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The structure of dairy products modifies the kinetics of protein hydrolysis and the release of bioactive peptides in the gut during digestion

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



2011 ADSA-ASAS Joint Annual
Meeting
New Orleans July 11-14

DIET
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ENVIRONMENT



Context

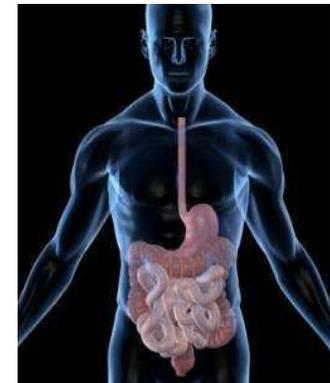
Link between food and human health = top research priority

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

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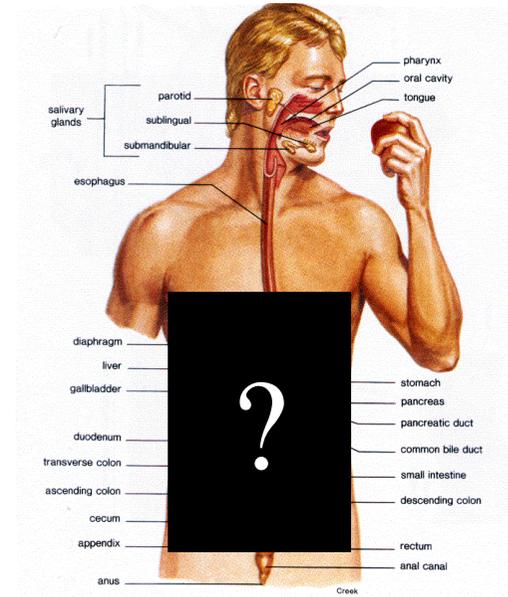


Past & present

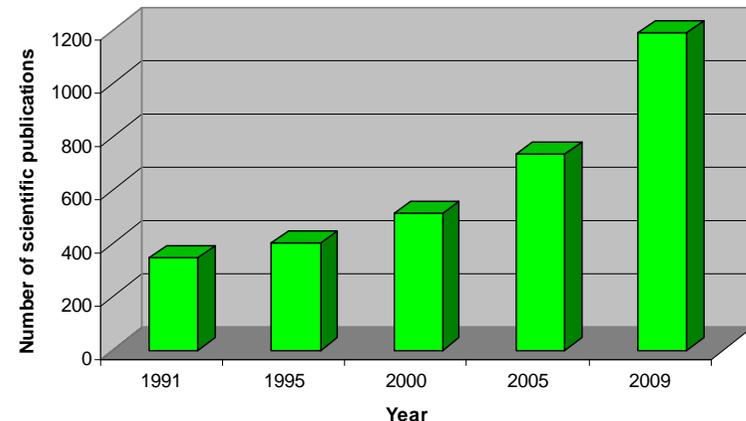
Gut = interface between food and the body

Digestion = key step for delivering beneficial food components (BFC) to the body

- ☞ In the past, food digestion has mainly been investigated by nutritionists and gut physiologists
- ☞ Food was considered by its composition rarely by its structure
- ☞ Digestive tract was seen as a « black box »

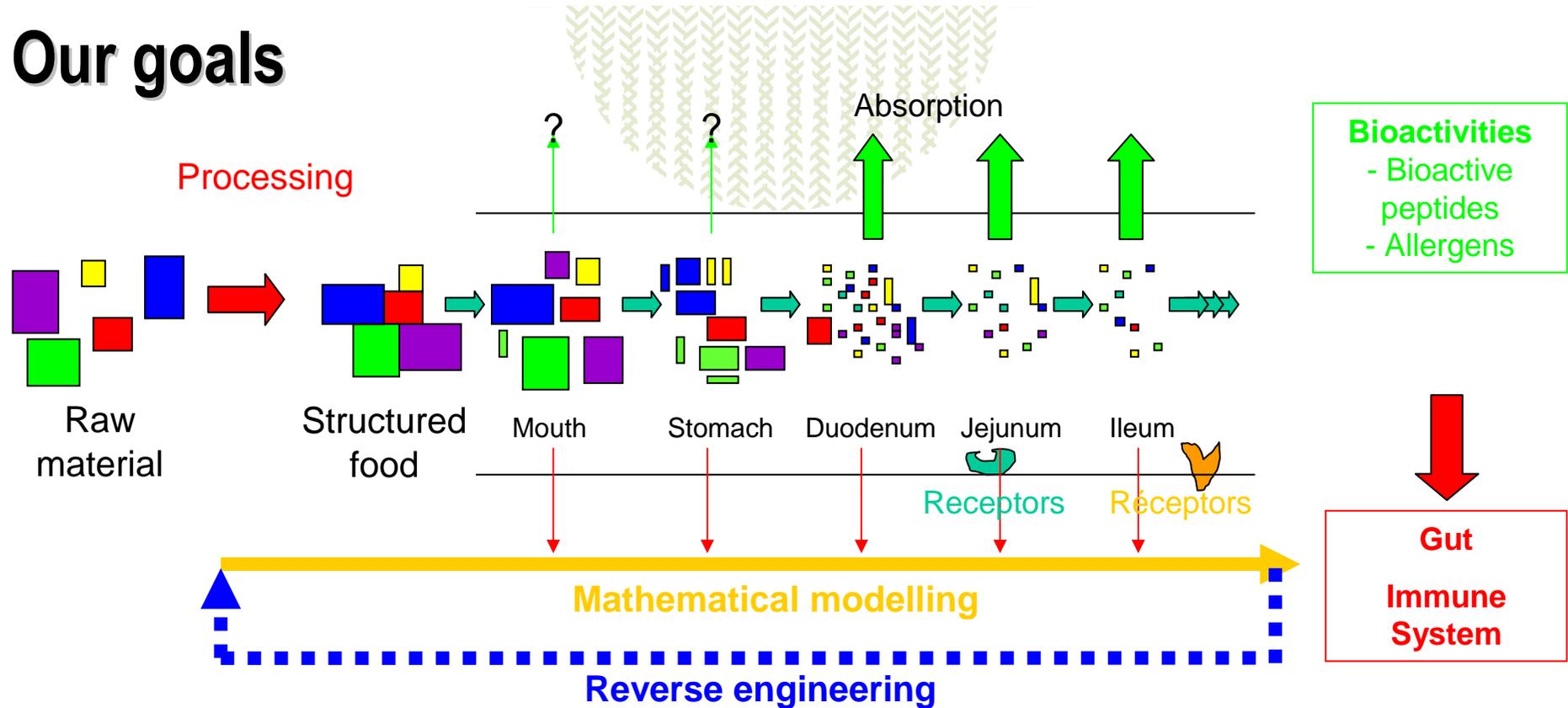


- ☞ In the last 10 y, ↑ in the number of publication on food digestion
- ☞ Mainly associating food scientists, nutritionists and gut physiologists



Does the food matrix structure influence dietary proteins digestion?

Our goals



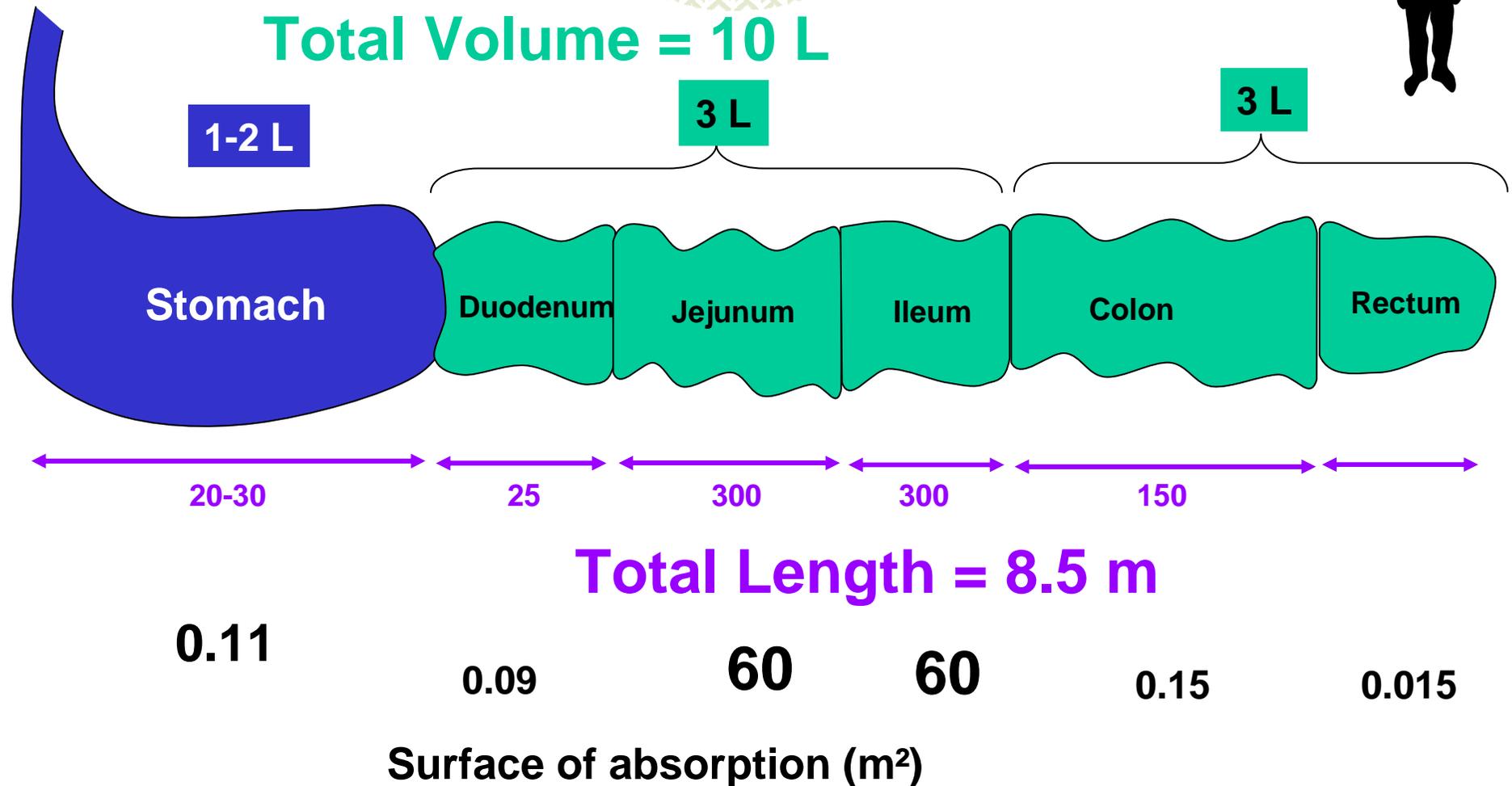
- ☞ To understand the mechanisms of breakdown of food matrices and their constituents in the gut and identify the beneficial food components released
- ☞ To determine the impact of the structure of food matrices on these mechanisms
- ☞ To model these phenomena in order to develop a reverse engineering approach

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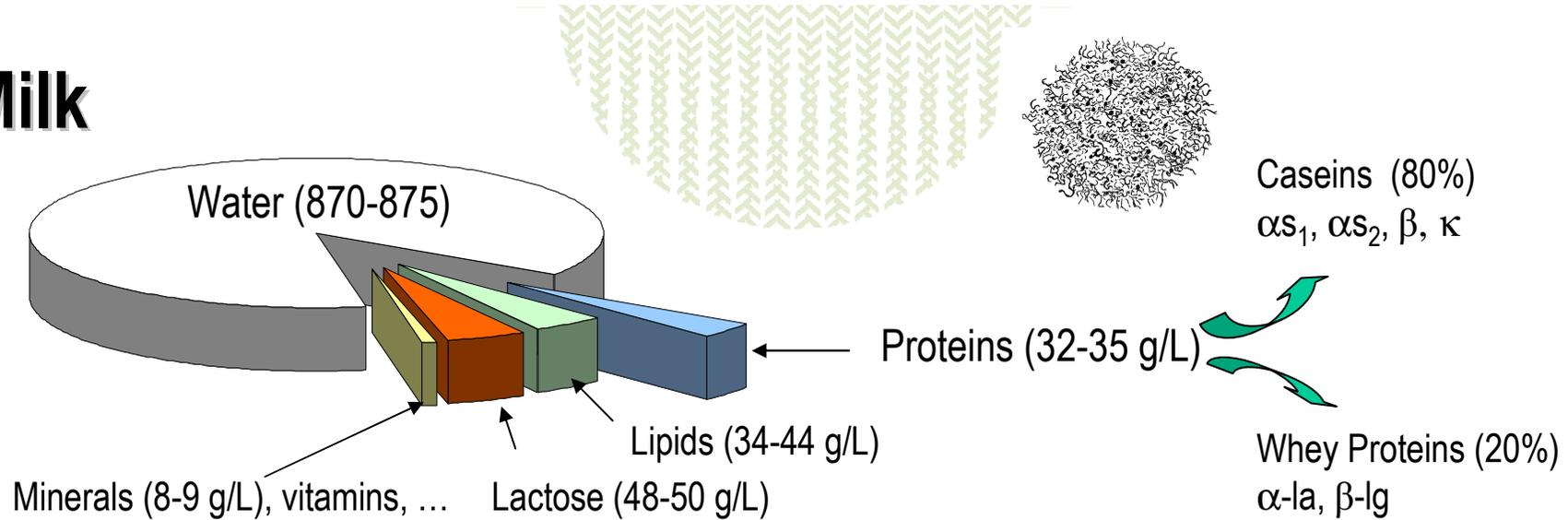
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Volume (L) & length (m) of the different compartments of the human gut

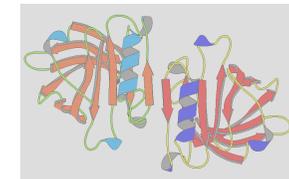
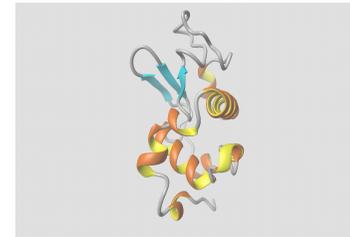


Milk

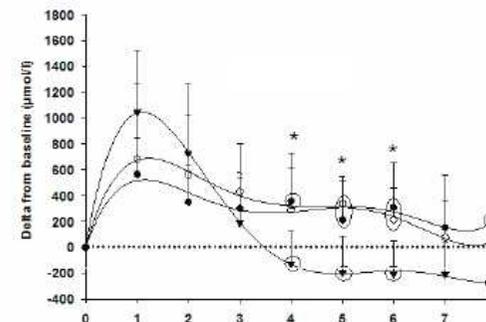


Caseins and whey proteins are:

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



Total amino acid



(Lacroix et al, 2006)

- ▼ whey protein
- casein
- Total milk protein

Two recent examples of our work on the digestion of dairy products

- ☞ *In vivo* digestion of infant formula using the piglet as a model of the human newborn
- ☞ Effect of the microstructure of dairy matrices on the kinetics of protein digestion and the bioavailability of amino acids

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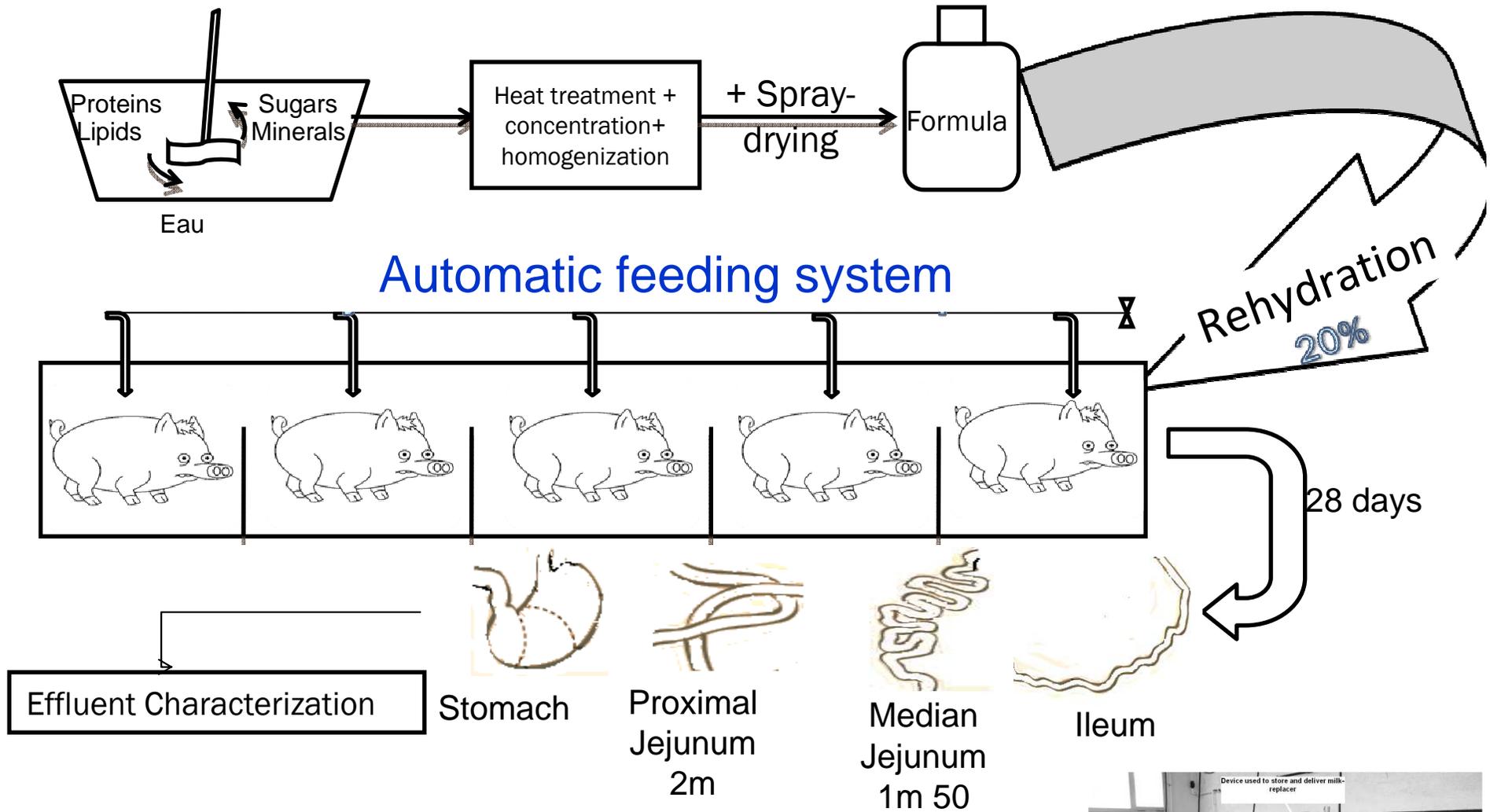
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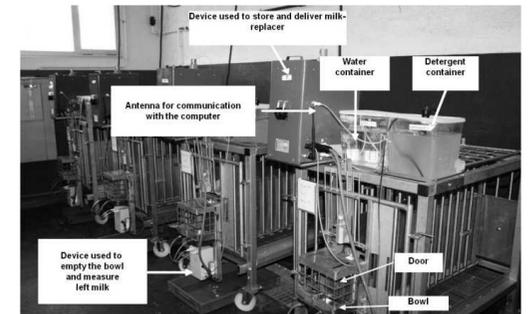
Infant formula

- ☞ 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

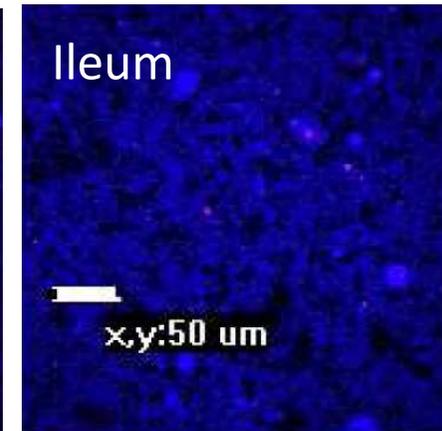
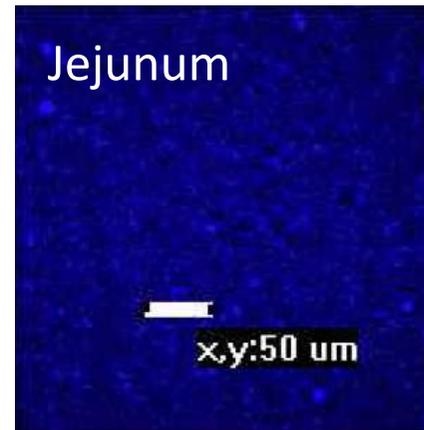
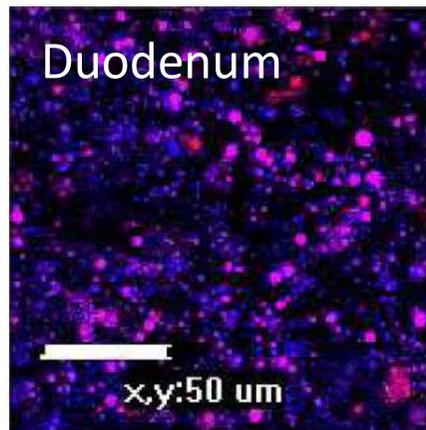
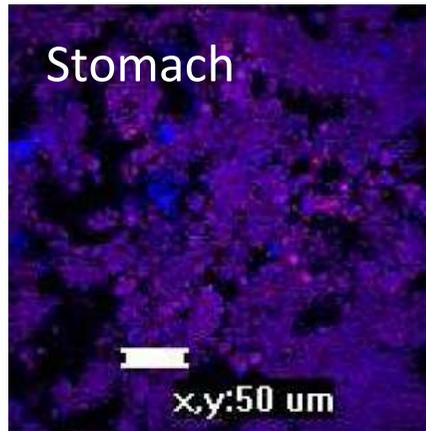


Multi-scale characterization of digested infant formula

Proteins

Lipids

Microscopic scale

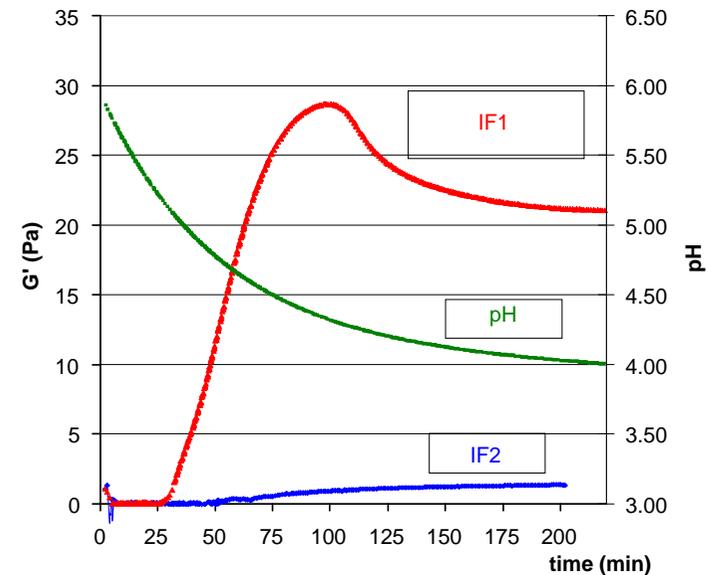


Will the IF coagulate when entering in the stomach???

↳ Prediction of the rheological behaviour of an IF in gastric conditions

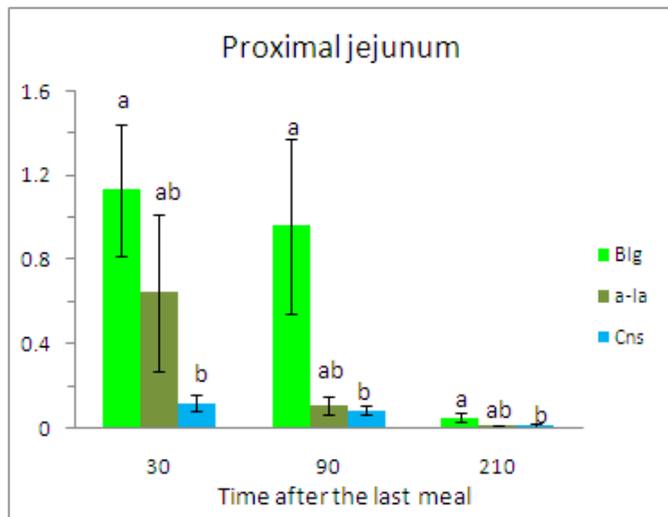
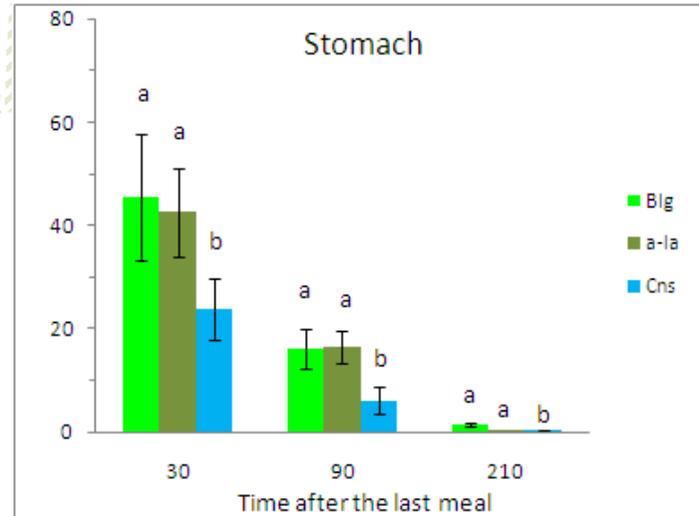
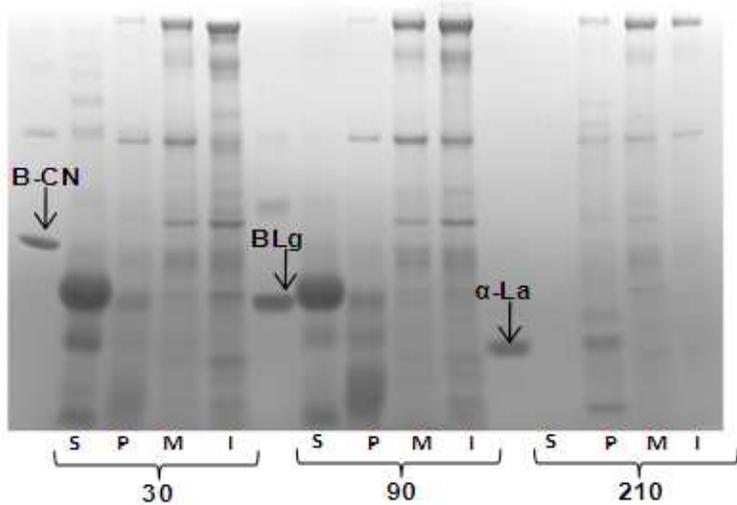
Viscosity of the gel

Macroscopic scale

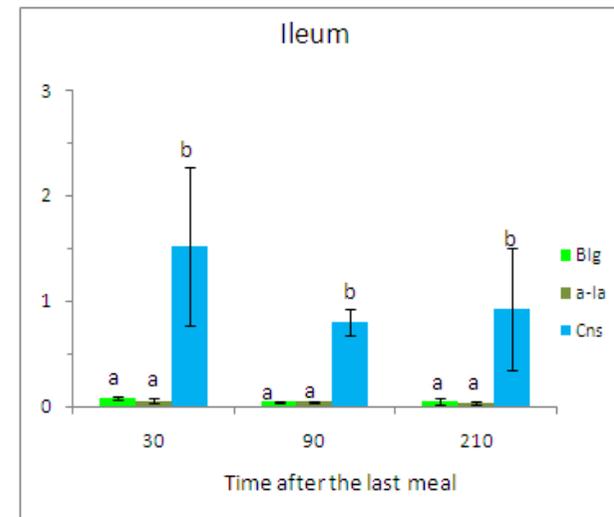


Kinetics of Infant Formula proteins digestion

Molecular scale

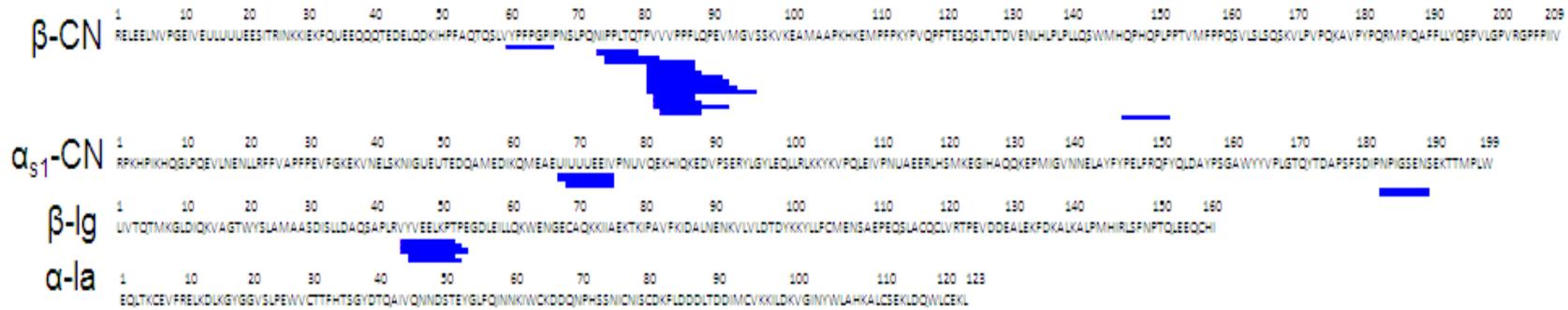


In g/100g of ingested protein

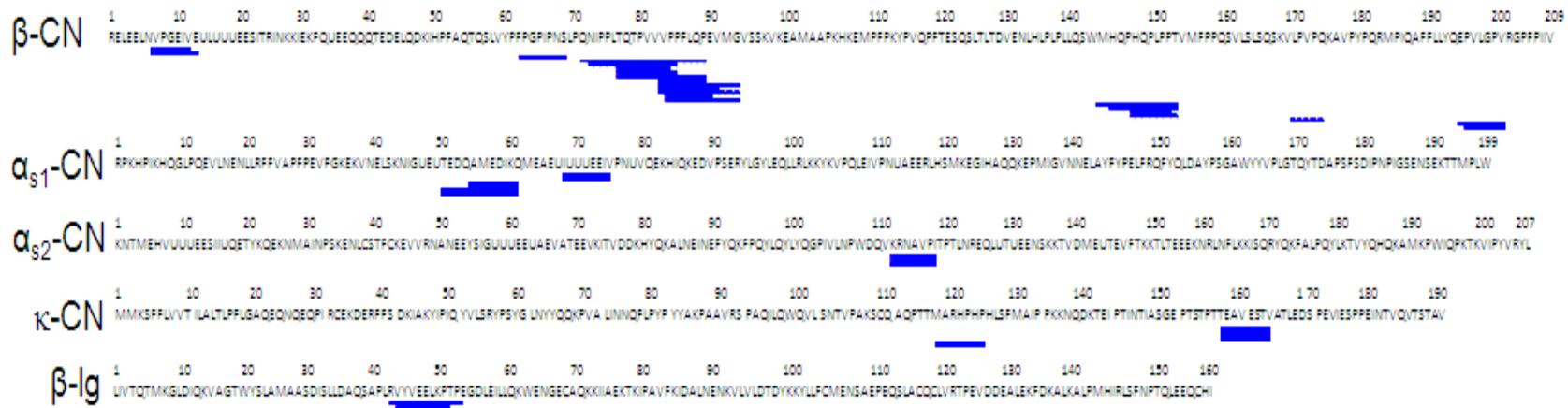


Peptides identified *in vivo*

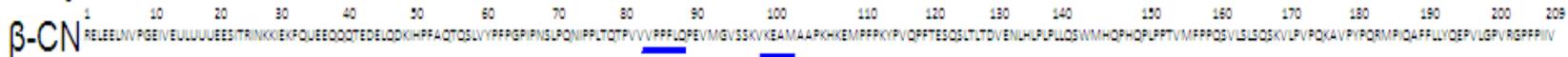
Jejunum at 30 min



Jejunum at 90 min



Jejunum at 210min



Peptide identification – some drawbacks

In vivo effluents are complex samples and need pre-treatment before analysis



Conclusion

- Caseins are more sensitive to digestion than whey proteins (at low concentration, caseins don't form a coagulum but soft flocks that are rapidly digested and transferred from the stomach to the small intestine)
- β -lg and I' α -la are more resistant to digestion and have a similar behaviour during digestion
- Casein fragments resist digestion and can be identified in the lower part of the small intestine (ileum)
 - ↳ characterization of their biological effect?
 - ↳ effect on gut microbiota???

Current research

- Digestion of infant formula with different models

Dynamic Model



pH regulation
Dynamic flow
[Enzymes] regulation

■ Logiciel SToRM
Acquisition des données, stockage, représentations
graphique, commandes,...



Large *In vivo* trial on piglets



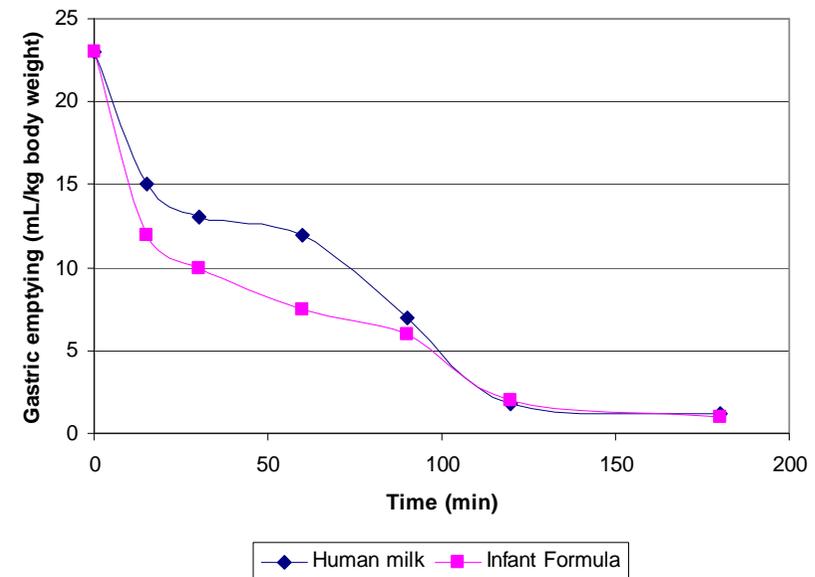
Effect of infant formula
composition on the milk
protein kinetics of digestion

Perspectives

- Study of the digestion of human milk



- Structuring infant formulas in order to mimic the « functional » behaviour of human milk when entering into the gut



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☞ *In vivo* digestion of infant formula using the piglet as a model of the human newborn

☞ Effect of the microstructure of dairy matrices on the kinetics of protein digestion and the bioavailability of amino acids

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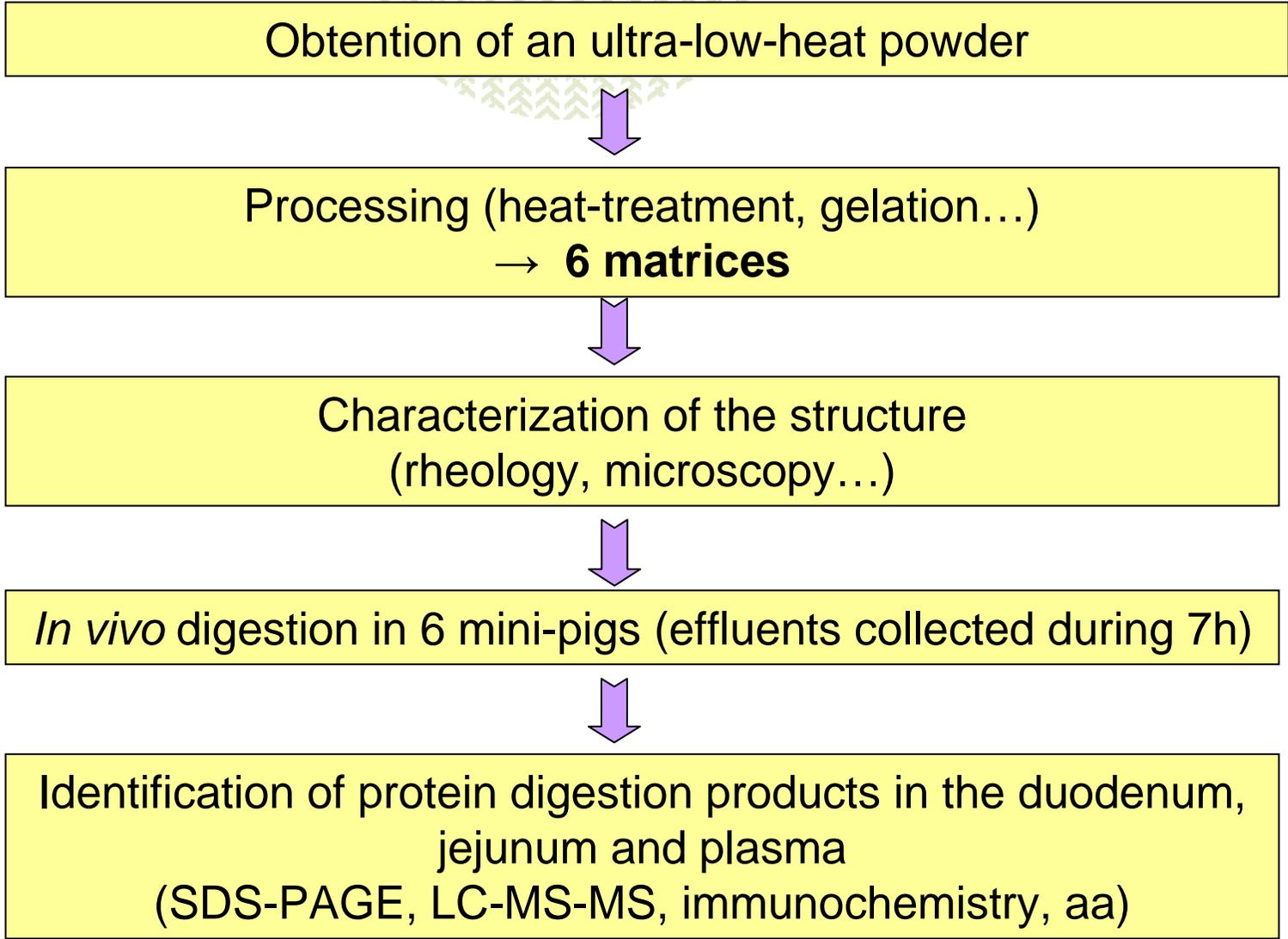
Context

- ☞ Processing conditions affect the structure of the food matrix and generate interactions between the food constituents
- ☞ Possible to manufacture dairy products with different microstructures but similar composition
- ☞ The kinetics of protein digestion can significantly modify the aa bioavailability
 - ex : whey proteins = fast proteins
 - caseins = slow proteins
- ☞ Kinetics of aa bioavailability can be critical for some specific populations
 - ex : sportsman, elderly need fast aa bioavailability

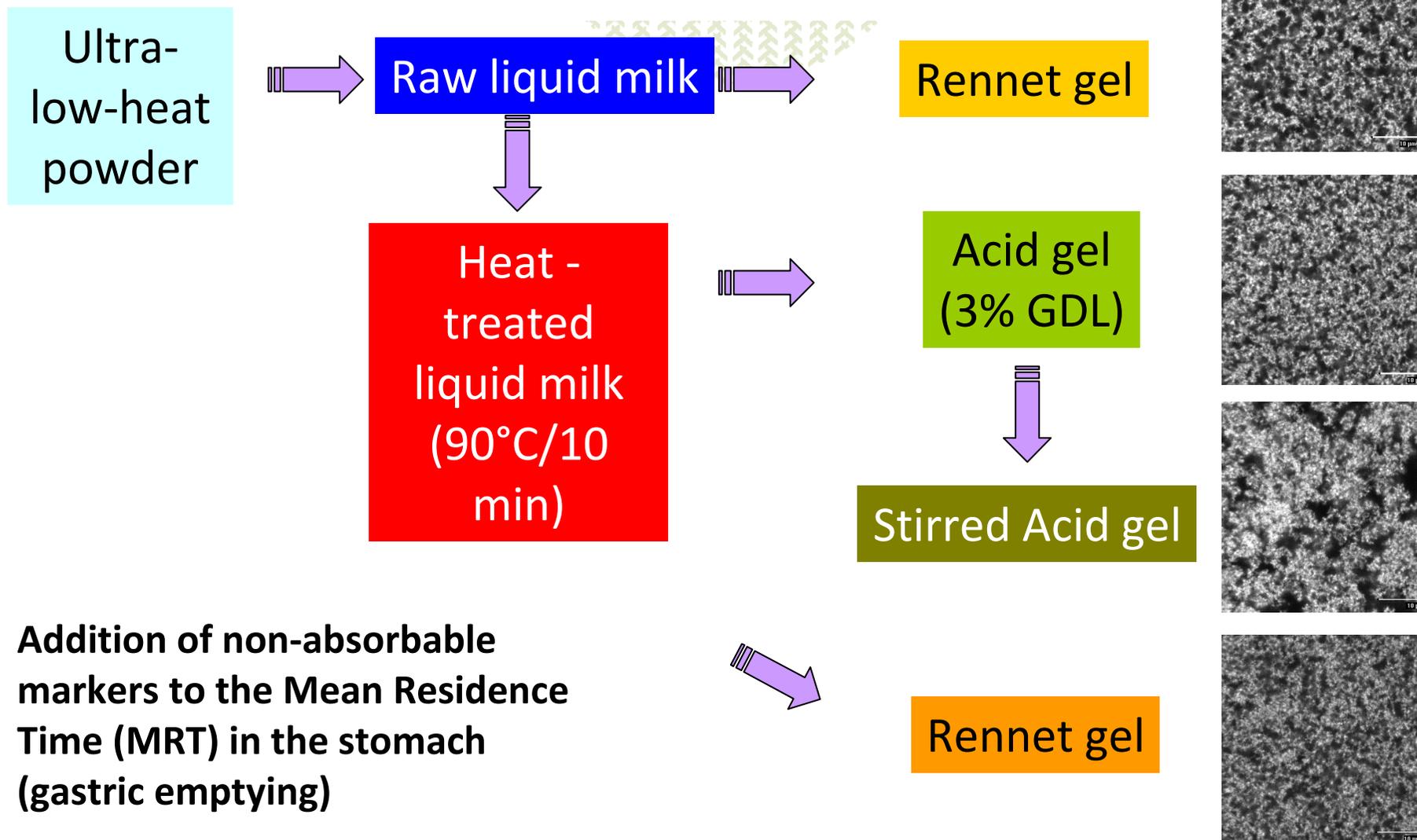
Does the microstructure of dairy products affect the kinetics of protein digestion and aa bioavailability?

Strategy

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



The 6 matrices

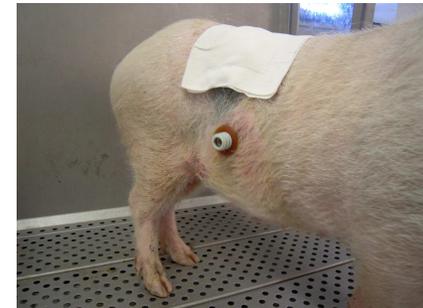


Addition of non-absorbable markers to the Mean Residence Time (MRT) in the stomach (gastric emptying)

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

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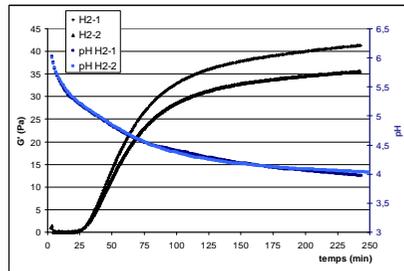
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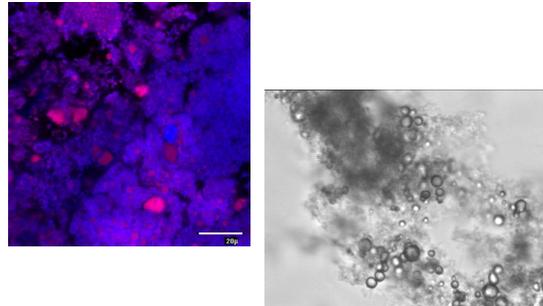
Analyses

Multi-scale characterization of dairy matrices

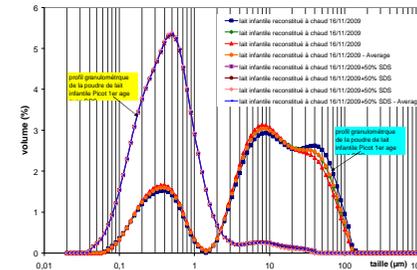
Rheology



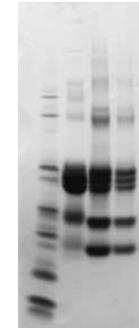
Optical and confocal microscopy



Granulometry



SDS-PAGE, ELISA

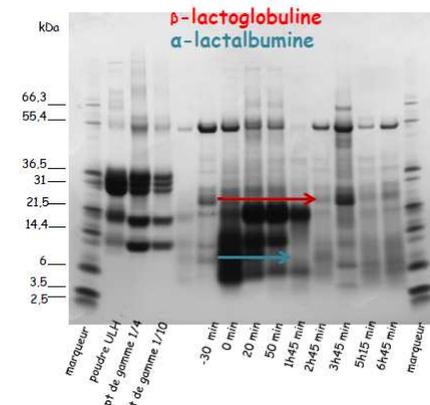


Digestive effluents characterization

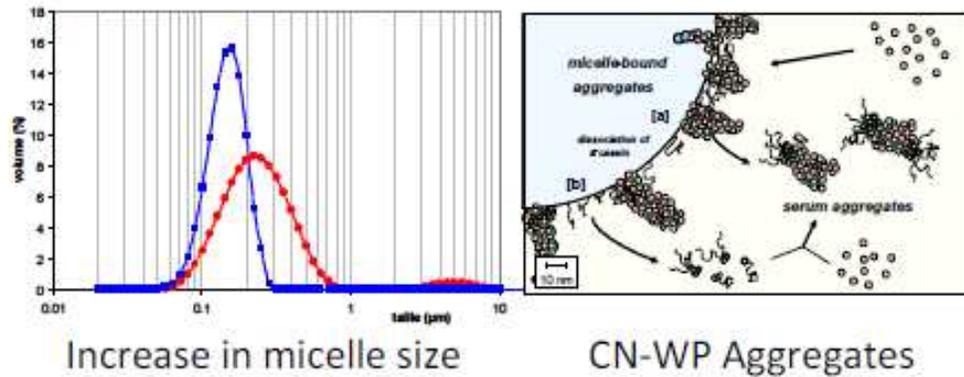
- Nitrogen content
- Ytterbium and chrome quantification by atomic absorption
- Protein characterization (SDS-PAGE, ELISA)
- Peptides characterization (LC-MS-MS)

Plasma characterization

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

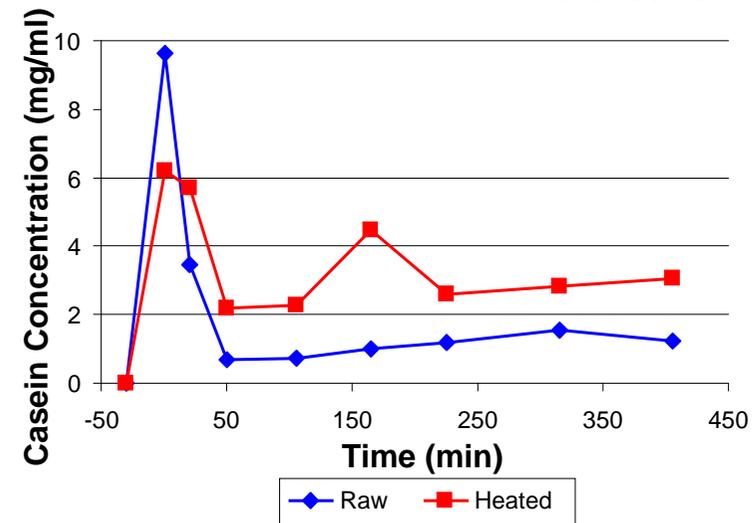
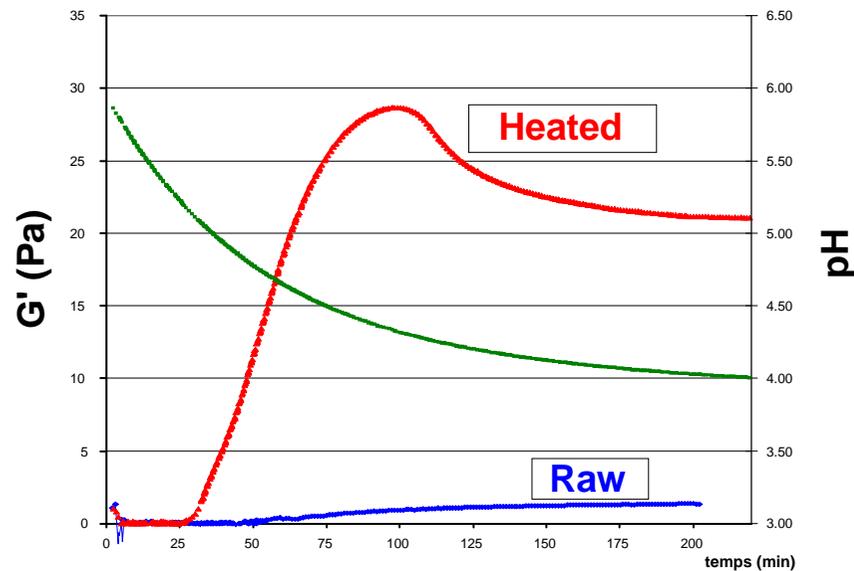


Example of results - Comparison raw liquid milk / heated liquid milk



Mean residence time in the stomach

Raw — **63 min**
 Heated — **90 min**

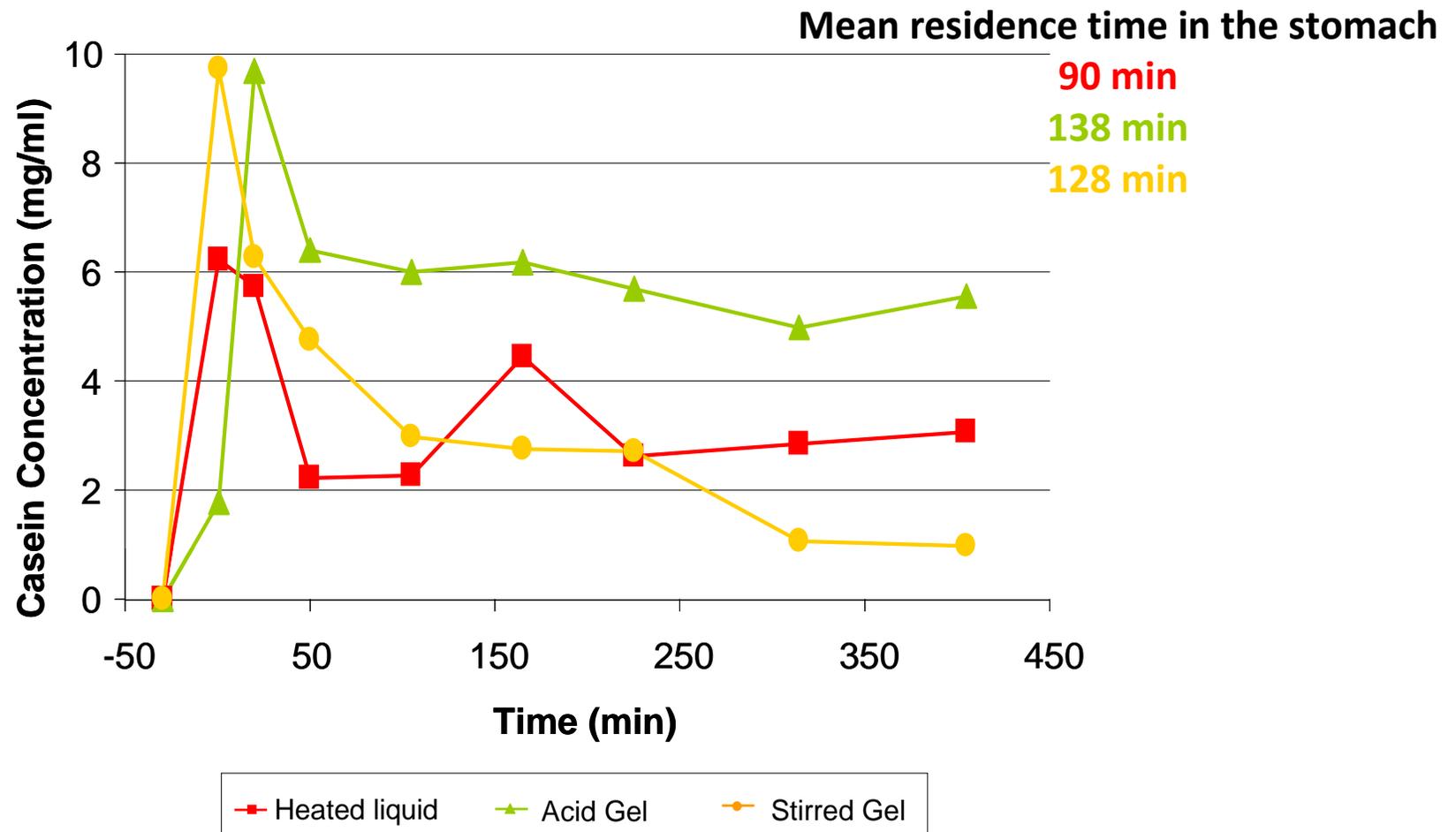


Heated liquid makes a stronger coagulum in the stomach → impact on gastric emptying



Prediction of the rheological behaviour in gastric simulated conditions

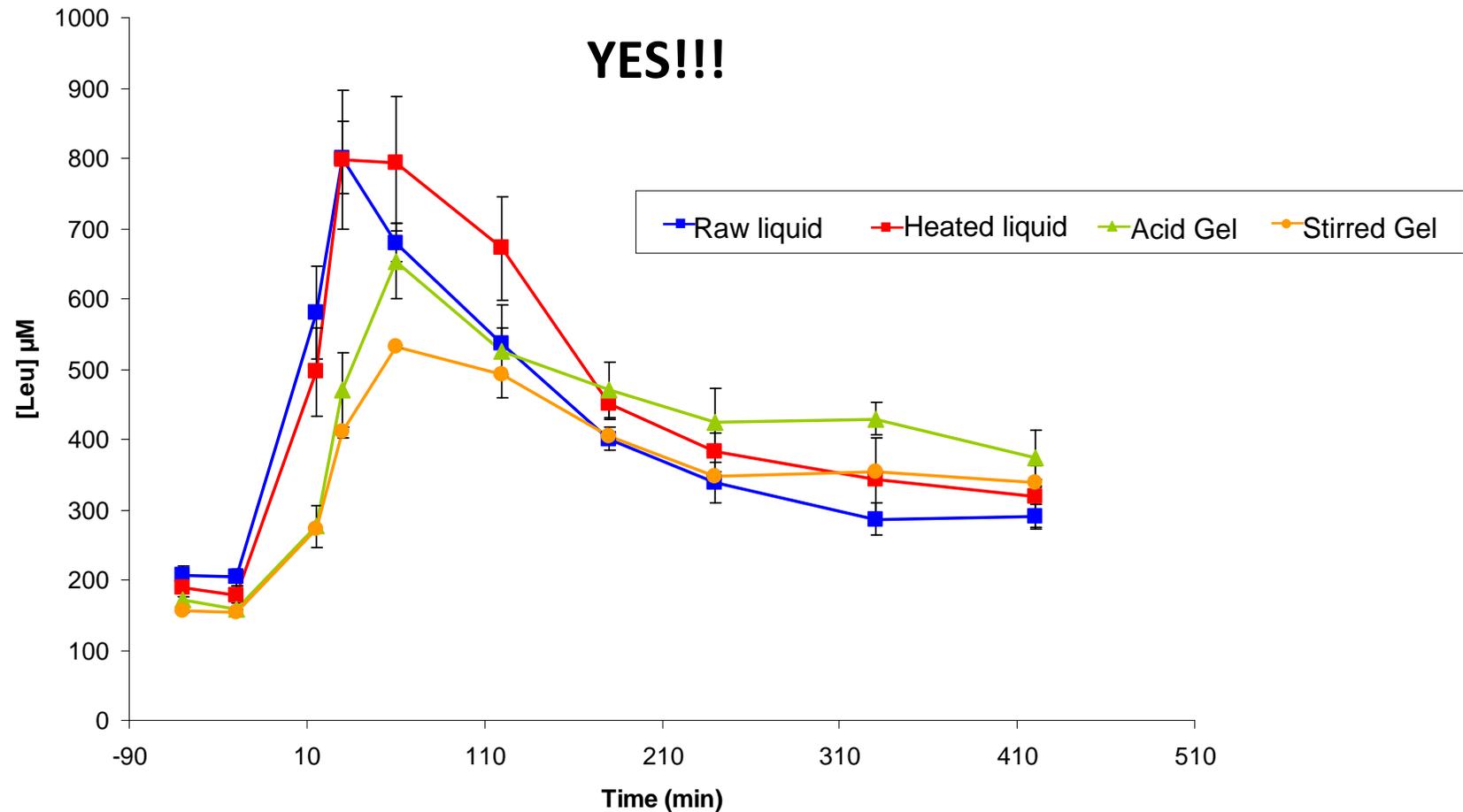
Effect of the microstructure on the kinetics of digestion



☞ The microstructure of dairy products affects the kinetics of caseins transfer from the stomach to the small intestine

Kinetics of aa release in the plasma

- Do the differences observed in protein release in the small intestine modify aa release and bioavailability in the plasma?



Microstructure of food influences nutrient bioavailability

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

Beneficial food component characterization
Stability of bioactives during processing
Multi-scale characterization of food

Harmonization of *in vitro* digestion models
Comparison *in vitro* / *in vivo*
Characterization of the digestion products
Resistance to peptidases and absorption
Active form of food components in the organism

Characterization of raw materials and processed food matrices for optimized nutrient bioaccessibility
WG1

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

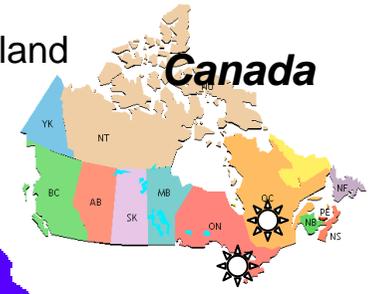
Dairy
Fruits & Vegetables
Egg

Evaluation of the health effects
WG3

- Food allergenicity and immunomodulatory properties
- Kinetics of digestion / regulation of appetite and satiety
 - Protein metabolism on human microbiota
- Impact of ACE inhibitors on cardiovascular diseases



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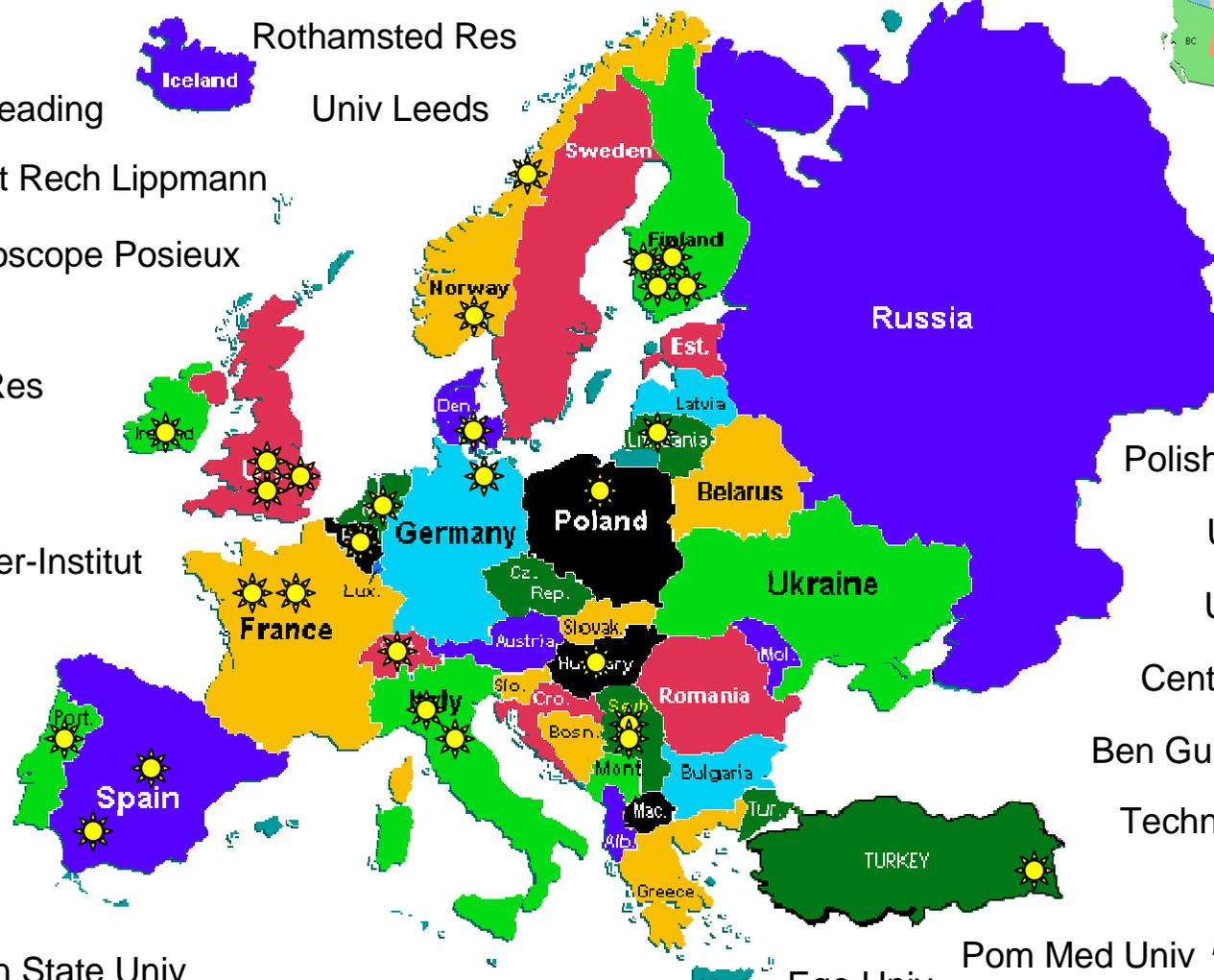
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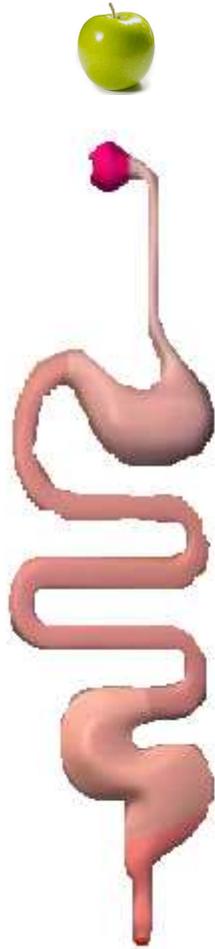
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Thank you for your kind attention