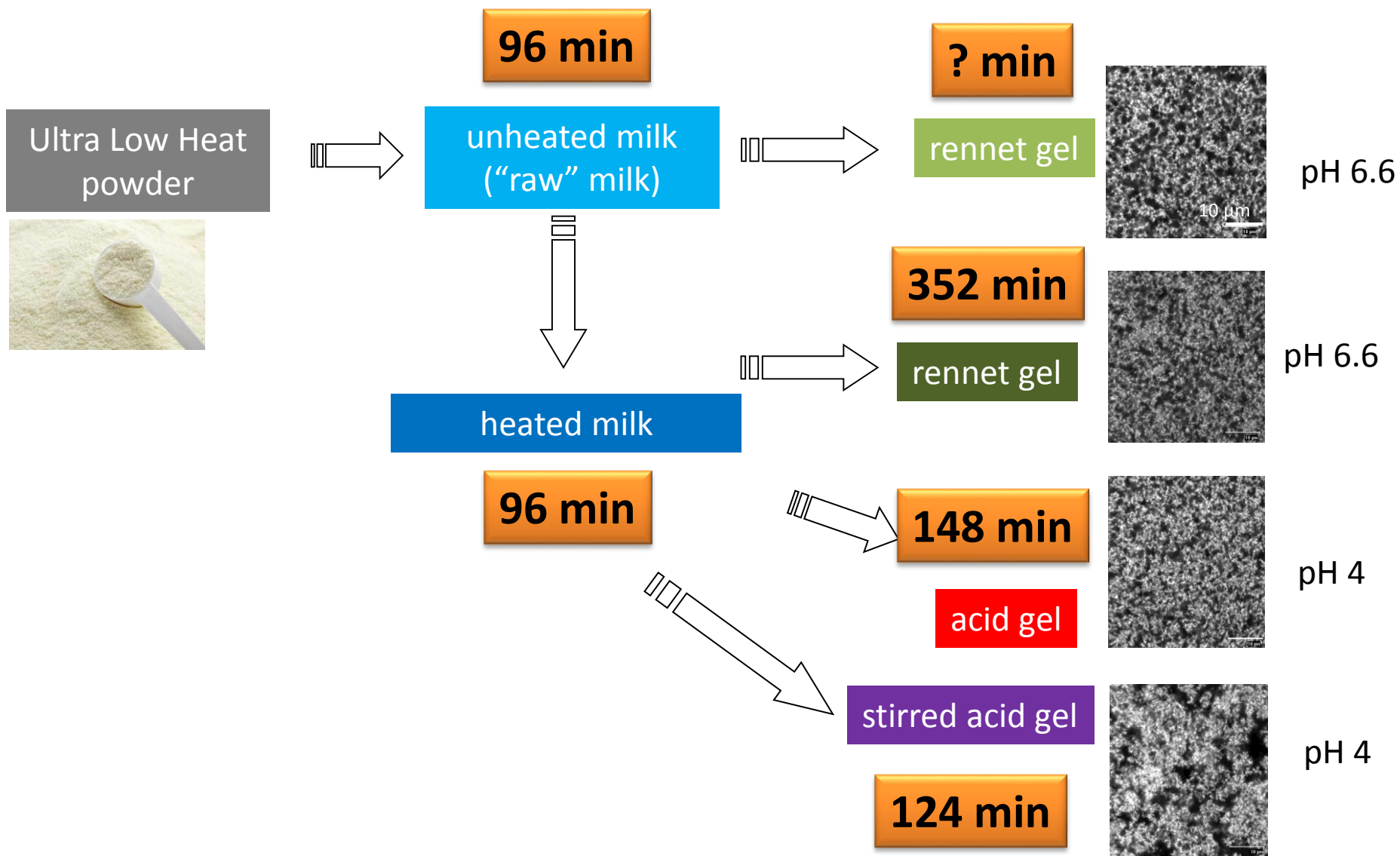
6 minipigs
× 6 matrices
× 8 sampling times after ingestion
=
288 plasma samples collected

2 cannulas:
end of stomach and mid-jejunum

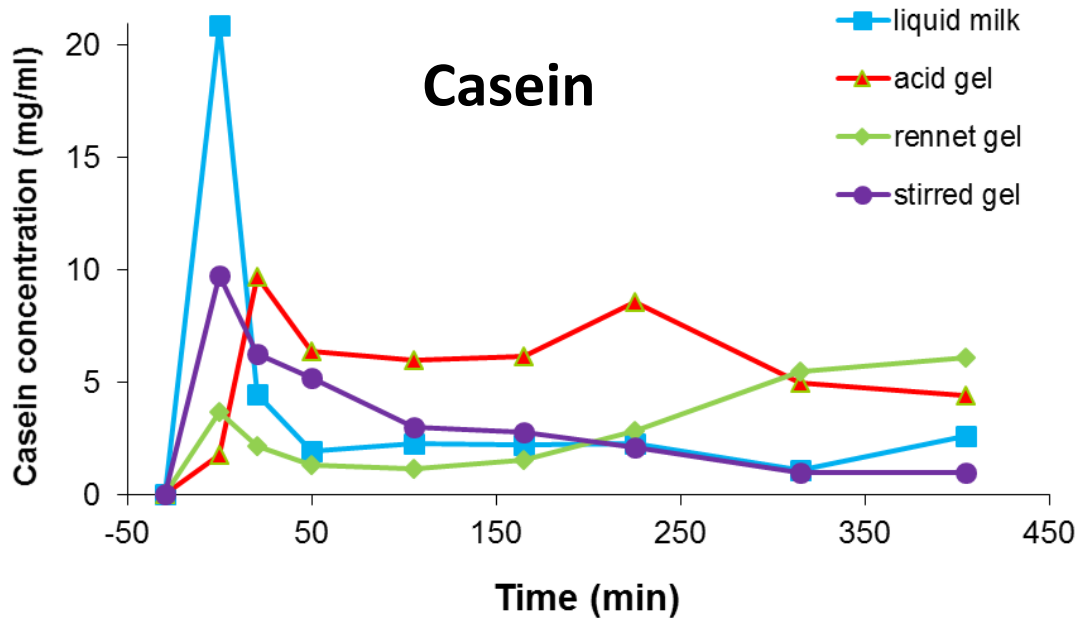
6 minipigs
× 6 matrices
× 8 sampling times after ingestion
× 2 sampling sites
=
576 effluent samples collected



Time of residence in the stomach

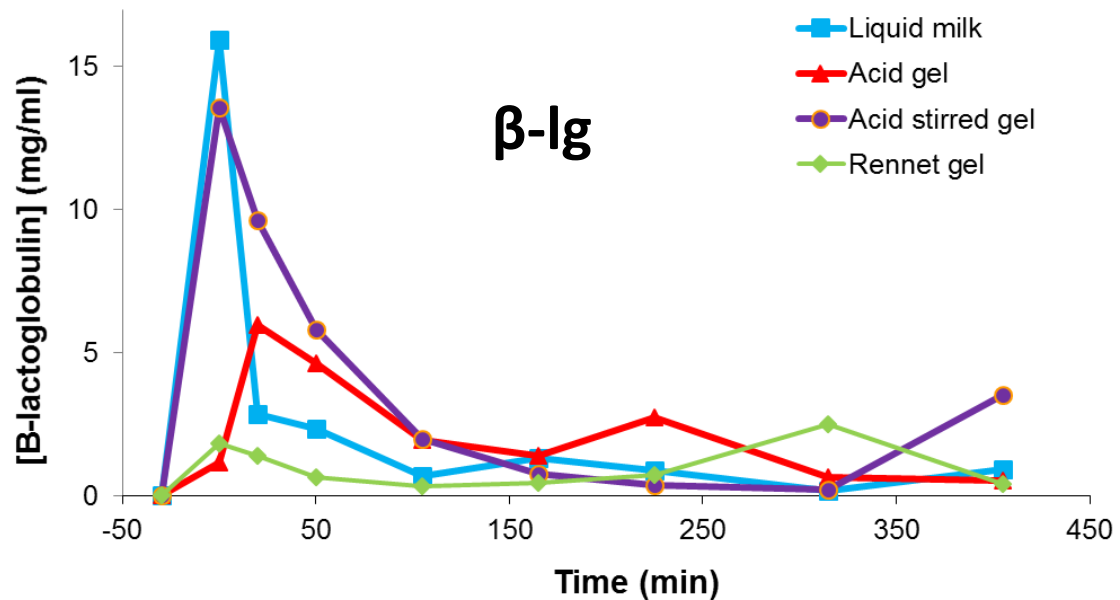


Milk proteins in the duodenum (ELISA)



- 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

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

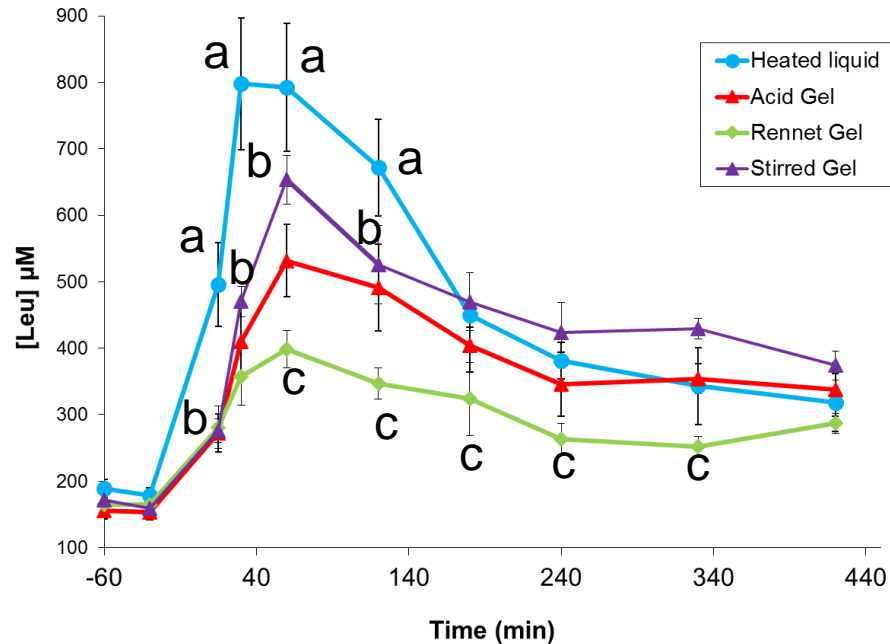
Protein	Sequence	Activity	Reference	4	20	50	105	165	225	315
α s1	40-52	MB	Adamson & Reynolds (1996)							█
α s1	43-58	MB	Meisel et al. (1991)	█	█					█
α s1	99-109	MIC	McCann et al. (2006)							
α s1	167-180	MIC	Hayes et al. (2006)							
α s1	180-193	MIC	Hayes et al. (2006)	█	█					
α s2	1-24	MB	Miquel 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



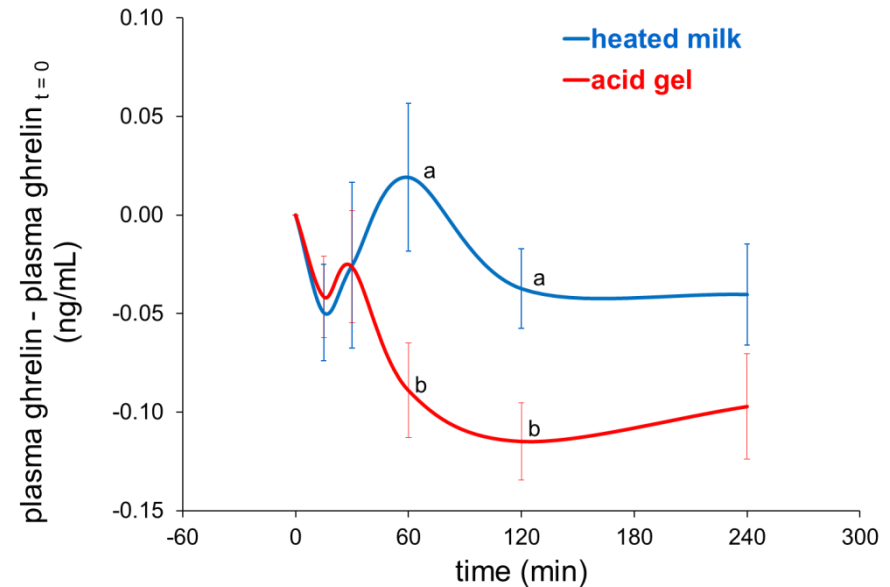
milk gelation:

→ delayed proteins transit → delayed AA absorption

↘ maximal AA concentration in the plasma

3) potential effect on satiety

ghrelin (gastrointestinal hormone → appetite stimulation)



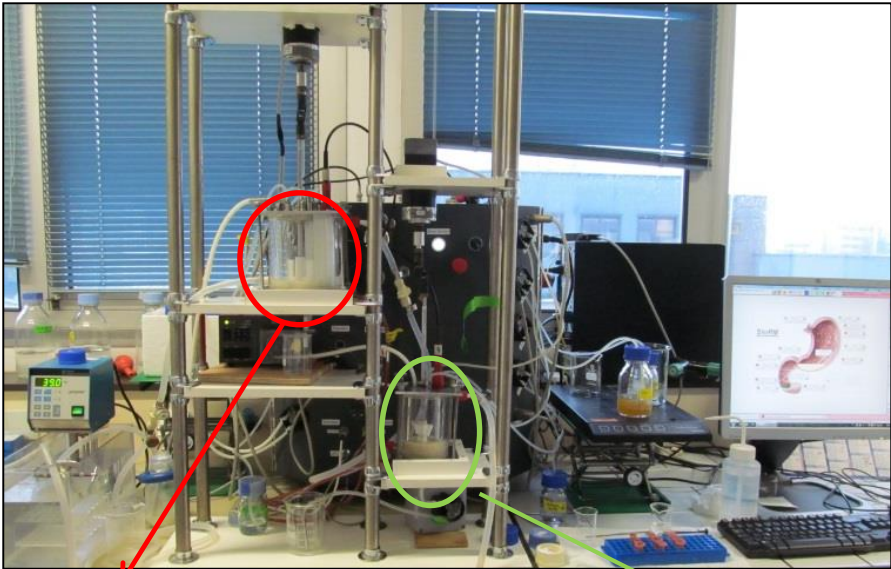
milk gelation:

↘ 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



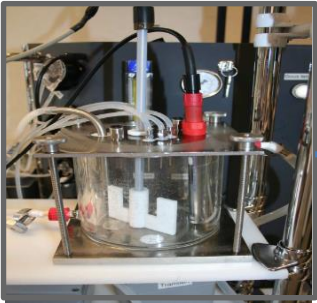
DIDGI®

StoRM® software

Stomach

Small intestine

- Pepsine
- Gastric lipase
- Simulated gastric fluid
- HCl



Emptying :
Elashoff's model



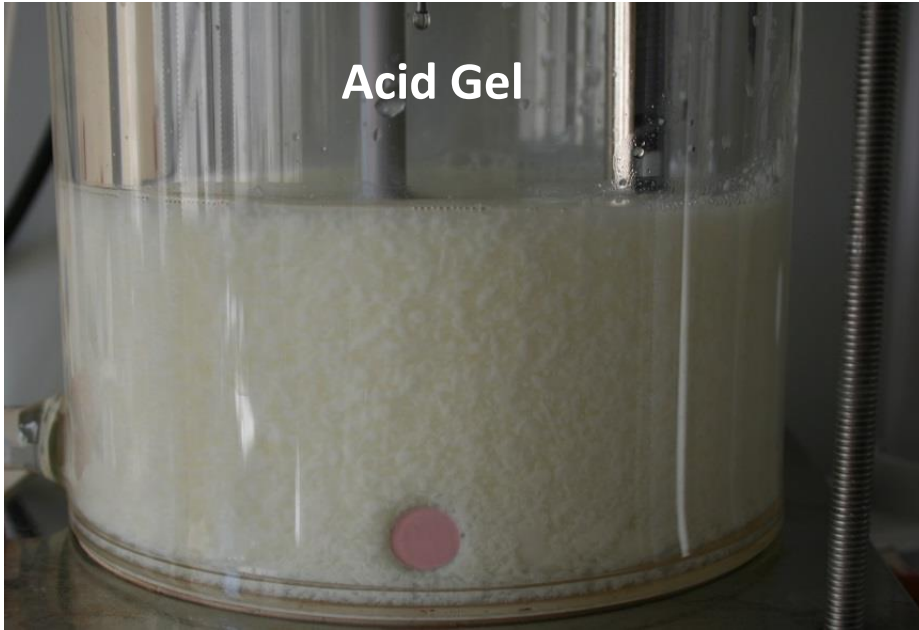
- Pancreatin
- Bile
- Simulated intestinal fluid
- NaHCO₃

Emptying :
Elashoff's model

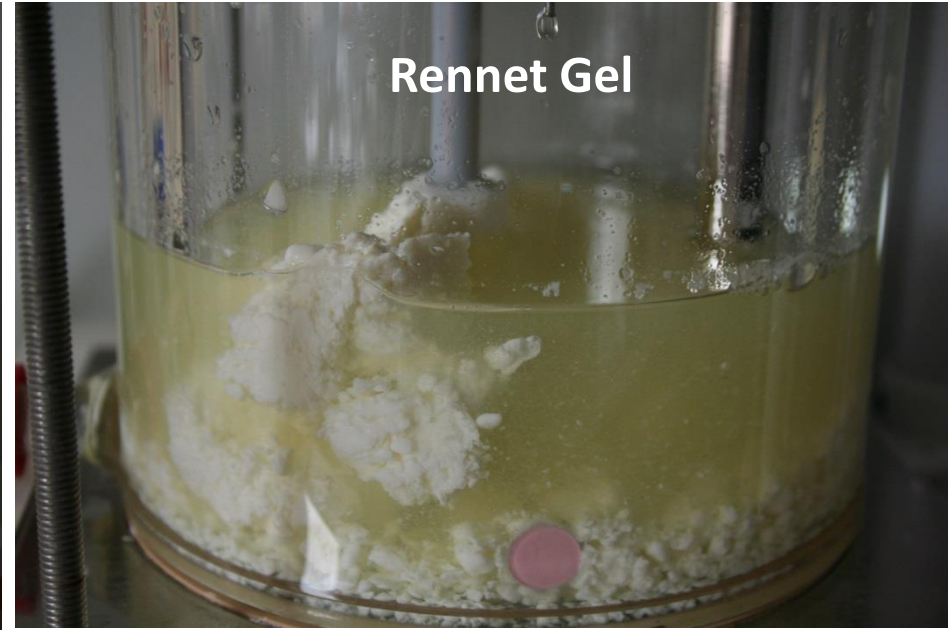
Behaviour of acid and rennet gels in the stomach during *in vitro* dynamic digestion

Barbé et al.
Food Chem. 2014

Acid Gel



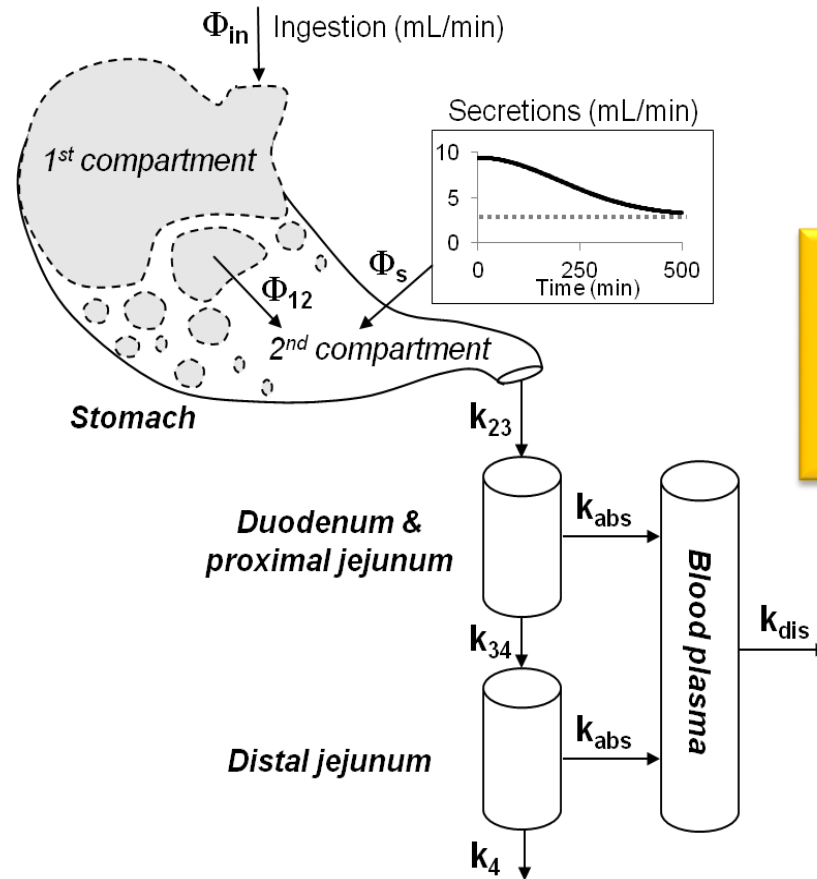
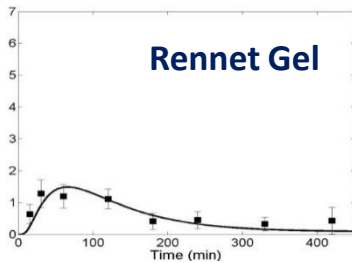
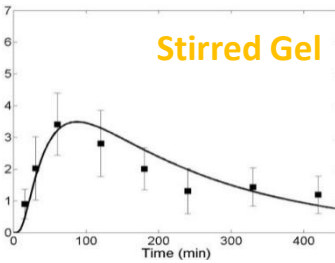
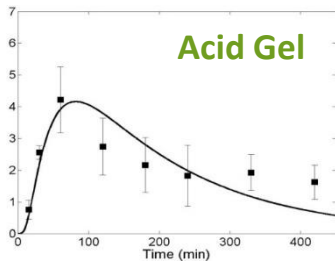
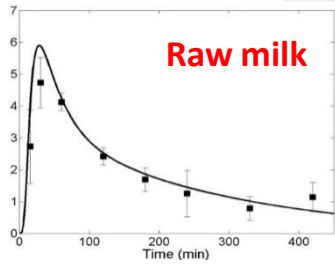
Rennet Gel



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

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???



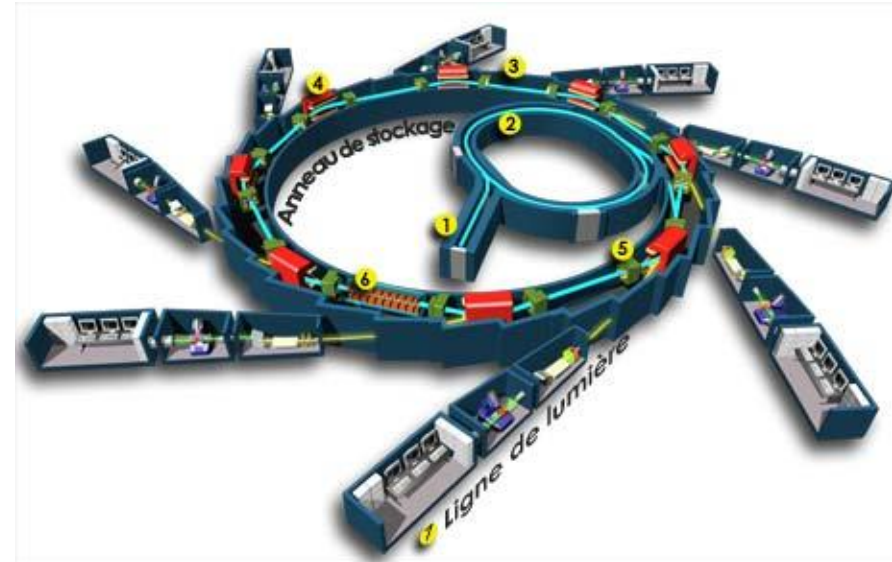
Understanding the mechanisms of dairy gel particles degradation in the stomach

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



Protocol



Ultra-low-heat skim milk powder
rehydrated at 30 g/l

+ GDL

+ Chymax

Acid Gel

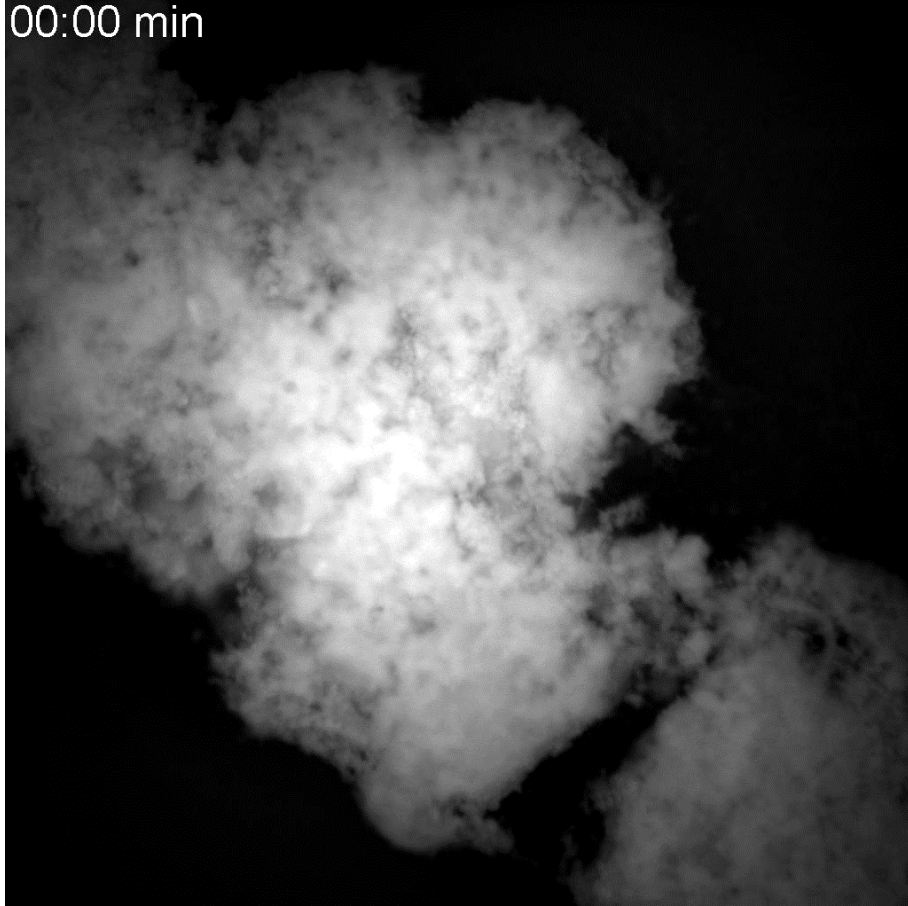
Rennet Gel

Gels soaked in SGF at pH 2.0 with or without pepsin (2000 U/mL)

Observation 2h UV microscope (x10 and x100)

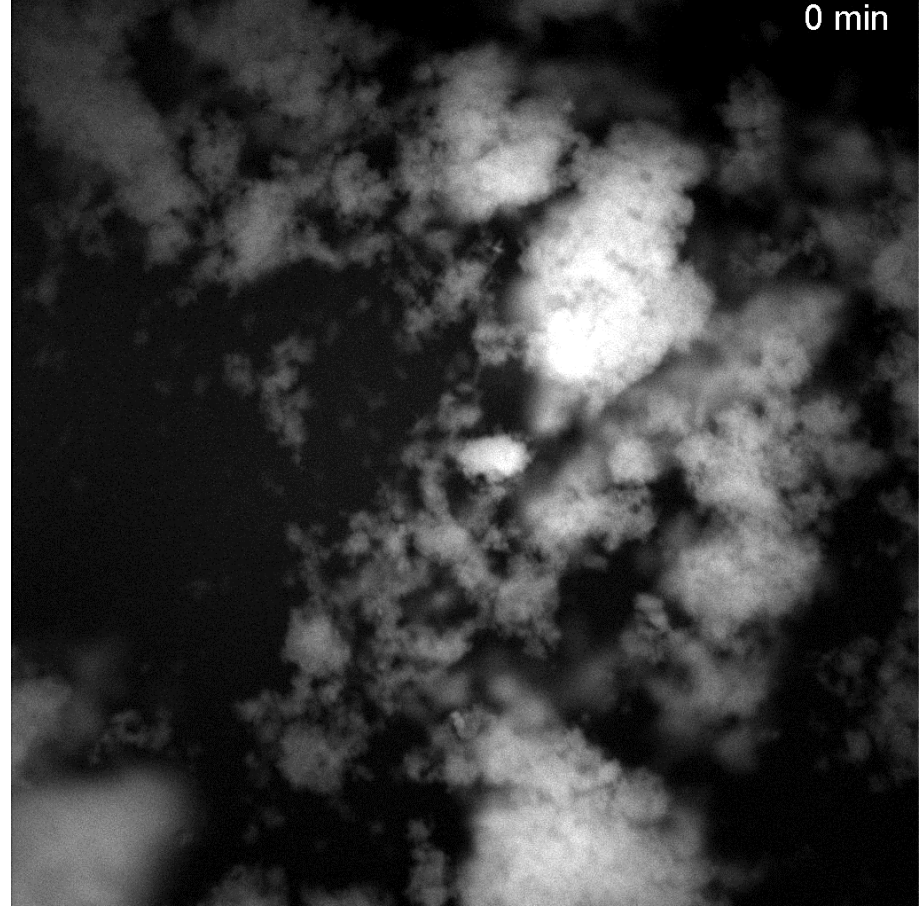
Kinetics of gel particles disintegration

00:00 min

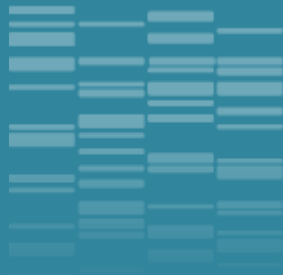


Rennet Gel

0 min



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

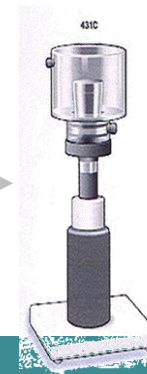
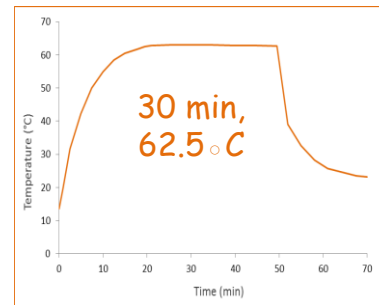
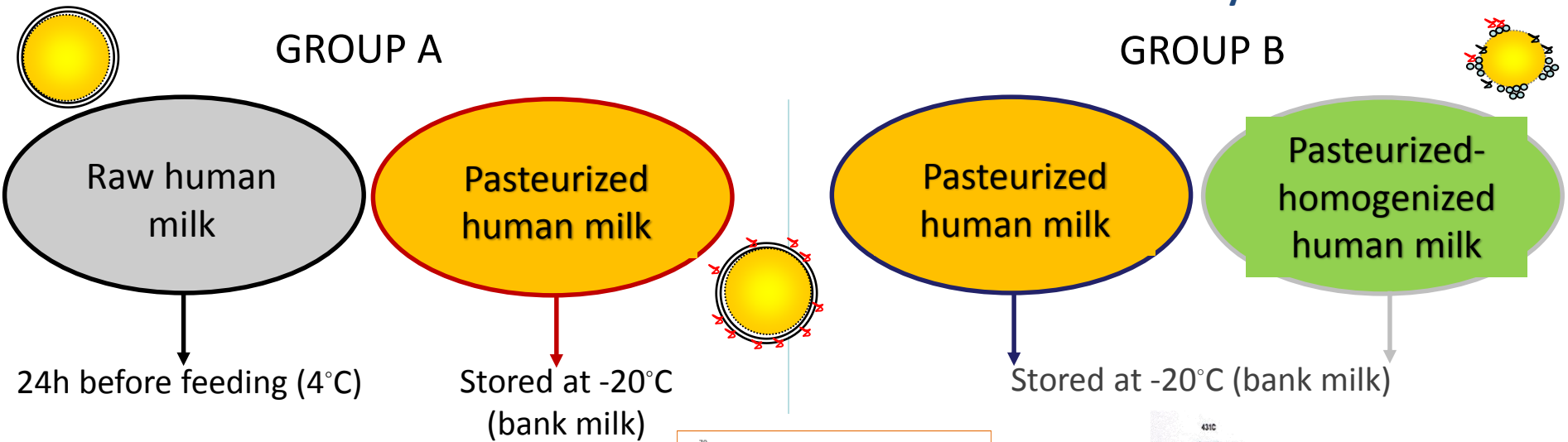
Aim: to compare meals with similar composition but different structure

Human milk from their **own mother**

Human milk from **anonymous donor**

GROUP A

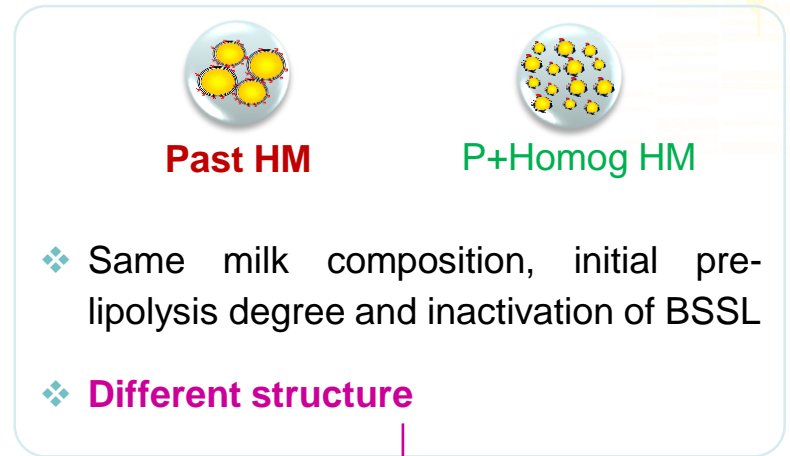
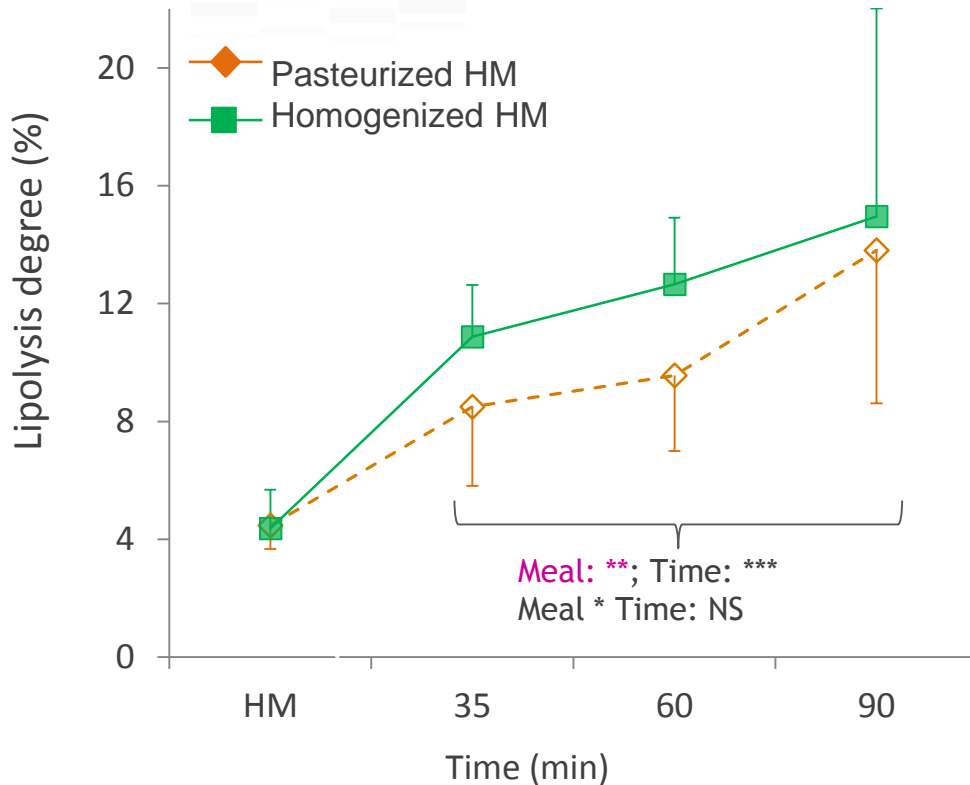
GROUP B



Homogenization by sonication

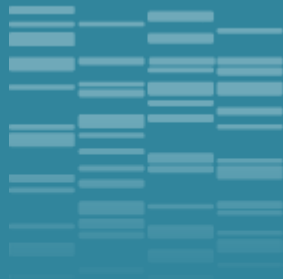
Homogenization impacted gastric lipolysis

Instantaneous lipolysis level



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?

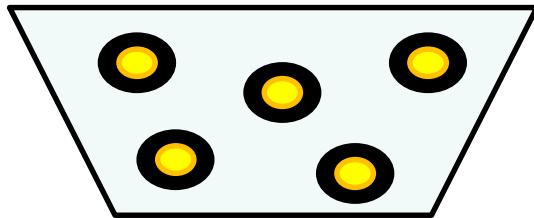


Infant formulas:
Can we create lipid structures
biomimetic on the native fat globule?



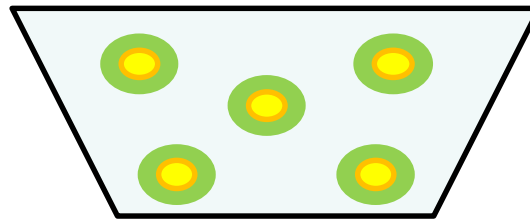
Infant formulas: can we create lipid structures biomimetic on the native fat globule?

Formula
T1



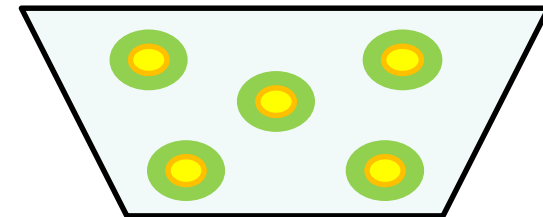
Interface 100 % Proteins
100% vegetable oil

Formula
T2

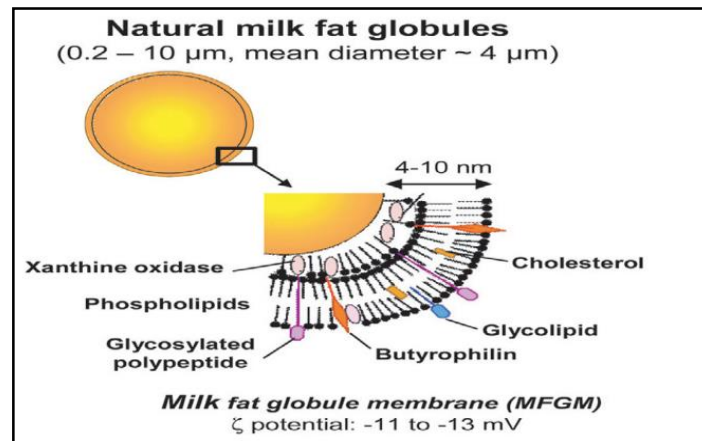


Interface 100 % phospholipids
100% vegetable oil

Formula
T3

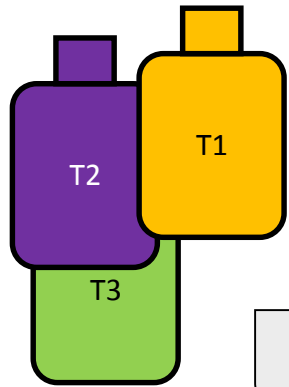


Interface 100 % phospholipids
40% vegetable oil + 60% milk fat



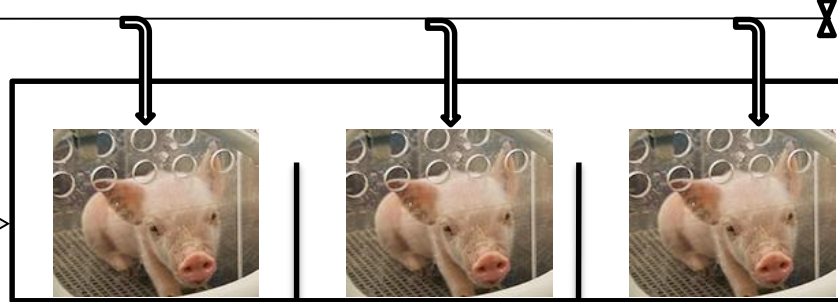
Lopez, (2007)

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)

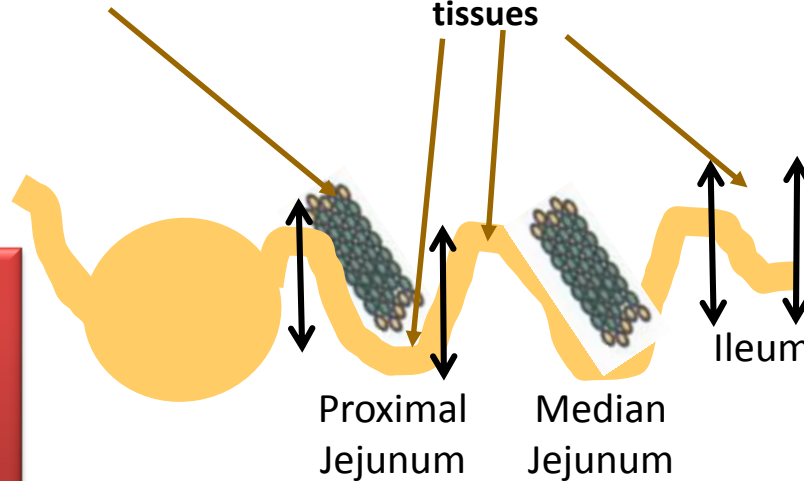
Mesenteric Lymph Nodes (MLN)

Collect of effluents and tissues

Effluents:
-SDS-PAGE
-Elisa

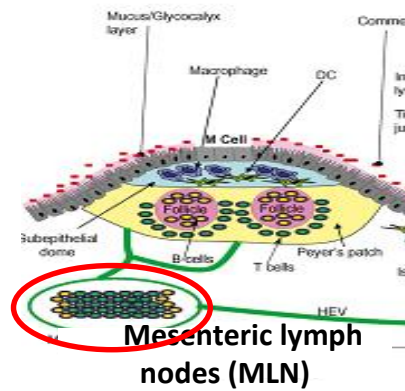
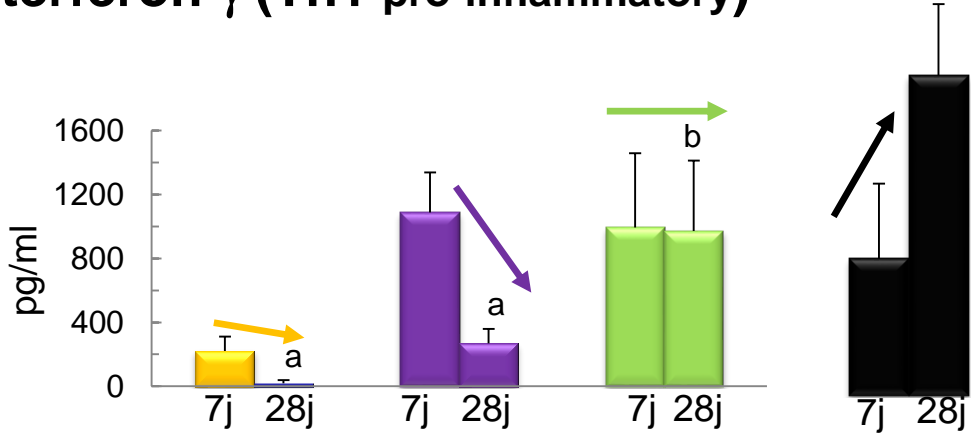
Tissues:

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



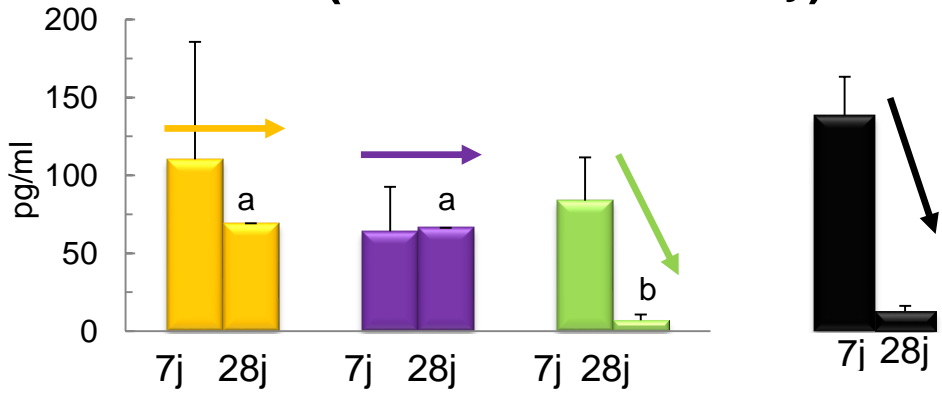
Secretory activity of MLN

Interferon- γ (Th1 pro-inflammatory)



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

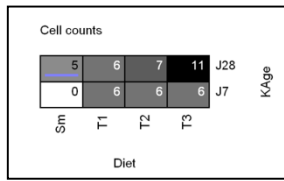
Interleukine-10 (Th2 anti-inflammatory)



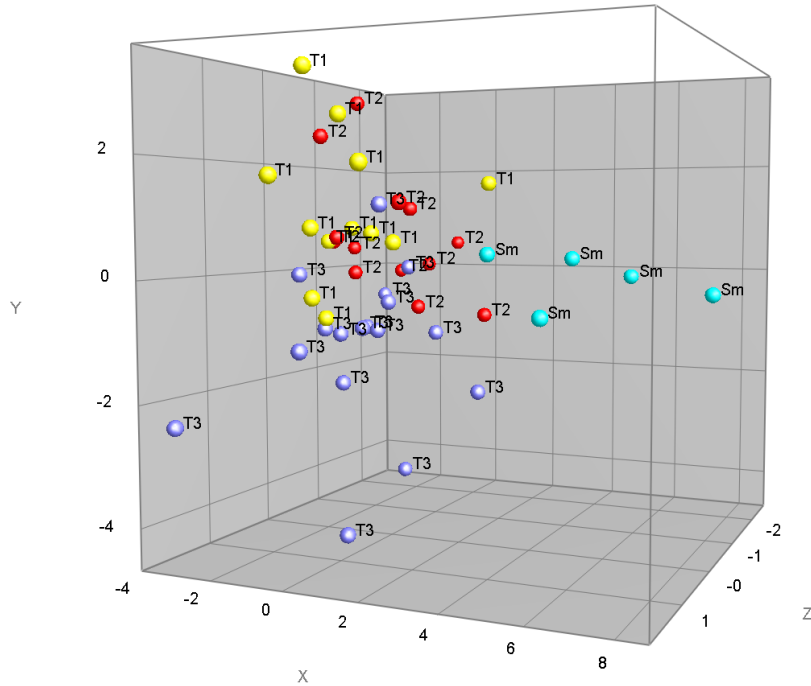
Milk lipids → maturation of the piglet's immune system more similar than with sow's milk

Le Huerou et al.
Eur J Nutr 2017

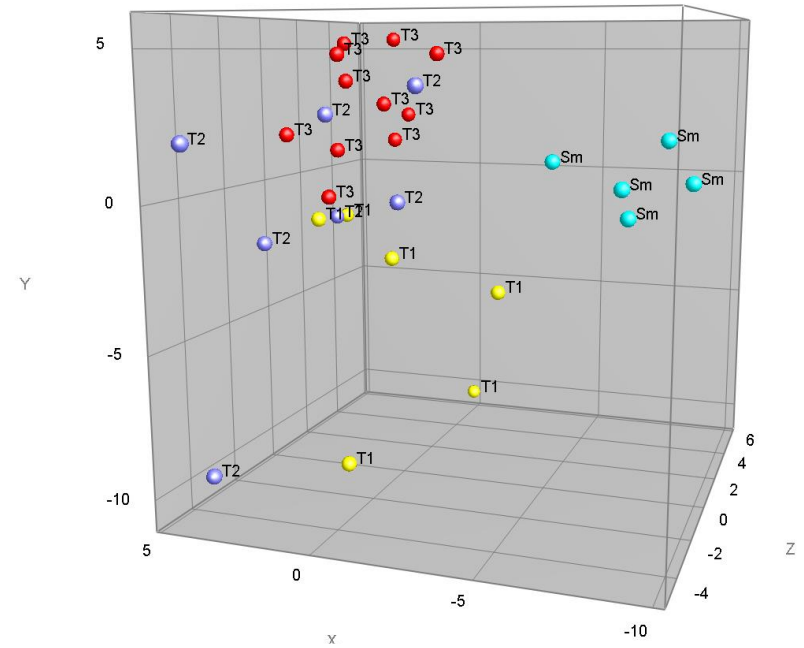
Microbiota by DHPLC



D7 & D28

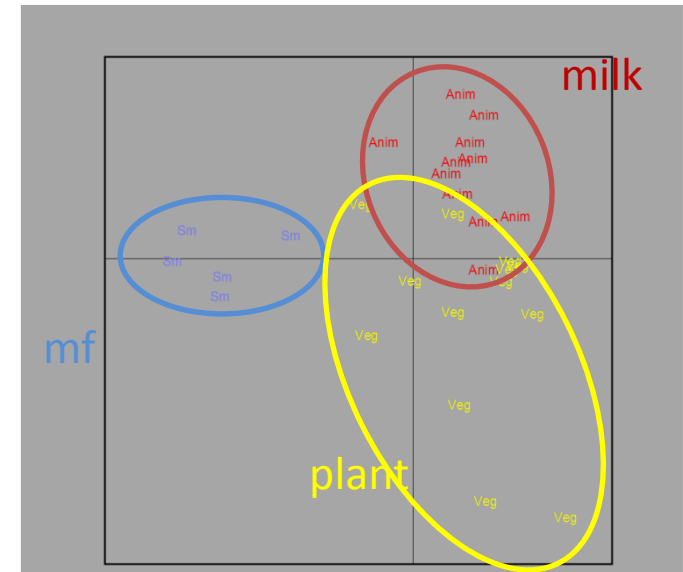


D28

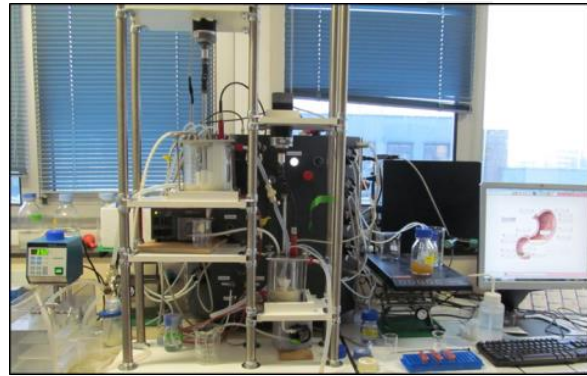


The composition/structure of the infant formula « orientates » the microbiota

More Proteobacteria with milk fat /
More Firmicutes with plant oil



Validation of the in vitro dynamic digestion simulator



DIDGI®

Infant Formula



In vitro

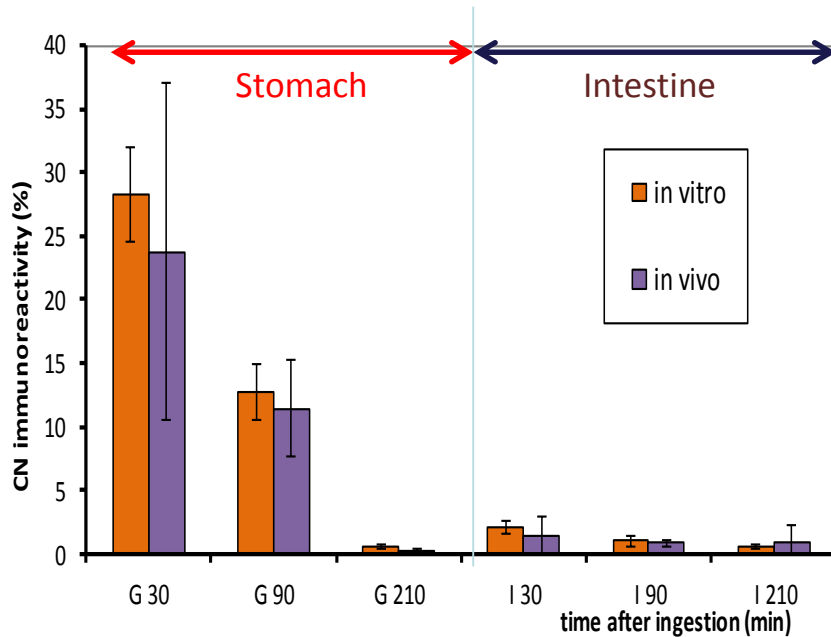


N=3

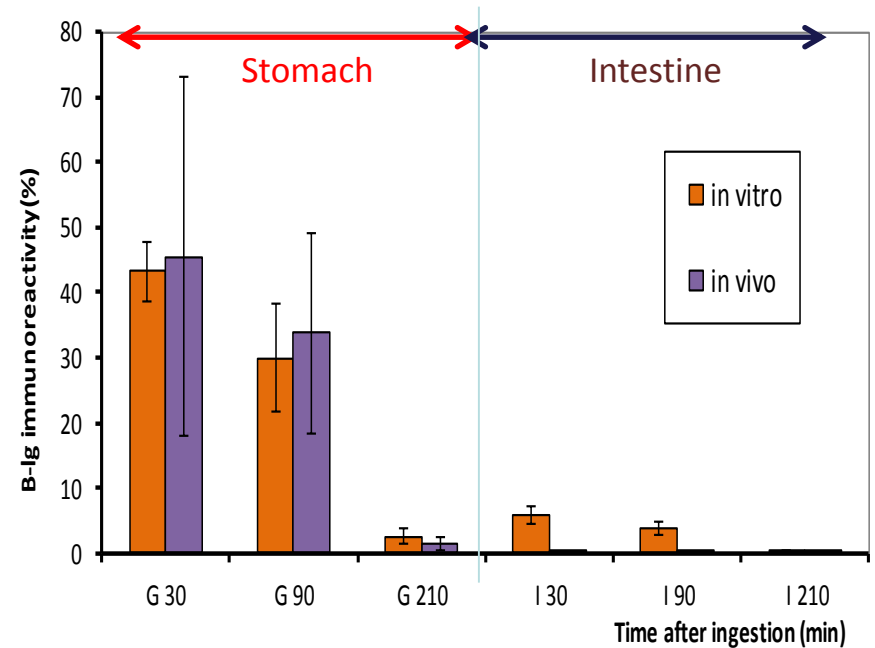
In vivo



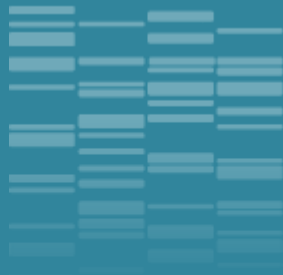
18 piglets



Caseins



β-lactoglobulin

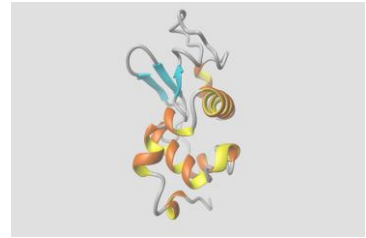


May bioactive peptides released
during digestion have an effect *in*
vivo?



In vivo digestion of milk proteins

- 16 subjects were fed with 30g of either:
 - Caseins
 - Whey proteins

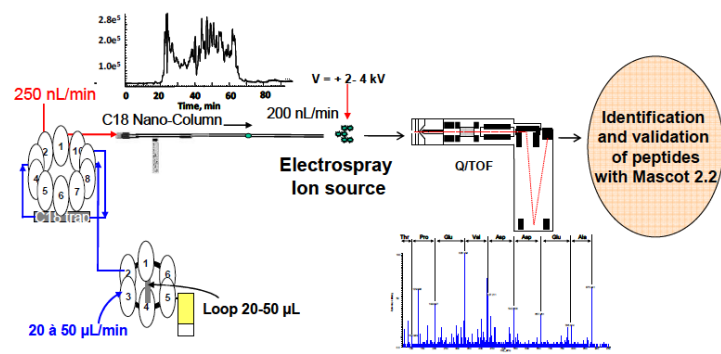


- Intestinal contents were collected through a double lumen nasogastric tube placed in their jejunum during 6 h after ingestion (location of the sampling site was controlled by radiography)



- Effluents were then freeze-dried until further use. Before analysis, effluents were rehydrated in 50 mM Tris HCl buffer pH 8.0 and 2M urea, centrifuged for 10 min a 2000 g

- Samples were characterized by ESI-MS-MS. Only peptides larger than 5 amino acids are considered



A great variability in patterns but some peptides present in all subjects

↳ 4704 dietary peptides unambiguously identified

31 peptides present throughout digestion

14 peptides found in all the subjects

β-CN

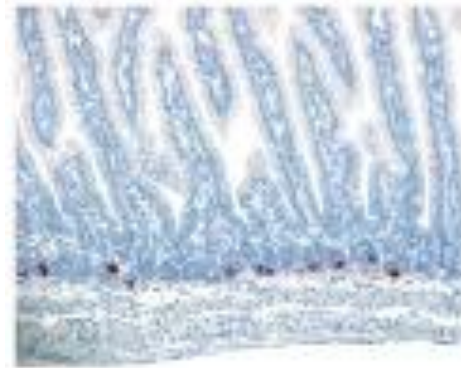
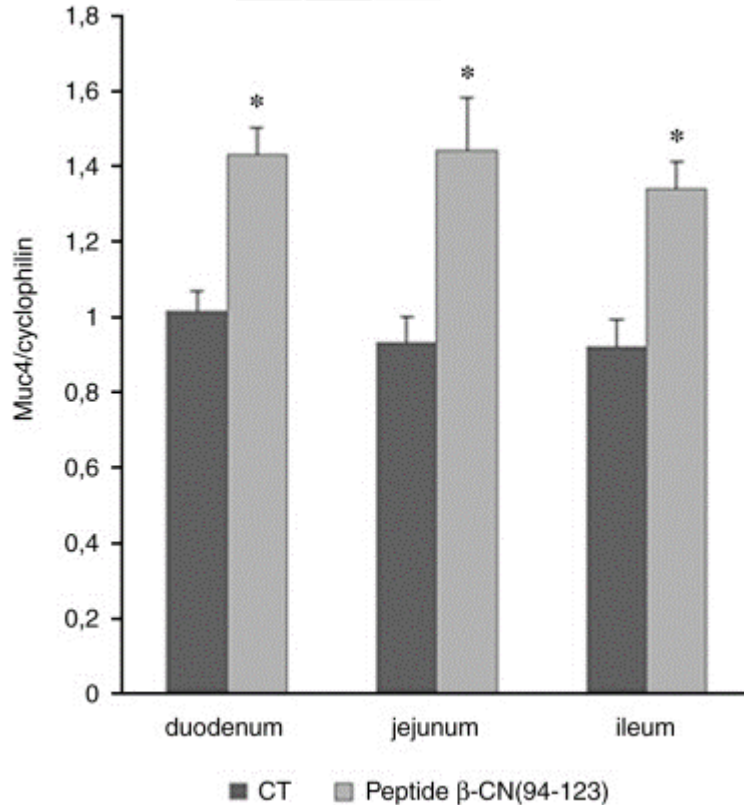
1-6	RELEEL		
57-66	SLVYFPFGPI	57-66	SLVYFPFGPI
58-66	LVYFPFGPI		
58-68	LVYFPFGPIP		
59-66	VYFPFGPI	59-66	VYFPFGPI
59-67	VYFPFGPIP		
59-68	VYFPFGPIP	59-68	VYFPFGPIP
60-66	YFPFGPI	60-66	YFPFGPI
61-66	PFGPI	60-67	YFPFGPIP
73-79	NIPPLTQ		
73-80	NIPPLTQT		
73-82	NIPPLTQTPV		
80-91	TPVVVPFLQPE		
81-87	PVVVPPF		
81-91	PVVVPPFLQPE	81-91	PVVVPPFLQPE
81-92	PVVVPPFLQPEV	81-92	PVVVPPFLQPEV
83-91	VPPFLQPE		
84-91	VPPFLQPE		
85-091	PPFLQPE		
107-113	KEMPFK		
108-113	EMPFK	108-113	EMPFK
114-119	YPVEPF	114-119	YPVEPF
134-139	HLPLPL		
135-139	LPLPL		
156-160	MFPPQ		
168-173	VAPFPQ	168-173	VAPFPQ
170-175	VLPVPQ	170-175	VLPVPQ
171-175	LPVPQ		
194-201	QEPVLGPV	177-182	AVPYPQ
195-201	EPVLGPV	194-201	QEPVLGPV
196-201	PVLGPV	195-201	EPVLGPV

Among those 5 bioactive peptides quantified

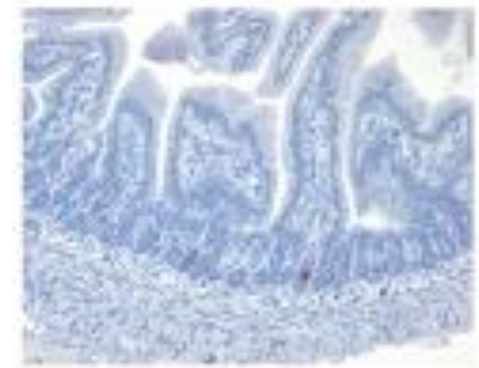
59-66	VYFPFGPI	} Anti-hypertensive Opioid
59-68	VYFPFGPIP	
60-66	YFPFGPI	
108-113	EMPFK	
114-119	YPVEPF	

Boutrou et al. 2013
Am J Clin Nutr

Bioactive peptides released during digestion can reinforce the defense of the intestinal epithelium



Before



After

Sections of duodenum after 10 d of administration of peptide β -CN (94-123)

β -CN(94-123) stimulates the mucus production
in vitro (HT-29 MTX) and *in vivo* (rat)

Plaisancie et al. 2013, J Nutr Biochem
Plaisancie et al. 2015, J Dairy Res

Conclusion

The structure/composition of food 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 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



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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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 CONICET
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 Agric Univ Tirana

Montenegro

New Zealand
 Riddett Inst
 Plant Food Res



USA

China
 Soochow Univ

360 scientists - 140 institutes – 39 countries

Industry involvement

☞ ~ 40 European companies are involved in INFOGEST





Chair
Didier Dupont - France

INFOGEST



Vice-chair
Alan Mackie - UK



www.cost-infogest.eu

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



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Alan Mackie



Uri Lesmes



Myriam Grundy



Nadja Siegert



Choi-Hong Lai

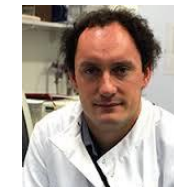


Guy Vergeres

The "Mind-the-Gap" group



Frederic Carriere



Fred Warren



Steven Le Feunteun

In vitro gastro-intestinal digestion

Consensus INFOGEST protocol

Oral phase

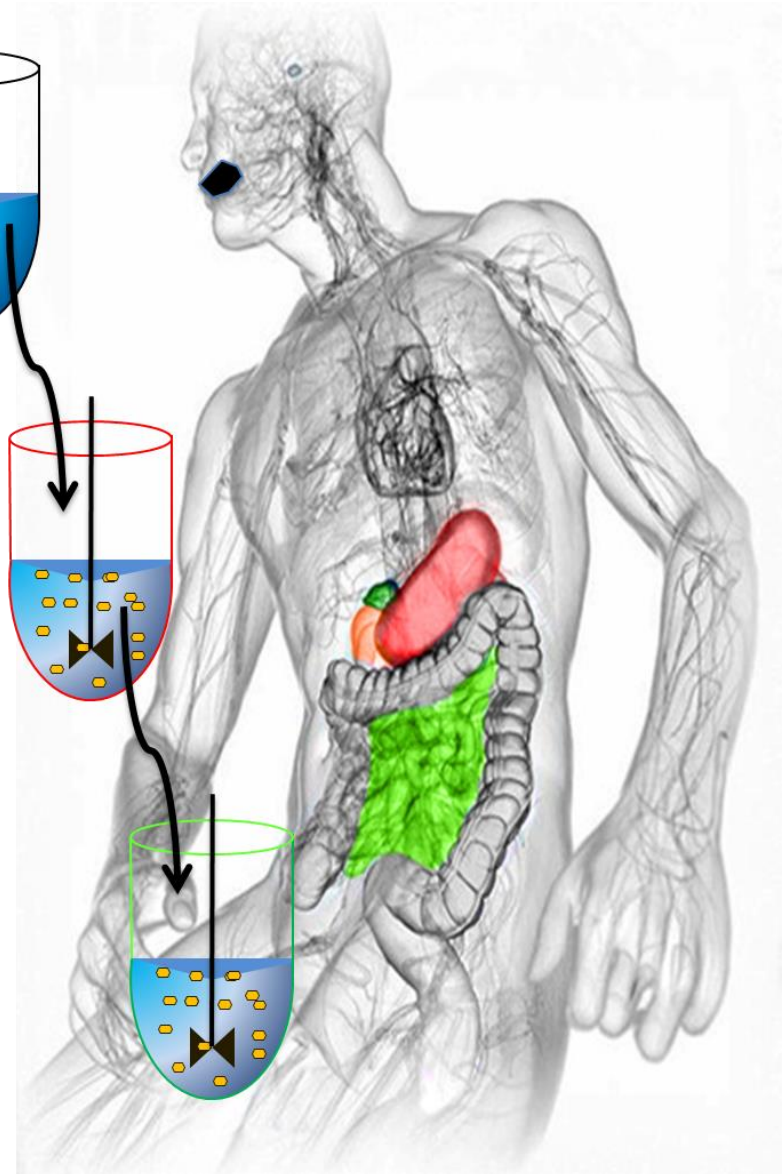
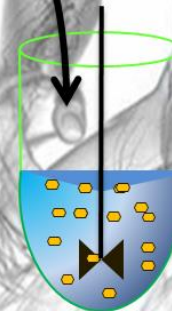
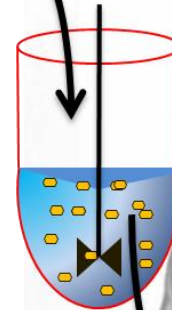
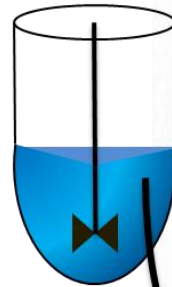
Mix 1:1 with Simulated Salivary Fluid (SSF)
salivary amylase (75 U/mL)
2 min, pH 7

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



The consensus model can be learned with videos on YouTube

Fichier Édition Affichage Historique Marque-pages Outils ?

Intranet UMR STLO - Accueil x GRR (Gestion et Réservatio... x YaZiba: 30/3 - 3/4 x In vitro food digestion - C... x +

https://www.youtube.com/channel/UCdc-NP9kTDGyH_kZCgpQWg youtube

YouTube FR cost infogest

Mettre en ligne Connexion

Vidéos à regarder

LE MEILLEUR DE YOUTUBE


- Populaire sur YouTube
- Musique
- Sport
- Jeux vidéo et autres
- Films
- Émissions TV
- Actualité

Parcourir les chaînes

Connectez-vous maintenant pour consulter vos chaînes et les recommandations.

Se connecter

In vitro food digestion - COST action INFOGEST



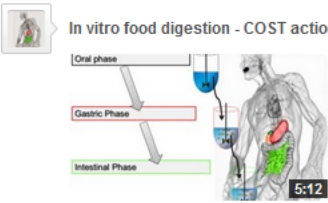
Food Digestion Article S'abonner 36

Accueil Vidéos Playlists Chaînes Discussion À propos

Toutes les activités

In vitro food digestion - COST action INFOGEST a mis en ligne une vidéo. il y a 10 mois

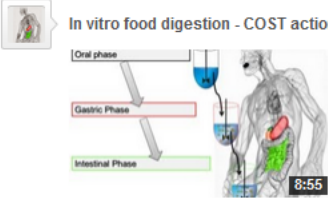
Alpha Amylase Activity Assay for In Vitro Food Digestion
de In vitro food digestion - COST action INFOGEST
il y a 10 mois • 846 vues
A step-by-step description of a static α -amylase activity assay for an in vitro digestion method presented suitable for food; recently published and available online (open access...)



5:12

In vitro food digestion - COST action INFOGEST a mis en ligne une vidéo. il y a 10 mois

Static In Vitro Digestion Method for Food
de In vitro food digestion - COST action INFOGEST
il y a 10 mois • 723 vues
A step-by-step description of a static in vitro digestion method presented suitable for food (international consensus); recently published and available online (open access), see ...



8:55

Chaînes populaires sur YouTube

- Seb la Frite S'abonner
- MissCreatives S'abonner
- LanguedePub / M... S'abonner
- JunkFoodTasterD... JFT S'abonner
- Madame Patachou S'abonner
- halawiyat khadija... S'abonner

https://www.youtube.com



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International Conference
Granada, Spain
April 2019

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in Granada, Spain, 2-4 April 2019