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Structuring foods to improve the bioavailability of bioactives and nutrients

Didier Dupont

► **To cite this version:**

Didier Dupont. Structuring foods to improve the bioavailability of bioactives and nutrients. Nutrition Symposium Institut Pasteur de Lille: Nutrevent conference, Jun 2017, Lille, France. 2017. hal-01542570

HAL Id: hal-01542570

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Submitted on 2 Jun 2020

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The structure of dairy products drives the kinetics of proteolysis and lipolysis in the GI tract and the bioavailability of nutrients

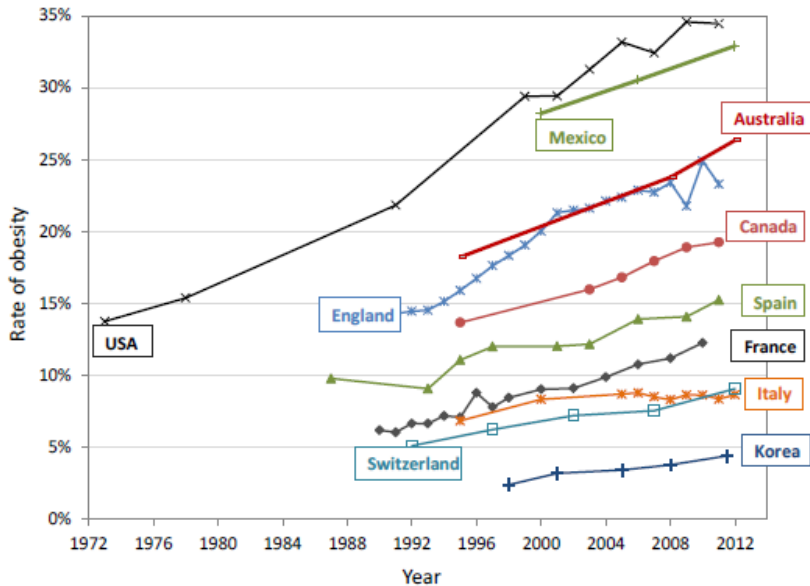


Dr Didier DUPONT

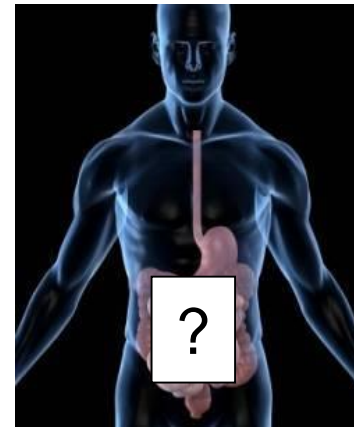
INRA, Rennes, France



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

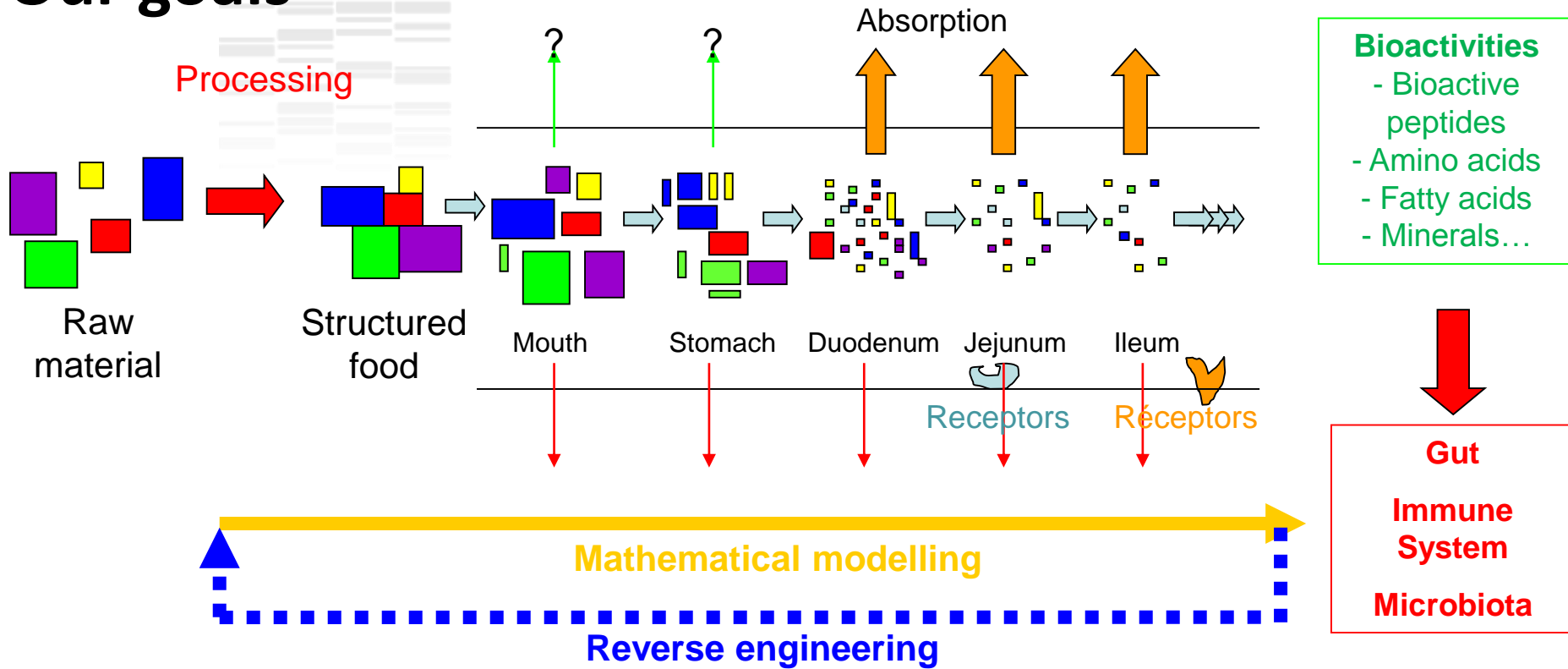
Digestion releases food components that can have a beneficial or a deleterious effect on human health

... 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

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 structure of dairy products modulate their kinetics of digestion



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



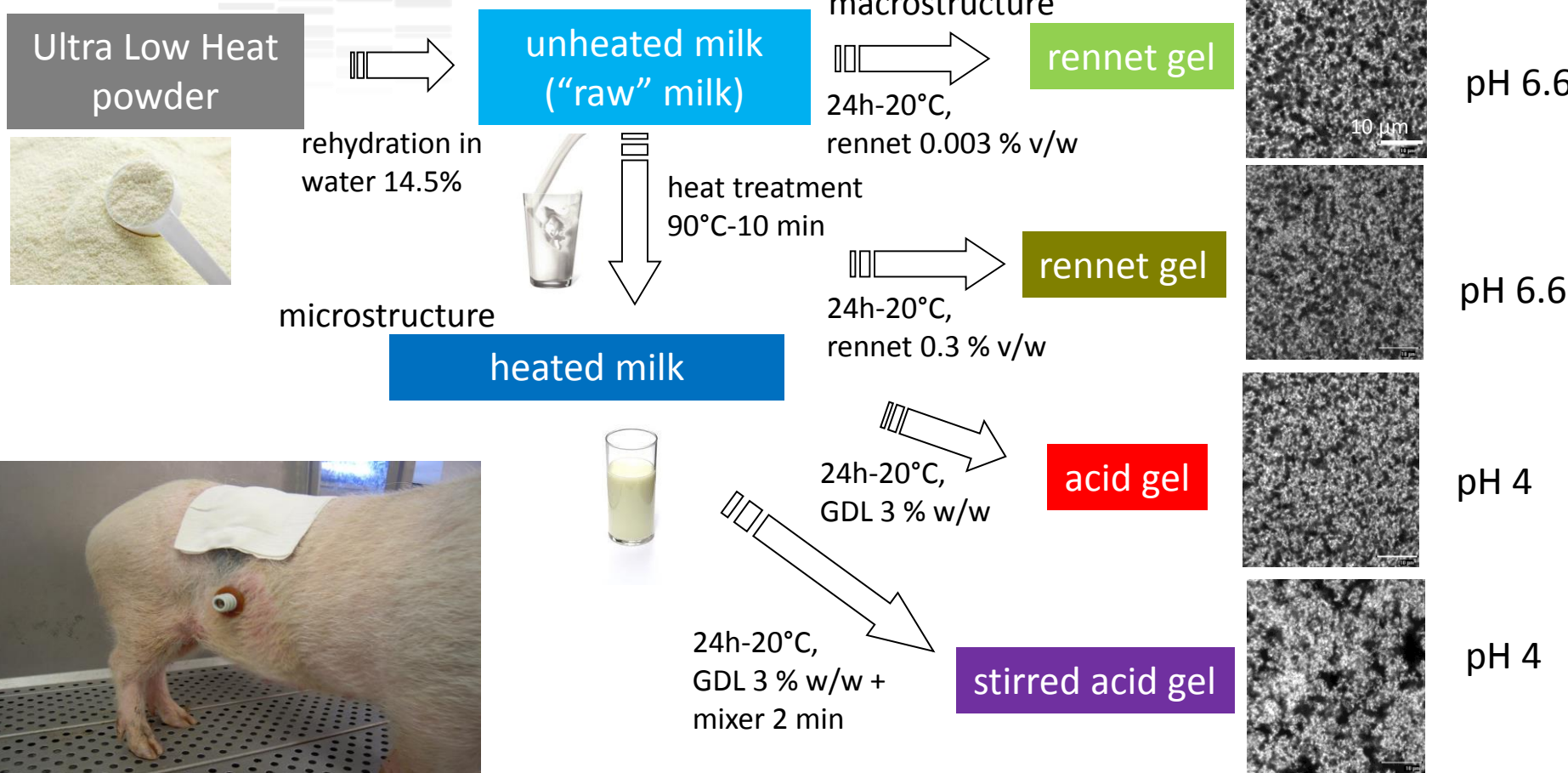
¹ INRA STLO Rennes, France

² INRA UNH Clermont-Ferrand, France

³ INRA MIA Jouy-en-Josas, France

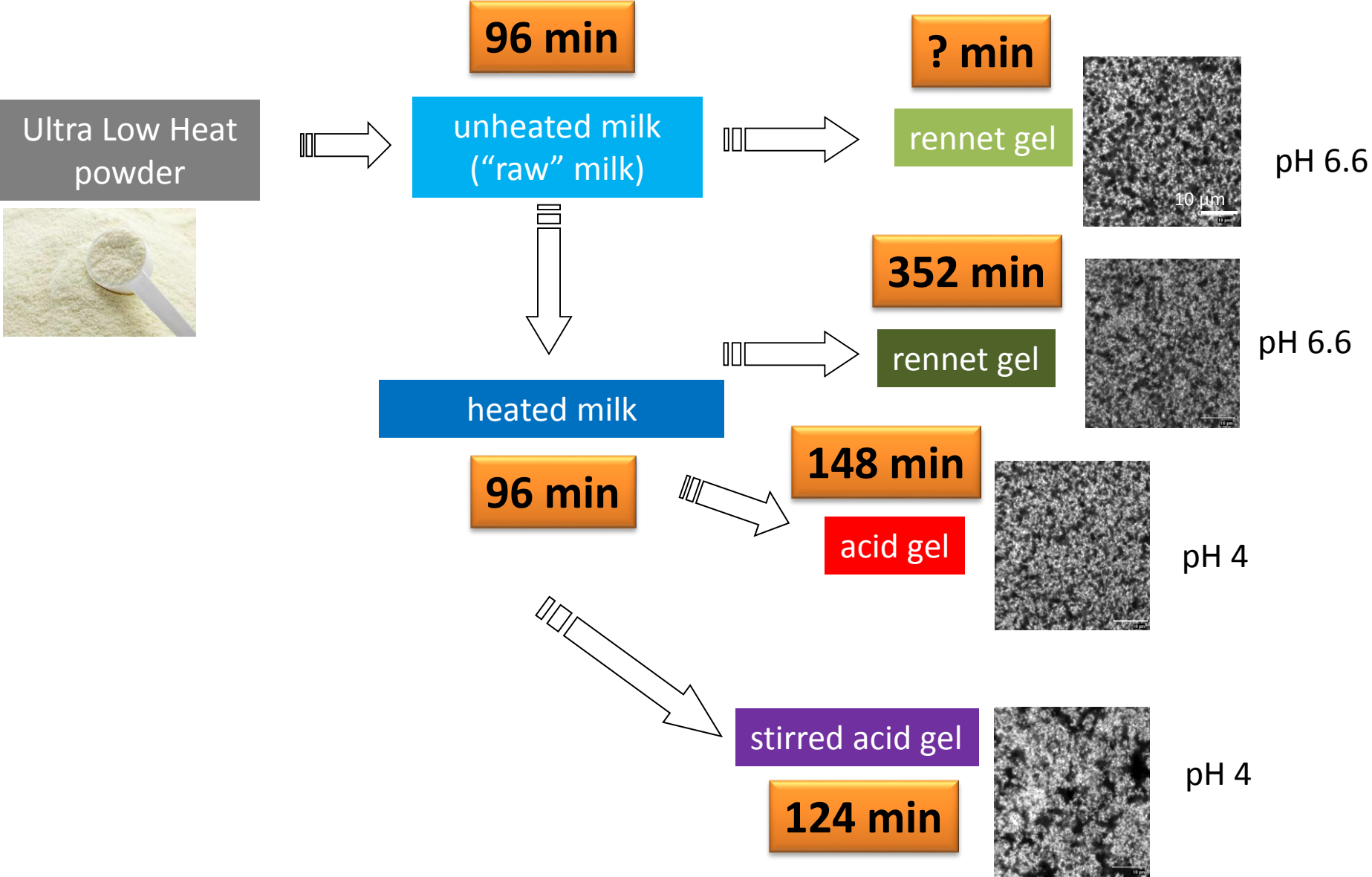
⁴ INRA GMPA Grignon, France

Objective: to compare kinetics of digestion of dairy products of identical composition but different structure

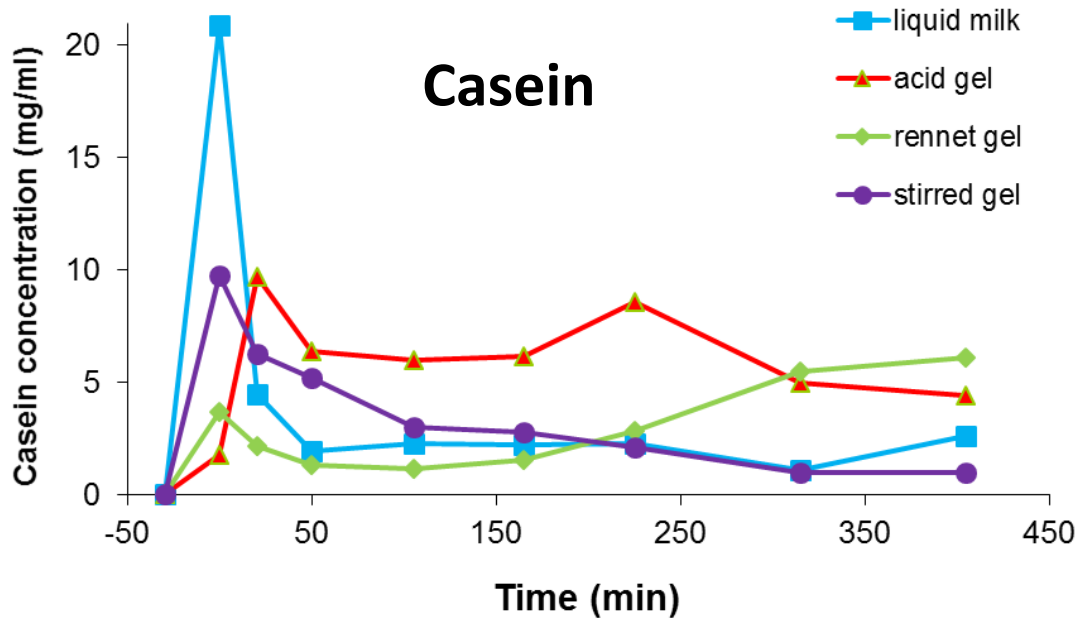


Fat-free matrices: 40 g/L caseins, 10 g/L whey proteins, 95 g/L lactose and minerals
 + marker of the meal transit (Cr²⁺-EDTA) → Gastric emptying half-time

Gastric emptying half-time

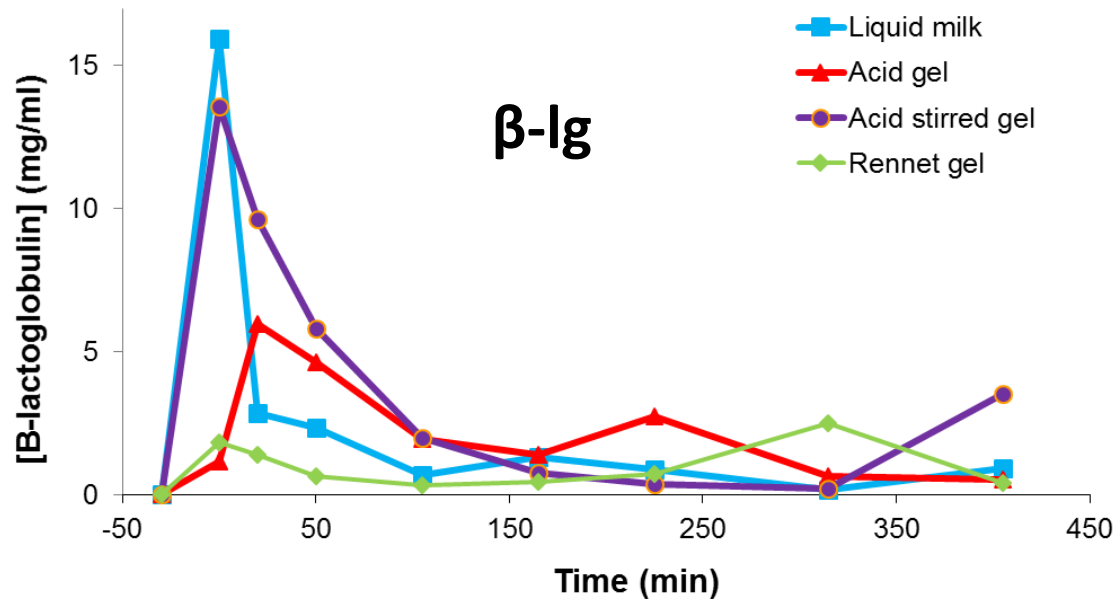


Milk proteins in the duodenum (ELISA)



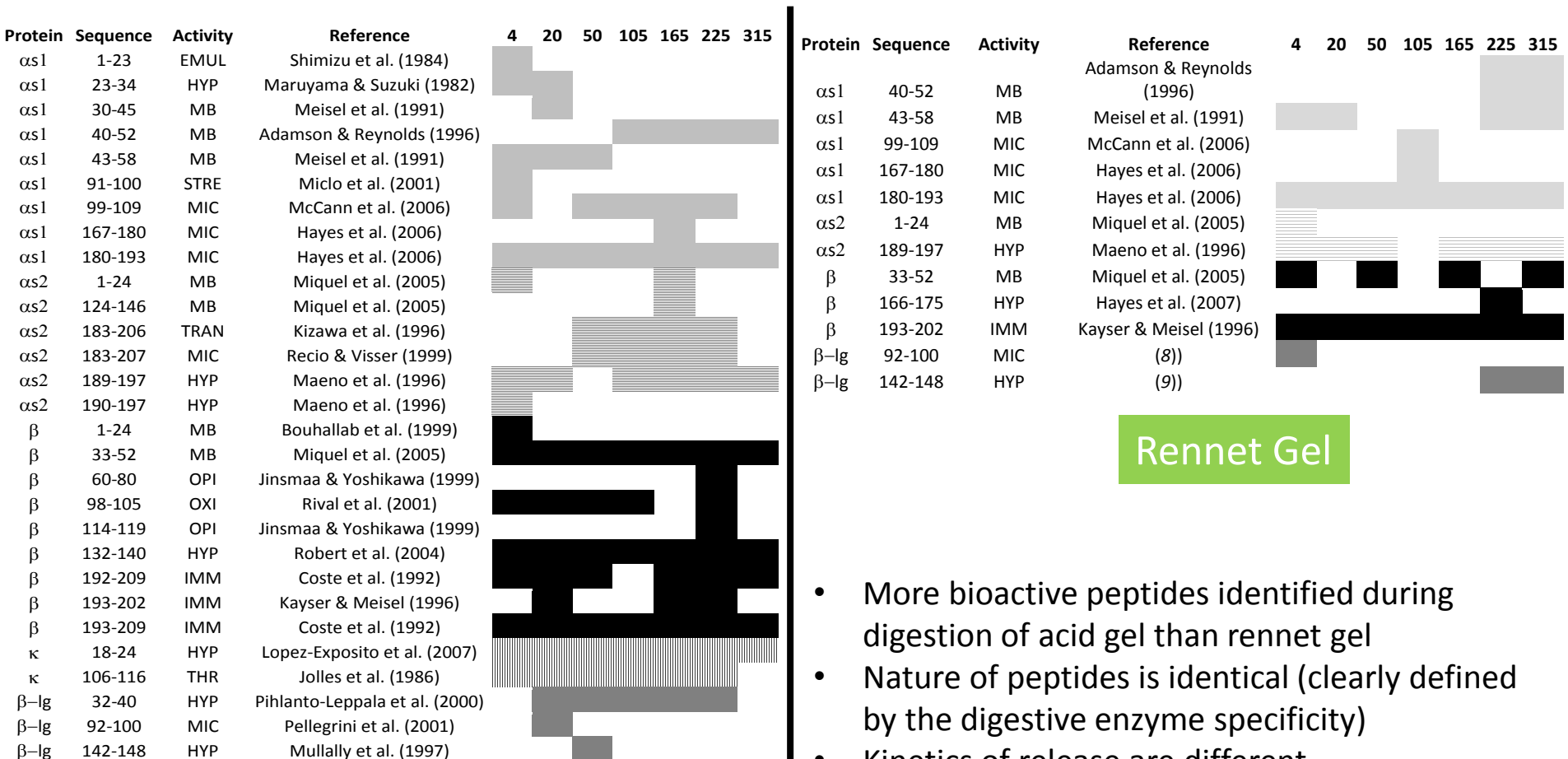
- Intense and early peak with milk
- Lower and delayed with gels
- Intermediate behaviour with stirred gel
- Low concentrations with rennet gel but casein release tends to increase over time

- 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!!!



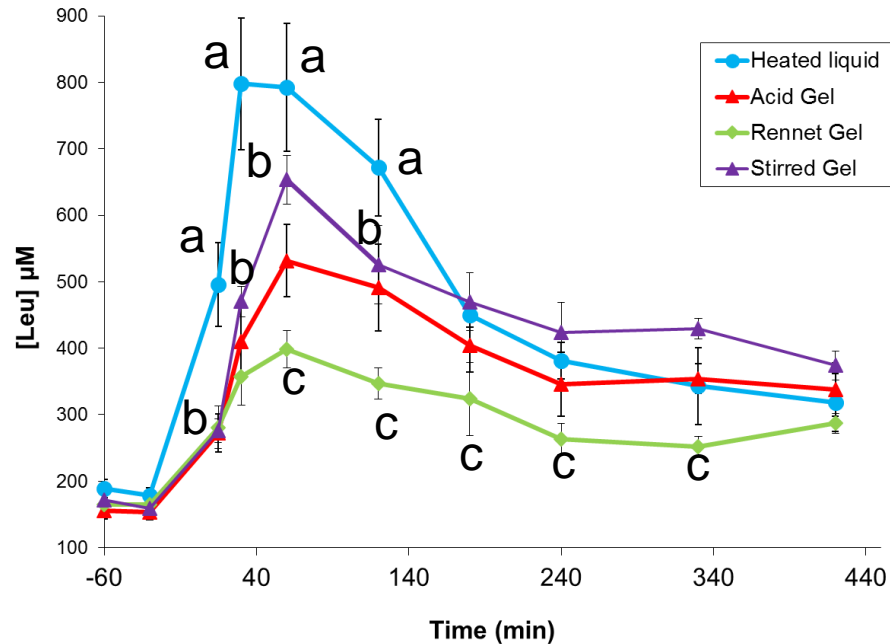
Rennet Gel

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

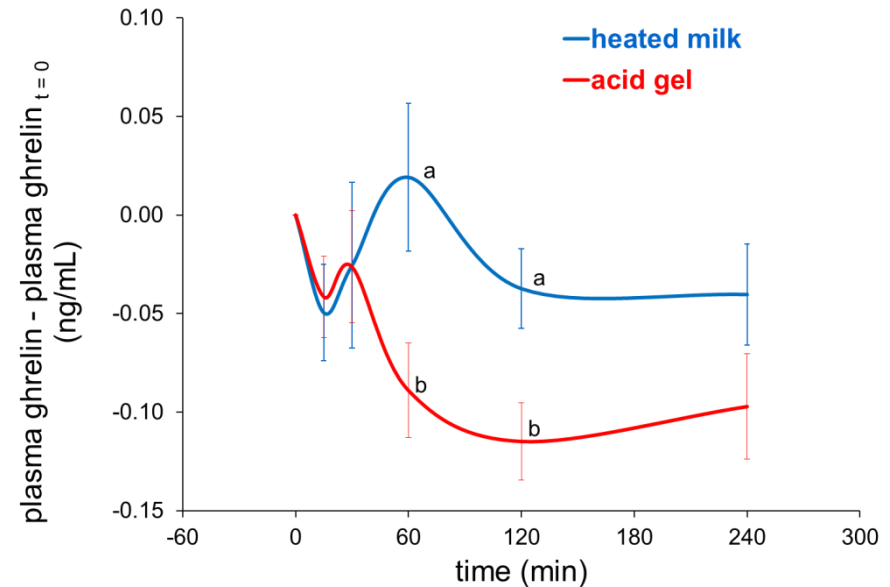


milk gelation:

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

3) potential effect on satiety

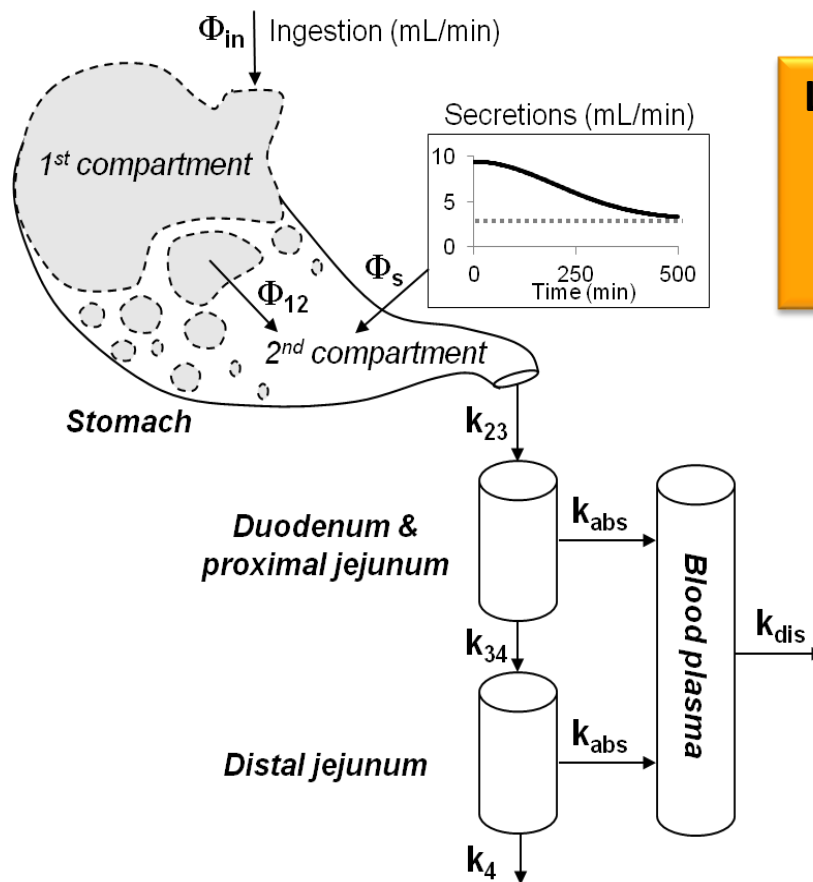
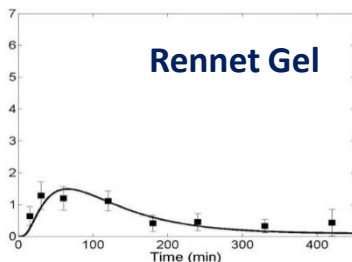
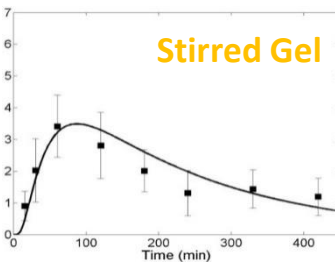
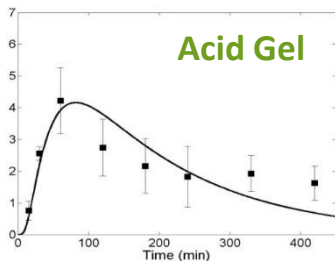
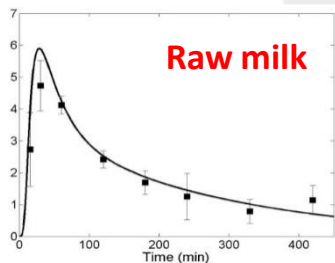
ghrelin (gastrointestinal hormone → appetite stimulation)



milk gelation:

↘ postprandial ghrelin concentration =
 ↗ satiety ?

In silico model of transit and absorption



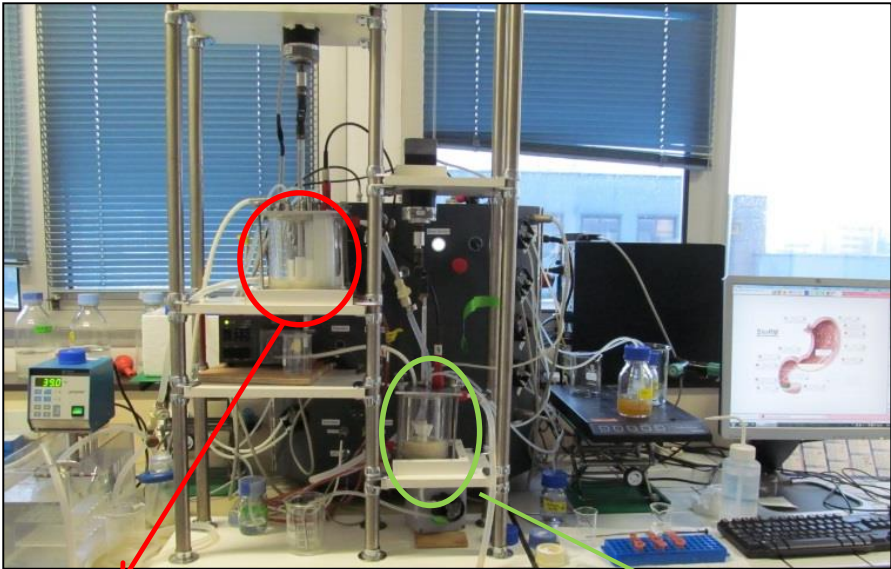
Le Feunteun et al. Food Bioprocess Tech 2014

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



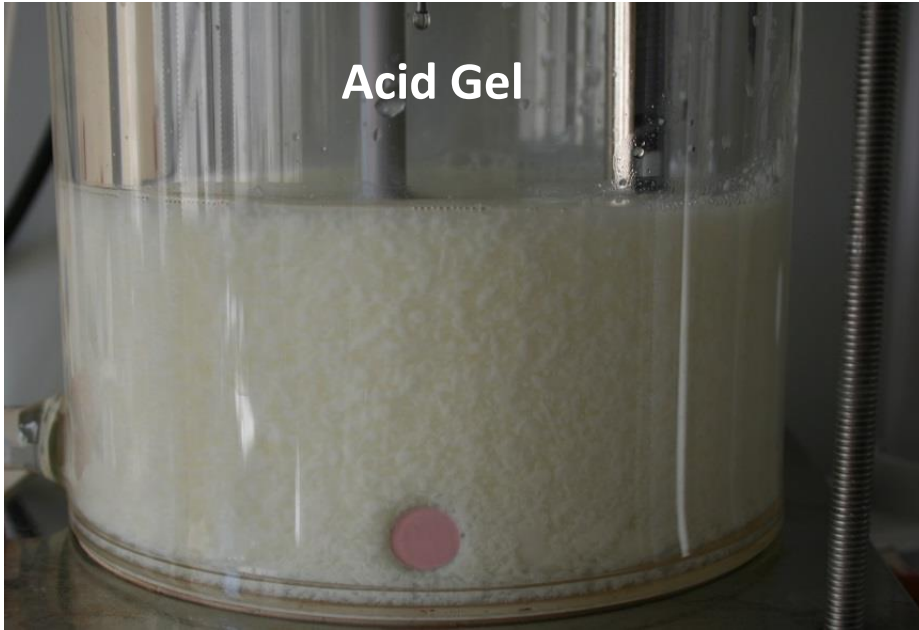
- Pancreatin
- Bile
- Simulated intestinal fluid
- NaHCO₃

Emptying :
Elashoff's model

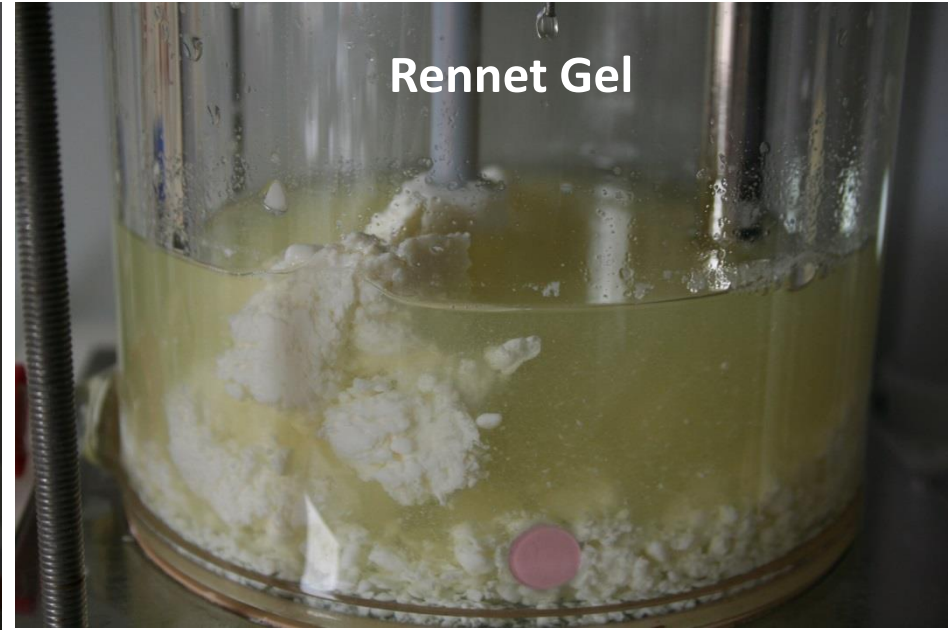
Behaviour of acid and rennet gels in the stomach during *in vitro* dynamic digestion

Barbé et al.
Food Chem. 2014

Acid Gel

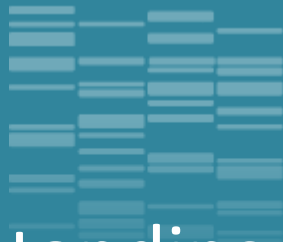


Rennet Gel



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



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



¹ INRA STLO Rennes, France

² SOLEIL Synchrotron Gif-sur-Yvette, France

³ INRA GMPA Grignon, France

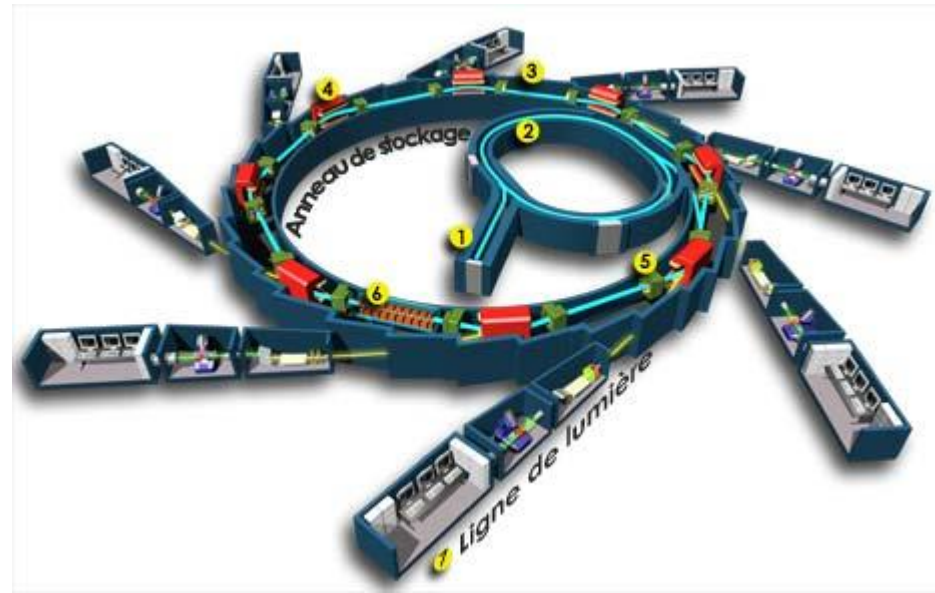


Soleil is a particle (electron) accelerator that produces the synchrotron radiation, an extremely powerful source of light that permits exploration of inert or living matter

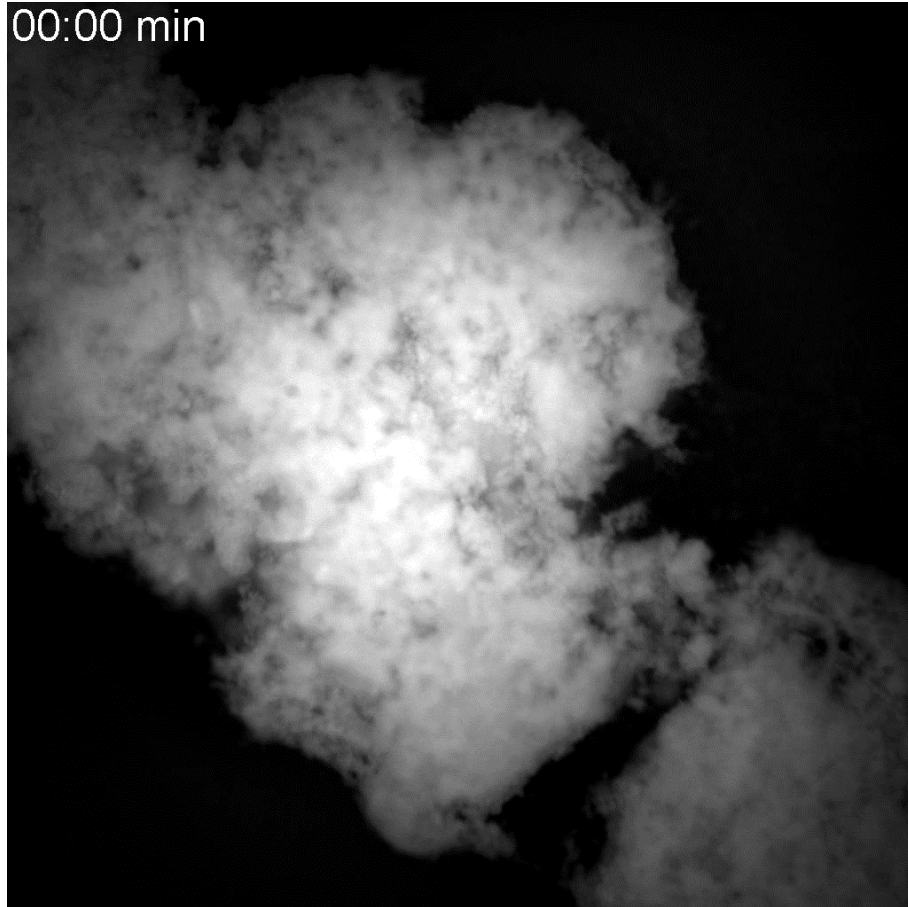
DISCO

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

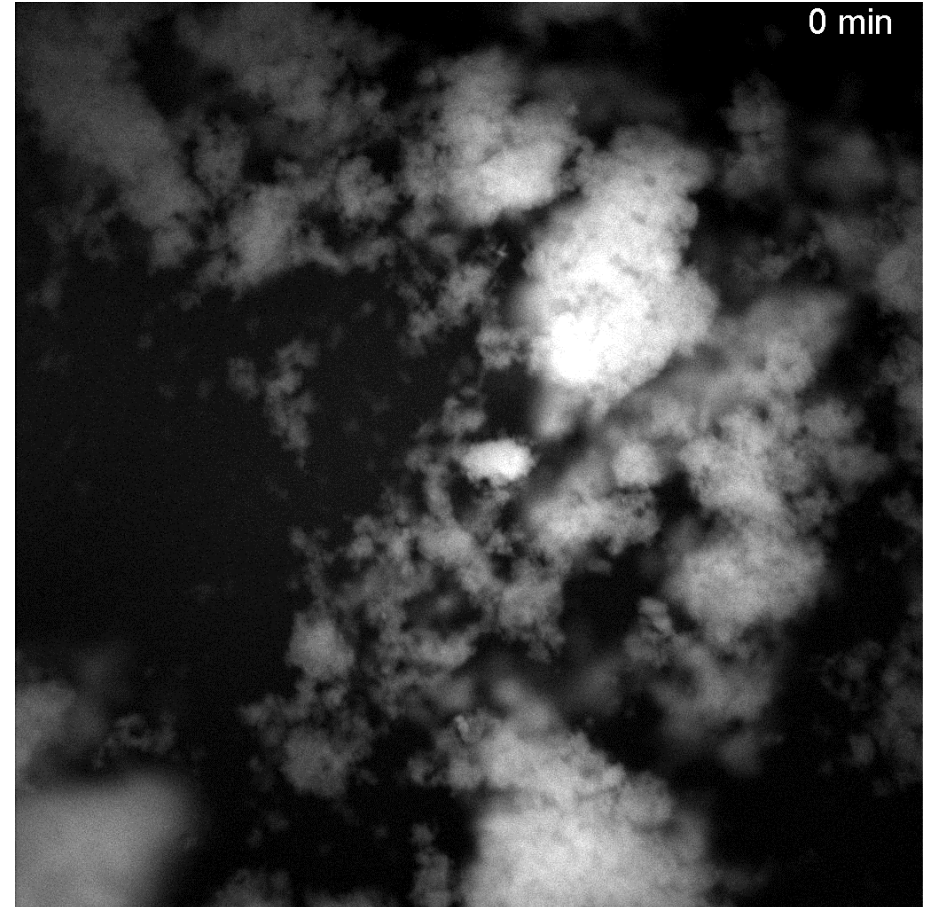
☞ Allow the imaging of protein intrinsic fluorescence with a UV microscope



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



Rennet Gel



Acid Gel

Nutrition of the neonate - Effect of the fat globule homogenization on the digestion of milk macronutrients



Bourlieu C.¹, Ménard O.¹, De Langle A.¹, Rousseau F.¹, Madec M.-N.¹, Deglaire A.¹,
Pezennec S.¹, Robert B.¹, Bouhallab S.¹, Carrière F.², Dupont D.¹



¹ INRA STLO Rennes, France

² CNRS EIPL Marseille, France

Human/ bovine milk / Infant Formula

Protein structures

Human milk



Bovine milk

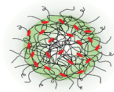


Infant Formula

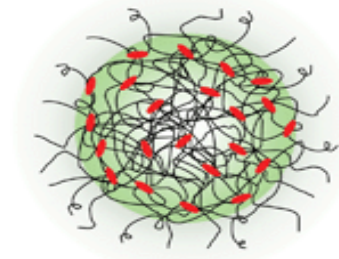


(Turck *et al*, 2010) $\varnothing = 64 \text{ nm}$
(β , κ -casein)

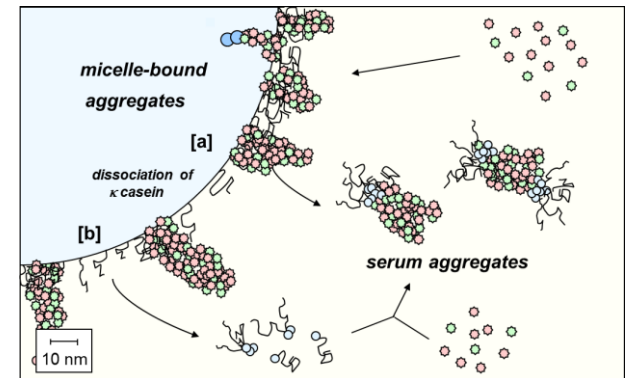
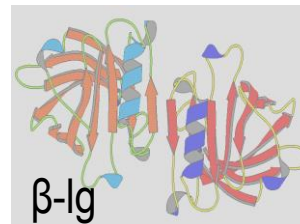
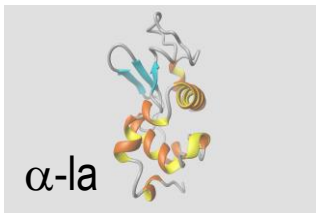
Casein micelle



$\varnothing = 182 \text{ nm}$
(α s1, β -casein)



Whey Proteins



Human/ bovine milk / Infant Formula

Lipid globule structure

Human milk

Bovine milk

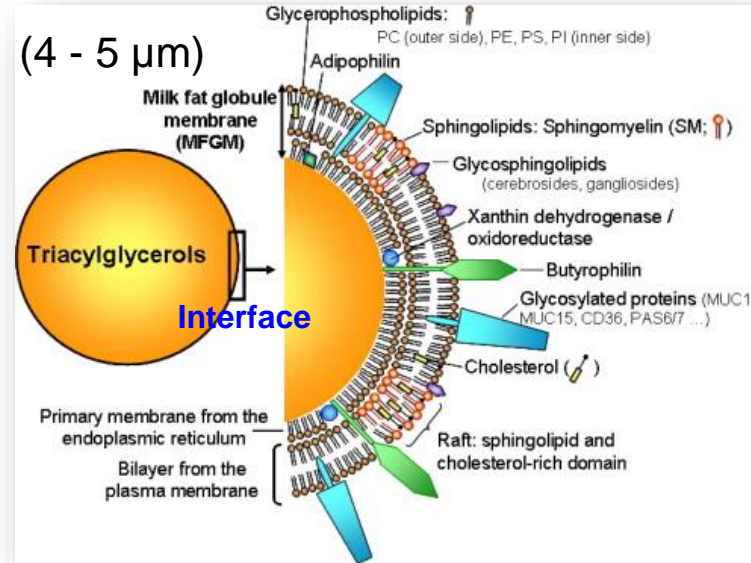
Infant Formula



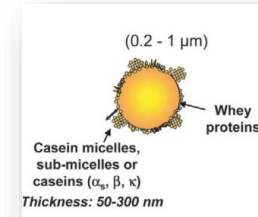
Native milk fat globule

Lipid droplets

Triacylglycerols



(Lopez, 2010)



(0,2 - 1 μm)

(Lopez and Briard-Bion, 2007)

Do technological processes have an impact on the kinetics of lipolysis in the stomach?

Effect of homogenization

2 model infant formulas standardized in fat and proteins

(1.8 % proteins 40:60 caseins/whey proteins, 3.2 % fat with either native or homogenized globules)

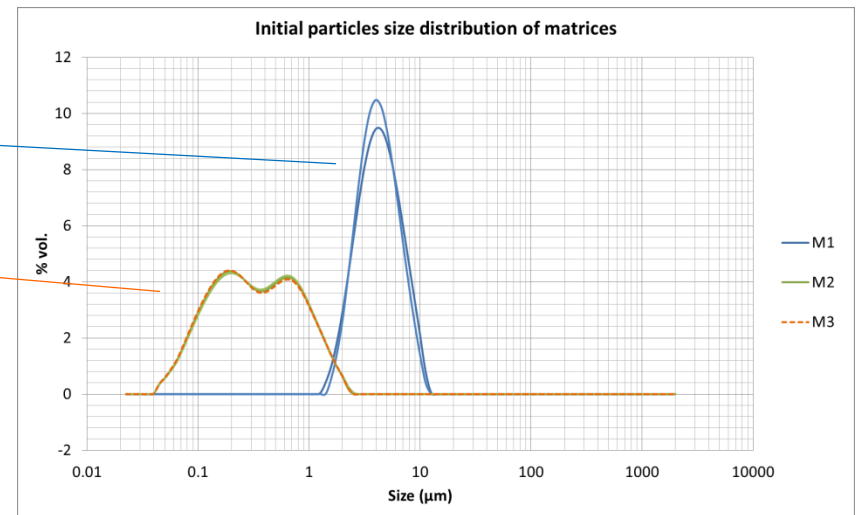
Raw formula
(M1)

Homogenized formula
(M2)

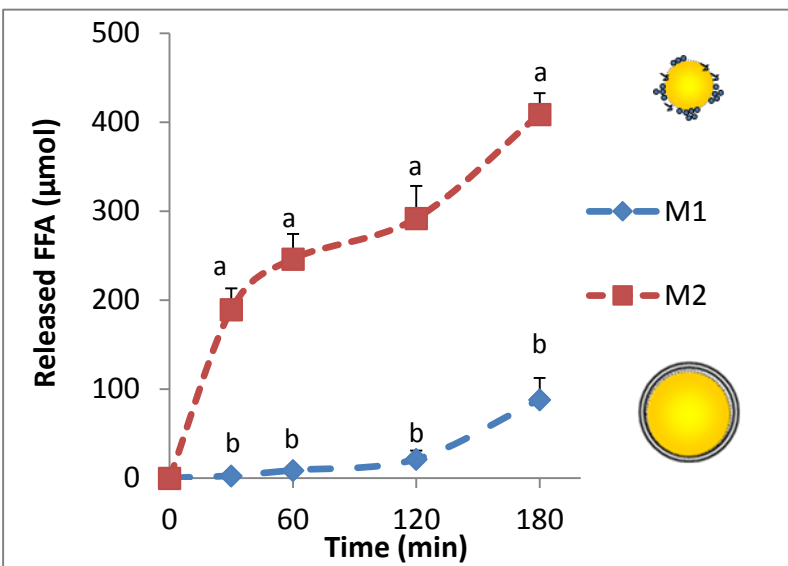
Raw (M1)



Homogenized (M2)

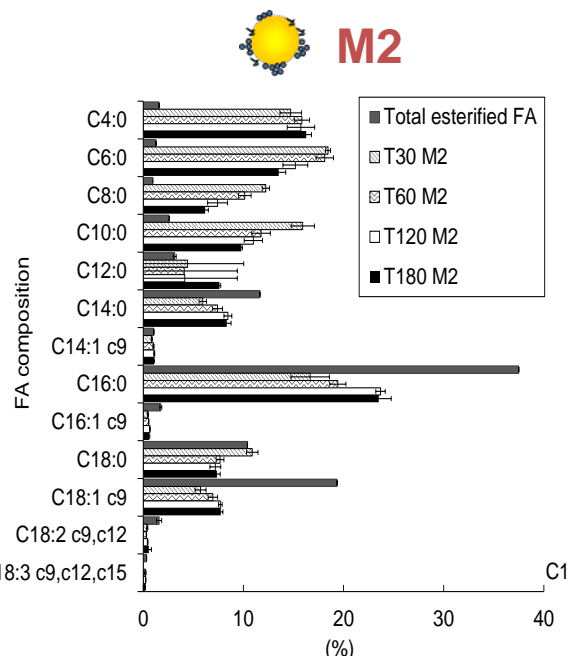
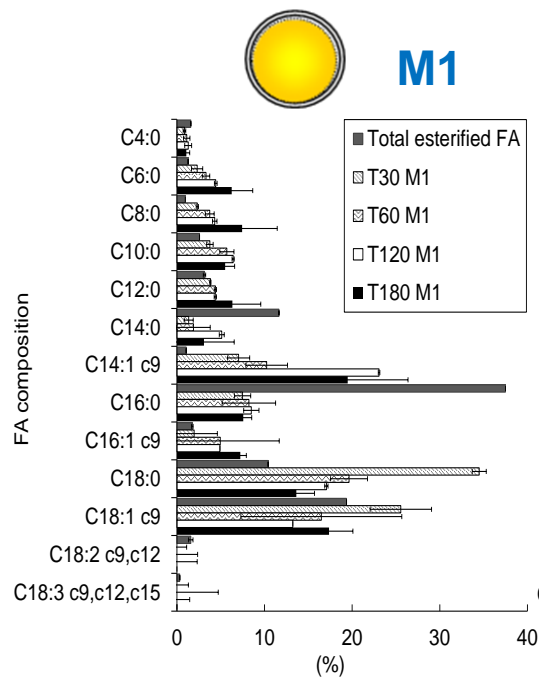


The increased lipolysis of the homogenized formula can be explained by the increase in specific surface of the o/w interface



Specific surface [m ² /g of lipid]	M1	M2
	1.81	31.90

Bourlieu *et al.* Food Chem. 2015



In vivo study in the preterm infant

NCT02112331 (ClinicalTrials.gov)



- Preterm hospitalized infants (GA < 32 wk)
- Nasogastric tube feeding
- Enteral feeding ≥ 120 mL/kg/day at 3 h intervals

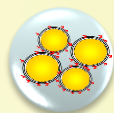
GROUP A

HM from their **own mother**



Raw HM

→ collected < 24h
before feeding

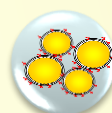


Past HM

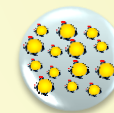
→ 1 pool aliquoted
in 6 bottles

GROUP B

HM from **anonymous donor**



Past HM



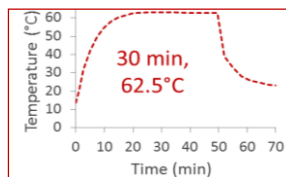
P+Homog HM

→ The same pool from one donor
was used for the two types of milk

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

HM bank

Holder pasteurization



Indirect homogenization
by ultrasonication



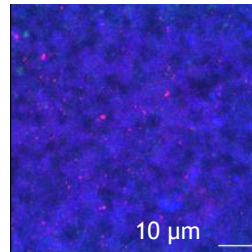
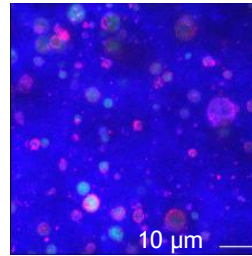
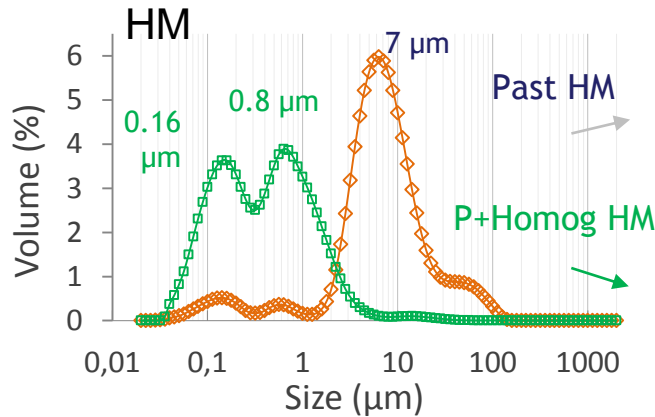
→ 595 W, 3 periods of
5 min interrupted by
30s of pause

Homogenization affected the initial structure and the emulsion disintegration of HM

(n = 5 infants)

Gastric disintegration

Initial structure



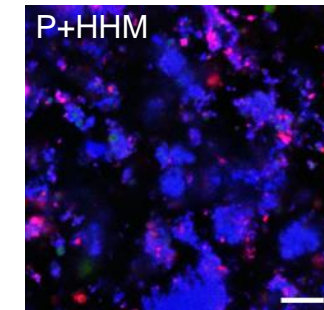
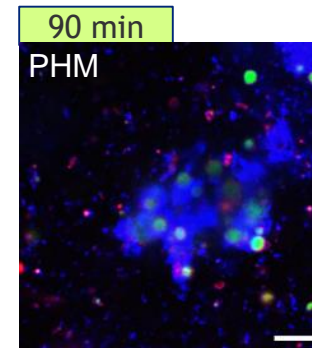
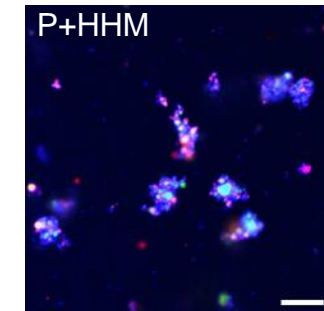
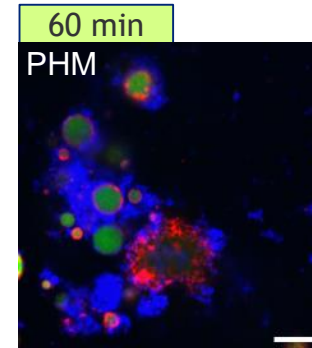
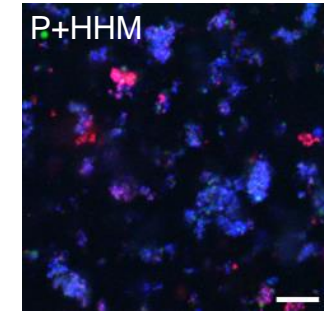
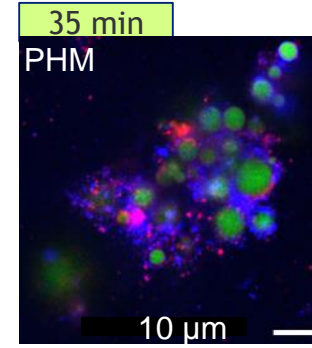
Past HM: $4.1 \pm 1.2 \text{ m}^2/\text{g}$ of fat

P+Homog HM: $25.5 \pm 3.8 \text{ m}^2/\text{g}$ of fat

Disintegration of the emulsion structure after 35 min of gastric digestion

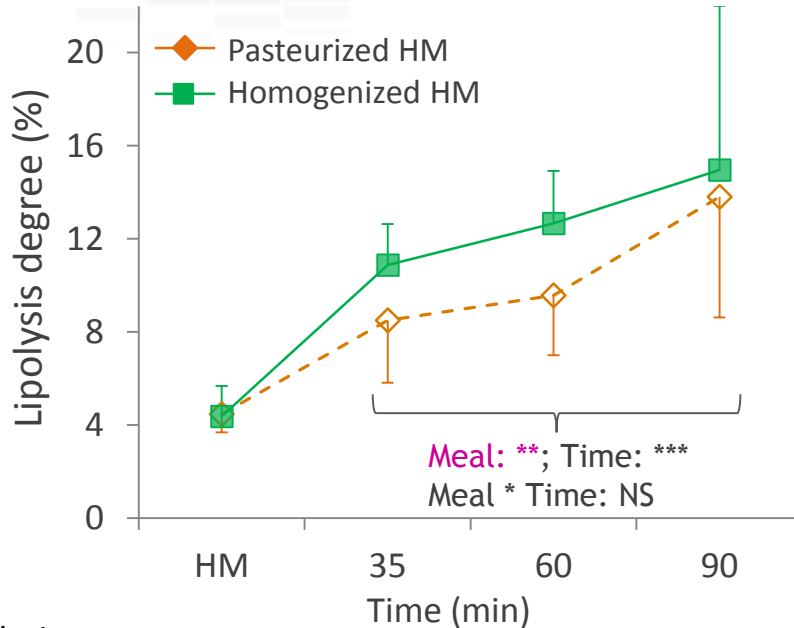
Differences in terms of aggregates morphology

Persistence of native fat globules throughout gastric digestion



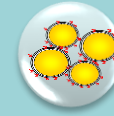
Homogenization impacted gastric lipolysis

Instantaneous lipolysis level

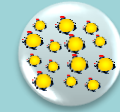


Pre-lipolysis: $4.4 \pm 1.0\%$

De Oliveira *et al.*
Clin Nutr. 2017



Past HM

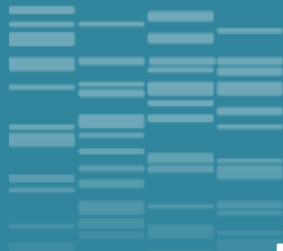


P+Homog HM

- ❖ Same milk composition, initial pre-lipolysis degree and inactivation of BSSL
- ❖ **Different structure**

➔ Increase of specific surface of droplets facilitating HGL adsorption

Human milk homogenization accelerates gastric lipolysis: what are the consequences on the growth and health of pre-term neonates?



Infant formulas

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



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



¹ INRA ADNC Rennes, France

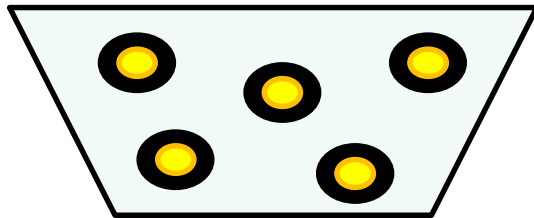
² INRA STLO Rennes, France

³ BIOFORTIS, Saint-Herblain, France

⁴ LACTALIS, Retiers, France

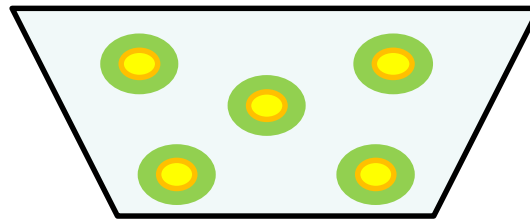
Infant formulas: can we create lipid structures biomimetic on the native fat globule?

Formula T1



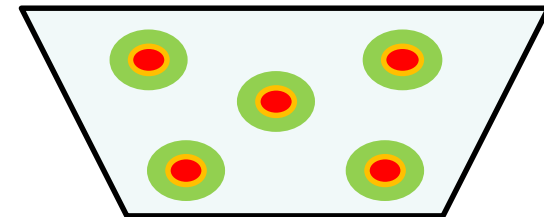
Interface 100 % Proteins
100% vegetable oil

Formula T2

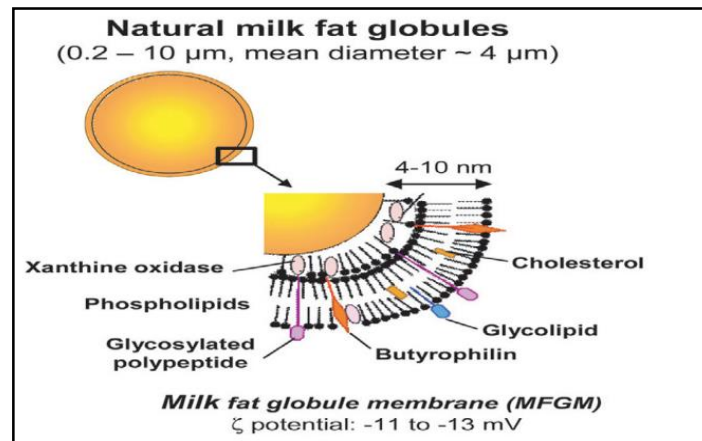


Interface 100 % phospholipids
100% vegetable oil

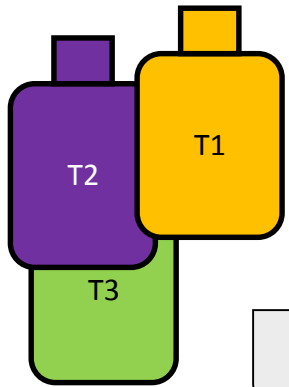
Formula T3



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



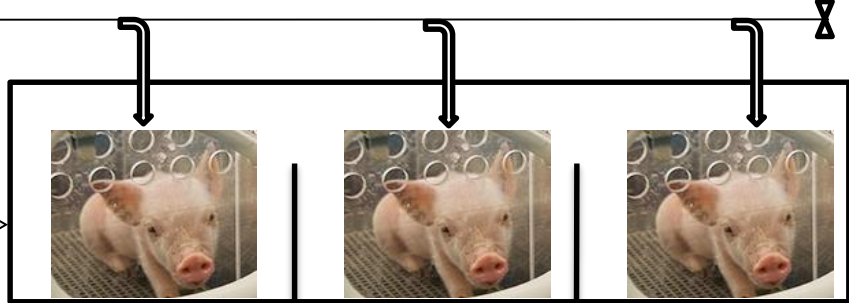
Can the composition of Infant Formula modulate the physiological response of the neonate?



- Veg
- Veg + PL
- Dairy Fat + PL

Rehydration at 20%

Automatic meal delivery (10 meals/ day)



+
Mother-fed piglets
(MF = + control)



Slaughtering after

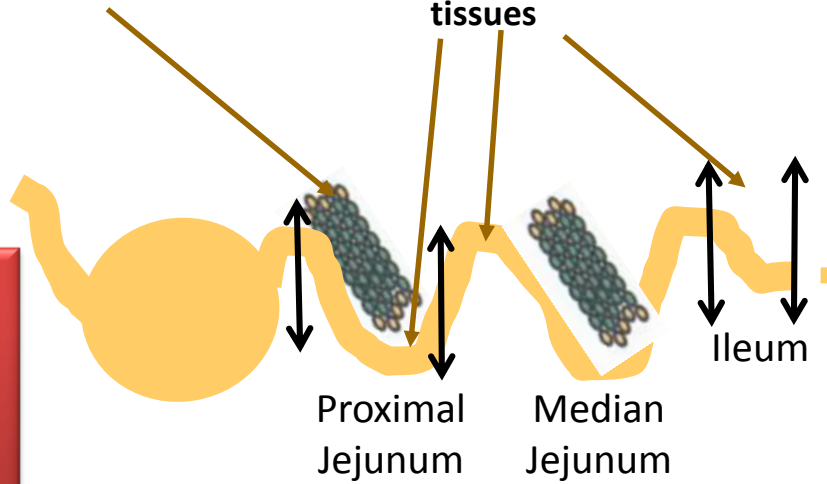
7 days

28 days

(90 min postprandial)

Mesenteric Lymph Nodes (MLN)

Collect of effluents and tissues



Effluents:
-SDS-PAGE
-Elisa

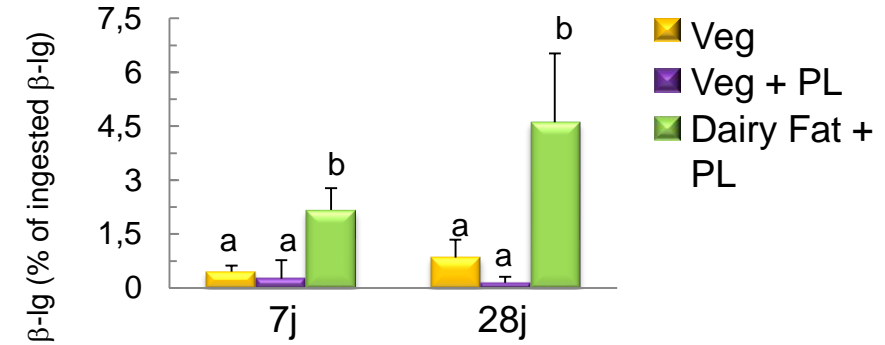
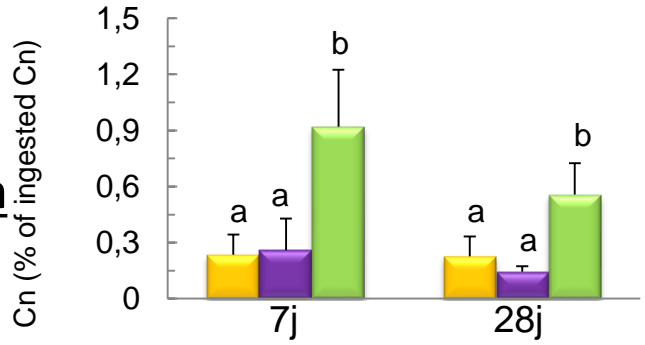
Tissues:
-Morphometry
-Enzyme Activities
-Intestinal Permeability
-Local immune response
-Microbiota

Protein Digestion

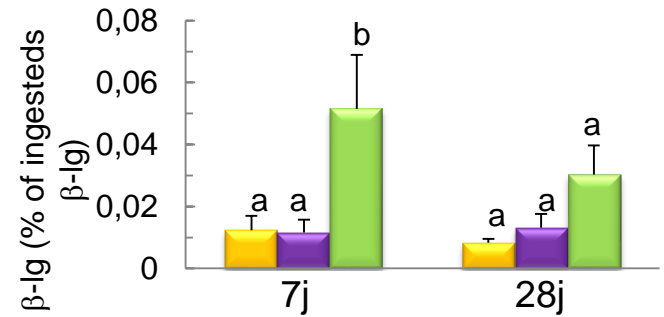
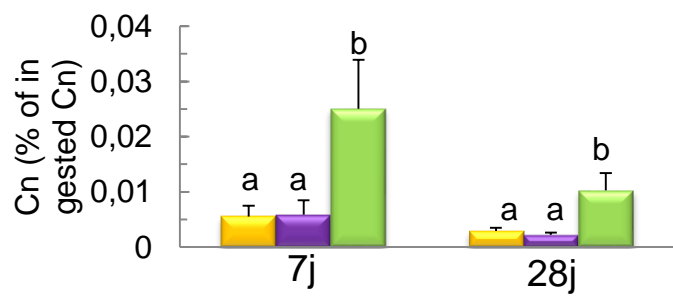
Casein

β -lactoglobulin

Jejunum



Ileum



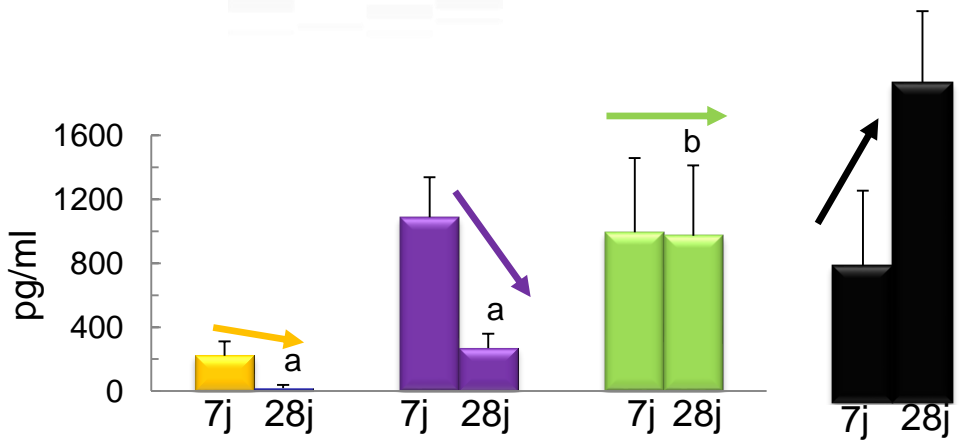
Milk Proteins better resist to intestinal digestion in the presence of dairy fat

➔ Modification of the interface

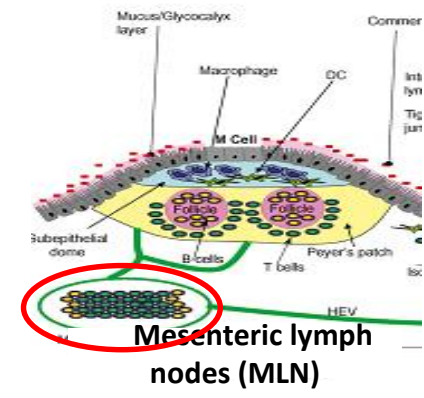
(Granger *et al* 2005; Davies *et al*, 2001)

Secretory activity of MLN

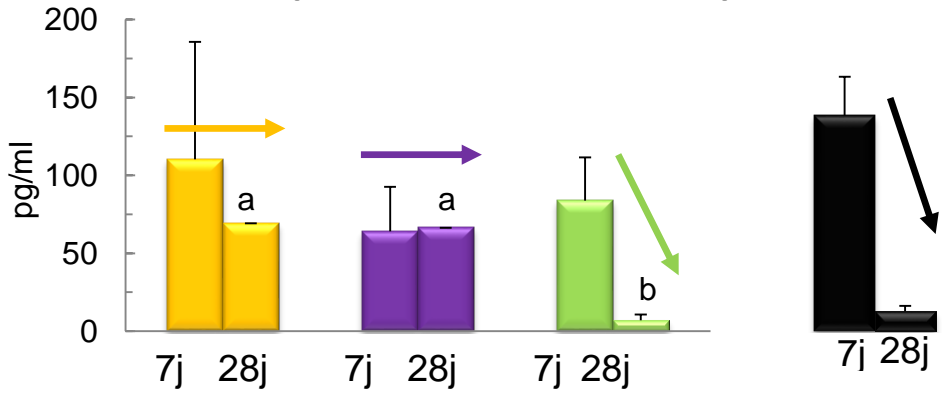
Interferon-g (Th1 pro-inflammatory)



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



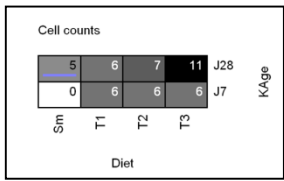
Interleukine-10 (Th2 anti-inflammatory)



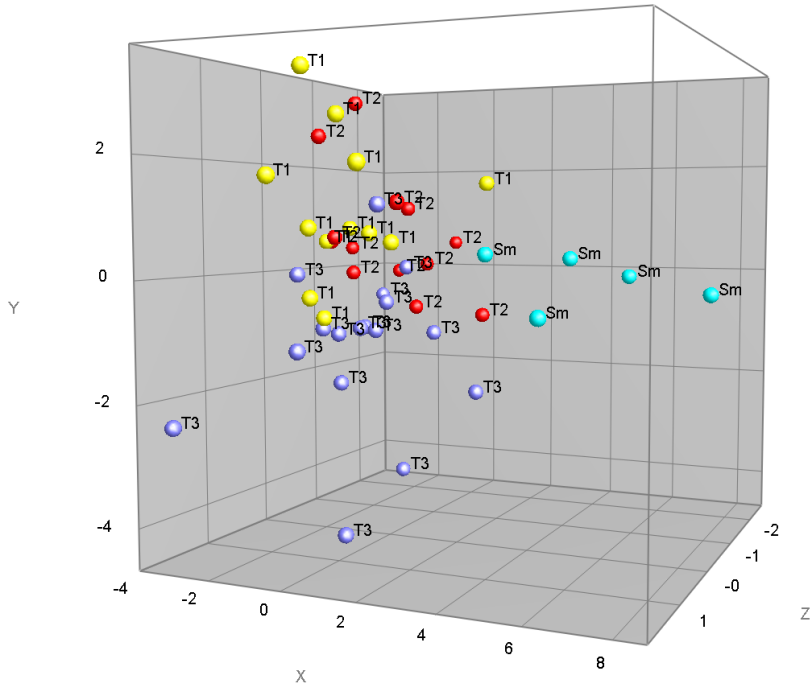
Milk lipids → maturation of the piglet's immune system more similar than with sow's milk

**Le Huerou-Luron *et al.*
Eur J Nutr. 2016**

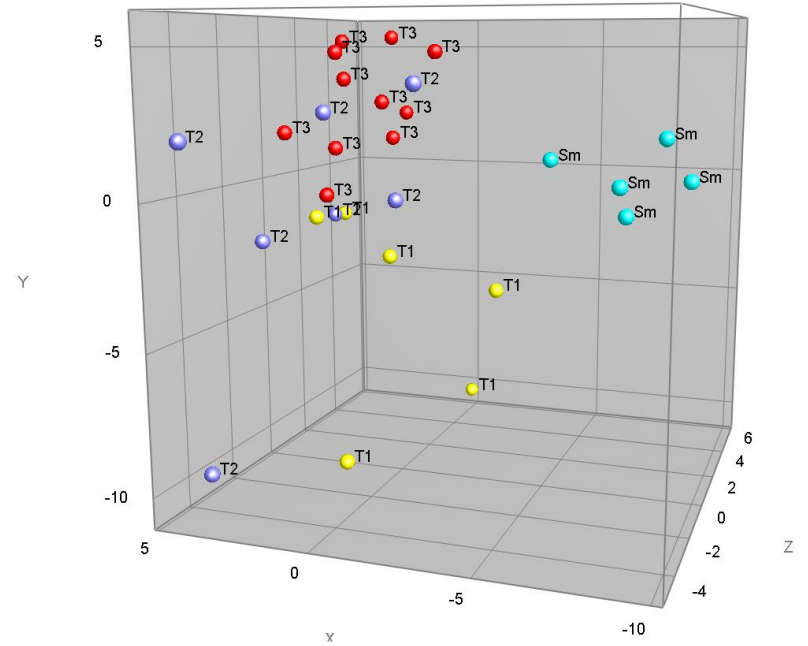
Microbiota by DHPLC



D7 & D28



D28



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

More Proteobacteria with milk fat /
More Firmicutes with plant oil



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 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

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●
INFOGEST
●





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 Plant Food Res



Argentina



Australia



Albania



Montenegro



USA



New Zealand

350 scientists - 130 institutes – 38 countries

Industry involvement

☞ ~ 40 European companies are involved in INFOGEST





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Didier Dupont - France



Vice-chair
Alan Mackie - UK

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In vitro/in vivo
correlations
WG1

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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

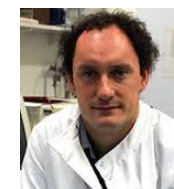


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The "Mind-
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Fred Warren



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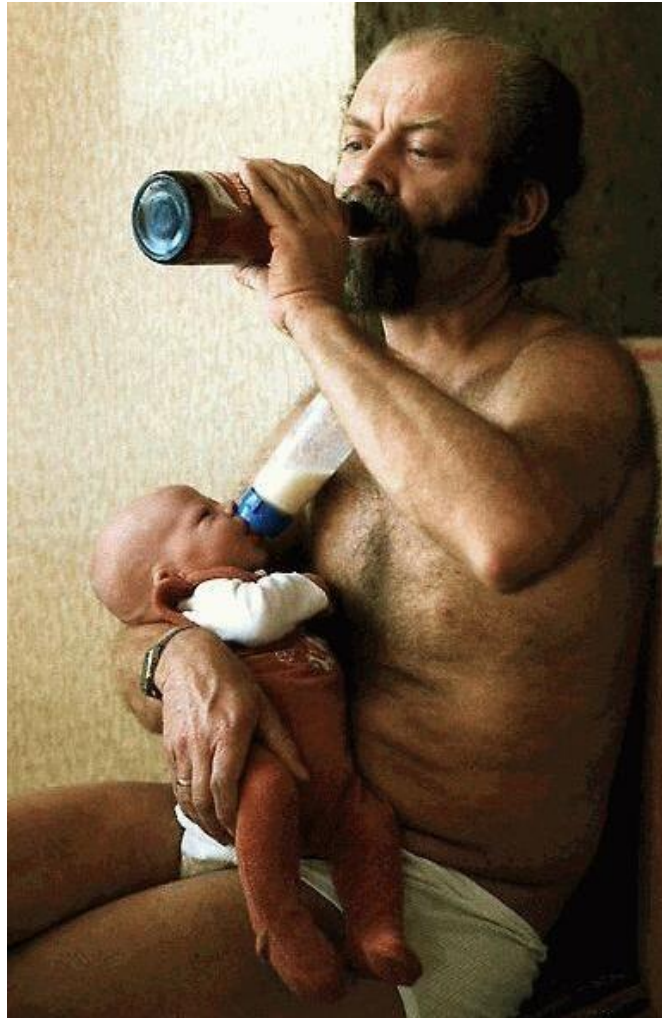
INFOGEST
International Conference
Granada, Spain
April 2019

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



in Granada, Spain, April 2019

Improving infant formula for improving human life...



Thanks for your kind attention !!!