



An overview of the models available for simulating food digestion

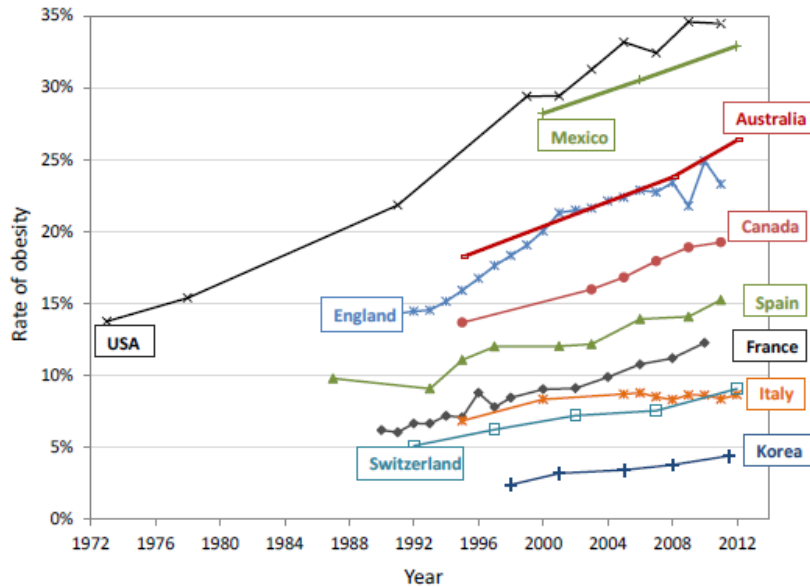


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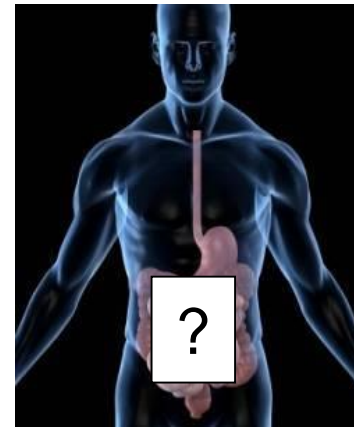
INRA Agrocampus Ouest – Milk and Egg Science & Technology
Rennes FRANCE



Food and human health: the key role of digestion



Diet-related diseases ↑
Prevent these pathologies rather than
cure them



Gut = interface between food and human body

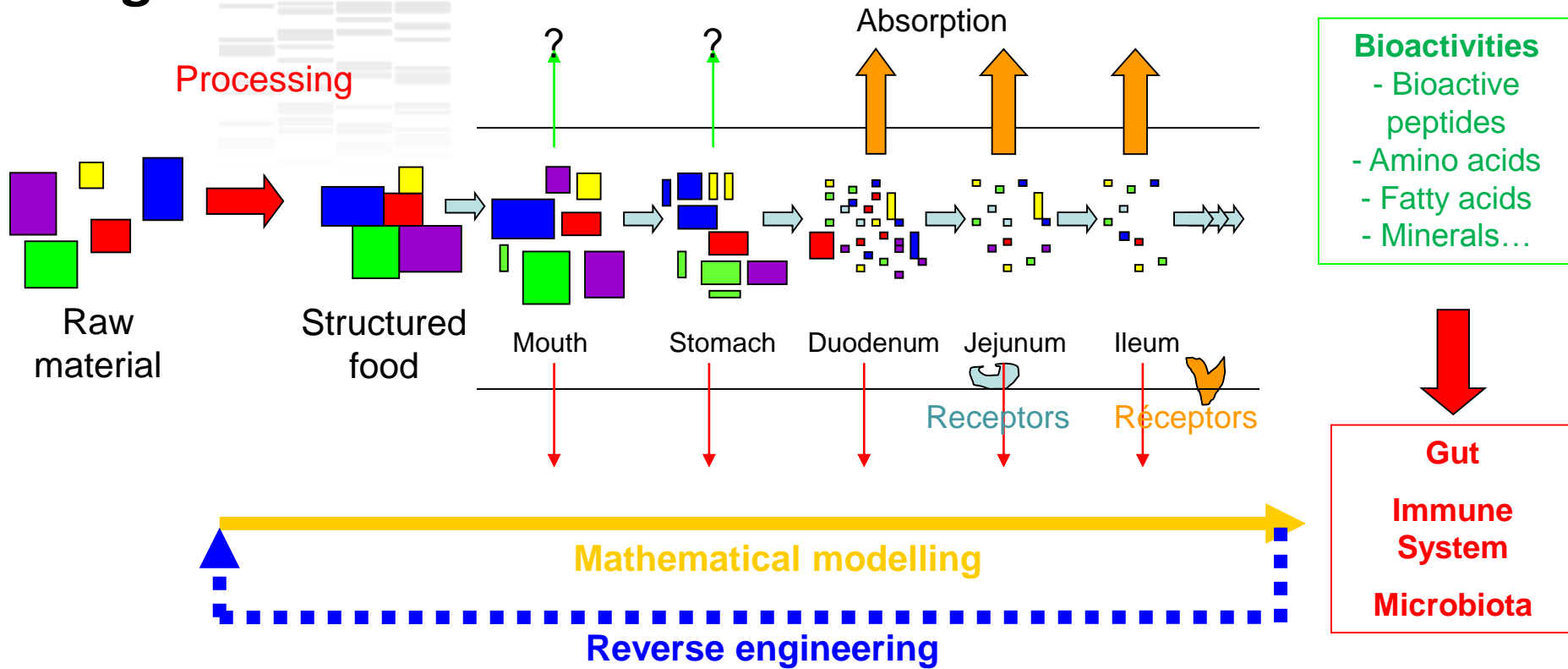
Digestion releases food components that can have a beneficial or a deleterious effect on human health

... 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

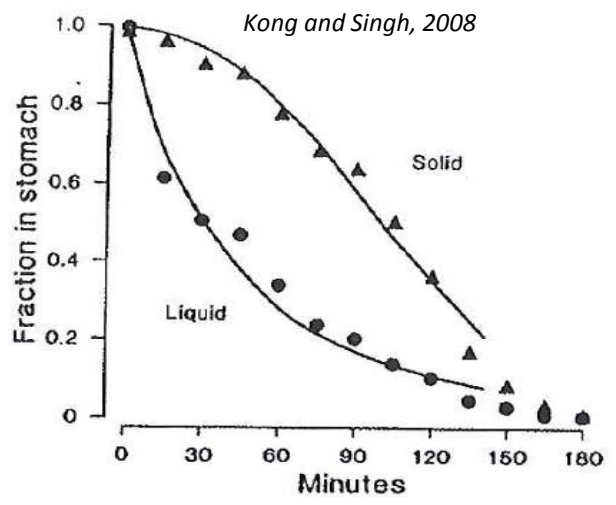
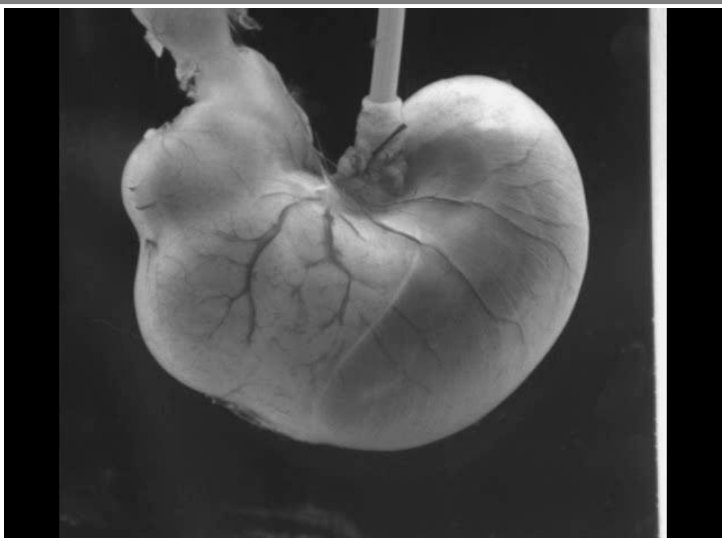
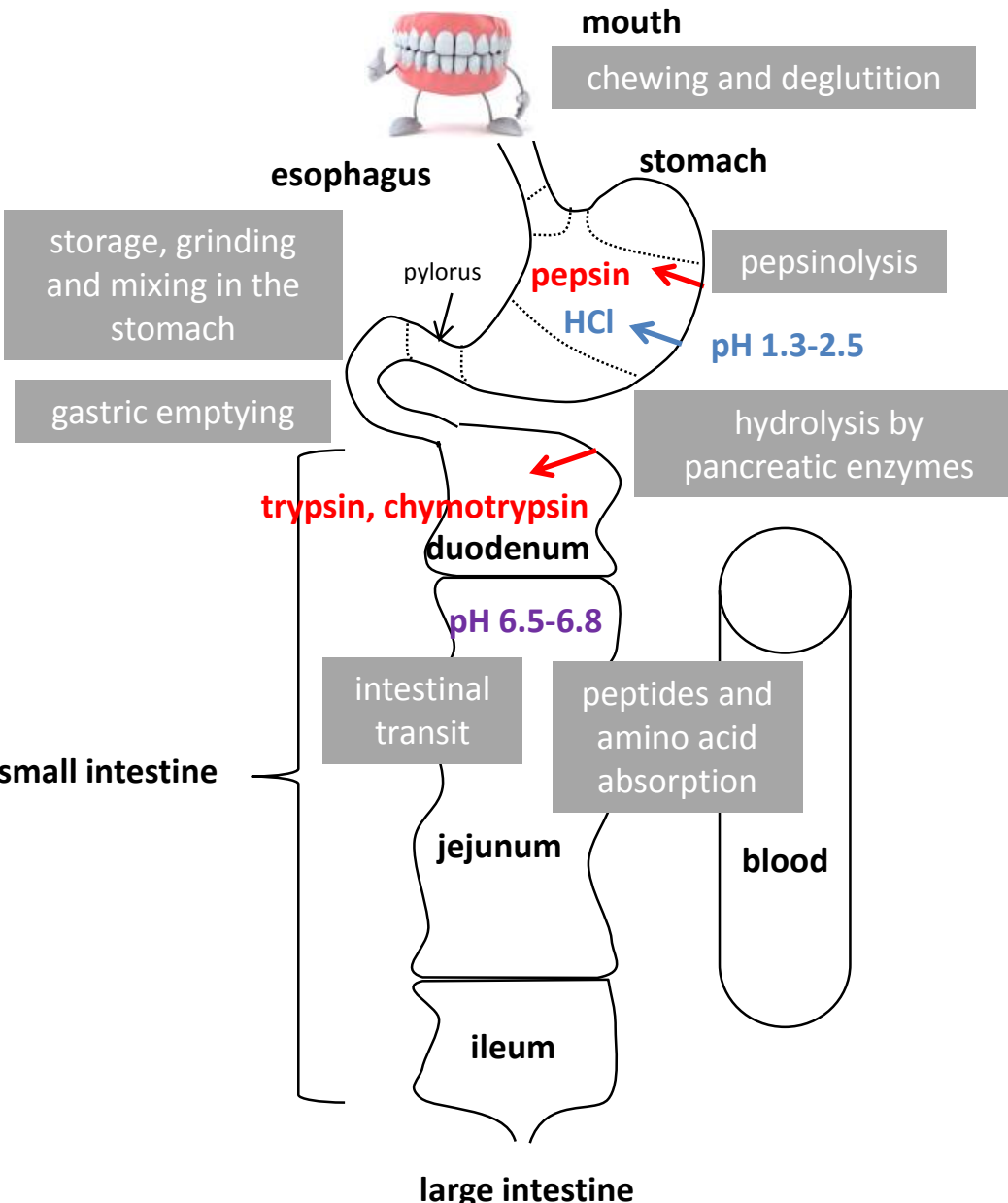
Our goals

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 digestive process



→ Gastric phase = key step for the whole digestion process

Models available at INRA for simulating digestion

Menard et al. 2014,
Food Chem
Sanchez et al. 2015
Food Res Int

Dupont et al.
2010ab,
Mol Nutr Food Res



*In vitro static models
(infant, adult)*

Le Feunteun et al.
2014
Food Bioprocess
Tech

*In silico
models*

$$\Phi_{12} = k_{12whey} \times (V_1 - m_{caswpd1} \times \alpha) + k_{12aggr} \times m_{caswpd1} \times \alpha$$



*In vitro dynamic models
(infant, adult, elderly)*



*Human
models*



Animal models



De Oliveira et al. 2016
Am J Clin Nutr
De Oliveira et al. 2017
Clin Nutr



Barbé et al. 2013, 2014
Food Chem
Le Huerou-Luron et al.
2016 Eur J Nutr

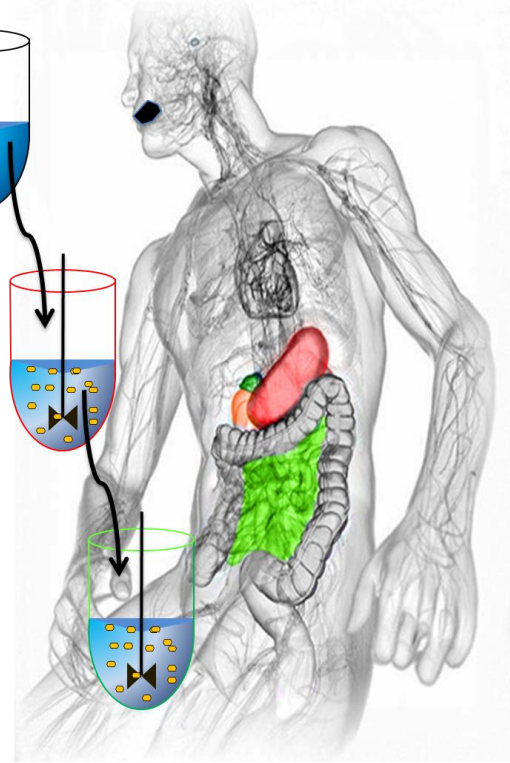
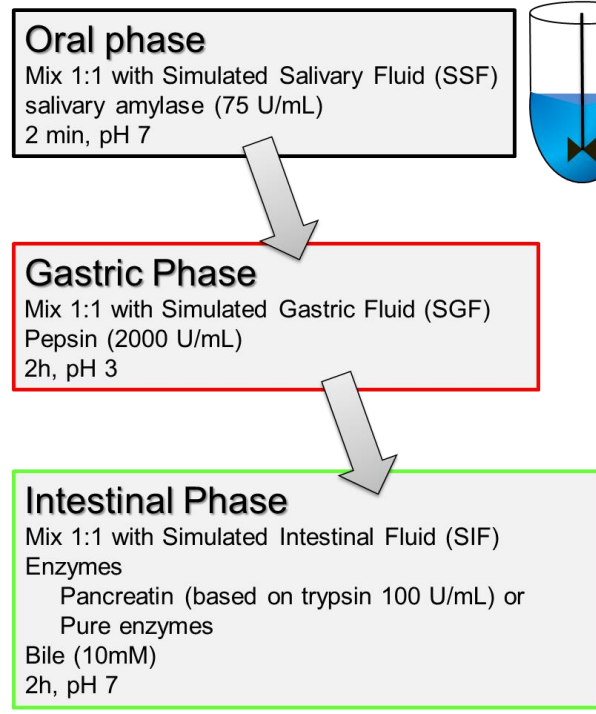
Static *in vitro* digestion models

- ☞ Huge diversity between the models mimicking the GI tract of the adult (E/S, pH...)
- ☞ Impossible to compare results from one study to another – Need for harmonization

Consensus *in vitro* digestion method for food

INFOGEST

International network
– 400 researchers
– 140 institutes
– 41 countries



A standardised static *in vitro* digestion method suitable for food- an international consensus, Food & Function, Minekus et al. 2014 – Highly Cited Paper 500 citations in 4 years!

The INFOGEST model can be learned through videos on YouTube

The screenshot shows a web browser window displaying a YouTube channel page. The browser's address bar shows the URL: https://www.youtube.com/channel/UCdc-NP9kTDGyH_kZCgpQWg. The YouTube search bar contains the text "cost infogest". The channel banner features a diagram of the human digestive system. The channel name is "In vitro food digestion - COST action INFOGEST". Below the banner, there are navigation tabs for "Accueil", "Vidéos", "Playlists", "Chaînes", "Discussion", and "À propos". A "S'abonner" button shows 36 subscribers. The main content area displays a list of videos. The first video is titled "Alpha Amylase Activity Assay for In Vitro Food Digestion" with a duration of 5:12. The second video is titled "Static In Vitro Digestion Method for Food" with a duration of 8:55. Both videos include a diagram of the digestive system with arrows indicating the Oral, Gastric, and Intestinal phases. On the right side, there is a "Chaînes populaires sur YouTube" section listing several channels with "S'abonner" buttons.

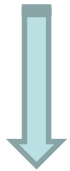
Static *In vitro* digestion models: pro's & con's



Main Reasons:

Ethical - Technical – Financial

in vivo



in vitro

Advantages:

Standardisation of the experimental conditions
Good reproducibility and repeatability
Easy sampling, possibility to follow kinetics

Disadvantages:

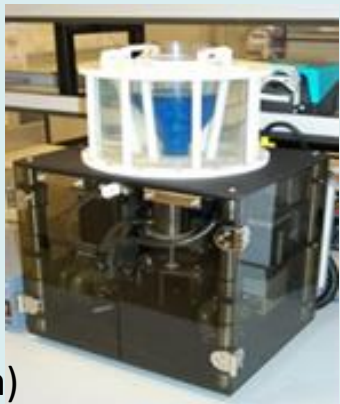
You cannot mimic the complexity of the GI tract in a test tube!!!

Bohn et al. 2017
Crit Rev Food Sci
Nutr

Dynamic *in vitro* digestion models



DGM
(stomach)



HGS
(stomach)

ARCOL
(colon)



Mono-compartmental models

DIDGI (stomach + small intestine)



Dupont et al. 2017
Crit Rev Food Sci
Nutr

TIM
(TIM1 =
duod+jej+ile
TIM2 = colon)



Multi-compartmental models

SIMGI (whole GI tract)



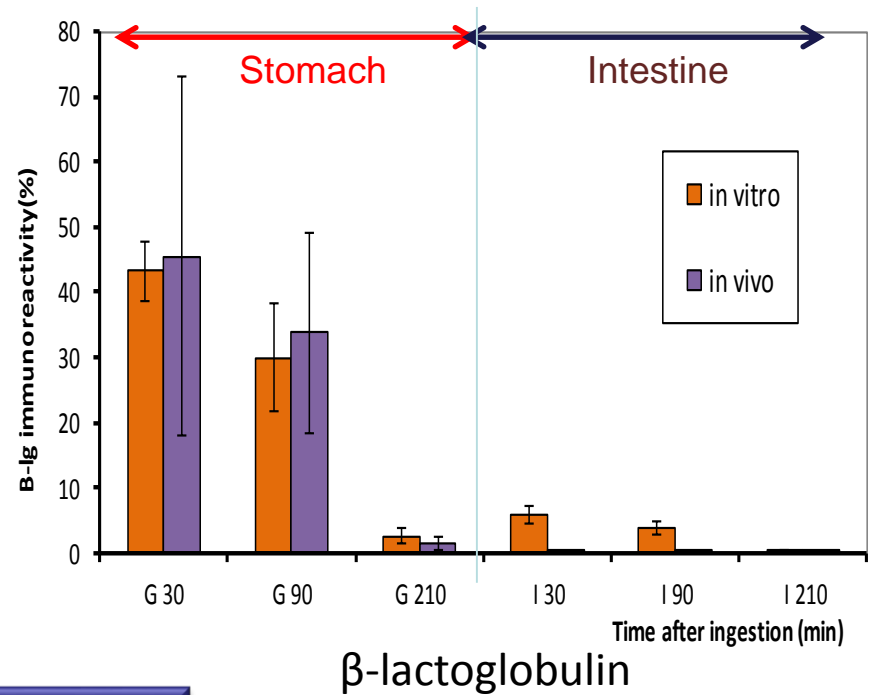
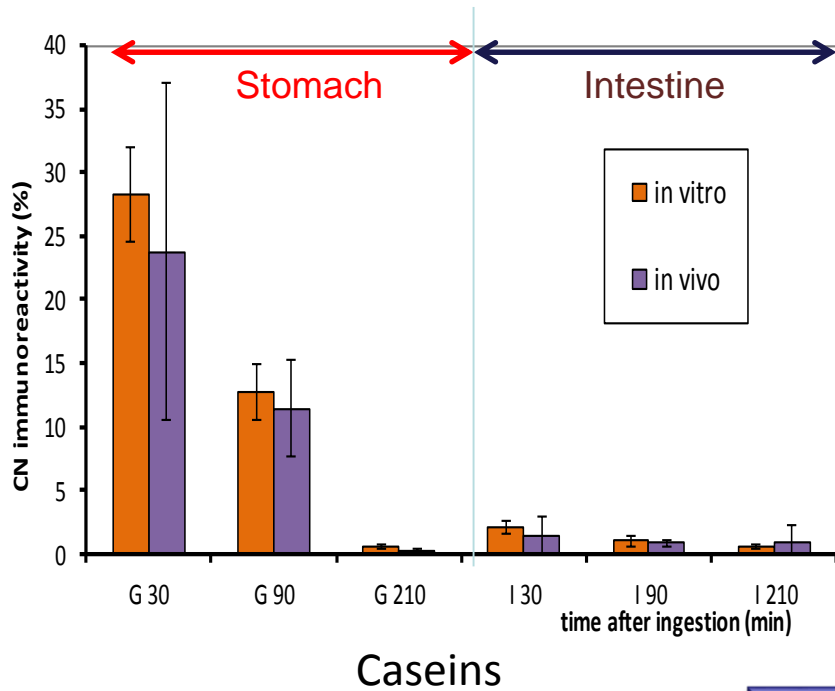
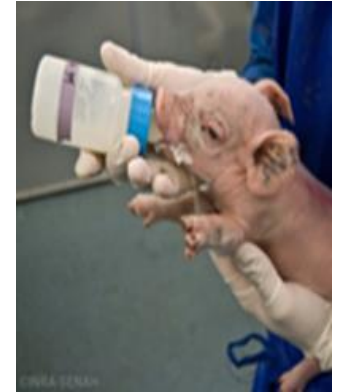
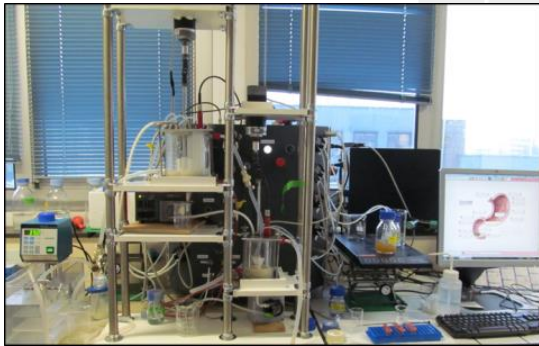
SHIME (whole GI tract)



ESIN
(stomach
+ small
intestine)



Validation of the dynamic *in vitro* digestion system

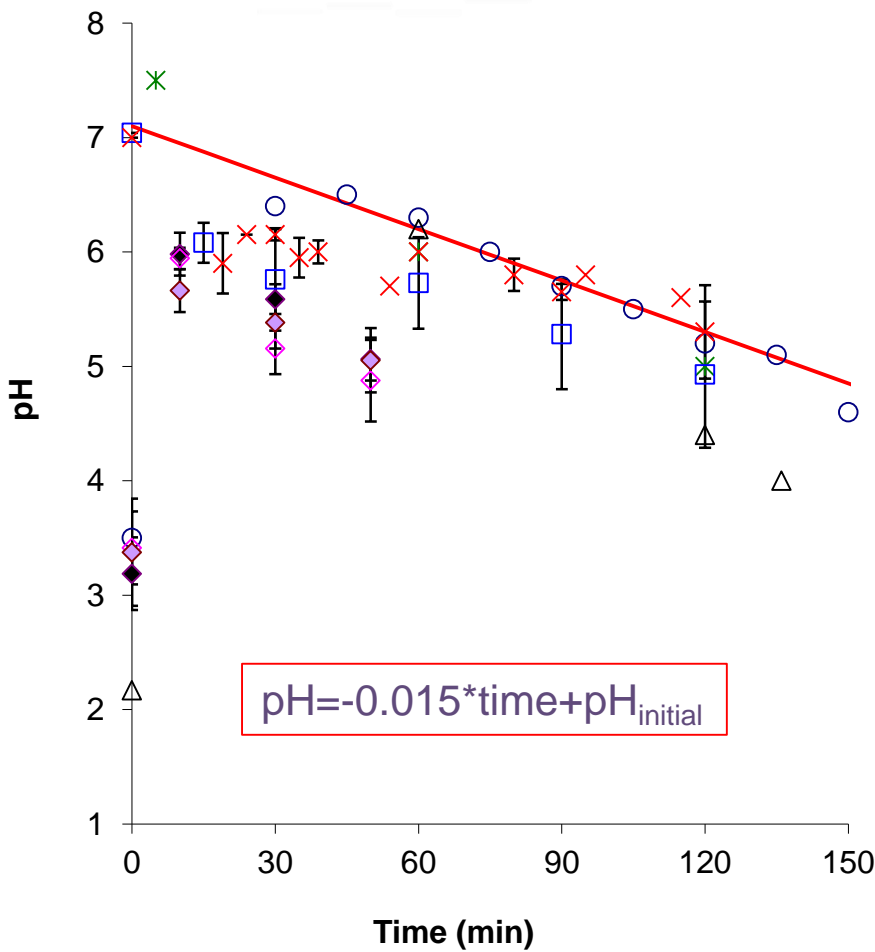


Menard et al.
2014
Food Chem

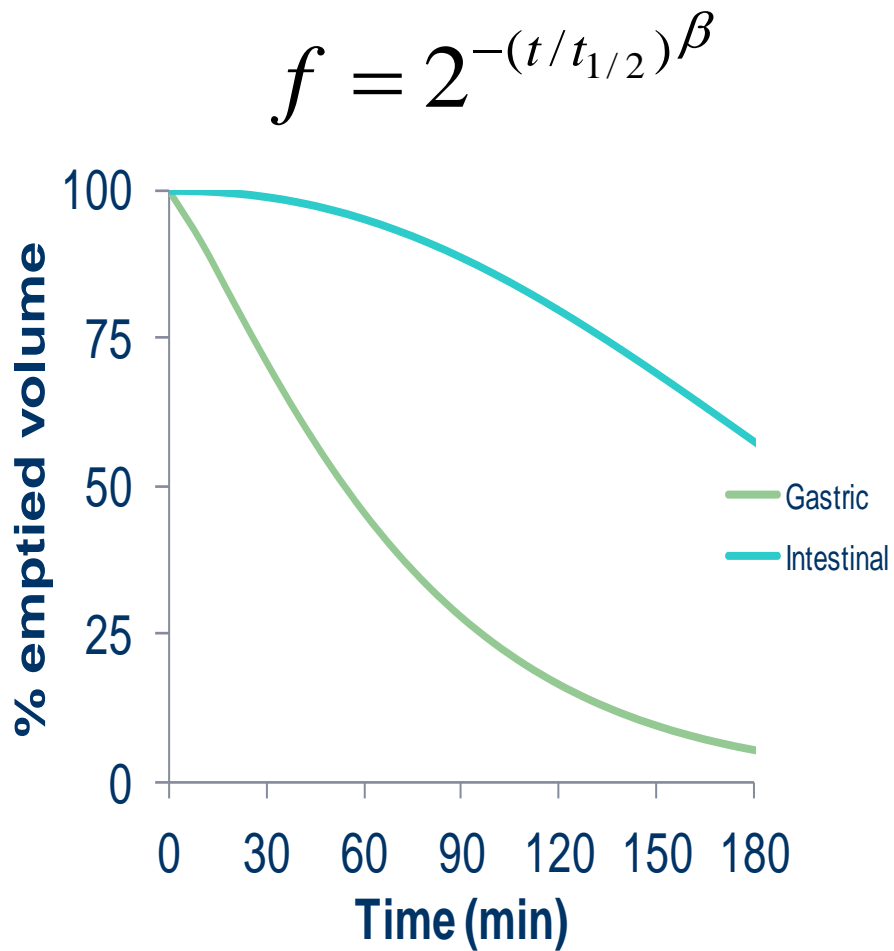
Need parameters to set up the simulator

Parameters taken from previous *in vivo* studies

pH evolution in the stomach



Gastric emptying rate

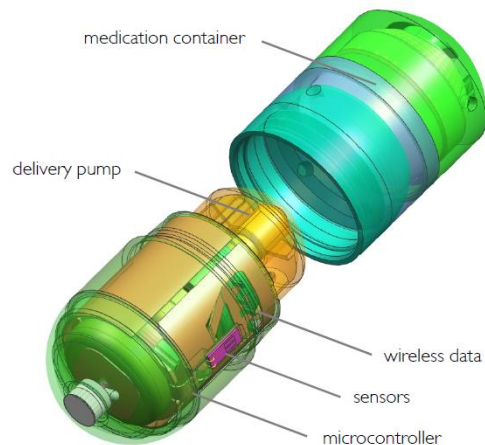


When parameters are not available, you need to determine them

For example, for the pH, the Intellicap[®] System

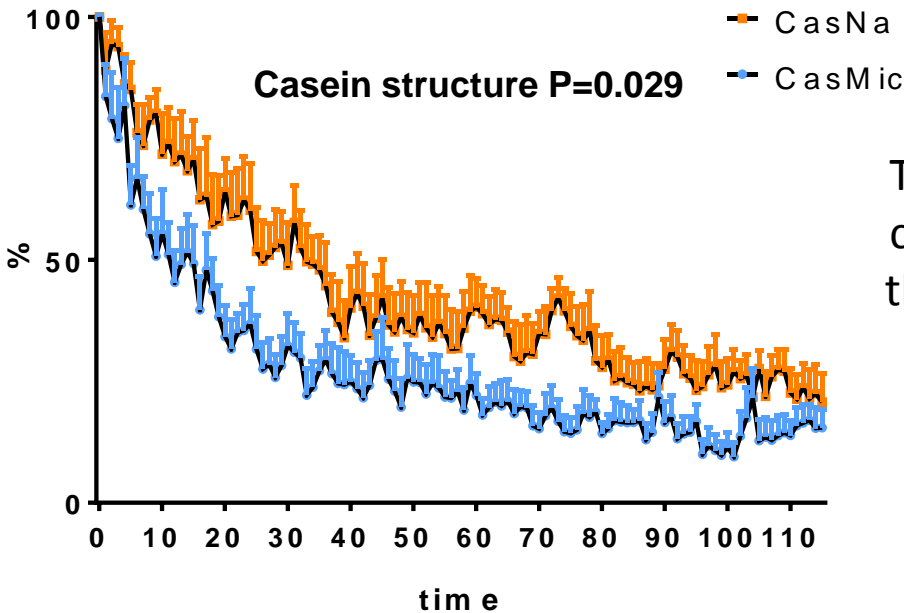
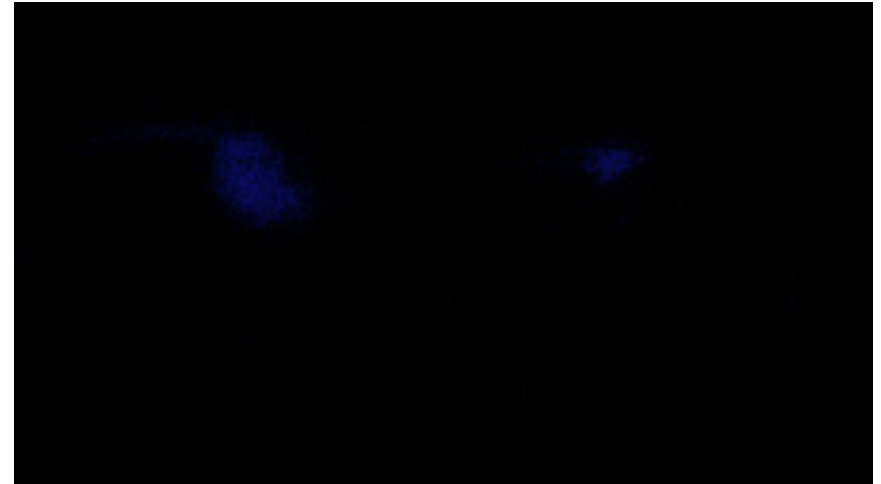
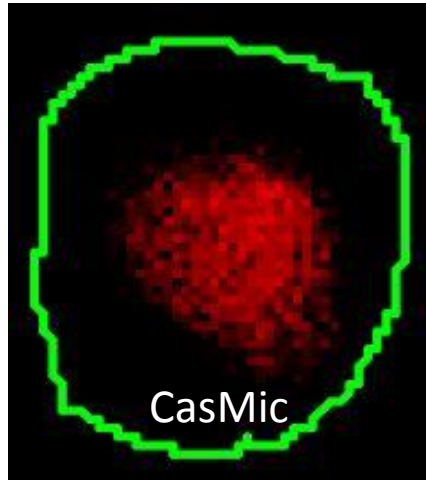
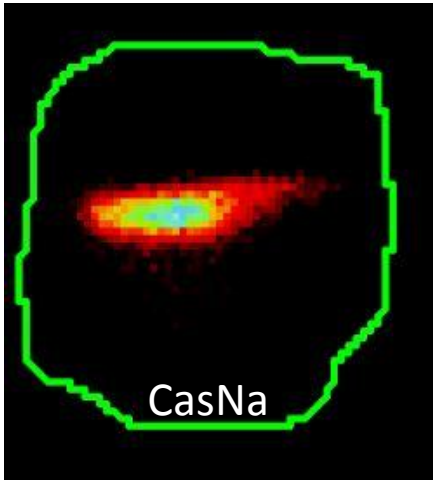


- ingestible capsules
- real-time monitoring of physiological parameters
- Controlled drug delivery unit
- Size: 11 x 26 mm
- IntelliCap[®] measurements:
 - pH (relative accuracy: ± 0.3 pH units)
 - Temperature (relative accuracy: ± 0.1 °C)

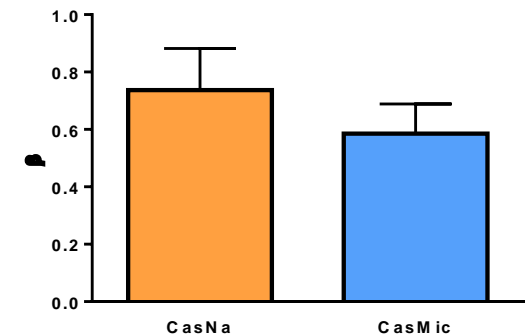
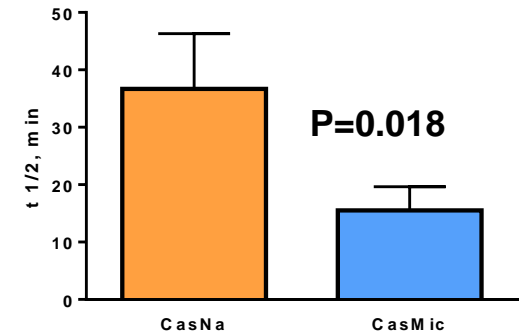


Gastric emptying by gamma-scintigraphy on pigs

Comparison of sodium caseinate/ casein micelles



The structure of caseins regulate their behavior in the stomach



Dynamic *in vitro* digestion models: Pro's & con's

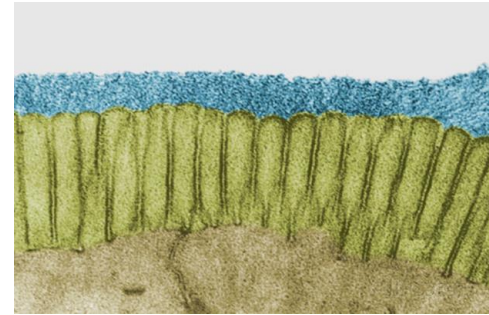
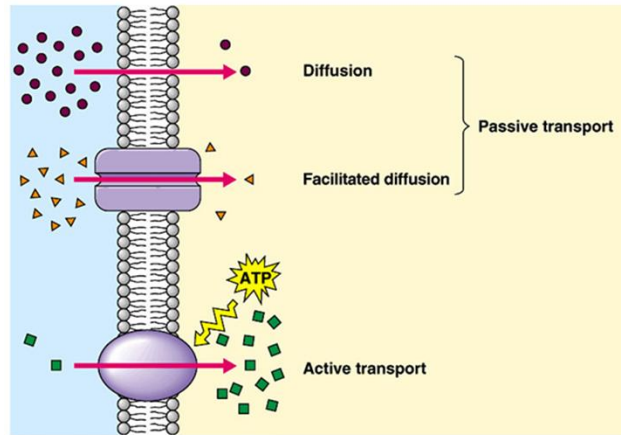


- Highly reproducible
- Physiologically relevant if parameters are available

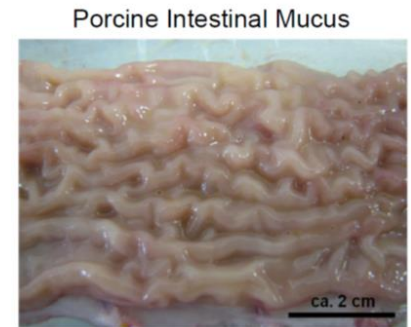


- More expensive than static models
- Too « large » to use pure enzymes (gastric lipase)
- Low throughput

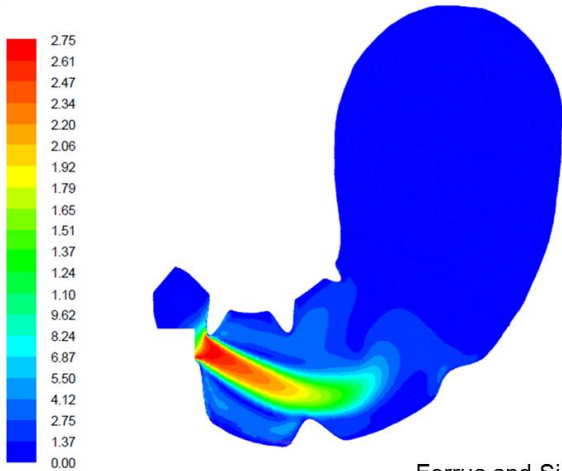
Limitations



Role of the brush border



Role of the mucus layer



Ferrua and Singh, 2010

Shape of the stomach

Absorption is usually poorly mimicked

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***In vivo* (animal) models**

Rodents



Probably not the best model to mimic the upper part of the human GI tract
Gnotobiotic animals (« humanized » mice) are of interest to study the effect of food on the microbiota

Pigs



Piglets



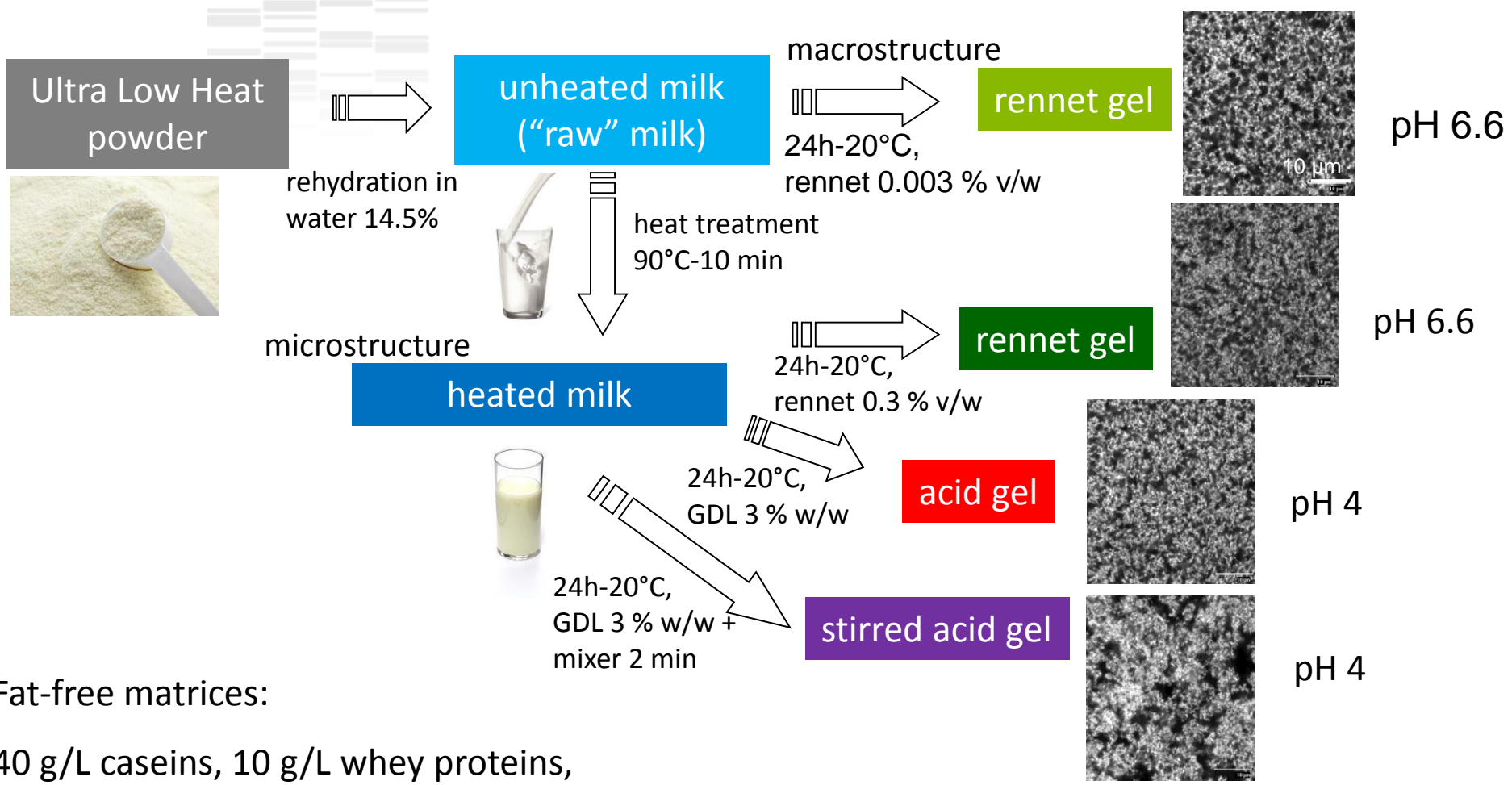
Mini-pigs



Multi-canulated and catheterized pigs

Pretty good model of the upper GI tract
Canulas and catheters allow to collect effluent and plasma throughout digestion (kinetics)

Does the food matrix regulate protein digestion and aa bioavailability?



Fat-free matrices:

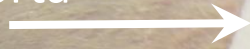
40 g/L caseins, 10 g/L whey proteins,
95 g/L lactose and minerals

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

The multi-cannulated mini-pigs

6 minipigs (20 ± 1kg)

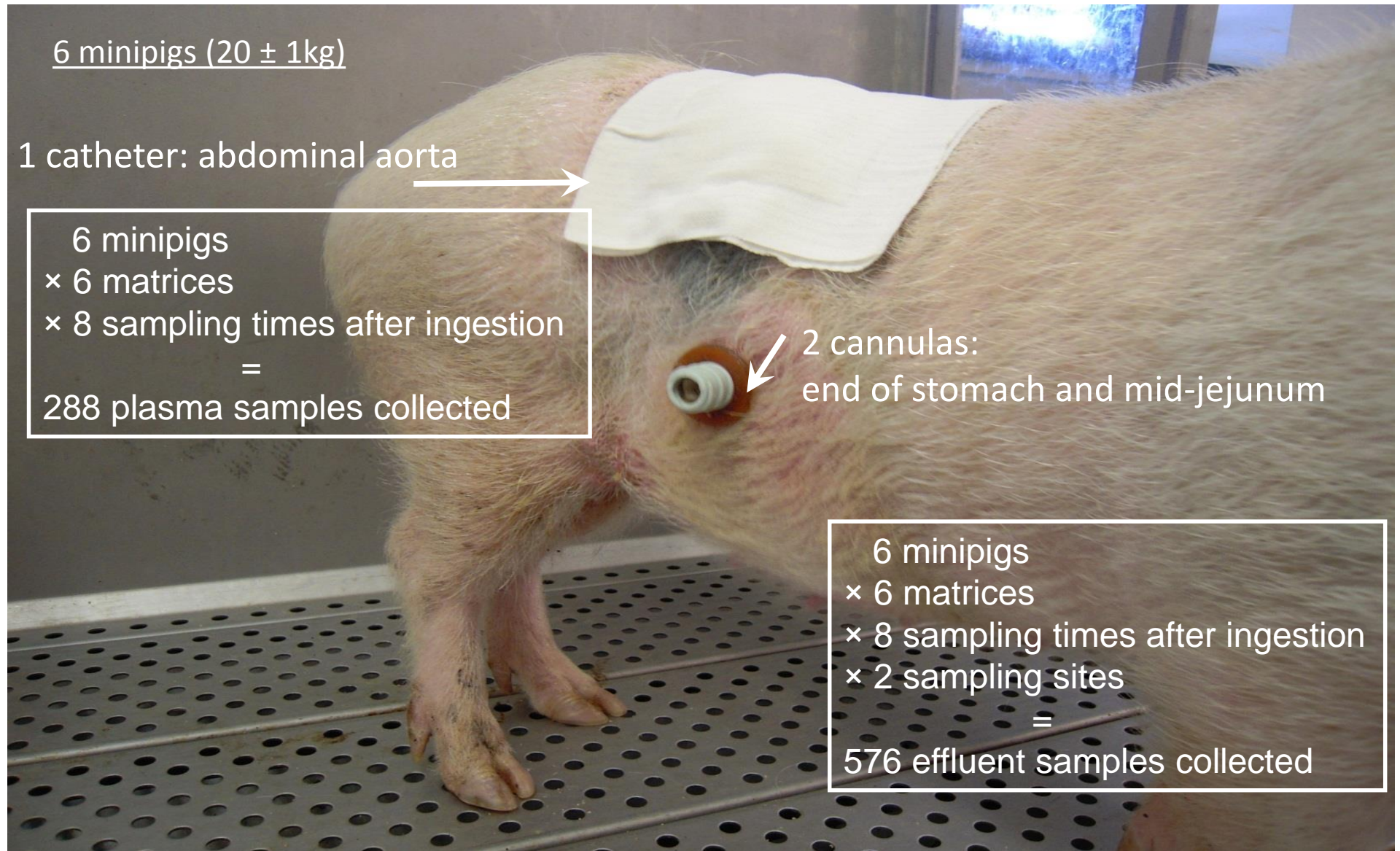
1 catheter: abdominal aorta



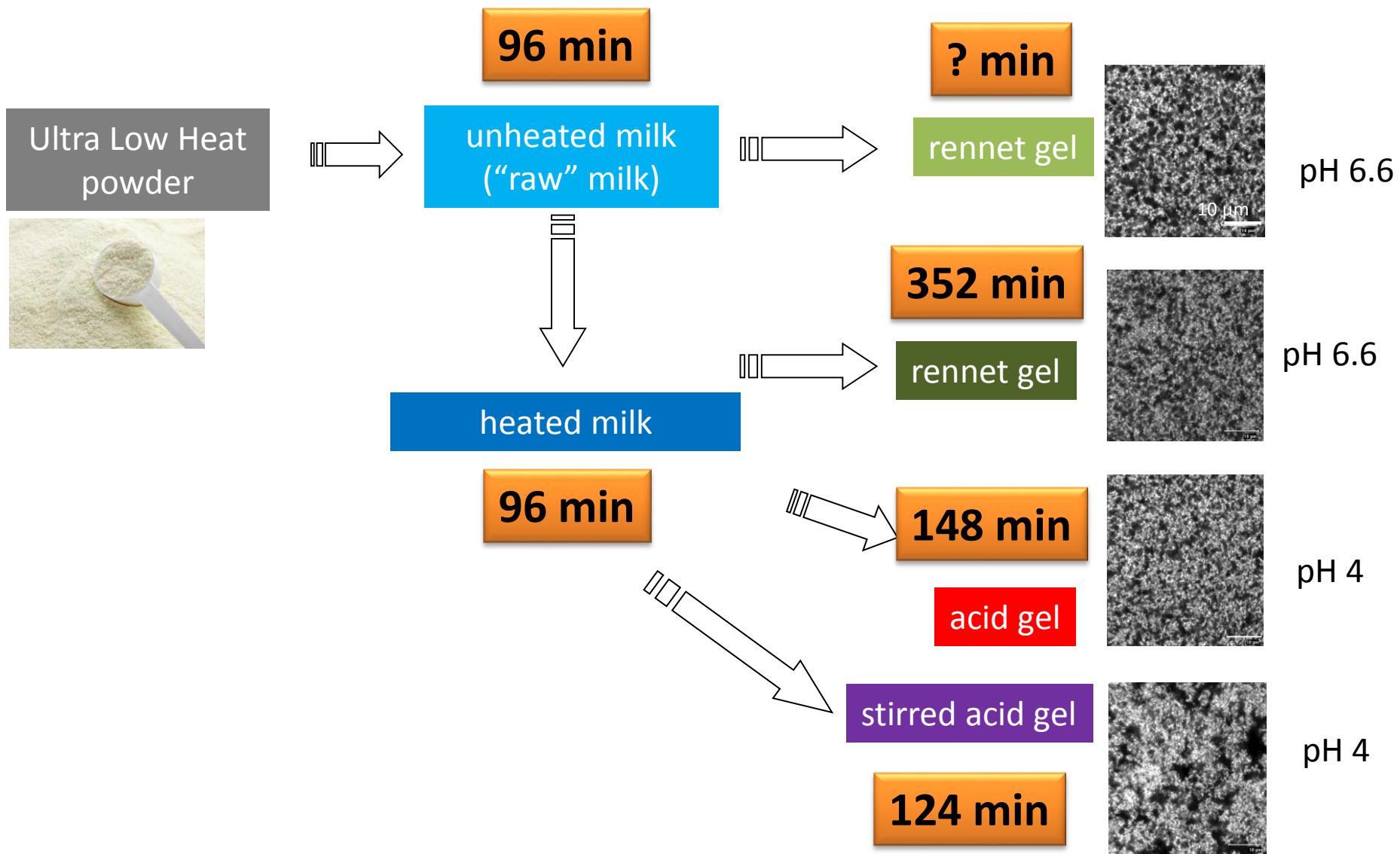
6 minipigs
× 6 matrices
× 8 sampling times after ingestion
=
288 plasma samples collected

2 cannulas:
end of stomach and mid-jejunum

6 minipigs
× 6 matrices
× 8 sampling times after ingestion
× 2 sampling sites
=
576 effluent samples collected



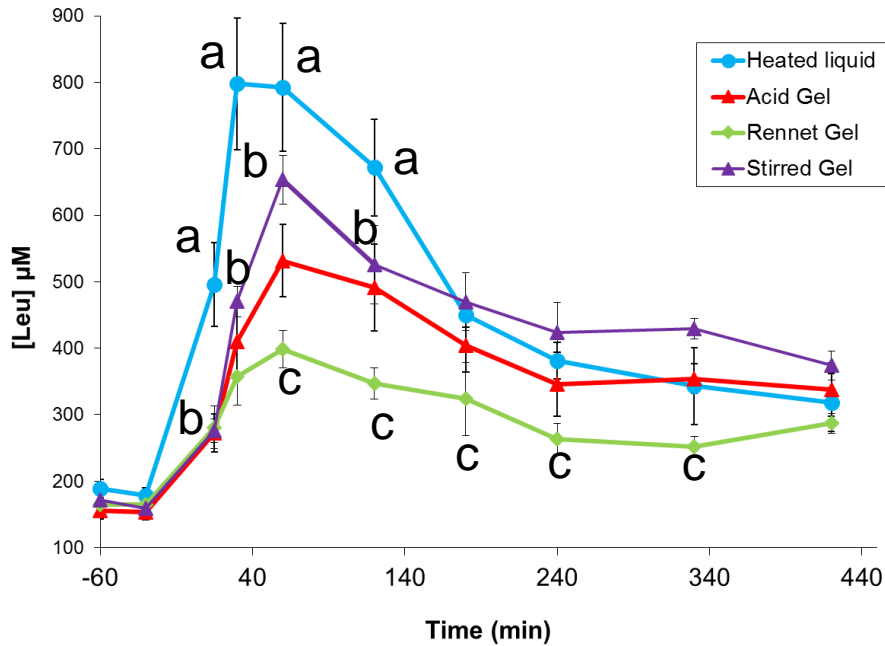
Time of residence in the stomach



The structure of foods regulates the nutrient bioavailability

2) effect on absorption

Barbé *et al.* Food Chem 2013
Highly cited paper

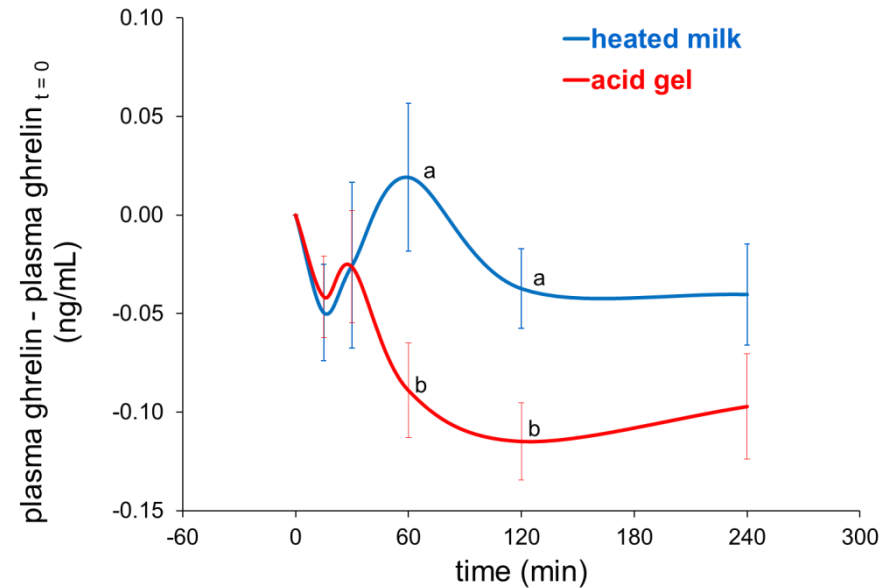


milk gelation:

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

3) potential effect on satiety

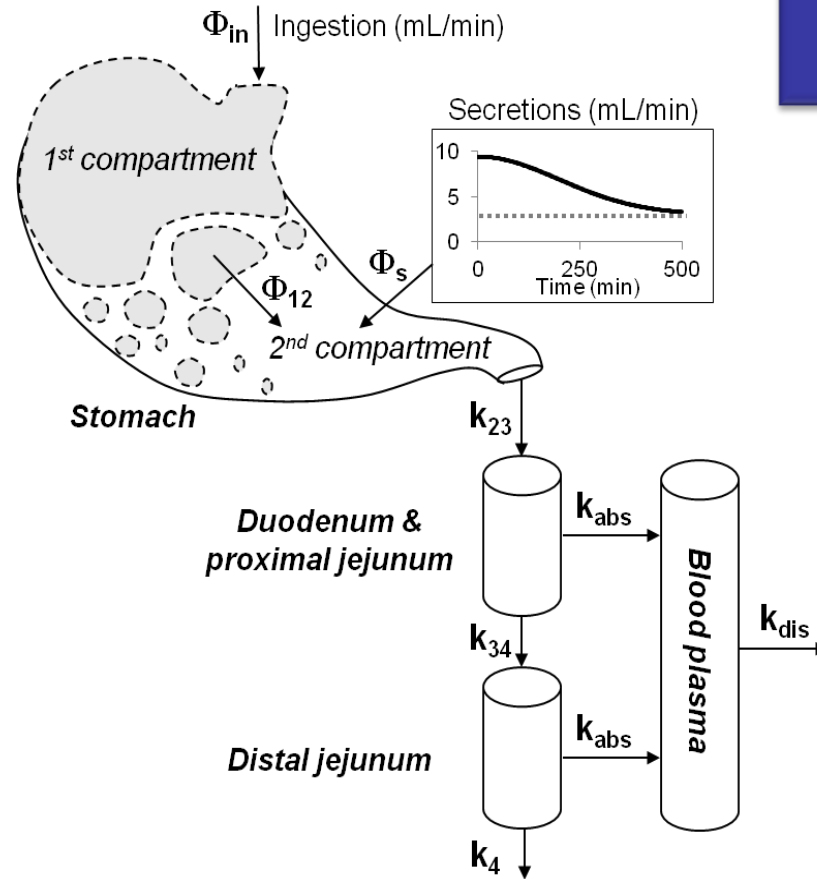
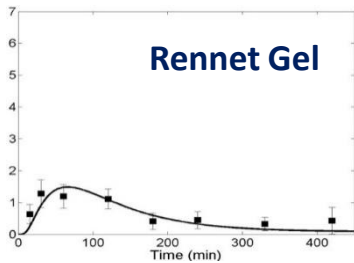
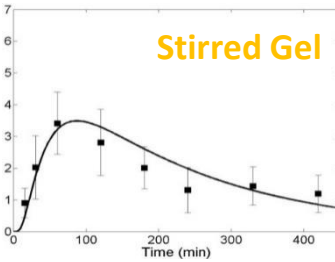
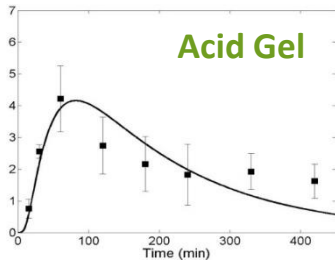
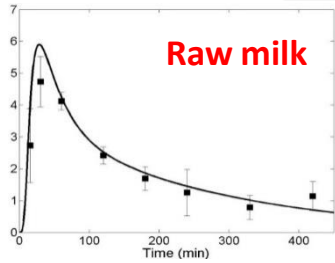
ghrelin (gastrointestinal hormone → appetite stimulation)



milk gelation:

↘ postprandial ghrelin concentration =
↑ satiety ?

In silico model of transit and absorption



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

Human Models

Patients with ileostomy

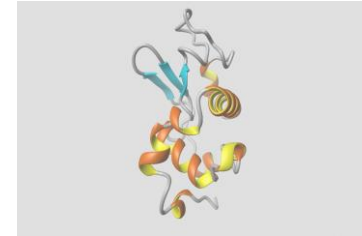


Naso-gastric or naso-jejunal probes



Identification of bioactive peptides in the human GI tract

- 16 volunteers fed 30 g of:
 - Caseins
 - Whey Proteins
 - 50/50 Mix

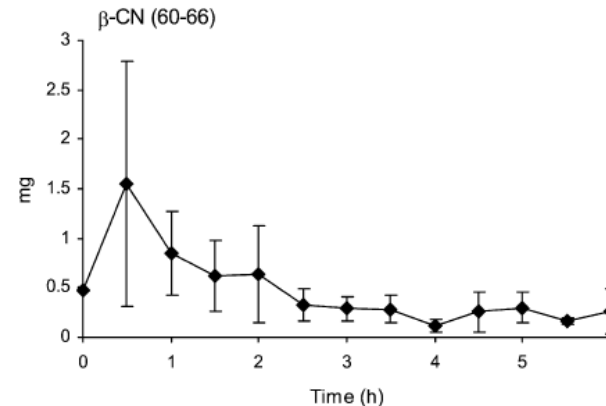


- Collect of effluents during 6h and analysis by MS-MS

4704 milk peptides identified = a unique database!

59-66	VYPFPGPI
59-68	VYPFPGPIP
60-66	YPFPGPI
108-113	EMPFPK
114-119	YPVEPF

Anti-hypertensive



Bioactive peptides concentrations are high enough in the lumen to generate a biological effect

Boutrou et al. Am J Clin Nutr 2013
Highly cited paper

But identifying a bioactive peptide in the gut lumen does not mean that it will exert a biological activity

The Bioactivity & Nutrition team



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

International Network

Dr. Didier DUPONT, Senior Scientist, INRA, France

INFOGEST





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 Norwegian Univ Life Sci Chalmers Univ Tech VTT Nofima Riga Stradin Univ Univ Ljubljana
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 Technion

Pom Med Univ

Ege Univ
 Univ California Davis

Riddett Inst
 Plant Food Res



Japan

400 scientists - 140 institutes - 41 countries



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



in Granada, Spain, 2-4 April 2019

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