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

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

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

- **Ultra Low Heat powder**
- **unheated milk (“raw” milk)**: 96 min → ? min
  - **re混合 gel pH 4**
  - **re混合 gel pH 6.6**
- **heated milk**: 96 min → 148 min → 352 min
  - **酸 gel pH 4**
  - **stirred acid gel**
  - **stirred acid gel pH 4**
  - **stirred acid gel pH 6.6**

pH values:
- pH 4
- pH 6.6
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

Casein

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

β-lg
### β-cn peptides released in the duodenum during digestion of acid gels

<table>
<thead>
<tr>
<th>Time of digestion</th>
<th>β-casein sequence</th>
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<tr>
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<tr>
<td>5h 15 min</td>
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Bioactive peptides released during digestion differ from one matrix to another

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<tr>
<th>Protein</th>
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<th>Activity</th>
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<tr>
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<td>EMUL</td>
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<td>HYP</td>
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<td>167-180</td>
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<td>1-24</td>
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<td>124-146</td>
<td>MB</td>
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- 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
The liquid-gel transition

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

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

Le Feunteun et al. Food Bioprocess Tech 2014
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

- Pepsine
- Gastric lipase
- Simulated gastric fluid
- HCl

Stomach

Small intestine

- Pancreatin
- Bile
- Simulated intestinal fluid
- NaHCO₃

Emptying: Elashoff’s model

DIDGI®

StoRM® software
Behaviour of acid and rennet gels in the stomach during \textit{in vitro} dynamic digestion

Formation of a strong coagulum with rennet gel $\rightarrow$ 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

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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: comparison of rennet/acid gel
Effect of processing on the digestion of milk macronutrients – The case of homogenization

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

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

2 model infant formulas standardized in fat and proteins

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

**Effect of homogenization**

- **Raw formula (M1)**
- **Homogenized formula (M2)**

![Initial particles size distribution of matrices](graph.png)
The increased lipolysis of the homogenized formula can be explained by the increase in specific surface of the o/w interface.

Bourlieu et al. Food Chem. 2015
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
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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% phospholipides, 40% vegetable oil + 60% milk fat

![Image of natural milk fat globules](link)
Can the composition of Infant Formula modulate the physiological response of the neonate?

Automatic meal delivery (10 meals/ day)

Mesenteric Lymph Nodes (MLN)

Collect of effluents and tissues

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

Effluents:
- SDS-PAGE
- Elisa

+ Mother-fed piglets (MF = + control)

Rehydration at 20%

Slaughtering after
- 7 days
- 28 days
(90 min postprandial)
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)
Interferon-γ (Th1 pro-inflammatory)

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

Interleukine-10 (Th2 anti-inflammatory)
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.

[Diagram showing Release Rate with Overweight/diabetic and Elderly/Athletes at opposite ends]
The Bioactivity & Nutrition team

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Rachel BOUTROU – Junior Scientist
Amélie DEGLAIRE – Lecturer
Juliane FLOURY – Lecturer
Catherine GUERIN - Lecturer
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Olivia MENARD
Jordane OSSEMOND

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

COST Action FA1005

Dr. Didier DUPONT, Senior Scientist, INRA, France

INFOGEST

June 2011 – May 2015
340 scientists - 130 institutes – 37 countries
We are pleased to announce the next

5th International Conference on Food Digestion

in Rennes, France, 4-6 April 2017