# Understanding and modeling the disintegration of food in the gastrointestinal tract and its consequences on human health

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INRA Agrocampus Ouest – Milk and Egg Science & Technology
Rennes FRANCE

Trilateral Workshop on
**Innovative Health Promoting Food**
**Berlin 29-30 September 2011**

# Milk & Egg Science & Technology

75 permanent staffs

135 people in total

## Our disciplinary skills

**Biochemistry**
**Microbiology**
**Molecular biology**
**Process & technology**

*In situ* systems

Model systems

## Our facilities

**Mass spectrometry**
**Confocal microscopy**
**Quantitative PCR**
**Isothermal calorimetry**
**Technology platform**
**Biological Resource Centre**

# Understanding the disintegration of food in the GI tract

Link between food and human health = top research priority

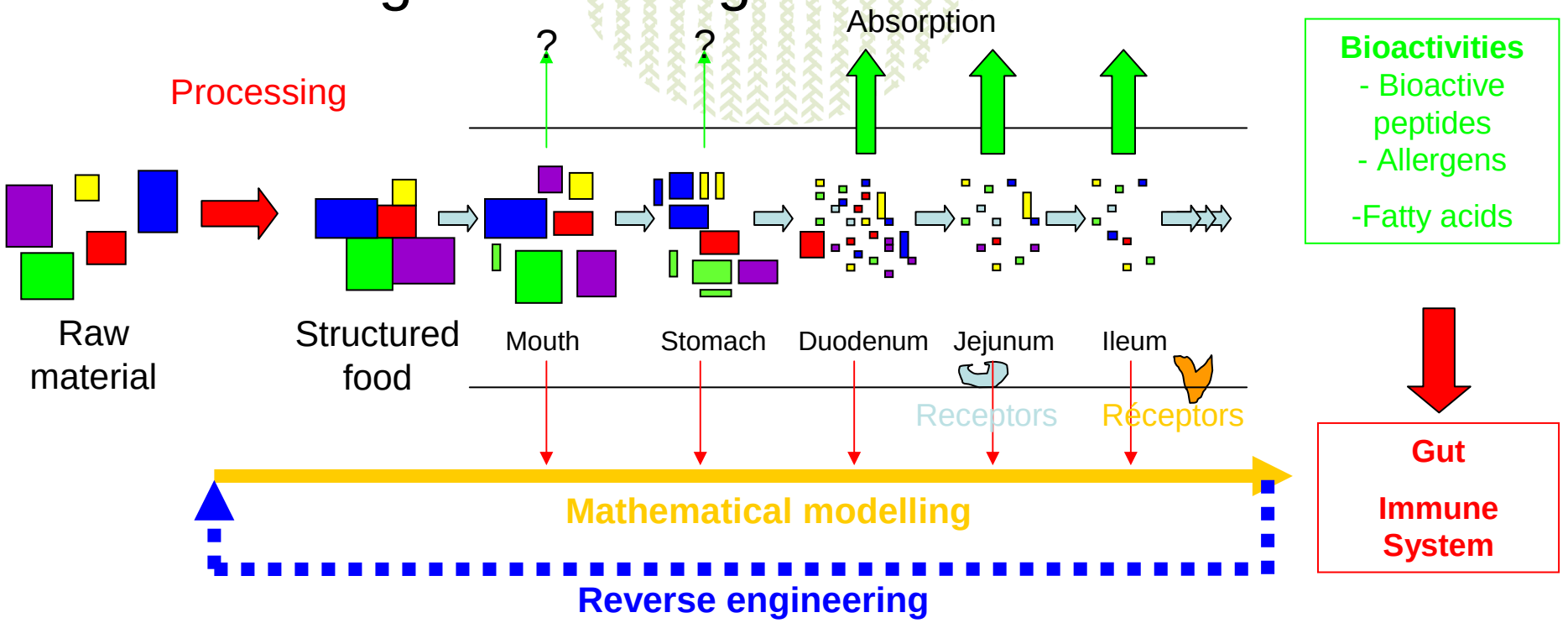
It is also a consumer demand

After ingestion, food are broken down in the gut during digestion, delivering nutrients and biological signals to the body

↳ It is of crucial importance to understand how food are disintegrated in the GI tract and to identify the bioactive molecules released during digestion

**Understanding the effect of food on human health**

# Understanding the disintegration of food in the GI tract

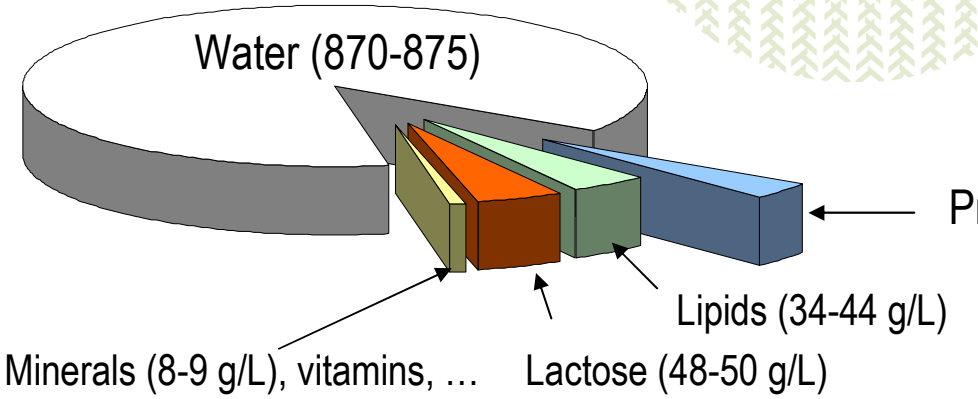



☞To understand the mechanisms of breakdown of food matrices and their constituents in the gut and identify the beneficial/deleterious food components released

☞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

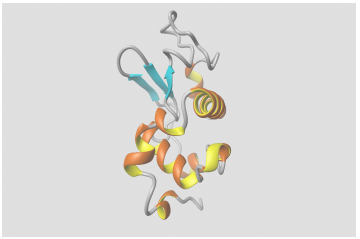
# Milk

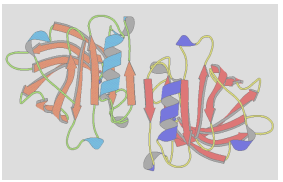



Proteins (32-35 g/L)

Caseins (80%)
$\alpha s_1$, $\alpha s_2$, $\beta$, $\kappa$

Whey Proteins (20%)
$\alpha$-la, $\beta$-lg

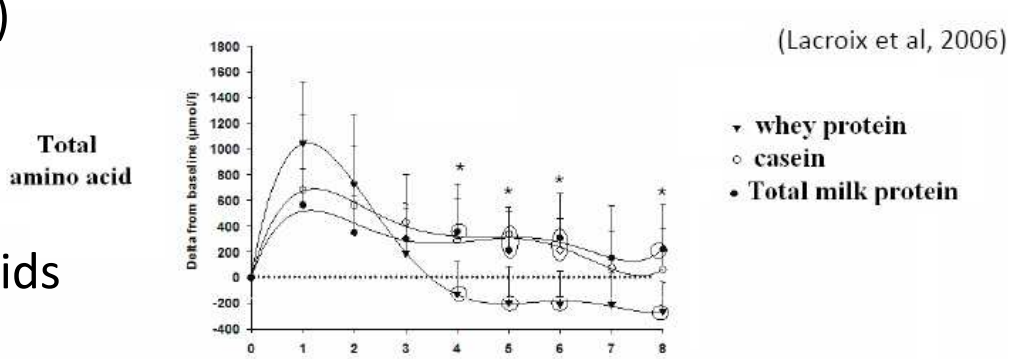




Caseins and whey proteins are:

- Structurally opposite (globular/flexible)
- Differently metabolized (fast/ slow proteins)
- Highly digestible (>95%)
- Excellent sources of essential amino acids

(Lacroix et al, 2006)



# Infant formula

☞ Only alternative to the newborn when breast-feeding is not possible

☞ A key food at a key stage of human life

Only stage of life where milk is the only food in the human diet

Nutritional imprinting (effect of the newborn diet on the pathologies he will develop later)

☞Efforts have been made in order to mimic human milk composition

CN/WP = 40/60

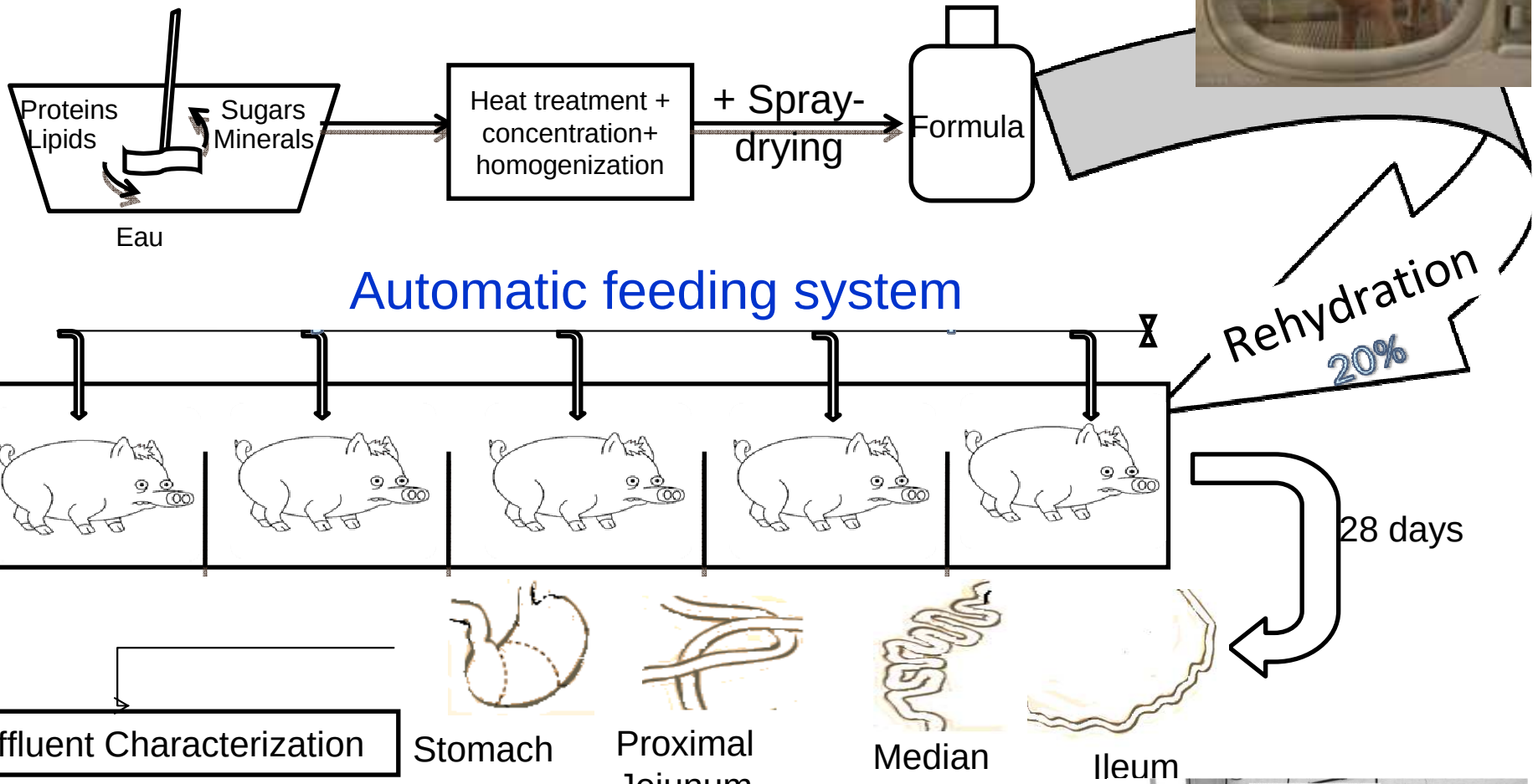
Up to 50 ingredients are added

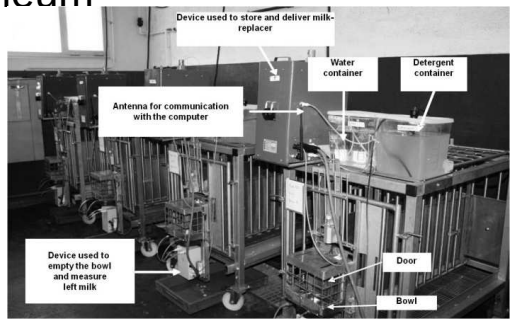
☞ Difficult (impossible?) to study IF digestion in the newborn for ethical reasons

☞ Needs relevant *in vitro* and animal models

☞ **Study of the IF protein kinetics of digestion in the piglet**

# *In vivo* digestion using the piglet as model



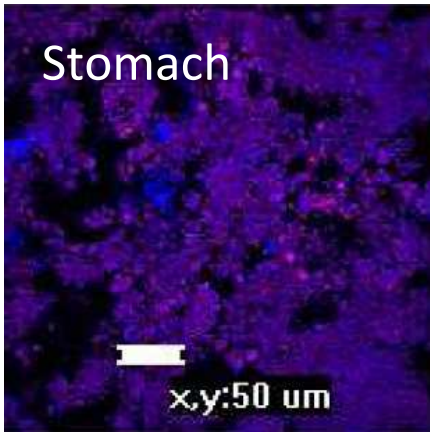



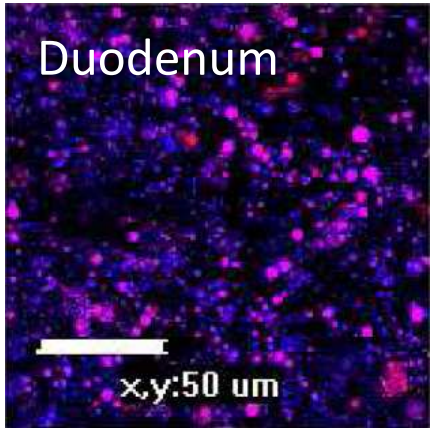

Collaboration I. Luron
INRA St Gilles

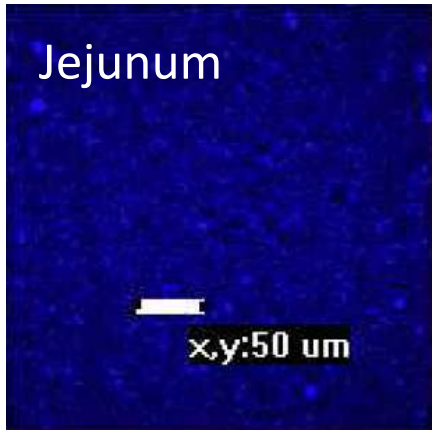
# Multi-scale characterization of digested infant formula

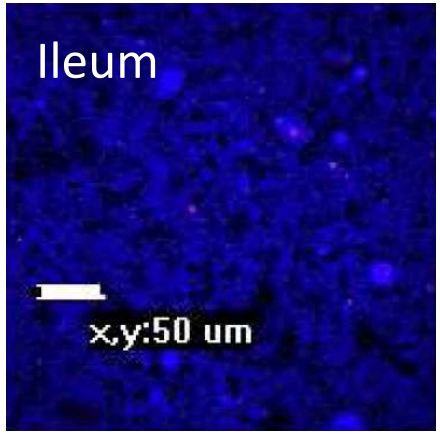
Proteins Lipids

Microscopic scale



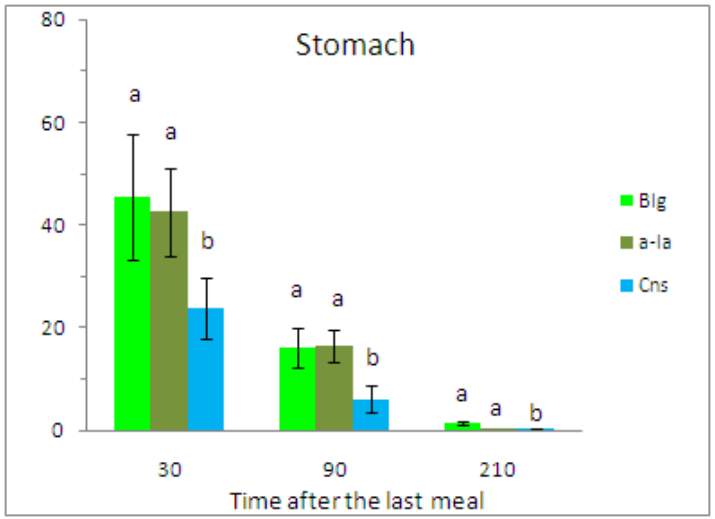



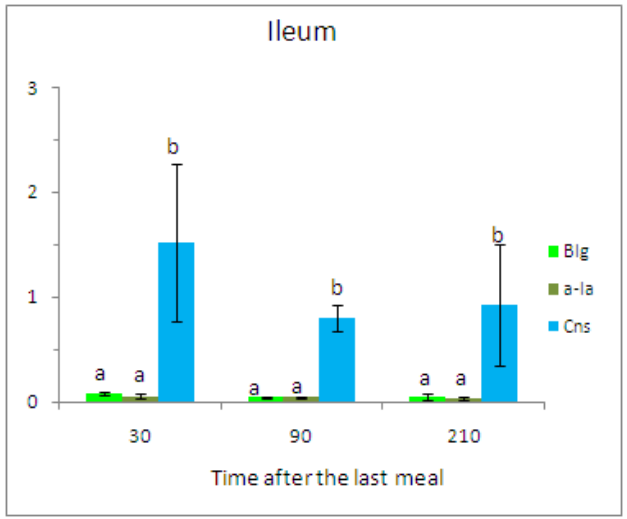




Caseins are rapidly hydrolyzed in the stomach but generate peptides resistant to digestion

Viscosity of the bolus

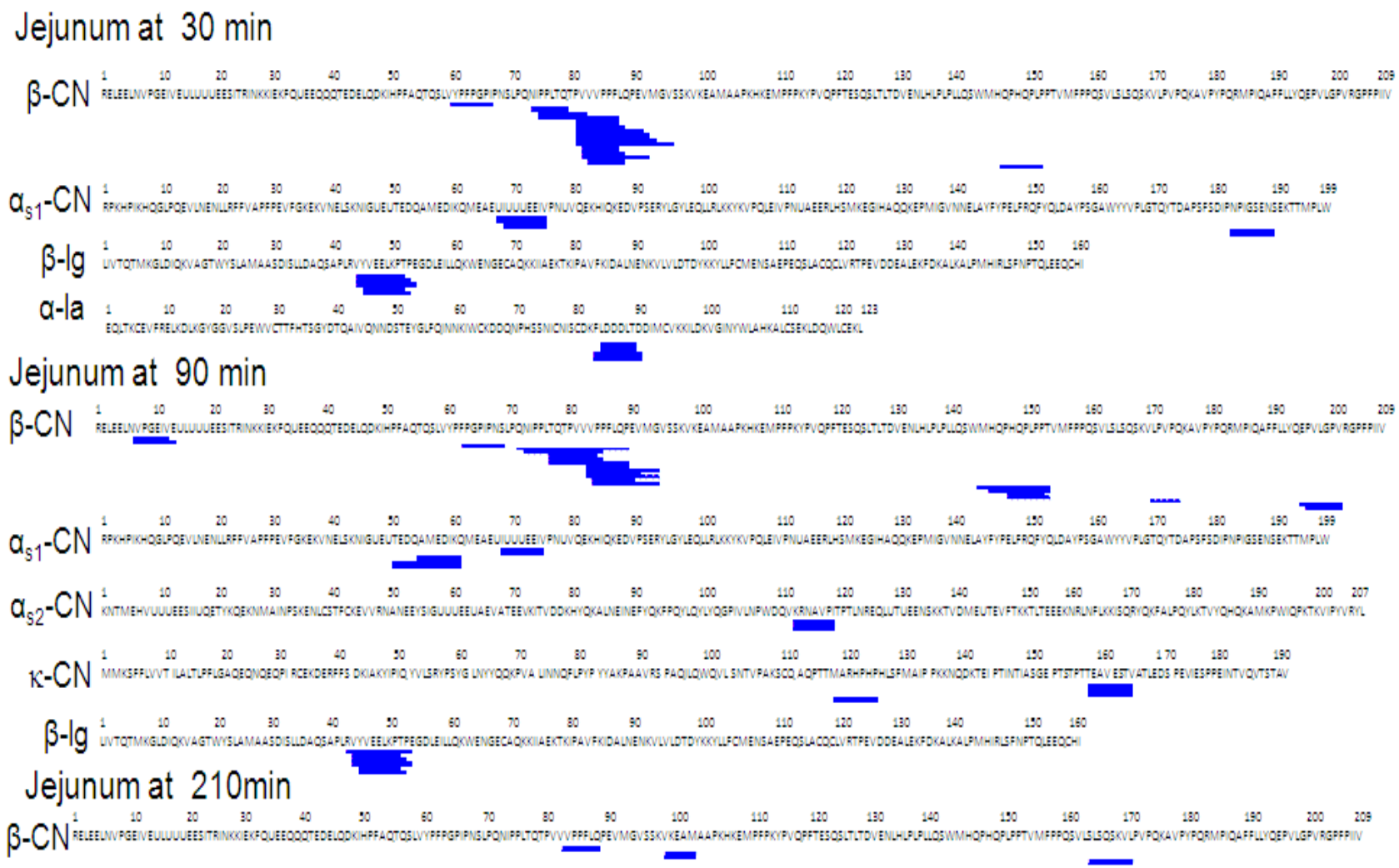
Macroscopic scale




Molecular scale - ELISA

# Peptides identified *in vivo*



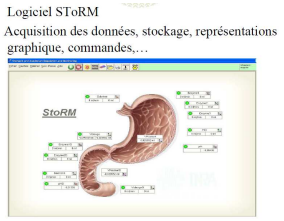
# Current research

- Digestion of infant formula with more sophisticated models

**Digestion of human milk**

**Dynamic Model**

pH regulation
Dynamic flow
[Enzymes] regulation




Proteomic characterization of effluents

# Understanding and modelling the hydrolysis of milk proteins according to the structure of the dairy matrix

**F BARBE, D DUPONT, INRA Rennes**
**D REMOND, INRA Clermont-Ferrand**
**S LE FEUNTEUN, INRA Grignon**
**C GAUDICHON, AgroParisTech Paris**
**B LAROCHE, CNRS Gif-sur-Yvette**

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dépasser les frontières

# Context

☞ Kinetics of aa bioavailability can be critical for some specific populations
ex : athletes, elderly need fast aa bioavailability

☞β-lactoglobulin is a milk protein rich in leucine and has been shown to restore muscle protein metabolism after food intake in elderly people suffering from sarcopenia (Rieu et al. 2006, 2007)

☞β-lactoglobulin is rarely consumed as a purified protein but mostly in processed foods

☞ Possible to manufacture dairy products with different microstructures but similar composition

**Does the microstructure of dairy products affect the kinetics of protein digestion and aa bioavailability?**

# Strategy

Modelling of the kinetics of hydrolysis of β-Lg and β-CN according to the food microstructure

Manufacture of an « ultra-low-heat » milk powder

↓

Processing (heat-treatment, gelation…)
→ **6 matrices**

↓

Multi-scale characterization of the structure
(rheology, microscopy…)

↓

*In vivo* digestion in 6 mini-pigs (effluents collected during 7h)

↓

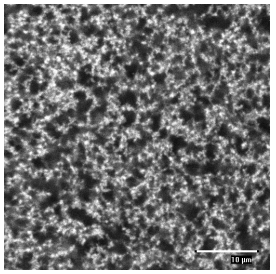
Identification of protein digestion products in the duodenum, jejunum and plasma
(SDS-PAGE, LC-MS-MS, molecular immunology…)

# The 6 matrices

Ultra-low-heat powder

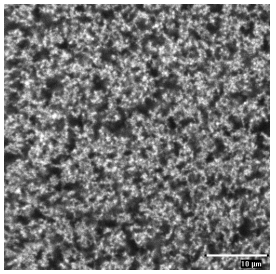
Raw liquid milk

Rennet gel

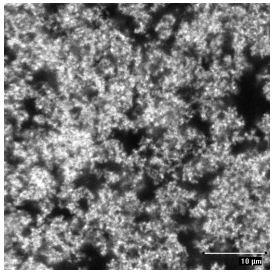


Heat - treated liquid milk (90°C/10 min)

Acid gel (3% GDL)

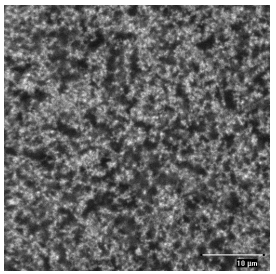


Stirred Acid gel

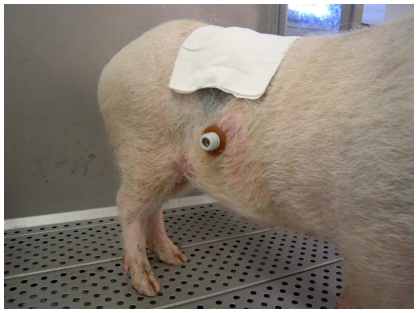


**Addition of non-absorbable markers to the Mean Residence Time (MRT) in the stomach (gastric emptying)**

Rennet gel



# *In vivo* trial



**6 female Göttingen mini-pigs** (around 30kg)

Collaboration D. Remond
INRA Theix

2 canulas: * end of stomach
* mid-jejunum
↳sampling of digestive contents

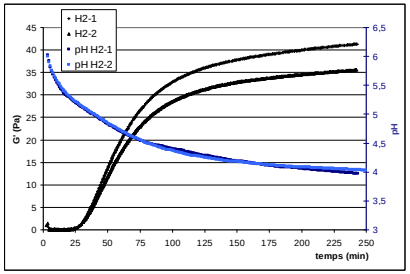
1 catheter (abdominal aorta)
↳blood sampling

**648 samples collected and analyzed**

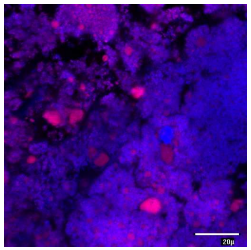
# Analyses

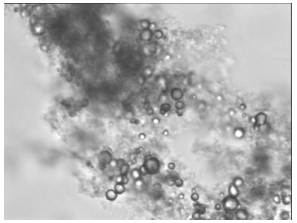
## Multi-scale characterization of dairy matrices

Rheology

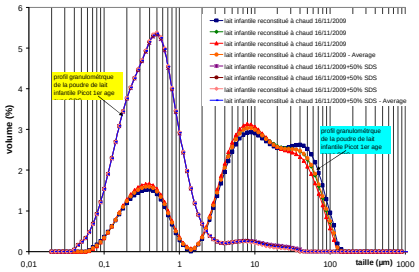



Optical and confocal microscopy

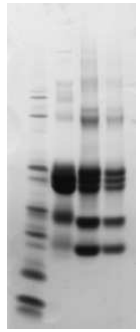




Granulometry

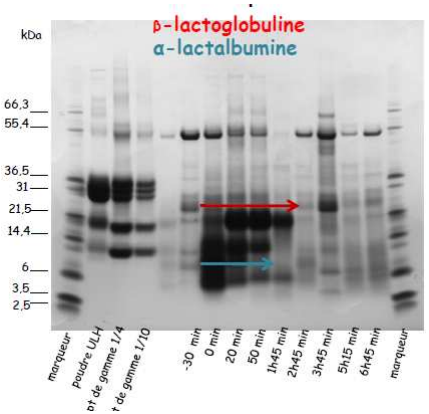



SDS-PAGE, ELISA



## Digestive effluents characterization

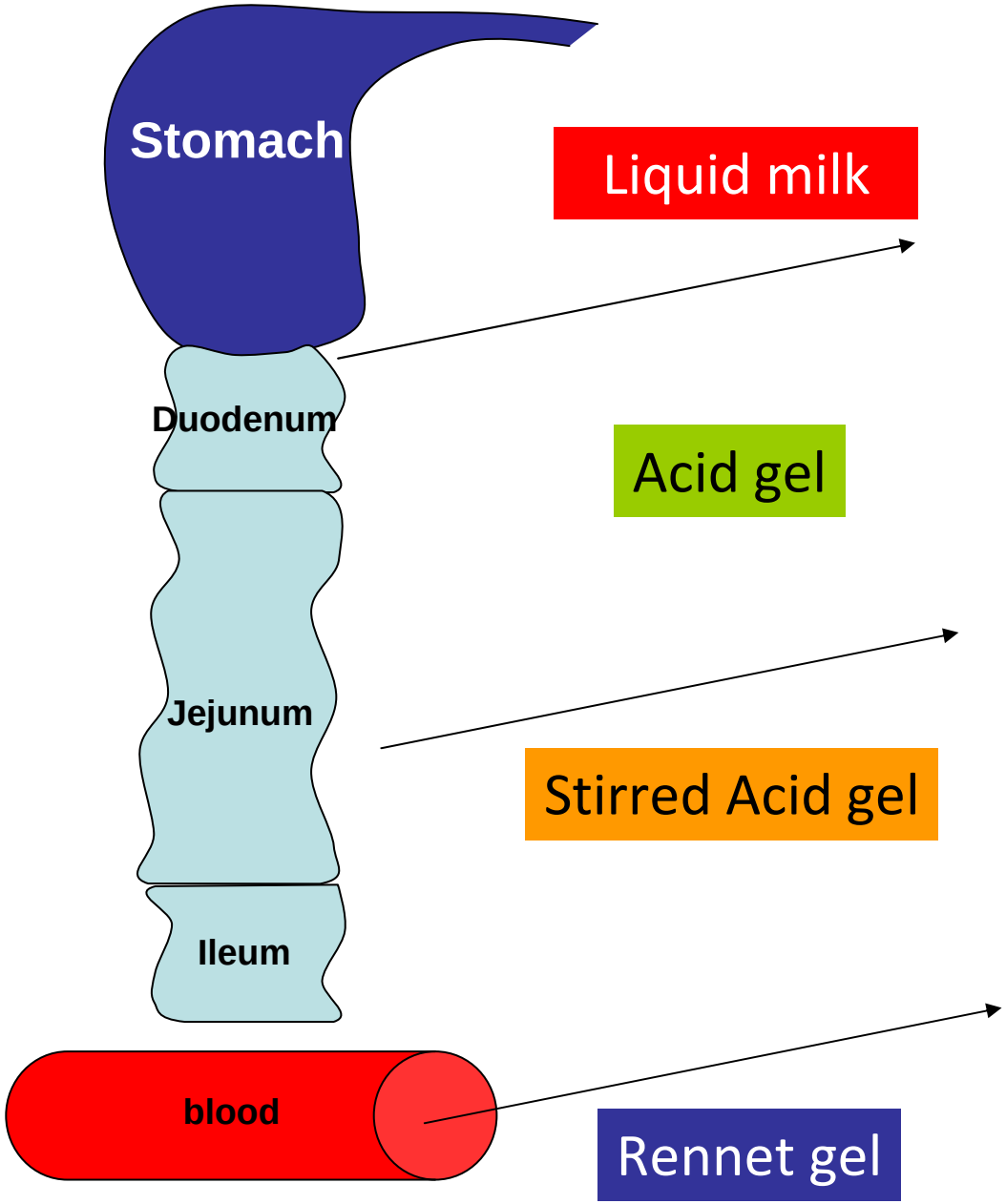
-Nitrogen content
-Ytterbium and chrome quantification by atomic absorption
-Protein characterization (SDS-PAGE, ELISA)
-Peptides characterization (LC-MS-MS)




## Plasma characterization

-Amino acid analysis by ion-exchange chromatography
-Peptidome characterization by LC-MS-MS

# Evolution of the β-lg concentration along the GI tract




**The structure of food affects the bioavailability of nutrients**

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

COST Action FA1005

**INFOGEST**

**Chair: Dr. Didier DUPONT, Senior Scientist, INRA, France**

Trilateral Workshop on

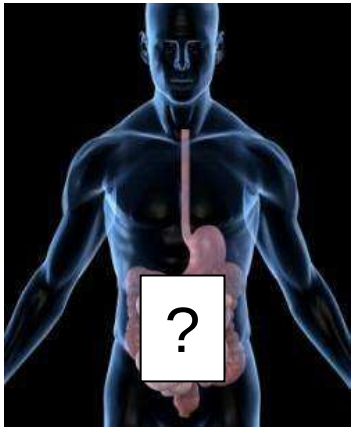
**Innovative Health Promoting Food**

**Berlin 29-30 September 2011**

# Scientific context and objectives

**Diet-related diseases + age EU population ↑**

↳ **Prevent these pathologies rather than cure them**




**Gut = interface between food and human body**

**Digestion releases beneficial food components**

**Need to increase our knowledge on the effect of food on human health by increasing our knowledge on food digestion**

## FA1005 objectives

- Spread and improve current basic knowledge on food digestion
- Identify the beneficial food components released in the gut during digestion
- Support the effect of beneficial food components on human health
- Promote harmonization of currently used digestion models

# Working groups

Chair
Didier Dupont - France

**INFOGEST**

Dairy
Fruits & Vegetables
Egg

Vice-chair
Alan Mackie - UK

**Relationship between food structure and nutrient bioaccessibility - bioavailability**
**WG1**

BFC identification
Stability during processing
Food multi-scale characterization

F Capozzi
Italy

B. De Meulenaer
Belgium

***In vitro, in vivo* and *in silico* models of mammalian gastrointestinal digestion**
**WG2**

Digestion models harmonization
Comparison *in vitro* / *in vivo*
Digestion products identification
BFC absorption /bioavailability

A. Brodkorb
Ireland

I. Recio
Spain

**Evaluation of the health effects**

**WG3**

Immunomodulatory properties
Regulation of appetite and satiety
Effect of BFC on human microbiota

Tor Lea
Norway

A. Bordoni
Italy

April 2011 – March 2015

INFOGEST cost

Tech Univ Denmark

Univ Aarhus

MTT

Univ Eastern Finland

Norwegian Univ Life Sci

VTT

Nofima

Wageningen UR

Rothamsted Res

Teagasc

Univ Reading

Univ Leeds

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Univ Ghent

Agroscope Posieux

Inst Food Res

Leatherhead Food Res

Univ Greifswald

Max Rubner-Institut

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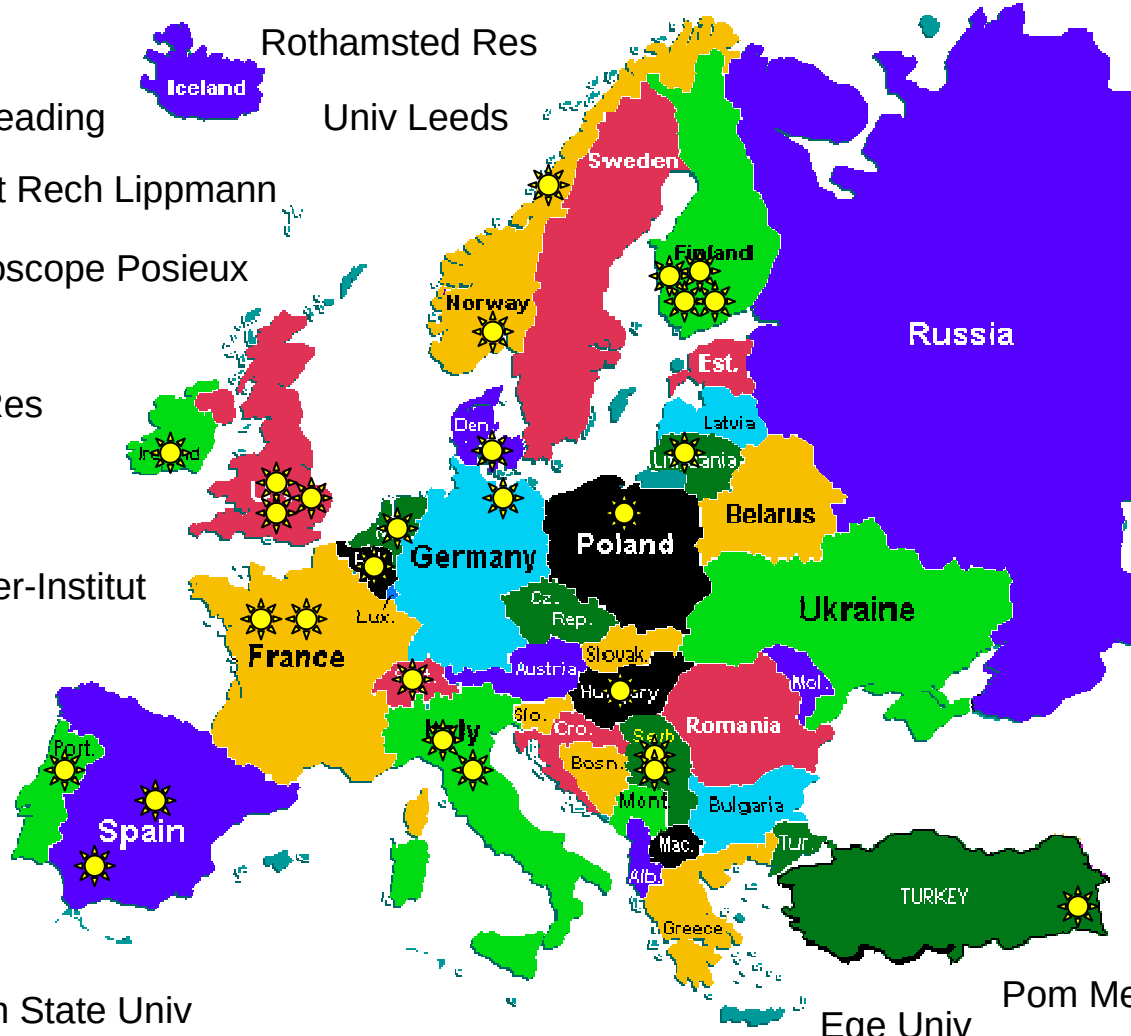
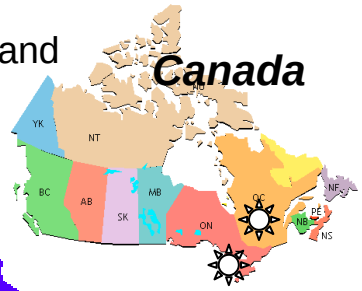
Technion





140 scientists - 44 institutions – 23 countries

# A strong industrial support

30 companies (large groups and SMEs) from all over Europe

# Future events

☞ 2nd Workshop in Le Croisic (France) on 19-21 October 2011

☞ **1st International Conference on Food Digestion** (+Annual Industry Workshop) in Cesena (Italy) on 19-21 March 2012