



Digestion of dairy products; consequences on human health

Didier Dupont

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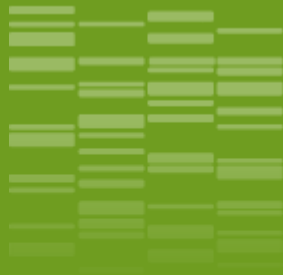
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Submitted on 5 Jun 2020

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Digestion of dairy products; consequences on human health



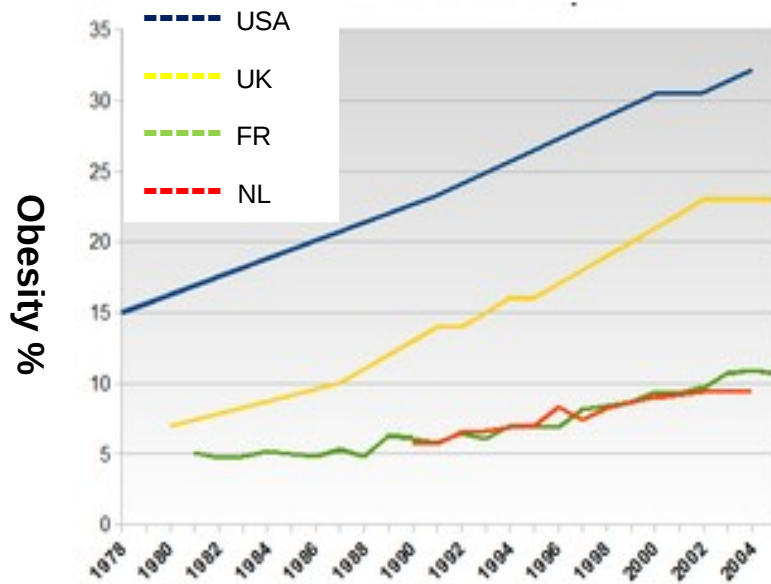
Dupont D

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



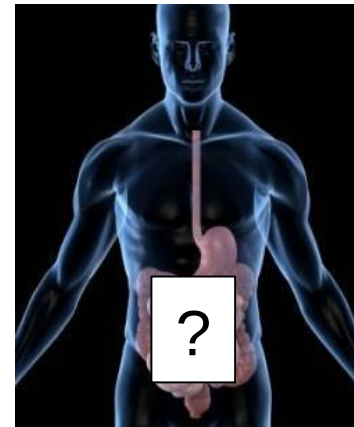
Food and quality of life Conference, Olsztyn, 22-23
May 2014

• Scientific Context



Diet-related diseases ↑

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



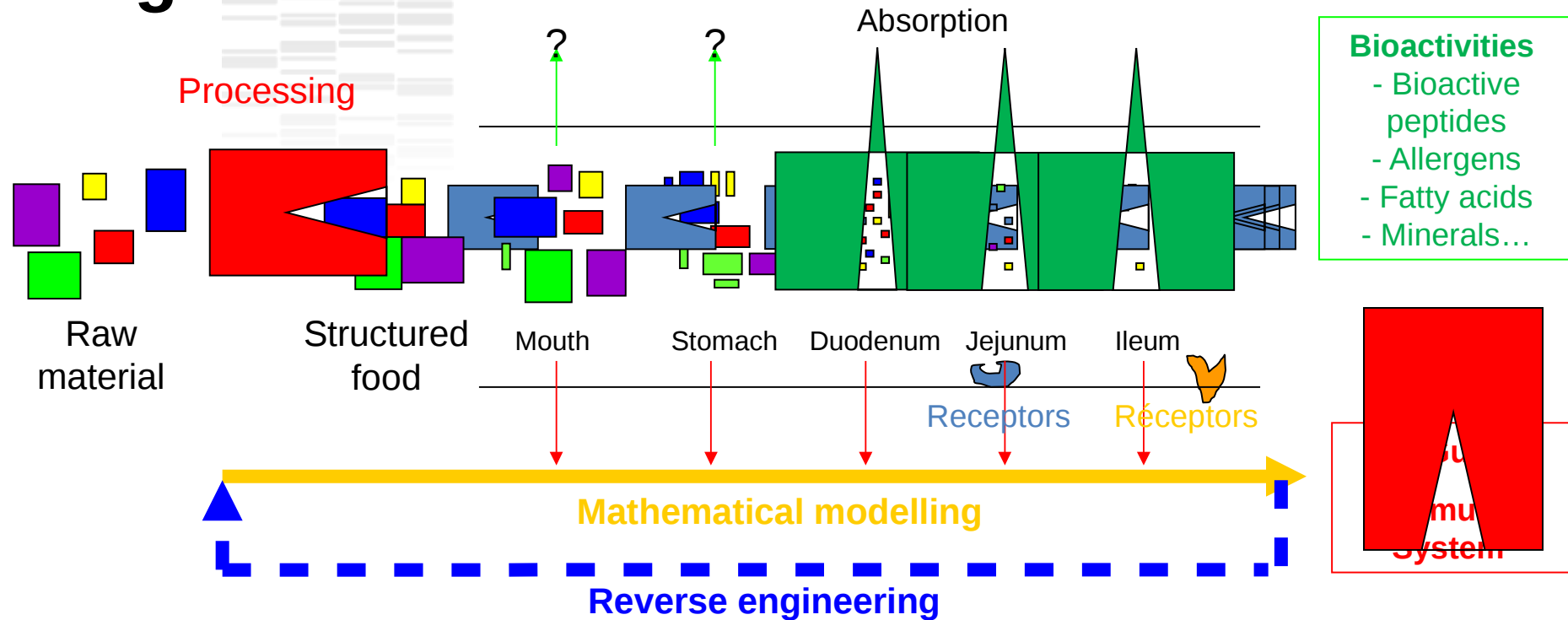
Gut = interface between food and human body

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 digestion has been considered as a black box so far

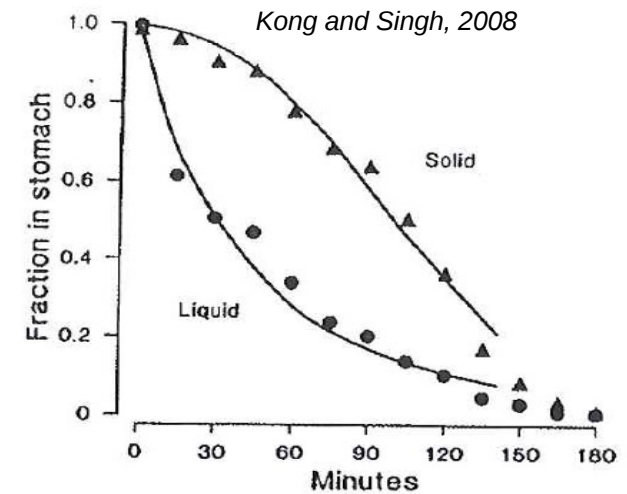
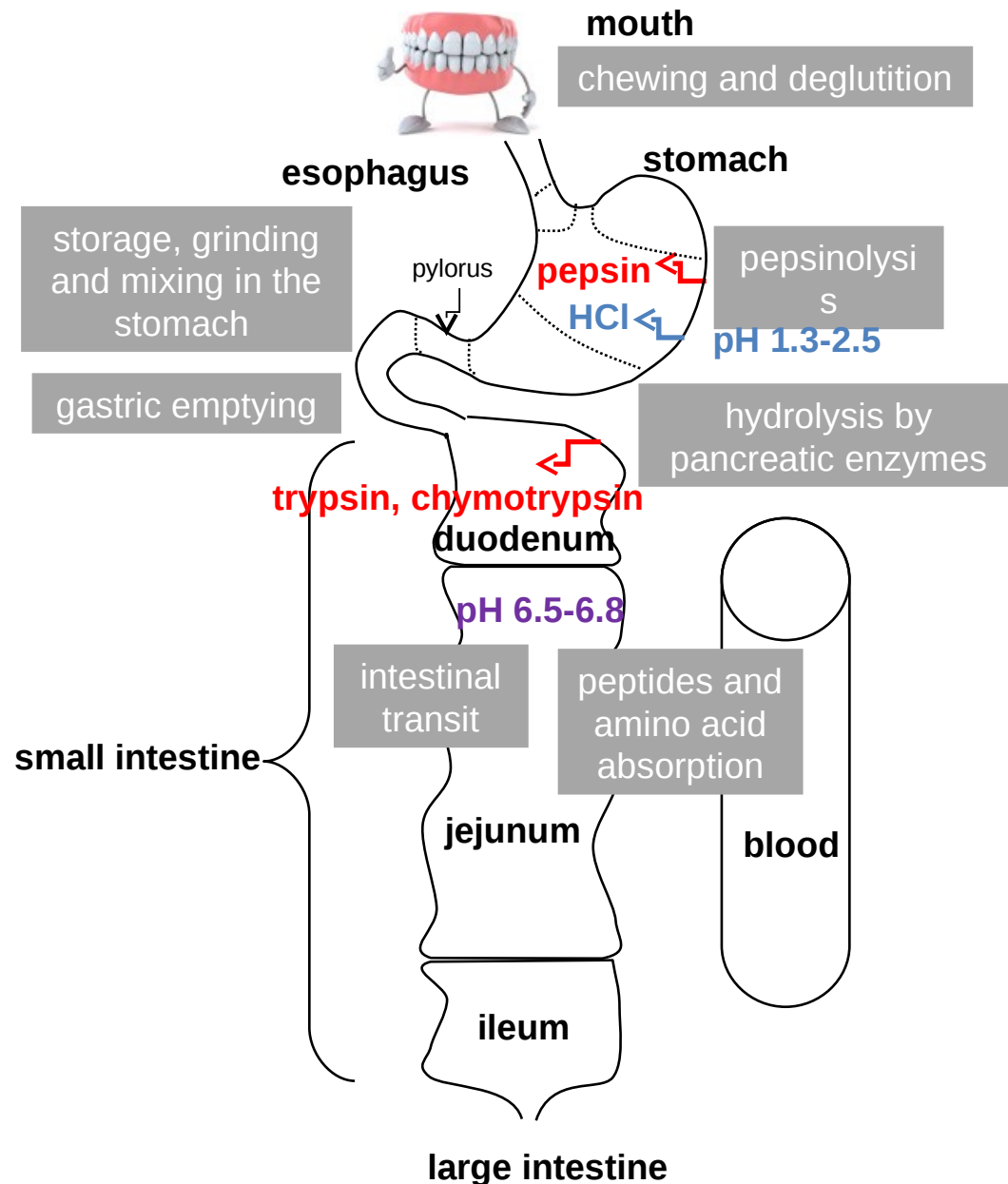
By increasing our knowledge on food digestion, we will increase our knowledge on the effect of food on human health

Our goals



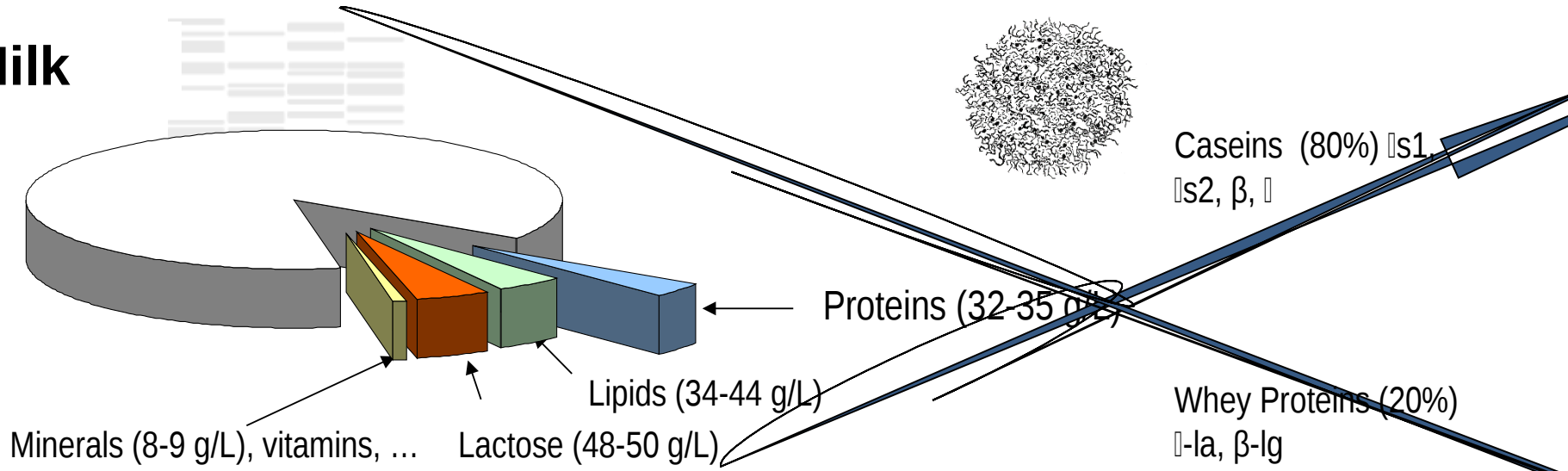
- To understand the mechanisms of breakdown of food matrices and their constituents in the gut and identify the beneficial/deleterious food components released during digestion
- To determine the impact of the structure of food matrices on these mechanisms
- To model these phenomena in order to develop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

The digestive process



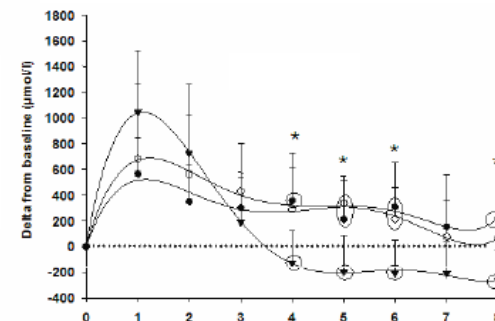
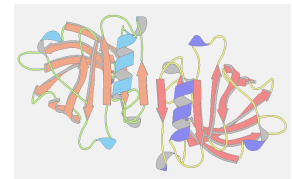
→ Gastric phase = key step for the whole digestion process

Milk



Caseins and whey proteins are:

- Structurally opposite (globular/flexible)
- Differently metabolized (fast/slow proteins)
- Highly digestible (>95%)
- Excellent sources of essential amino acids
- Milk can be transformed into several dairy products (liquids, gels, solids) of similar composition but different structure

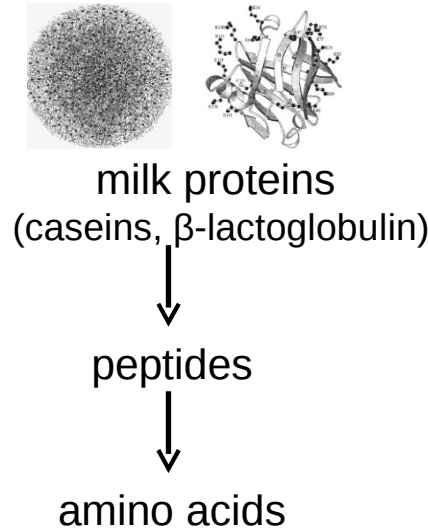


(Lacroix et al, 2006)

- ▼ whey protein
- casein
- Total milk protein

Does the food matrix regulate protein digestion and aa bioavailability?

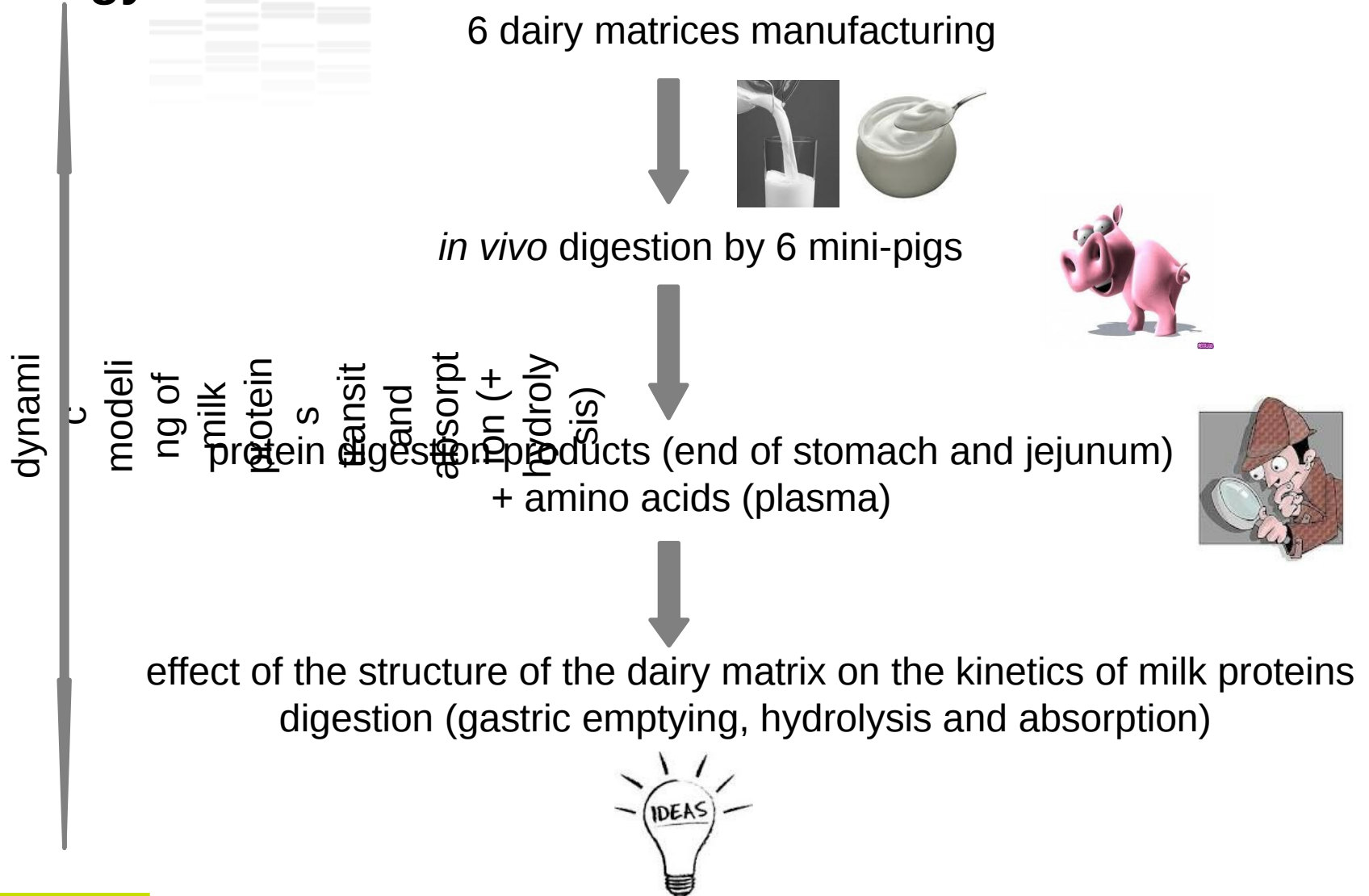
Understanding and modeling milk proteins digestion in the gastrointestinal tract of mini-pigs in relation with the dairy matrix ingested



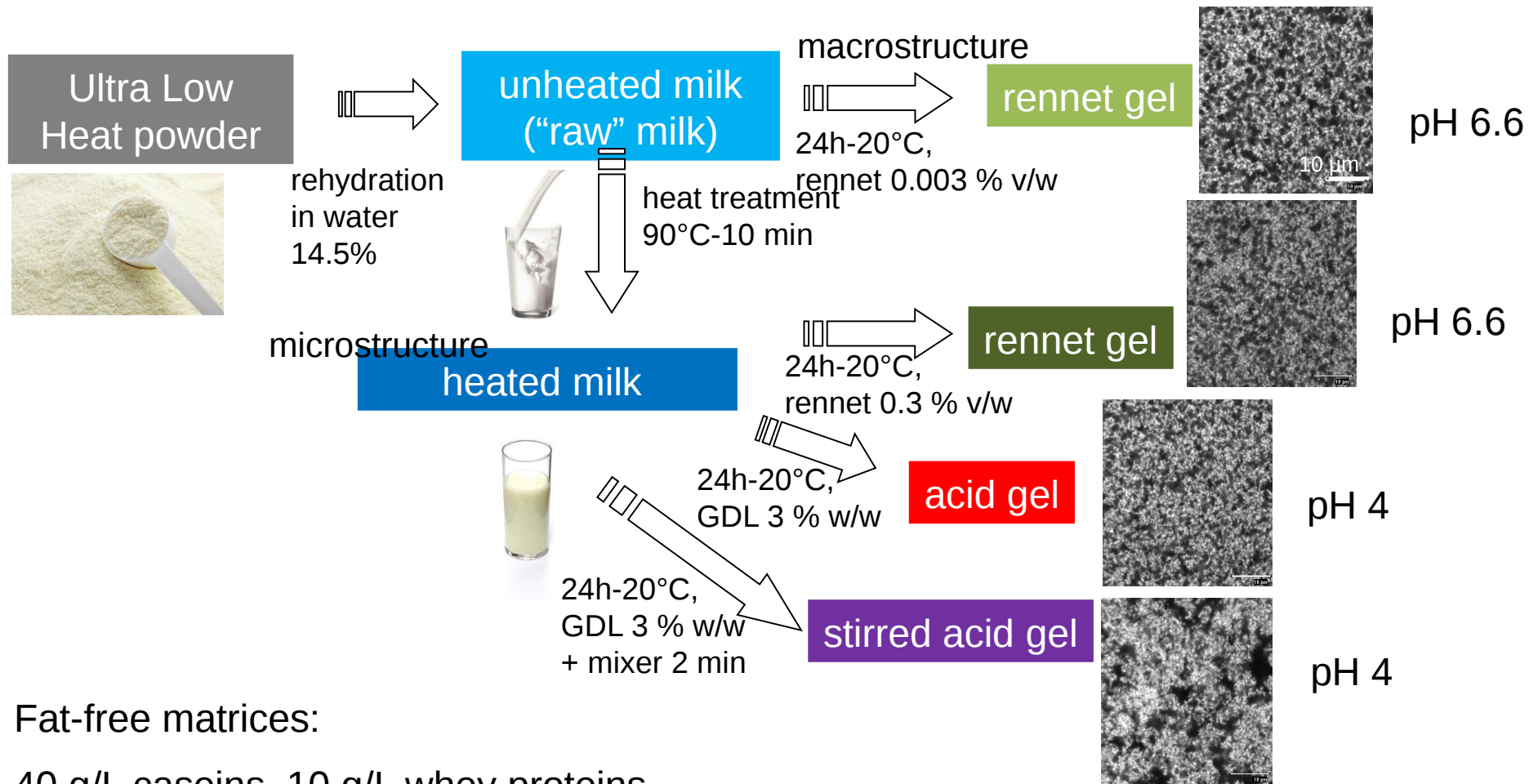
How does the milk product structure influence:

- 1) Transit and proteolysis in the gastrointestinal tract ?
- 2) Appearance of (bioactive) peptides in the lumen?
- 3) Release of amino acids in the blood compartment ?

Experimental strategy



The food matrices



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) □ Mean Retention Time in the stomach

The multi-canulated mini-pigs

6 minipigs ($20 \pm 1\text{kg}$)

1 catheter: abdominal aorta

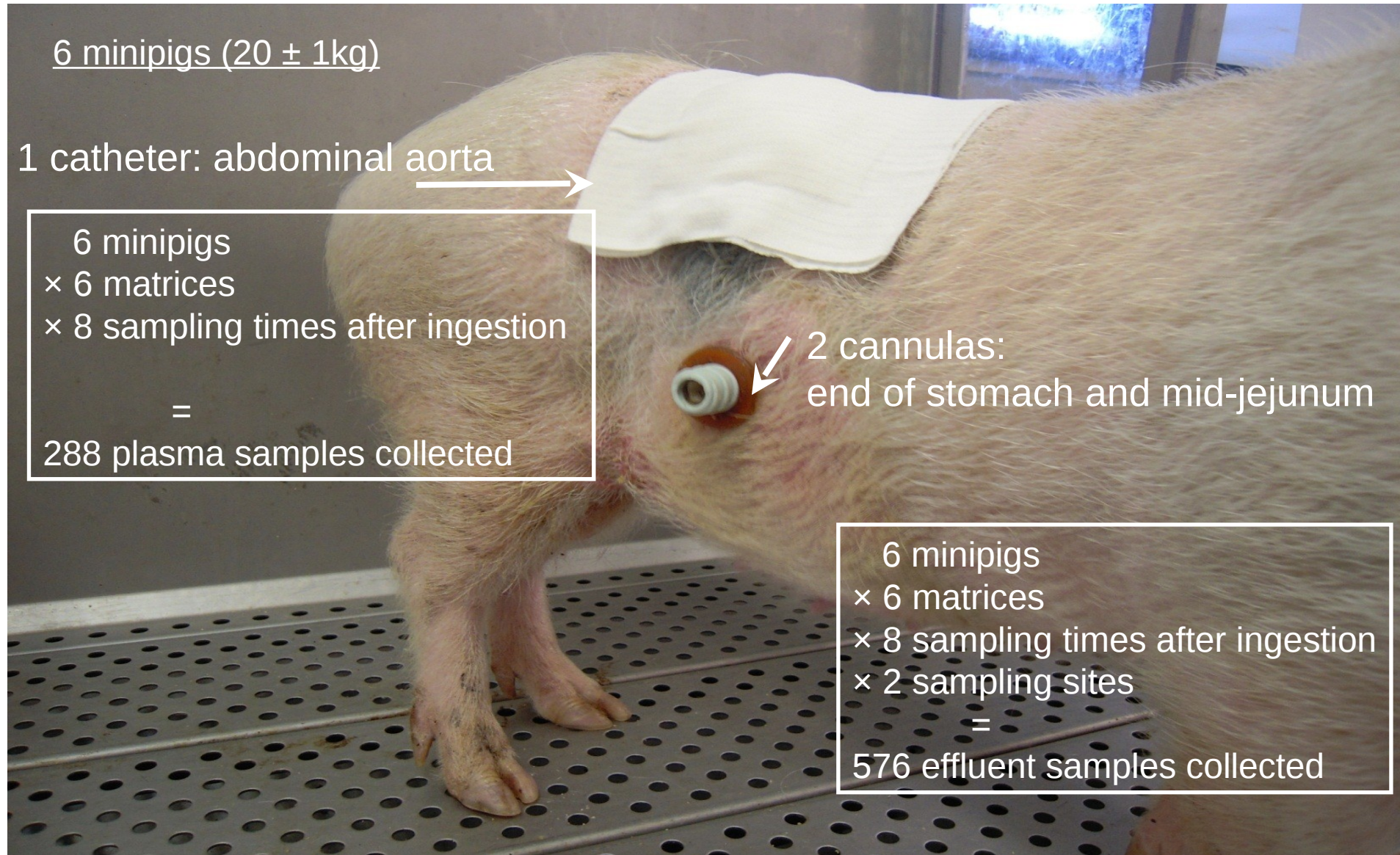
6 minipigs
× 6 matrices
× 8 sampling times after ingestion

=

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

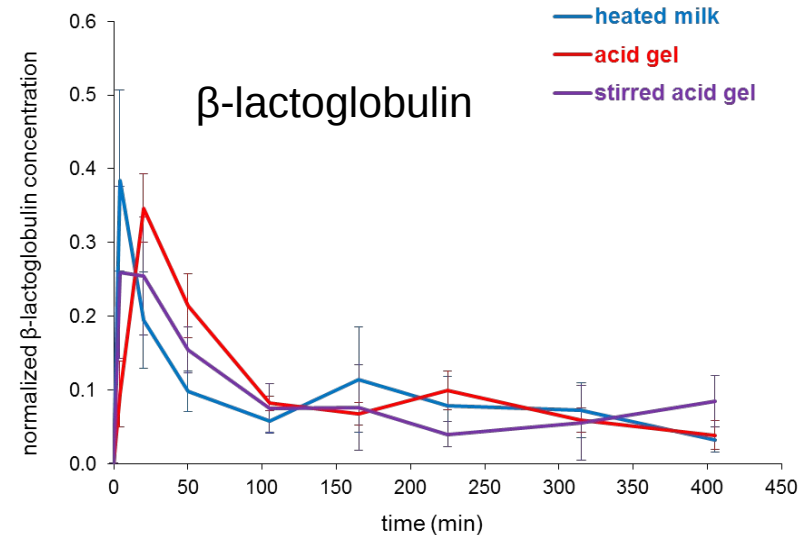
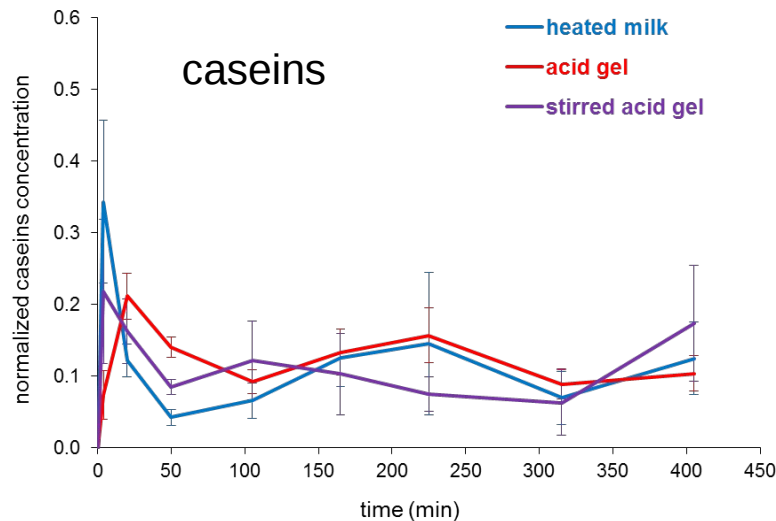


The liquid-gel transition



1) effect on transit

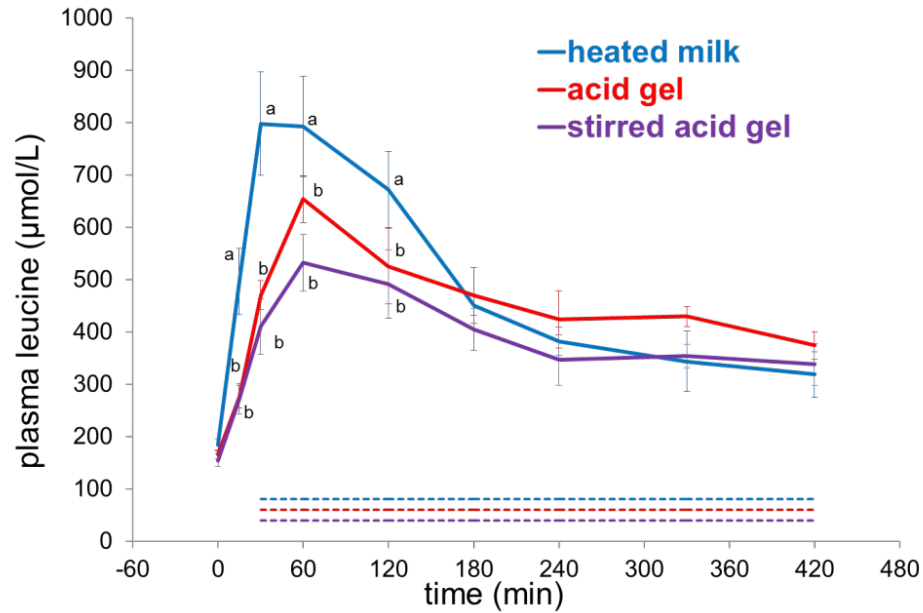
Mean Retention Time in the stomach (min) $96.9 \pm 14.3 \xrightarrow{\text{acid gelation}} 148.0 \pm 8.9 \xrightarrow{\text{stirring}} 124.0 \pm 14.2$



intermediate structure (stirring) $\square$ similar digestion kinetics liquid milk/stirred acid gel

The liquid-gel transition

2) effect on absorption

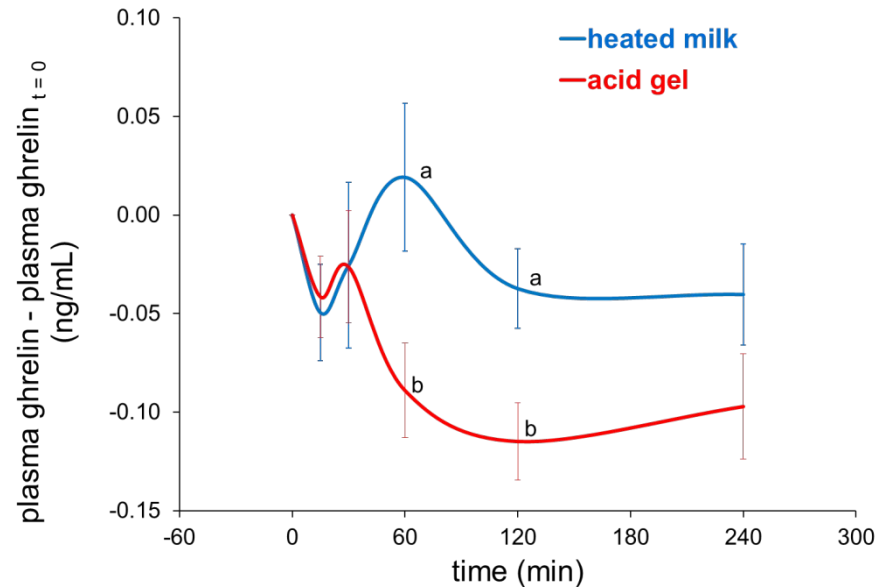


milk gelation:

□ 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 ?

Many bioactive peptides are released in the gut during digestion

More than
16000
peptides
identified in
the lumen

Barbé et al.
2014 Food Res
Int

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	Mido 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	Jnsmaa & Yoshikawa (1999)	■	■	■	■	■	■	■
β	98-105	OXI	Rival et al. (2001)	■	■	■				
β	114-119	OPI	Jnsmaa & 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	Jilles et al. (1986)							
β -Ig	32-40	HYP	Pihlanto-Leppala et al. (2000)		■	■	■	■	■	■
β -Ig	92-100	MIC	Pellegrini et al. (2001)		■					
β -Ig	142-148	HYP	Mullally et al. (1997)			■				

Impact of skim milk powder processing on casein digestion by an *in vitro* infant model

Hoarau B, Boutrou R, Jardin J, Molle D, Tanguy G, Gaucheron F, Schuck P, Léonil J,
Haab B* & Dupont D

INRA – Agrocampus Ouest, UMR STLO, 65 rue de St Briec 35042 Rennes France
* VAN ANDEL Institute, 333 Bostwick NE, Grand Rapids, MI 49503, USA



Objective: Determine if heat treatment affects casein digestion



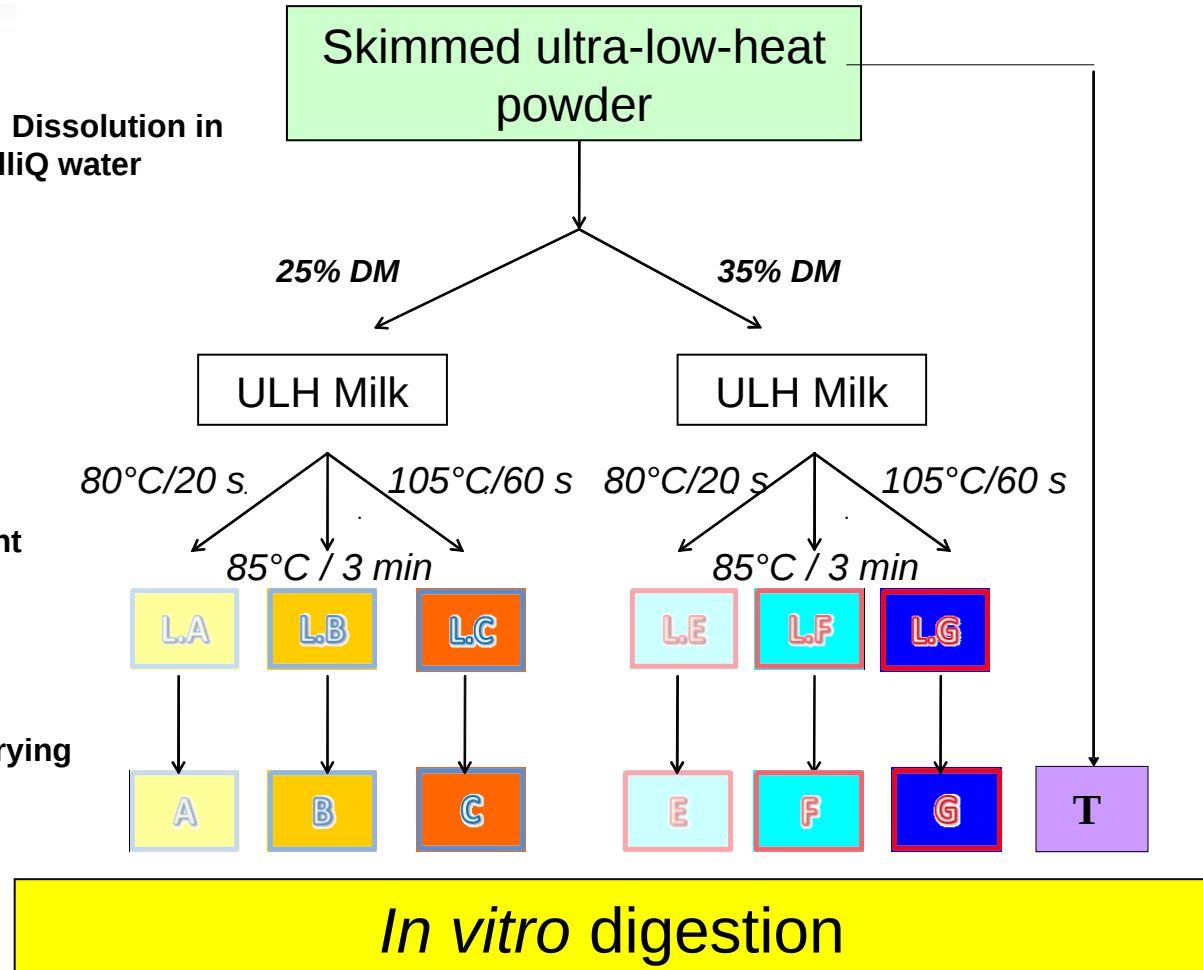
Step 1 : Dissolution in
milliQ water



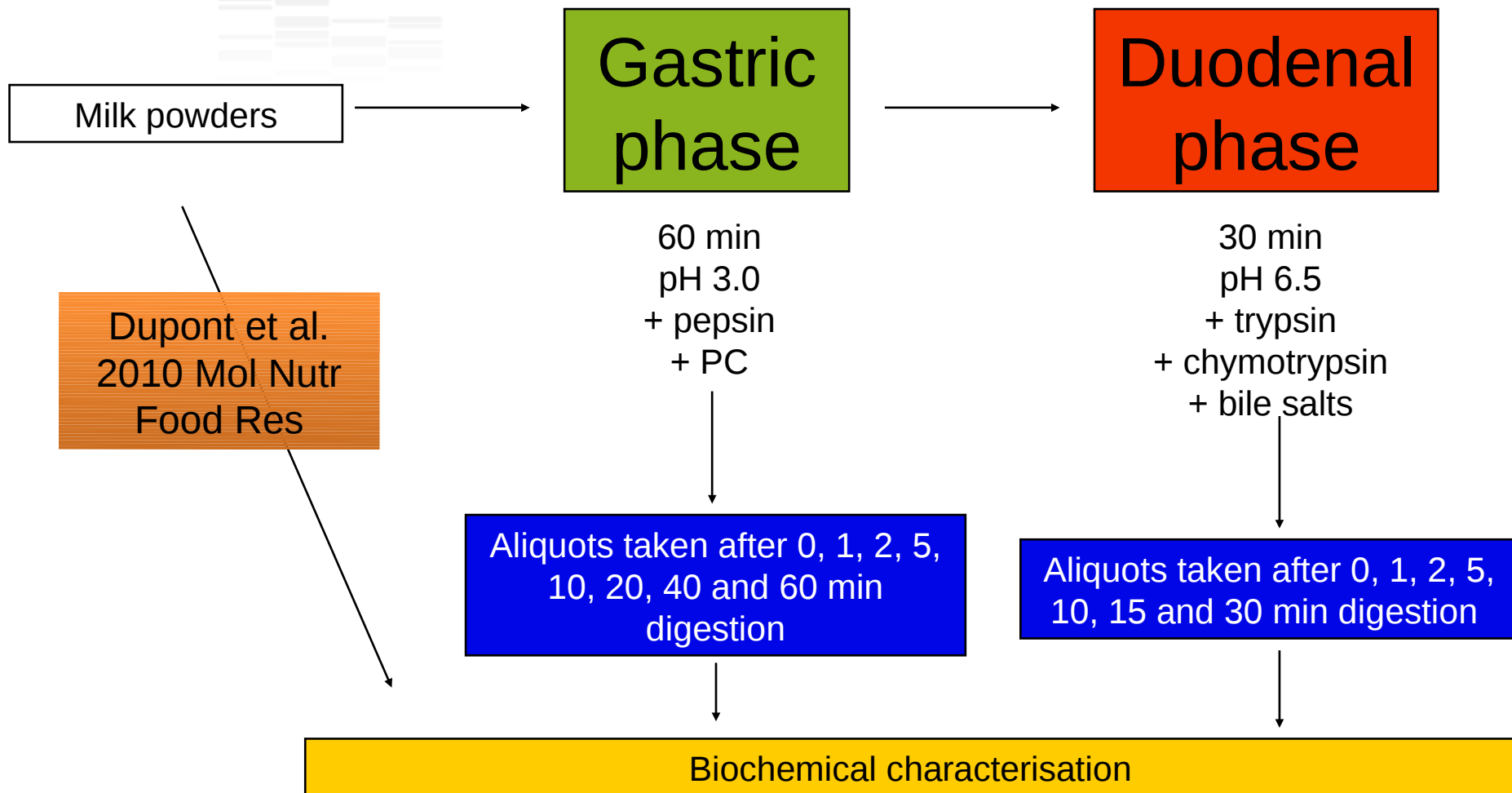
Step 2 :
Heat
treatment



Step 3 :
Spray drying

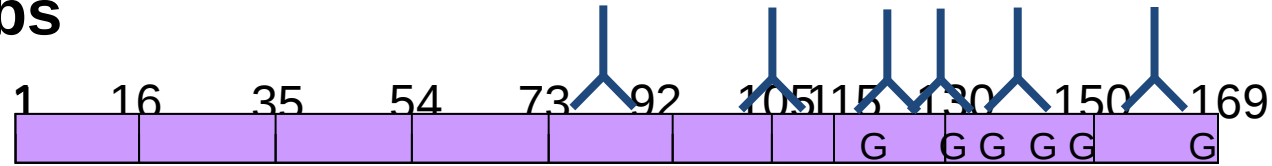


Infant gut Model

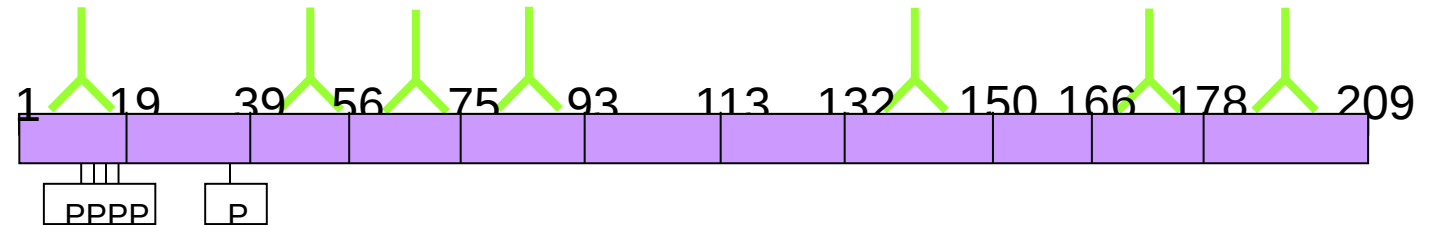


Identification of epitopes resistant to digestion using specific Mabs

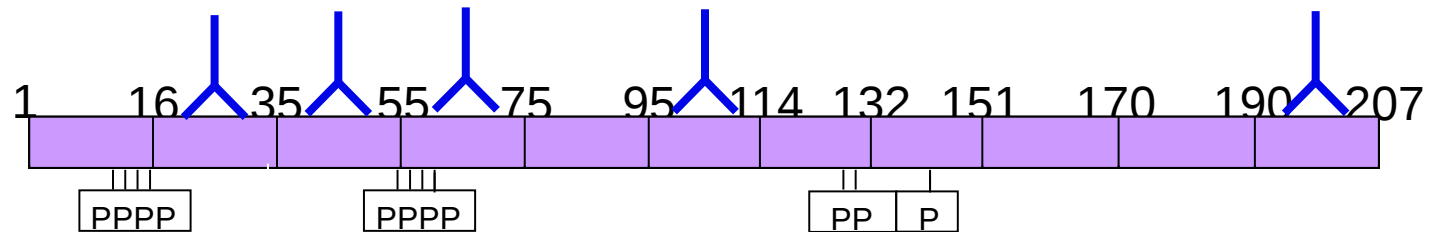
□ -
casein



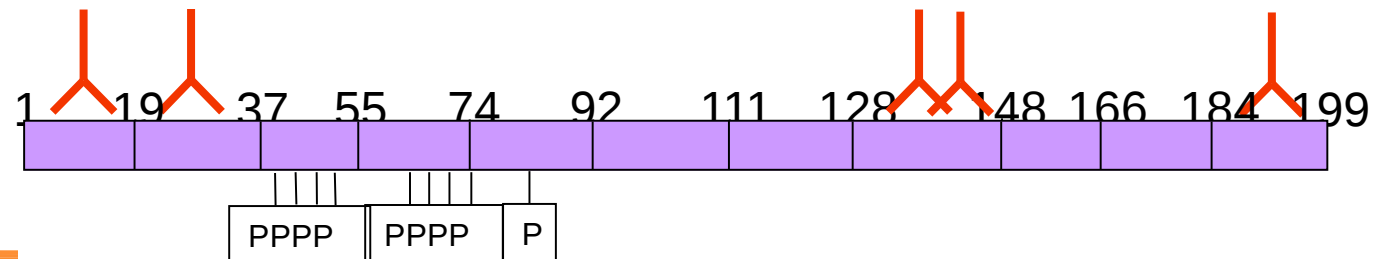
□ -
casein



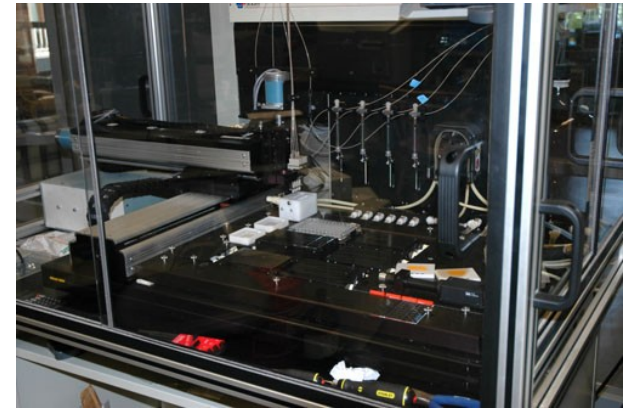
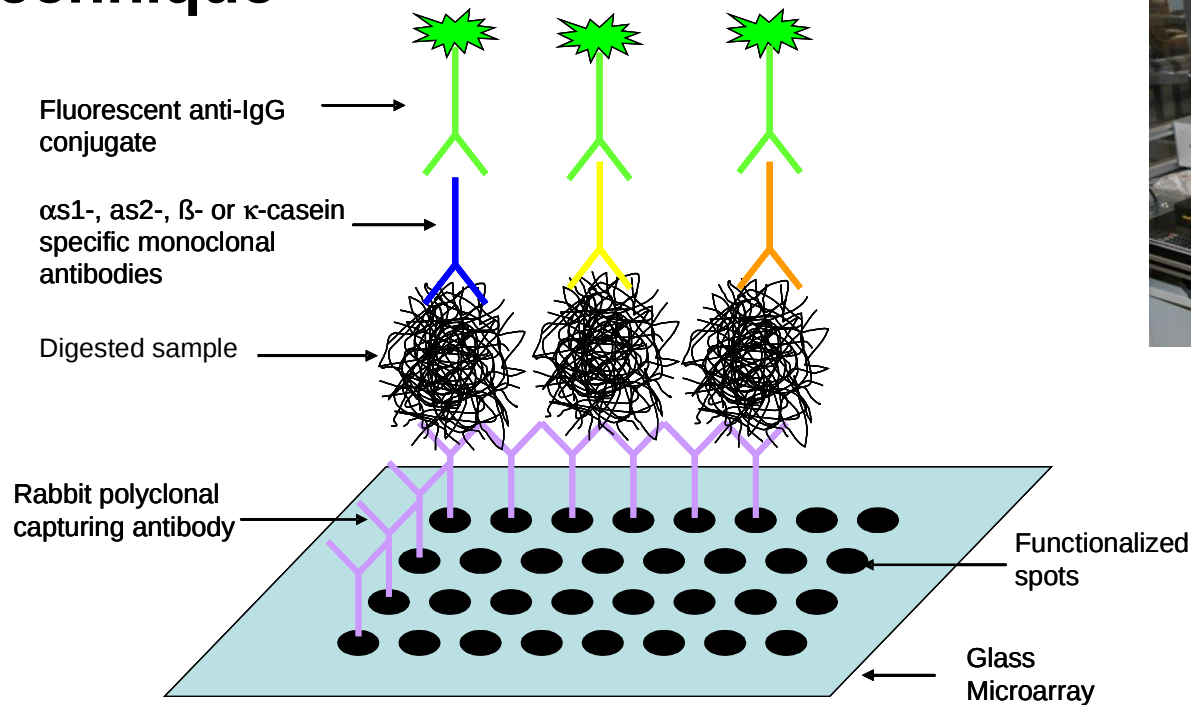
□ s2-
casein



□ s1-
casein



Principle of the technique

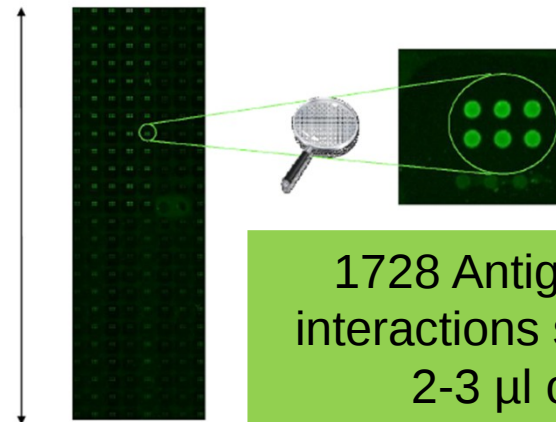


Dupont et al.
2010 Food Dig

Van Andel Inst.

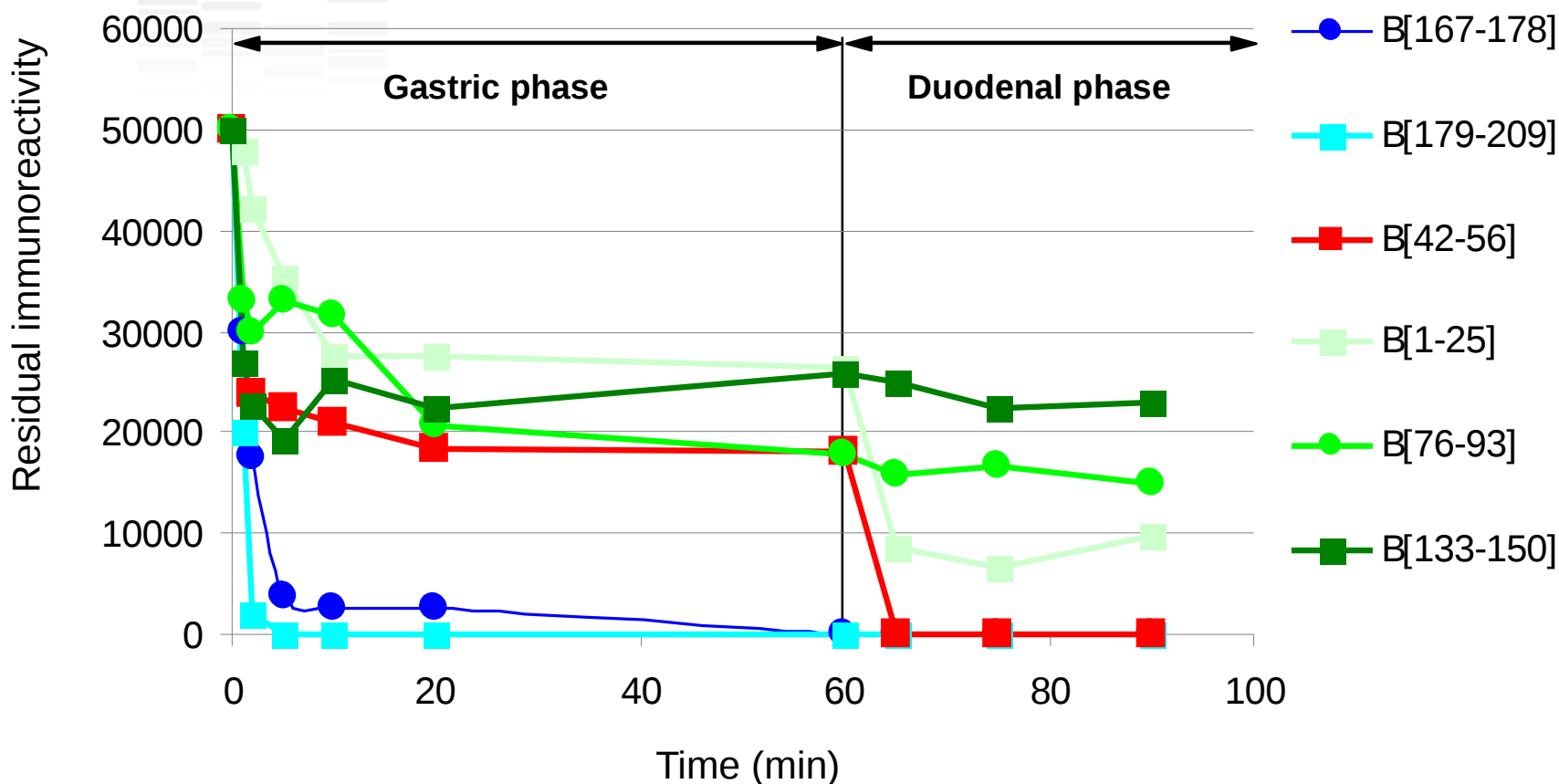


Microscope slide



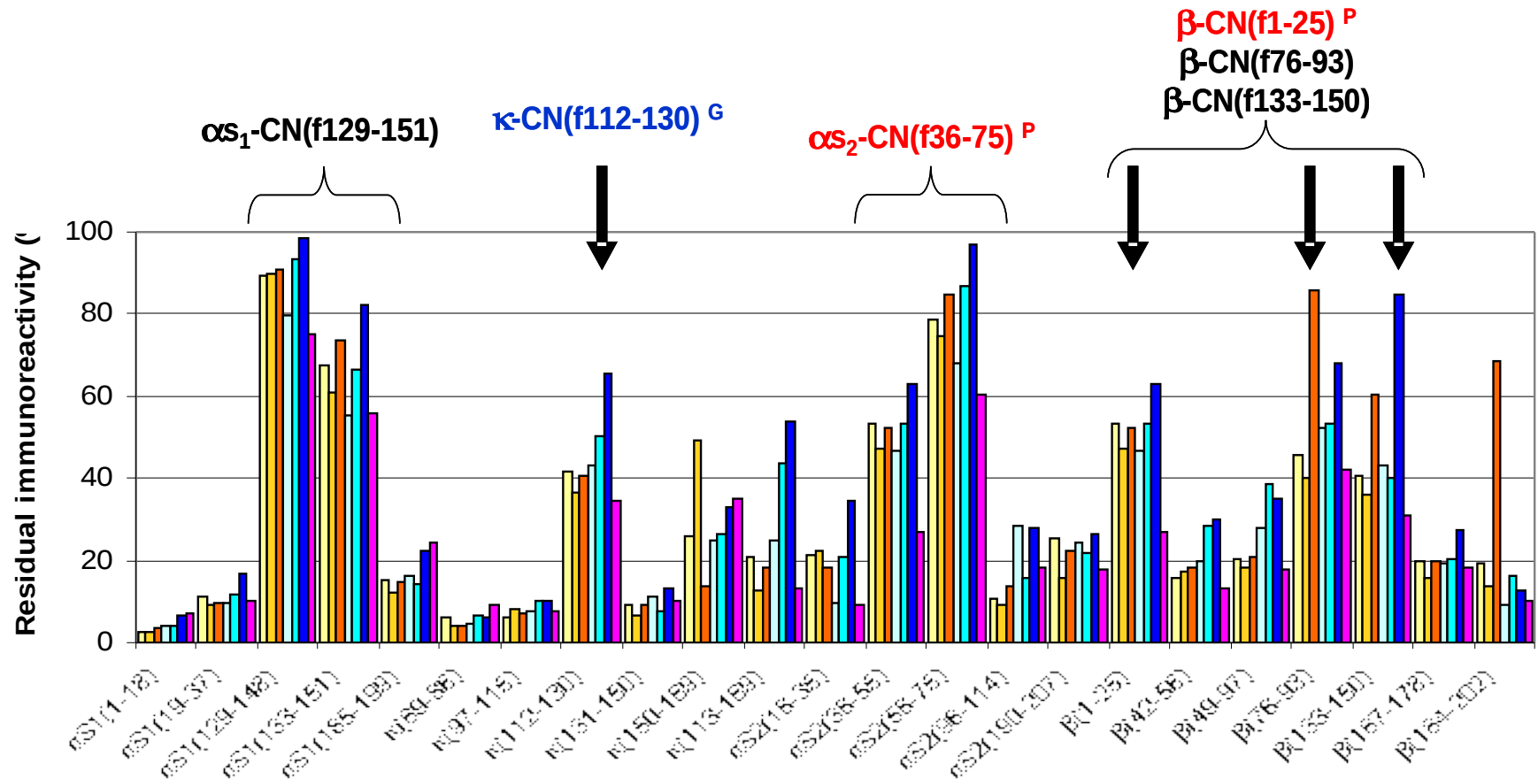
1728 Antigen-Antibody
interactions simultaneously
2-3 μ l of sample

Kinetics of β -casein digestion



□ Kinetics of □-casein digestion differ according to the area studied

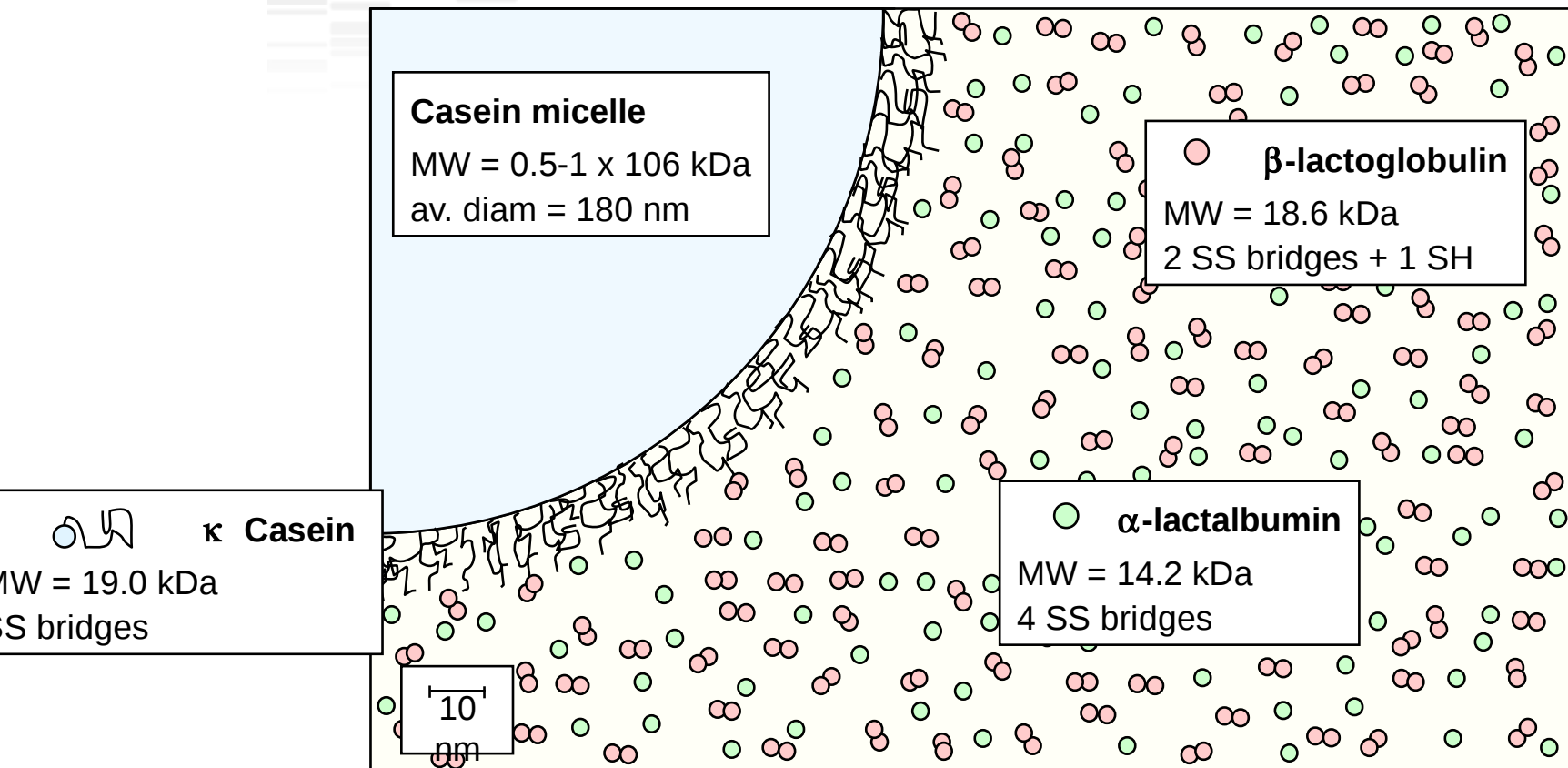
Residual immunoreactivity of casein fragments



Factor	p value	Significance
T	0.00001	***
% DM	0.00555	**
T:%DM	0.03262	*

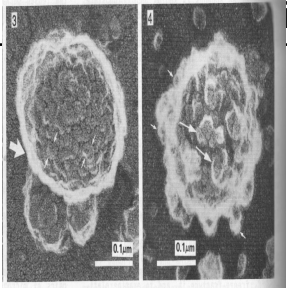
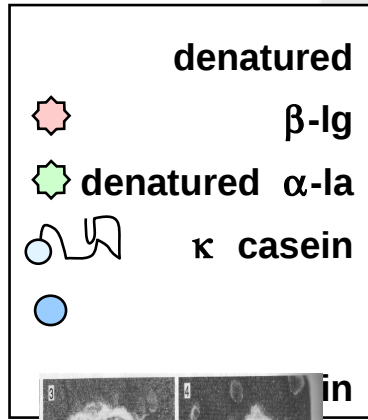
Increasing the heat-treatment makes casein more resistant to digestion

Thermal aggregation of whey proteins on the casein micelle

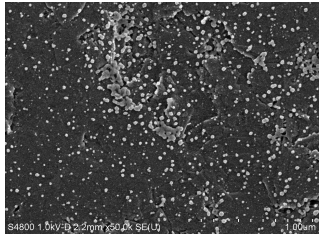


To scale schematic representation of the major whey proteins and of the casein micelle in unheated milk

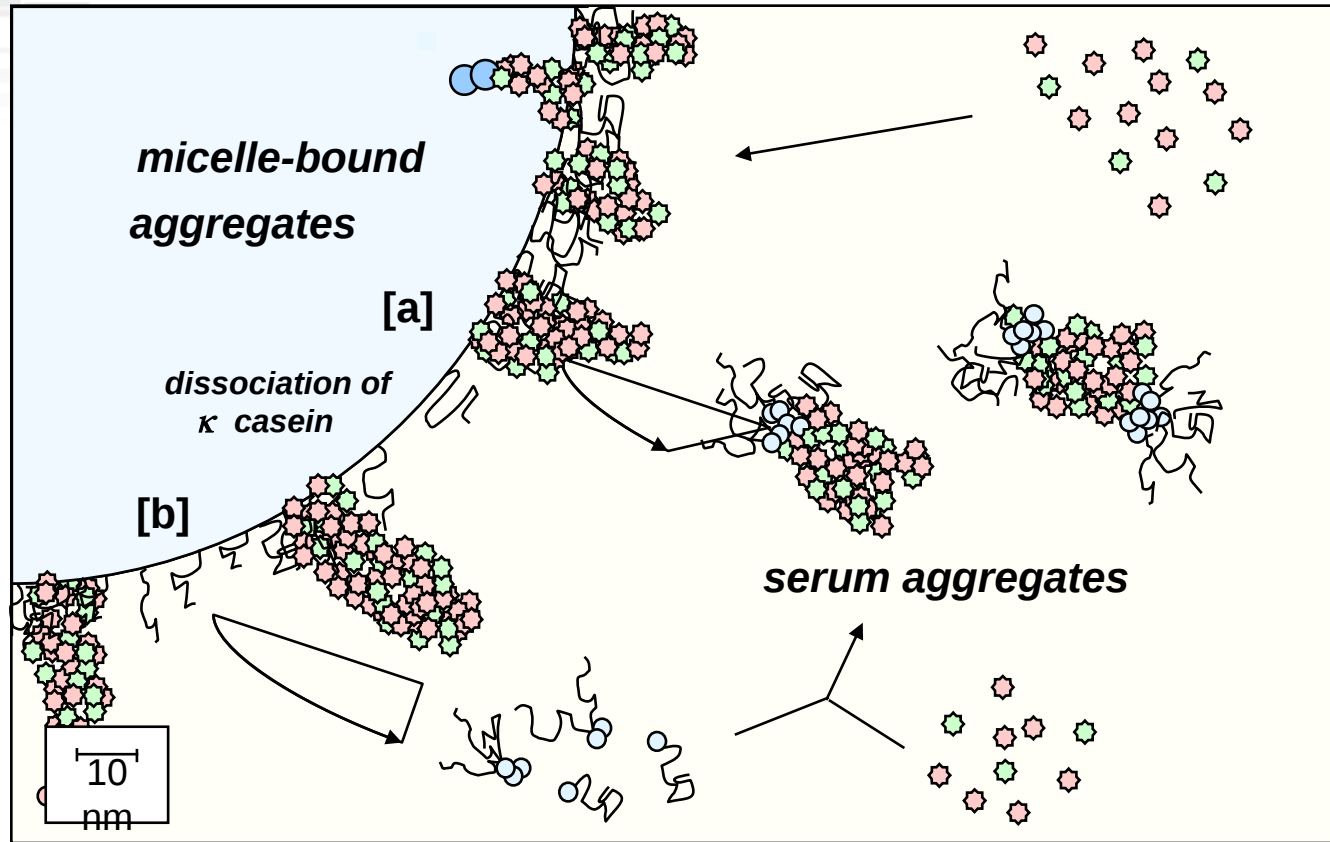
Thermal aggregation of whey proteins on the casein micelle



a (Harwalkar et al., 1989)

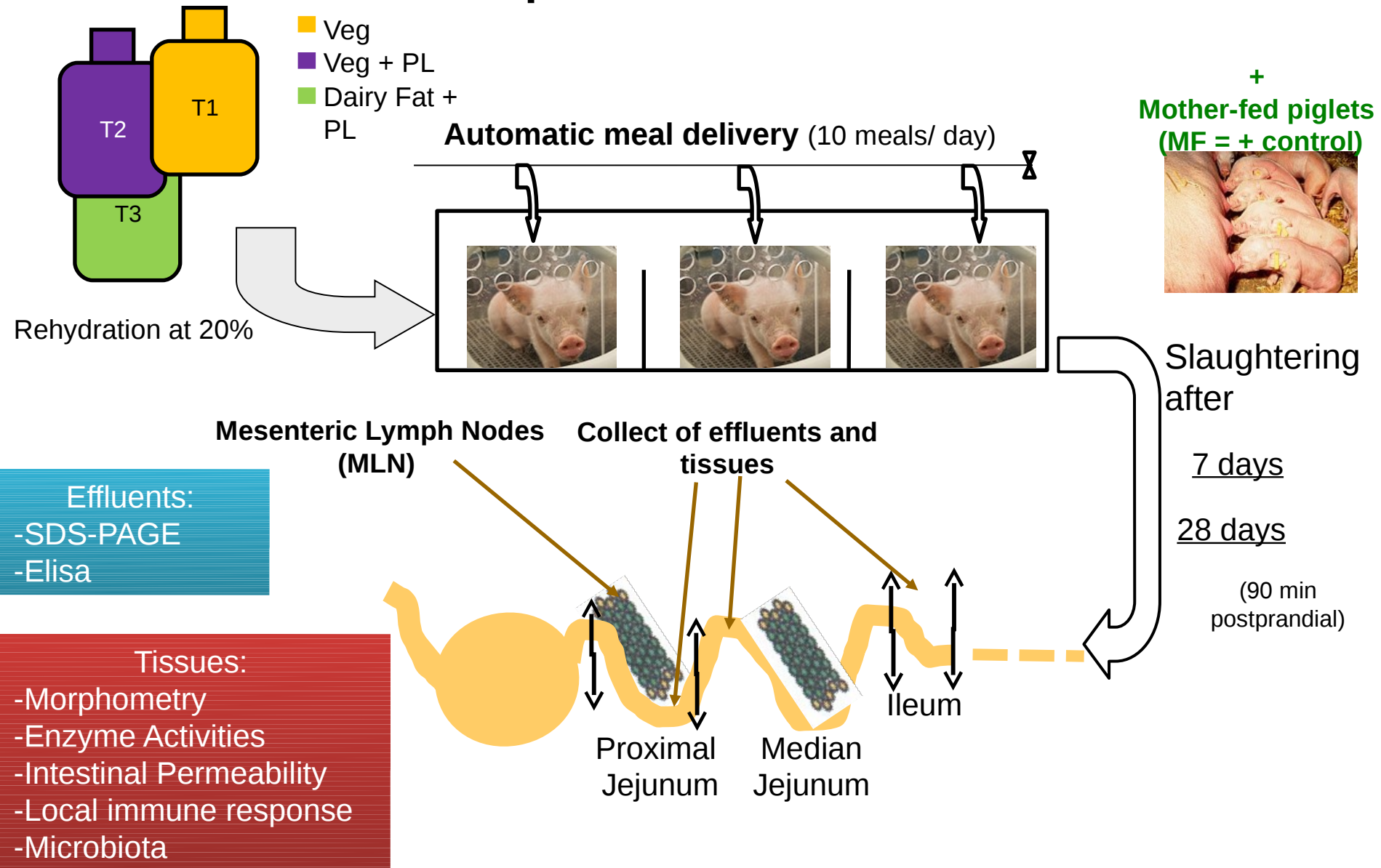


b (Rodriguez del Angel & Dalgleish, 2006)



Micelle-bound and serum aggregates are formed, containing denatured whey proteins, κ casein and possible traces of α s2 casein. [a] and [b] indicate the 2 possible ways for the formation of the serum aggregates.

Can IF of different composition modulate the physiological response of the host?

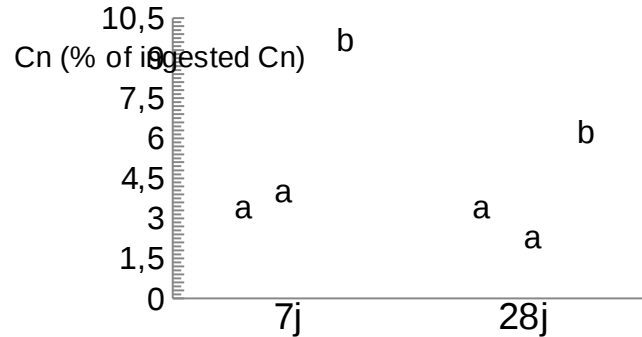


Protein Digestion

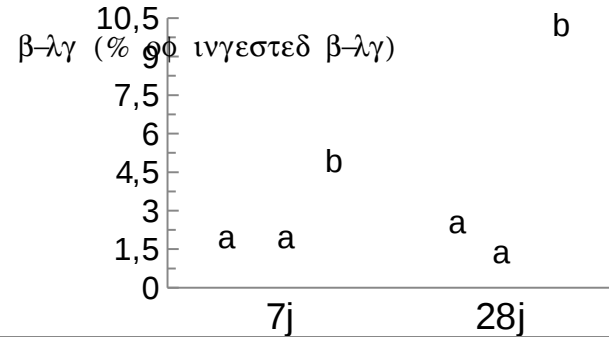
Casein

β -lactoglobulin

Cn (% of ingested Cn)

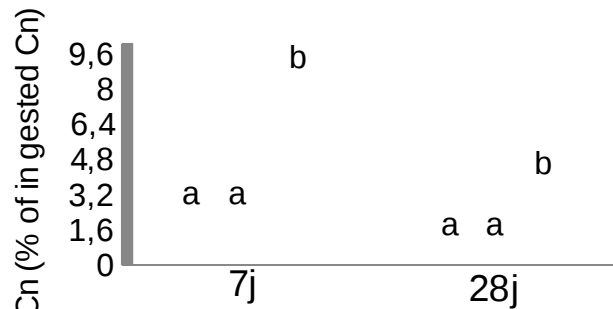


β -lg (% of ingested β -lg)

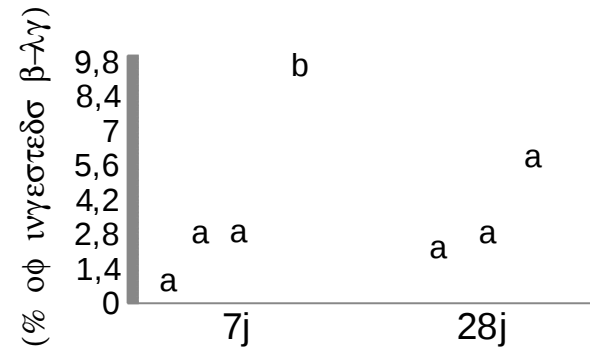


■ Veg
■ Veg + PL
■ Dairy Fat + PL

Cn (% of ingested Cn)



(% of ingested β -lg)

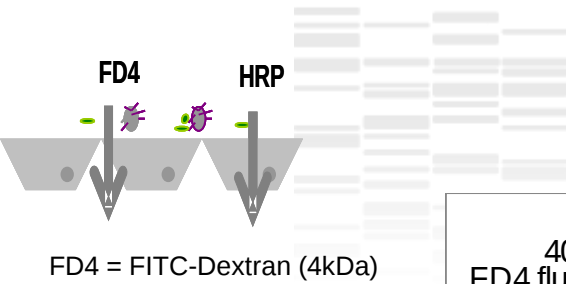


Milk Proteins better resist to intestinal digestion in the presence of dairy fat

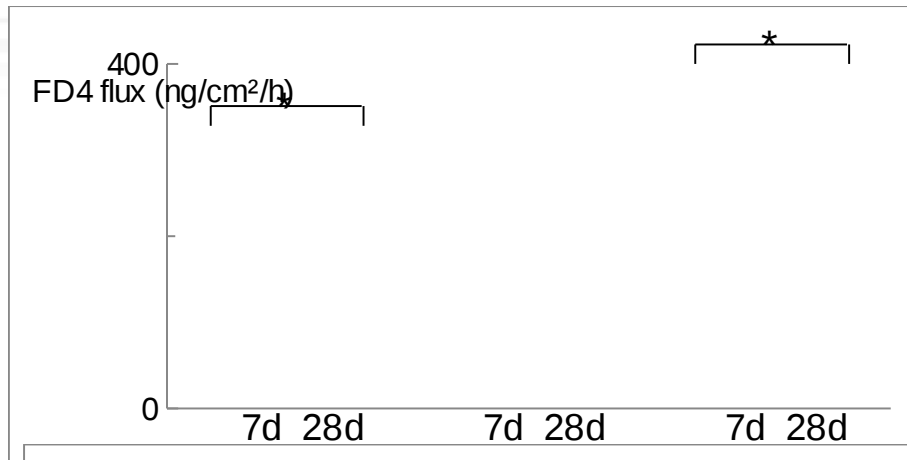
□ Modification of the interface

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

Paracellular Permeability

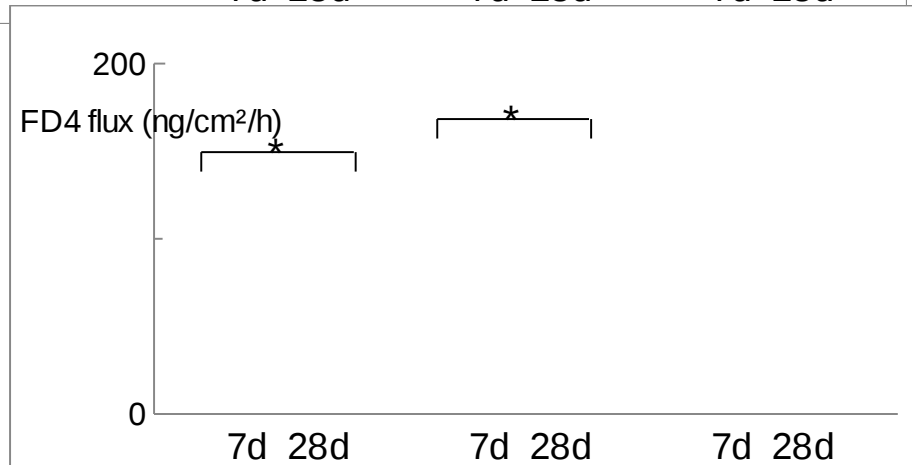


Jejunum



- Veg
- Veg + PL
- Dairy Fat + PL

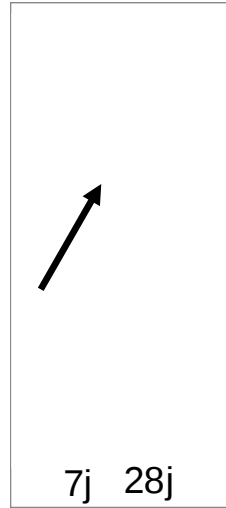
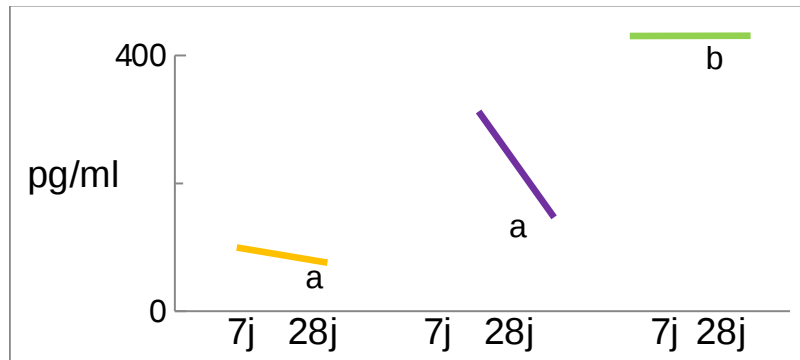
Ileum



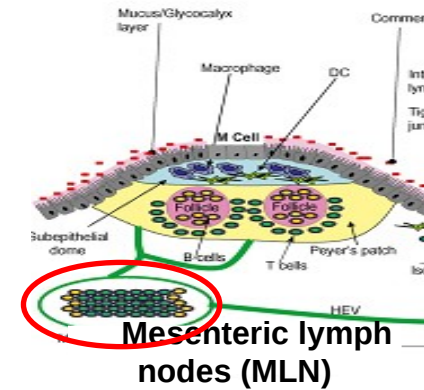
Limited effect of the infant formula structure/composition on paracellular permeability

Secretory activity of MLN

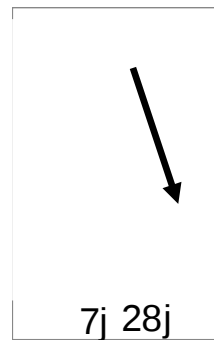
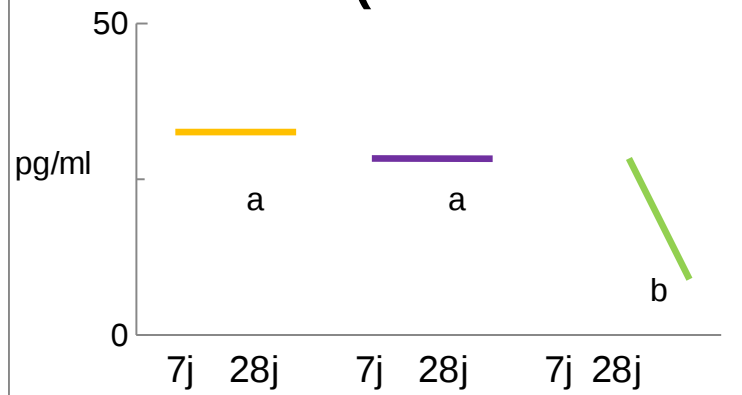
Interferon- γ (Th1 pro-inflammatory)



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

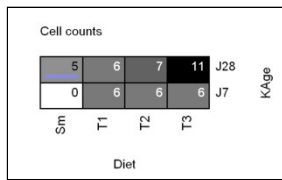


Interleukine-10 (Th2 anti-inflammatory)

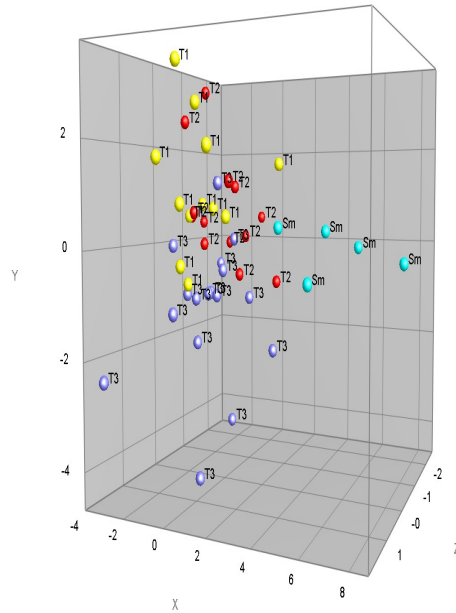


Milk lipids □ maturation of the piglet's immune system more similar than with sow's milk

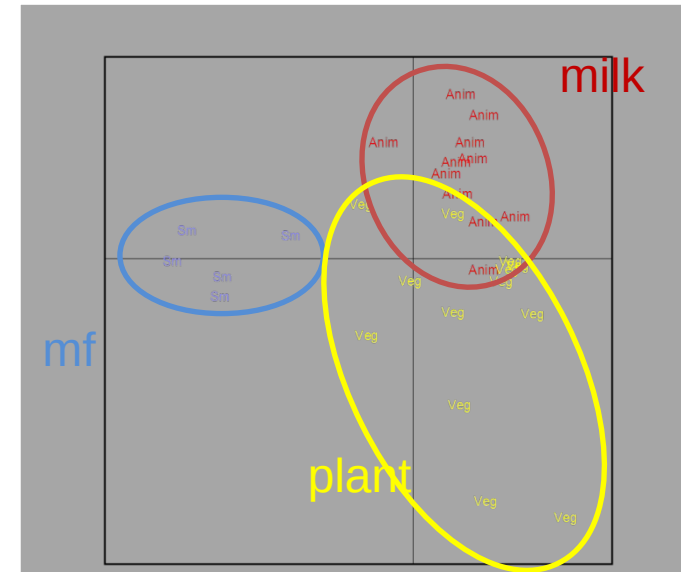
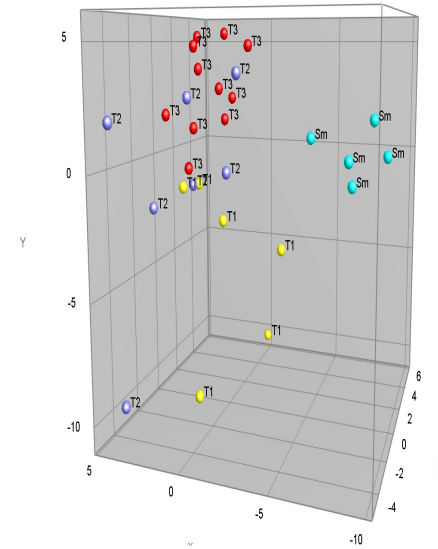
Microbiota by DHPLC



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 of dairy products, as modified by the processing conditions, regulates the kinetics of protein digestion and dietary amino acids bioavailability

For the neonate, substitution of vegetable oil by milk fat allows a better maturation of the immune system and a modification of the microbiota, but more work is needed to determine whether these modifications are transient or will remain with time

Understanding the disintegration of dairy products in the gastrointestinal tract is essential for designing new foods dedicated to specific sub-populations (elderly, athlete, infant, overweight people....)

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



320 scientists - 110 institutes – 34 countries



INFOGEST
International Conference
| Naples, Italy
6 March 2015

We are pleased to announce the next
4th International Conference on Food Digestion
organized by the
COST Action FA1005 INFOGEST



in Naples, 17-19 March 2015